ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

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Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

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PROVIDING A VOICE FOR TEXAS' MULTIDISCIPLINARY CANCER CARE TEAMS AND THE PATIENTS THEY SERVE SINCE 1988

Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Lung Cancer Faculty

Justin F Gainor, MD
Director, Center for Thoracic Cancers at Massachusetts General Hospital
Director of Targeted Immunotherapy in the Henri and Belinda Termeer Center for Targeted Therapies
Associate Professor of Medicine at Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

Corey J Langer, MD
Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

Contributing Oncologists

Susmitha Apuri, MD
Florida Cancer Specialists and
Research Institute
Lutz, Florida

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

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Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

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Agenda

Module 1: Cases from the Community

- Dr Apuri: A 69-year-old man with metastatic adenocarcinoma of the lung and brain metastases
- Dr Prakash: A 65-year-old man with metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Martins: A 59-year-old woman with extensive-stage SCLC and Eaton-Lambert syndrome

Module 2: Highlights of ASCO 2021 – Dr Langer

Module 3: Cases from the Community

- Dr Levin: A 60-year-old woman with mNSCLC with EGFR L8585R and MET exon 14 skipping mutations
- Dr Jasani: A 35-year-old woman with newly diagnosed mNSCLC – ALK mutation
- Dr Malik: A 56-year-old man with metastatic adenocarcinoma of the lung – HER2 amplification
- Dr Meerasahib: An 82-year-old man with metastatic NSCLC (mNSCLC) – PD-L1 75%, KRAS G12C mutation

Module 4: Highlights of ASCO 2021 – Dr Gainor

Highlights of ASCO 2021 – Immunotherapy
Corey J Langer, MD

- Wakelee HA et al. **IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIA non-small cell lung cancer (NSCLC).** ASCO 2021;Abstract 8500.
- Spicer J et al. **Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC).** ASCO 2021;Abstract 8503.
- Reck M et al. **First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): Two-year update from CheckMate 9LA.** ASCO 2021;Abstract 9000.
- Akinboro O et al. **Outcomes of anti-PD-(L1) therapy in combination with chemotherapy versus immunotherapy (IO) alone for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score 1-49%: FDA pooled analysis.** ASCO 2021;Abstract 9001.
- Spigel DR et al. **Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial.** ASCO 2021;Abstract 8511.

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Highlights of ASCO 2021 – Targeted Treatment
Justin F Gainor, MD

- Janne PA et al. **Efficacy and safety of patritumab deruxtecan (HER3-DXd) in EGFR inhibitor-resistant, EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC).** ASCO 2021;Abstract 9007.
- Bauml J et al. **Amivantamab in combination with lazertinib for the treatment of osimertinib-relapsed, chemotherapy-naïve EGFR mutant (EGFRm) non-small cell lung cancer (NSCLC) and potential biomarkers for response.** ASCO 2021;Abstract 9006.
- Skoulidis F et al. **Overall survival and exploratory subgroup analyses from the phase 2 CodeBreaK 100 trial evaluating sotorasib in pretreated KRAS p.G12C mutated non-small cell lung cancer.** ASCO 2021;Abstract 9003.
- Paik PA et al. **METex14 ctDNA dynamics & resistance mechanisms detected in liquid biopsy (LBx) from patients (pts) with METex14 skipping NSCLC treated with tepotinib.** ASCO 2021;Abstract 9012.
- Soo RA et al. **Early circulating tumor (ct) DNA dynamics and efficacy of lorlatinib: Analysis from the CROWN study.** ASCO 2021;Abstract 9011.

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Module 4: Highlights of ASCO 2021 – Dr Gainor

Regulatory and reimbursement issues aside, which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 0%?

- Chemotherapy +/- bevacizumab
- Anti-PD-1/PD-L1 antibody alone
- Carboplatin/pemetrexed/pembrolizumab
- Atezolizumab/carboplatin/*nab* paclitaxel
- Atezolizumab/carboplatin/paclitaxel/bevacizumab
- Ipilimumab/nivolumab
- Ipilimumab/nivolumab + chemotherapy
- Other (please specify)

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Case Presentation – Dr Apuri: A 69-year-old man with metastatic adenocarcinoma of the lung and brain metastases

Dr Susmitha Apuri

- 80 pack year tobacco use
- Presents with dizziness and progressive SOB x 2 months
- Imaging and biopsy: Lung mass c/w adenocarcinoma and liver and brain metastases
- Whole brain radiation therapy and carboplatin/pemetrexed/pembrolizumab
- Liquid NGS: EGFR A67T, FGFR and PDGFRA amplification, ROS1 VUS
- PD-L1 <1%

Questions

- Would you recommend ipilimumab/nivolumab in a patient on active steroid therapy, who just completed radiation therapy? How might it impact their treatment?
- Would penetration of the BBB be more than with a chemotherapy and immunotherapy combination approach?

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Case Presentation – Dr Prakash: A 65-year-old man with metastatic adenocarcinoma of the lung – PD-L1 95%

Dr Chris Prakash

- Presents with right lung mass and multiple liver metastases
  - Biopsy: Adenocarcinoma of the lung, PD-L1: 95%, no other mutations
- Nivolumab/ipilimumab

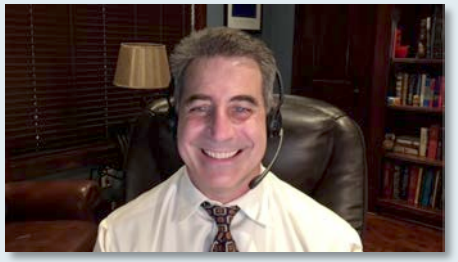
Question

- How would you approach first-line therapy in a patient with a high PD-L1 expression – immunotherapy doublet, chemoimmunotherapy or single-agent immunotherapy?

What is your preferred second-line treatment for a patient with extensive-stage small cell lung cancer and disease progression on chemotherapy/anti-PD-L1 antibody?

- Topotecan
- Topotecan + trilaciclib
- Irinotecan
- Lurbinectedin
- Nivolumab/ipilimumab
- Pembrolizumab
- Nivolumab
- Other (please specify)

Case Presentation – Dr Martins: A 59-year-old woman with extensive-stage SCLC and Eaton-Lambert syndrome



Dr Joseph Martins

- 2/2018: Eaton-Lambert syndrome treated with amifampridine
- 2/2020: Diagnosed with ES-SCLC, severe SIADH
- Disease progression on carboplatin/irinotecan, carboplatin/etoposide and paclitaxel/gemcitabine
- Ipilimumab/nivolumab initiated
  - Recently developed increasing weakness, requiring a walker to move around

Questions

- What would you have recommended for this patient? Would you have used lurbinectedin?

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Module 4: Highlights of ASCO 2021 – Dr Gainor

Wakelee HA et al. IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIA non-small cell lung cancer (NSCLC). ASCO 2021;Abstract 8500.

Dr Corey Langer

1. For which clinical situations is this data clinically relevant?

- Adjuvant setting in stage IB, stage II, and stage IIIA NSCLC, after R0 resection and completion of adjuvant platinum-based chemotherapy. Data are particularly robust in pts with node (+), PD-L1 (+) NSCLC

2. What are the key findings that are most relevant to patients in these clinical situations?

- First phase III study of CPI to demonstrate DFS improvement in the adjuvant NSCLC setting after platinum-based chemotherapy. In this regard, the study is trailblazing and a "game-changer."
- Adjuvant atezolizumab for up to 1 yr led to statistically significant DFS benefit in the PD-L1 TC ≥1% stage II-IIIA (HR, 0.66; 95% CI: 0.50, 0.88, p = 0.004) with 3 yr DFS of 60% vs 48.2% for BSC; median DFS NR vs 35.3 mos
  - Benefit much more pronounced in N1 (HR 0.59) and N2 (HR 0.66) NSCLC, c/w N0 NSCLC (HR 0.88)
- Less pronounced, but still significant benefit in all-randomized stage II-IIIA (HR, 0.79; 95% CI: 0.64, 0.96, p = 0.02) NSCLC pts: 3 yr DFS of 55.7% vs 49.4% and median DFS of 42.3 vs 35.3 mos
  - Benefit largely restricted to PD-L1 (+) population with HR of 0.43 in TC > 50%, HR of 0.66 in TC of >1% and HR of 0.97 in TC 0%
- DFS in the ITT population, including patients with stage IB disease, did not cross the significance boundary at this interim DFS analysis; HR 0.81 with p = 0.04

Wakelee HA et al. IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIA non-small cell lung cancer (NSCLC). ASCO 2021;Abstract 8500. (continued)

Dr Corey Langer

- OS data remain immature and were not formally tested, but early HR in the stage II/IIIA PD-L1 (+) pts was 0.77 with slight separation in the curves beyond 3 yrs
- Safety profile of atezolizumab consistent with prior experience; no new issues

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Assuming FDA approval is forthcoming, I will likely offer this agent to my "wild type" N1/N2 NSCLC post resection, as long as their tumors have some degree of PD-L1 expression. This agent sets the standard and benchmark for other, similar trials of CPIs in the adjuvant setting.
- If the approval is more expansive, I will have major "ambivalence" offering this agent to N0 or PD-L1 (-) patients, and I may have some doubts regarding those with 1-49% PD-L1 expression
- I will defer use in EGFR mt (+) pts where ADAURA has established a beachhead for osimertinib in a similar population of resected patients with much more impressive HRs
- Finally, we need to account for the 275 pts who completed adjuvant chemo and were registered and eligible, but did not proceed with randomization

Spicer J et al. Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). ASCO 2021;Abstract 8503.

Dr Corey Langer

1. For which clinical situations is this data clinically relevant?

- Neoadjuvant setting in resectable/curable stage IB/II/IIIA NSCLC

2. What are the key findings that are most relevant to patients in these clinical situations?

- Major improvement in pCR rates, particularly in IB NSCLC (40%) with commensurate improvement in MPR rates

Endpoint	Nivo/Chemo (%)	Chemo (%)	p value
pCR	24	2.2	<0.0001
MPR	36.9	8.9	NA

- No untoward safety issues
- No compromise in surgical outcomes, no delays in surgery or prolongation in hospitalization (LOS ~ 10 days each) and numerically fewer SAEs (41% vs 47%), especially pain
- Numerically higher rates of VATS, lobectomy and R0 resection

Spicer J et al. Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). ASCO 2021;Abstract 8503. (continued)

Dr Corey Langer

Endpoint	Nivo/Chemo (%)	Chemo (%)
VATS	30	22
Lobectomy	77	61
R0 resection	83	78

- Data do not match the results seen in the phase II NADIM trial, but are still impressive

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Relevance remains unclear since surgery upfront is still the “standard of care.”
- All correlations between pCR and MPR are retrospective; we have no prospective data yet in 2021 showing that these endpoints predict long term DFS and OS
- Not clear if the FDA will grant approval for these approaches based on “surrogate” endpoints

Spigel DR et al. Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial. ASCO 2021;Abstract 8511.

Dr Corey Langer

1. For which clinical situations is this data clinically relevant?

- All stage III unresectable NSCLC patients who have successfully completed combined platinum chemotherapy and XRT and who have no “contraindications” to CPIs, ie. no e/o ongoing immunologic disorders or residual chemo-XRT toxicity that would preclude CPI (e.g grade 2 pneumonitis, etc)

2. What are the key findings that are most relevant to patients in these clinical situations?

- Long term 5 yr f/u of landmark, practice-altering phase III trial showing a durable, statistically significant and clinically meaningful improvement for durvalumab vs placebo in locally advanced (LA) NSCLC
- PFS improvement with HR of 0.55 (CI 0.45 – 0.68)
- Benefit seen in all sites: Lung, CNS, Extra-thoracic
- OS improvement with HR of 0.72 (CI: 0.59 – 0.89)

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Spigel DR et al. Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial. ASCO 2021;Abstract 8511. (continued)

Dr Corey Langer

Endpoint	Median PFS	5 yr PFS	Median OS	5 yr OS
Durvalumab	16.9 mos	33.1%	47.5 mos	42.9%
Placebo	5.6 mos	19.0%	29.1 mos	33.4%

- PFS benefit particularly striking in those randomized within 14 days of completing chemo-XRT: HR of 0.39 vs 0.63
- Post-hoc analysis failed to show an OS benefit in pts without PD-L1 expression: HR 1.15 (dropping from 1.38 at prior analysis)
- Pneumonitis rates higher for Durva: 33.9 vs 24.8%, but predominantly grade 1-2

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Current standard of care in unresectable LA-NSCLC post chemoradiation
- F/U data show no decay in PFS or OS benefit

Spigel DR et al. Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial. ASCO 2021;Abstract 8511. (continued)

Dr Corey Langer

- Numerous caveats:
  - Trial does not account for the attrition that generally occurs during chemo-XRT due to PD or toxicity (~ 30% of the LA-NSCLC population) who would not have qualified for this study, and therefore these outcomes cannot really be compared to prior “defining” trials like RTOG 0617
  - Major ambivalence for many in pts with no PD-L1 expression
    - EU, unlike the US, has restricted approval to PD-L1 > 1%
    - However, PD-L1 analysis was post-hoc with nearly 40% of pts having insufficient tissue for PD-L1 assay; nor does this account for possible upregulation of PD-L1 post chemo and XRT.
  - Similar ambivalence for pts with EGFR mutation
    - Only 43 out of 713 pts accrued
    - Despite concerns that there might be harm with CPI, the HR for OS in EGFR mt (+) NSCLC was 0.85, albeit with VERY wide confidence intervals
  - Absence of “robust” biomarkers to really predict benefit – until then, we have a monolithic “one size fits all” approach

Reck M et al. First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): Two-year update from CheckMate 9LA. ASCO 2021; Abstract 9000.

Dr Corey Langer

1. For which clinical situations is this data clinically relevant?

- Advanced recurrent or metastatic NSCLC pts with no e/o pre-existing ALK or EGFR alterations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Large phase III trial; n = 719
- Durable PFS (HR 0.67) and OS (HR 0.72 [0.61-0.80]) benefit for combination ipilumumab and nivolumab with histology-specific chemo for 2 cycles c/w "standard" chemotherapy alone

Arm	Median PFS	2 yr PFS	Median OS	2 yr OS
Chemo/Ipi/Nivo	6.7 mos	20%	15.8 mos	38%
Chemo	5.3 mos	8%	11.0 mos	26%

Reck M et al. First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): Two-year update from CheckMate 9LA. ASCO 2021; Abstract 9000. (continued)

Dr Corey Langer

- OS Benefit independent of histology or PD-L1 status – Median PFS (mos)

Subgroup	Number	Chemo/Ipi/Nivo	Chemo	HR
SQ	227	14.1	9.1	0.63
NSQ	492	17.8	12	0.78
CNS (+)	123	19.9	7.9	0.47
PD-L1 < 1%	264	17.7	9.8	0.67
PD-L1 > 1%	407	15.8	10.9	0.70
Age > 75	70	8.5	11.5	1.04

- Institution of chemo over the first six weeks of treatment appeared to prevent early drop-off in OS seen in the CM227 trial
- Toxicity substantial: 17% discontinued Tx due to AEs vs 6% in control arm

Reck M et al. First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): Two-year update from CheckMate 9LA. ASCO 2021; Abstract 9000. (continued)

Dr Corey Langer

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Relevance unclear when KN189 and KN407 have become the standards of care in advanced, wild type NSCLC with PD-L1 < 50%
- Underscores need for prospective phase III trials comparing 9LA to KN189/407 in this population, a trial that can only be accomplished by cooperative groups since industry would find this “high risk”
  - If successful, this defers resumption of platinum-based chemo until PD on CPIs
  - Study did not identify nature of subsequent 2nd line strategies
  - Some clinicians have adopted an ipi/nivo approach in PD-L1 < 1%, especially SQ NSCLC
- Opens the door to other combined immunotherapy strategies in advanced NSCLC
- Highlights need to establish robust biomarkers – have not seen data on TMB
- Trepidation using this approach in the elderly (> 75 yrs)

Akinboro O et al. Outcomes of anti-PD-(L1) therapy in combination with chemotherapy versus immunotherapy (IO) alone for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score 1-49%: FDA pooled analysis. ASCO 2021;Abstract 9001.

Dr Corey Langer

1. For which clinical situations is this data clinically relevant?

- Advanced wild type NSCLC with PD-L1 expression of 1-49%

2. What are the key findings that are most relevant to patients in these clinical situations?

- Pooled analysis of 8 separate phase III randomized controlled trials in advanced, recurrent or metastatic NSCLC pts with PD-L1 expression of 1-49%
- Significant PFS benefit for combination platinum-based chemotherapy and CPI (n = 639) vs checkpoint inhibitor(s) alone (n = 529) with HR of 0.6 (CI: 0.48-0.76) and median PFS of 7.7 vs 4.2 mos respectively
- Pronounced OS benefit for chemo-IO vs IO alone with median OS of 21.4 mos vs 14.5 mos (HR 0.68, CIs: 0.52-0.90)
- Benefit seen across the board with the potential exception of those 75 years of age and older – Median OS (mos) by age range

Akinboro O et al. Outcomes of anti-PD-(L1) therapy in combination with chemotherapy versus immunotherapy (IO) alone for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score 1-49%: FDA pooled analysis. ASCO 2021;Abstract 9001. (continued)

Dr Corey Langer

Age Cohort	Number	Chemo and CPI	CPI alone
< 65	580	23.7	16.1
65- 75	443	22.5	14.8
≥ 75	132	13.9	10.3

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Underscores the benefits of combined chemotherapy and CPI vs CPI alone in this vulnerable population
- Major implications for the ongoing INSIGNA trial comparing single agent pembrolizumab vs Pembro in combination with pemetrexed and platinum in recurrent or metastatic NSQ-NSCLC; this study includes pts with 1-49% expression as well as PD-L1 expression 50% or higher.
- Analysis vitiated by failure to cull out CPI monotherapy vs combined PD-L1/CTLA-4 inhibition in the comparisons
- Does not account for toxicity differences between these regimens

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Module 4: Highlights of ASCO 2021 – Dr Gainor

Regulatory and reimbursement issues aside, which adjuvant systemic therapy would you generally recommend for a patient with Stage IIB nonsquamous NSCLC and an EGFR exon 19 deletion?

- Chemotherapy
- Osimertinib
- Chemotherapy followed by osimertinib
- Other (please specify)

Regulatory and reimbursement issues aside, in what line of therapy would you generally offer amivantamab to a patient with metastatic NSCLC and an EGFR exon 20 insertion mutation?

- First line
- Second line
- Third line
- Beyond third line
- I would not offer amivantamab
- I am not familiar with amivantamab

Case Presentation – Dr Levin: A 60-year-old woman with metastatic NSCLC with EGFR L8585R and MET exon 14 skipping mutations

Dr Pavel Levin

- Diagnosed with de novo metastatic NSCLC
- Liquid biopsy: EGFR L8585R and MET exon 14 skipping mutations
- Re-biopsy of tissue: EGFR L8585R mutation only
- Osimertinib

Questions

- What would you do in the situation where a patient's tumor harbors both an EGFR and a MET exon 14 mutation? Would you treat with an EGFR and MET inhibitor simultaneously?

Case Presentation – Dr Jasani: A 35-year-old woman with newly diagnosed mNSCLC – ALK mutation

Dr Nikesh Jasani

- Presented with cough, chest pain, and fatigue
- Diagnosed with stage IV NSCLC adenocarcinoma with right hilar mass, with metastases to multiple mediastinal nodes, bone and a solitary brain mass
- Molecular studies: ALK FISH +
- Stereotactic RT to brain lesion
- 1/2021: Alectinib → excellent response with resolution of all symptoms

Questions

- What is the optimal first-line therapy for NSCLC that is ALK mutation-positive?
- If her disease progresses, what would be the best next steps - repeat biopsy and assessment of resistance mutations to determine ideal treatment?
- How do you manage CNS disease in patients with NSCLC that is ALK mutation-positive?
- What are the side effects of note with the newer ALK inhibitors such as lorlatinib and brigatinib?

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Regulatory and reimbursement issues aside, in what line of therapy would you generally offer trastuzumab deruxtecan to a patient with HER2-mutated metastatic adenocarcinoma of the lung?

- First line
- Second line
- Third line
- Beyond third line
- I would not offer trastuzumab deruxtecan

Case Presentation – Dr Malik: A 56-year-old man with metastatic adenocarcinoma of the lung – HER2 amplification

Dr Henna Malik

- Presents with cough and treated for bronchitis with antibiotics and steroids, with minimal improvement
- CXR: Suspicious nodule in his RUL → CT scan: Multiple b/l pulmonary nodules
- Weight loss of 10 lbs over the past 3 months, worsening cough and back pain
- PET scan: Bone metastases mostly in the lumbar spine.
- Pathology: Adenocarcinoma of lung primary. PD-L1: 1%, no actionable mutations
- HER2 amplification detected
- Pembrolizumab/cisplatin/pemetrexed, with PD in 6 months
- Switched to docetaxel/trastuzumab, with response x 6 months

Question

- Would trastuzumab deruxtecan be helpful as upfront therapy for these patients with HER2-positive lung cancer, with or without chemotherapy?

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Case Presentation – Dr Meerasahib: An 82-year-old man with mNSCLC – PD-L1 75%, KRAS G12C mutation

Dr Anish Meerasahib

- 2015-2017: Retired family practitioner with 5-7 mm lung nodule followed and stable, but patient missed a few years of surveillance scans
- 3/2020 CT: Lung nodule grew to 1.9 cm, hypermetabolic by PET
  - Biopsy-confirmed adenocarcinoma, MSS, TMB-intermediate, PD-L1: 75%
  - NGS: ARID1A, KRAS G12C and RBM10 mutations
- Patient does not desire surgery → 5/2020: SBRT to primary lung lesion
- 8/2020: 1-cm satellite lesion LUL → patient declines systemic therapy → SBRT
- 12/2020: Right scapula lesion
- 2/2021: Pembrolizumab, with RT to right scapula, which resolved pain

Questions

- Are we seeing positive results with the KRAS 12GC-targeted agent sotorasib in lung cancer?
- Is immunotherapy the right treatment for him, and would you consider adding chemotherapy?

Agenda

Module 1: Cases from the Community

- Dr Apuri: A 69-year-old man with metastatic adenocarcinoma of the lung and brain metastases
- Dr Prakash: A 65-year-old man with metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Martins: A 59-year-old woman with extensive-stage SCLC and Eaton-Lambert syndrome

Module 2: Highlights of ASCO 2021 – Dr Langer

Module 3: Cases from the Community

- Dr Levin: A 60-year-old woman with mNSCLC with EGFR L8585R and MET exon 14 skipping mutations
- Dr Jasani: A 35-year-old woman with newly diagnosed mNSCLC – ALK mutation
- Dr Malik: A 56-year-old man with metastatic adenocarcinoma of the lung – HER2 amplification
- Dr Meerasahib: An 82-year-old man with metastatic NSCLC (mNSCLC) – PD-L1 75%, KRAS G12C mutation

Module 4: Highlights of ASCO 2021 – Dr Gainor

Bauml J et al. Amivantamab in combination with lazertinib for the treatment of osimertinib-relapsed, chemotherapy-naïve EGFR mutant (EGFRm) non-small cell lung cancer (NSCLC) and potential biomarkers for response. ASCO 2021; Abstract 9006.

Dr Justin Gainor

1. For which clinical situations is this data clinically relevant?

- Patients with EGFR-mutant (del19 or L858R) NSCLC and disease progression on osimertinib (chemotherapy-naïve)

2. What are the key findings that are most relevant to patients in these clinical situations?

- Amivantamab + lazertinib ORR (N=45): 36%, mDOR 9.6 months
- Median PFS 4.9 months
- ORR 47% among patients with EGFR/MET-based resistance based upon NGS
- ORR 29% among patients without EGFR/MET-based resistance on NGS
- ORR 90% among patients with IHC+ for EGFR/MET (combined EGFR/MET H score ≥400)
- Common adverse events – infusion reactions (78%), rash (78%), paronychia (49%)

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Amivantamab + lazertinib showed promising activity in a chemo-naïve, post-TKI setting.
- Biomarker analysis suggests that patients with EGFR/MET-dependent resistance are most likely to benefit.

Janne PA et al. Efficacy and safety of patritumab deruxtecan (HER3-DXd) in EGFR inhibitor-resistant, EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC). ASCO 2021; Abstract 9007.

Dr Justin Gainor

1. For which clinical situations is this data clinically relevant?

- Patients with NSCLC with EGFR mutations previously treated with EGFR TKIs and platinum-based chemotherapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- Overall population (N=57): confirmed ORR 39%, DCR 72%
- Prior osi population (N=44): confirmed ORR 39%, DCR 68%
- Median DOR 6.9-7.0 months; median PFS 8.2 months
- Activity observed regardless of prior treatment, resistance mechanism or history of CNS mets
- Responses observed in patients with a wide range of HER3 expression (based on H score)
- Manageable safety profile: dose reduction 21-22%, treatment discontinuation 9-11%

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- HER3-DXd was associated with clinically meaningful activity in the post-EGFR TKI/chemo setting. This agent remains investigational.
- A randomized phase II study is now ongoing testing two different dose strategies

Soo RA et al. Early circulating tumor (ct) DNA dynamics and efficacy of lorlatinib: Analysis from the CROWN study. ASCO 2021;Abstract 9011.

Dr Justin Gainor

1. For which clinical situations is this data clinically relevant?

- Treatment-naïve, ALK-rearranged NSCLC

2. What are the key findings that are most relevant to patients in these clinical situations?

- Presence of ctDNA at baseline was associated with greater tumor burden.
- Treatment with crizotinib and lorlatinib led to rapid reductions in ctDNA by week 4.
- Reduction in dVAF (VAF at week 4 minus VAF at baseline) was associated with longer PFS with lorlatinib.
- PFS was longer in molecular responders who achieved clearance with lorlatinib

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Early ctDNA dynamics may predict lorlatinib efficacy in ALK+ NSCLC

Skoulidis F et al. Overall survival and exploratory subgroup analyses from the phase 2 CodeBreaK 100 trial evaluating sotorasib in pretreated KRAS p.G12C mutated non-small cell lung cancer. ASCO 2021;Abstract 9003.

Dr Justin Gainor

1. For which clinical situations is this data clinically relevant?

- Patients with previously-treated, NSCLC harboring KRAS G12C mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Among 124 KRAS G12C-mutant NSCLC pts, ORR 37.1%; DCR 80.6%
- DOR 11.1 months
- Median PFS 6.8 months
- OS 12.5 months
- KEAP1 co-mutations associated with lower activity; STK11 mutant/KEAP1 WT higher activity (small numbers though)
- Manageable safety profile (GI and liver toxicity most common); dose reductions in 22%

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Sotorasib is first FDA-approved targeted therapy for KRAS
- Indication is for treatment of previously-treated KRAS G12C-mutant NSCLC
- Data is not compelling enough for front-line use; should be a second line agent
- Molecular testing for KRAS is now standard of care

Paik PA et al. METex14 ctDNA dynamics & resistance mechanisms detected in liquid biopsy (LBx) from patients (pts) with METex14 skipping NSCLC treated with tepotinib. ASCO 2021;Abstract 9012.

Dr Justin Gainor

1. For which clinical situations is this data clinically relevant?

- Patients with advanced NSCLC and MET ex14 skipping alterations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Among 99 patients enrolled on the VISION study of tepotinib using ctDNA, ORR was 52.5%
- Treatment naïve ORR 59.1%, previously-treated 47.3%
- Clinical activity of tepotinib was not different based upon types of MET ex 14 skipping events
- Trend towards improved efficacy in pts with concomitant MET amplification
- Molecular response correlated with clinical response
- Acquired resistance mechanisms include new MET mutations/amplification (7/35), EGFR/HER2 amp (4/35) and RAS/PI3K mutations (3/35)

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Tepotinib had comparable efficacy in patients genotyped using tissue or plasma
- Outside of MET, no baseline biomarkers were identified as predicting outcomes to tepotinib
- Liquid biopsy identified several mechanisms of resistance to tepotinib, but these mechanisms are currently not actionable.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Safety and Efficacy of Pralsetinib in Patients with Advanced *RET* Fusion-Positive Non-Small Cell Lung Cancer: Update from the ARROW Trial

Curigliano G et al.

ASCO 2021;Abstract 9089.

ARROW: Efficacy Summary

	Measurable disease population					
	RET fusion–positive NSCLC (n=216)	Treatment-naïve			Prior treatment	
		All (n=68)	Pre-eligibility revision (n=43)[a]	Post eligibility revision (n=25)[a]	Prior platinum (n=126)	Prior non-platinum (n=22)
ORR, % (95% CI)	**69** (62–75)	**79** (68–88)	**74** (59–87)	**88** (69–98)	**62** (53–70)	**73** (50–89)
Best overall response, n (%)						
CR	9 (4)	4 (6)	4 (9)	0	5 (4)	0
PR	139 (64)	50 (74)	28 (65)	22 (88)	73 (58)	16 (73)
SD	50 (23)	9 (13)	7 (16)	2 (8)	37 (29)	4 (18)
PD	10 (5)	3 (4)	3 (7)	0	5 (4)	2 (9)
NE	8 (4)	2 (3)	1 (2)	1 (4)	6 (5)	0
DCR, % (95% CI)[b]	92 (87–95)	93 (84–98)	91 (78–97)	96 (80–100)	91 (85–96)	91 (71–99)
CBR, % (95% CI)[c]	77 (71–82)	82 (71–91)	79 (64–90)	88 (69–98)	74 (65–81)	77 (55–92)
mDOR, mo (95% CI)	22.3 (15.1–NR)	NR (9.0–NR)	11.0 (7.4–NR)	NR (NR–NR)	22.3 (15.1–NR)	NR (9.2–NR)
mPFS, mo (95% CI)[d]	16.4 (11.0–24.1) n=233	13.0 (9.1–NR) n=75	10.9 (7.7–NR) n=47	NR (NR–NR) n=28	16.5 (10.5–24.1) n=136	12.8 (9.1–NR) n=22

Curigliano J et al. ASCO 2021;Abstract 9089.

Contributing Oncologists

Susmitha Apuri, MD
Florida Cancer Specialists and
Research Institute
Lutz, Florida

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

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Thank you for joining us!

CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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We are taking a short break!

The program will resume at 9:15 AM CT (10:15 AM ET)

Up Next…

Drs Arjun Balar and Robert Dreicer discuss the management of genitourinary cancers

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ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

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TO PRACTICE

Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Genitourinary Cancers Faculty

Arjun Balar, MD
Associate Professor, Department of Medicine
Director, Genitourinary Medical Oncology Program
Medical Director, Clinical Trials Office
NYU Perlmutter Cancer Center
New York, New York

Robert Dreicer, MD, MS
Section Head, Medical Oncology
Deputy Director, University of Virginia Cancer Center
Associate Director for Clinical Research
Professor of Medicine and Urology
University of Virginia School of Medicine
Charlottesville, Virginia

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Contributing Oncologists

Uday Dandamudi, MD
Florida Cancer Specialists and Research Institute
New Port Richey, Florida

Zanetta S Lamar, MD
Florida Cancer Specialists and Research Institute
Naples, Florida

Margaret Deutsch, MD
Duke Raleigh Cancer Center Raleigh
Raleigh, North Carolina

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Ina J Patel, DO
Assistant Professor of Internal Medicine
Division of Hematology/Oncology
Moncrief Cancer Institute
Fort Worth, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

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Highlights of ASCO 2021
Arjun Balar, MD

1. Choueiri TK et al. **Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for patients with renal cell carcinoma: Randomized, double-blind, phase III KEYNOTE-564 study.** ASCO 2021; Abstract LBA5.
2. Rini BI et al. **Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426.** ASCO 2021;Abstract 4500.
3. Galsky MD et al. **Phase 2 trial of gemcitabine, cisplatin, plus nivolumab with selective bladder sparing in patients with muscle-invasive bladder cancer (MIBC): HCRN GU 16-257.** ASCO 2021; Abstract 4503.
4. Balar AJ et al. **Pembrolizumab (pembro) in combination with gemcitabine (Gem) and concurrent hypofractionated radiation therapy (RT) as bladder sparing treatment for muscle-invasive urothelial cancer of the bladder (MIBC): A multicenter phase 2 trial.** ASCO 2021;Abstract 4504.
5. Friedlander TW et al. **Study EV-103: Update on durability results and long-term outcome of enfortumab vedotin + pembrolizumab in first line locally advanced or metastatic urothelial carcinoma (la/mUC).** ASCO 2021;Abstract 4528.

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Highlights of ASCO 2021
Robert Dreicer, MD, MS

1. Morris MJ et al. **Phase III study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION).** ASCO 2021;Abstract LBA4.
2. Fizazi K et al. **A phase 3 trial with a 2x2 factorial design of abiraterone acetate plus prednisone and/or local radiotherapy in men with de novo metastatic castration-sensitive prostate cancer (mCSPC): First results of PEACE-1.** ASCO 2021;Abstract 5000.
3. Agarwal N et al. **Health-related quality of life (HRQoL) and patient-reported outcomes at final analysis of the TITAN study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT).** ASCO 2021;Abstract 5068.
4. Gillessen S et al. **Decreased fracture rate by mandating bone protecting agents in the EORTC 1333/PEACEIII trial combining Ra223 with enzalutamide versus enzalutamide alone: An updated safety analysis.** ASCO 2021;Abstract 5002.
5. Graff JN et al. **Pembrolizumab plus enzalutamide for enzalutamide-resistant metastatic castration-resistant prostate cancer (mCRPC): Updated analyses after one additional year of follow-up from cohorts 4 and 5 of the KEYNOTE-199 study.** ASCO 2021;Abstract 5042.

Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 59-year-old man with metastatic hormone-sensitive prostate cancer
- Dr Malik: A 55-year-old man with de novo metastatic prostate cancer

Module 2: Highlights of ASCO 2021 – Dr Dreicer

Module 3: Cases from the Community

- Dr Patel: A 63-year-old man with metastatic ccRCC
- Dr Kodali: A 52-year-old woman with metastatic RCC who receives pembrolizumab/axitinib
- Dr Lamar: A 68-year-old man with metastatic urothelial carcinoma
- Dr Prakash: A 58-year-old man with metastatic transitional cell cancer of the bladder

Module 4: Highlights of ASCO 2021 – Dr Balar

Agenda

Module 1: Cases from the Community

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- Dr Malik: A 55-year-old man with de novo metastatic prostate cancer

Module 2: Highlights of ASCO 2021 – Dr Dreicer

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Module 4: Highlights of ASCO 2021 – Dr Balar

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Regulatory and reimbursement issues aside, what systemic therapy would you typically add to androgen deprivation therapy (ADT) for an asymptomatic 65-year-old man who presents with prostate cancer and multiple bone and soft tissue metastases?

- Abiraterone
- Apalutamide
- Enzalutamide
- Darolutamide
- Docetaxel
- Abiraterone + docetaxel
- None initially, but add secondary hormonal therapy if suboptimal response to ADT
- None initially, but add chemotherapy if suboptimal response to ADT
- Other (please specify)
- None

Case Presentation – Dr Jasani: A 59-year-old man with metastatic hormone-sensitive prostate cancer (mHSPC)

Dr Nikesh Jasani

- Presented with obstructive renal failure and diagnosed with mHSPC with bulky retroperitoneal lymphadenopathy (PSA 57 ng/mL)
- Molecular studies: no somatic HRD mutations
- ADT plus bicalutamide and RT to primary tumor due to obstruction
- Switched to abiraterone and prednisone plus ADT after hospitalization → PSA reduced to 0.21 ng/mL

Questions

- What is the role for radiation therapy in metastatic low-volume prostate cancer to the primary prostate?
- What is the ideal androgen receptor antagonist in the first line for castration-sensitive metastatic prostate cancer? How do you decide between chemotherapy versus androgen deprivation therapy plus androgen receptor antagonist in high volume disease?
- For an immediate response, should we be using the oral GnRH antagonist relugolix?
- What is the role for BRCA-mutated somatic or germline in metastatic prostate cancer as well as ATM and a whole host of other HRD mutations?

RTP RESEARCH TO PRACTICE

Which of the following genomic evaluations do you generally order for patients with castration-resistant metastatic prostate cancer?

- BRCA germline
- BRCA somatic
- BRCA germline and somatic
- Germline panel
- Somatic panel (eg, NGS)
- Germline and somatic panel
- Other (please specify)
- None

Case Presentation – Dr Malik: A 55-year-old man with de novo metastatic prostate cancer

Dr Henna Malik

- Presents with pain in his back and in his inguinal area, trouble with urination
- Prostate biopsies: Gleason 4 + 4 adenocarcinoma of the prostate
- PET: Diffuse bone metastases, significantly in the lumbar spine
- Docetaxel/prednisone x 2, with significant improvement and PSA decline to 75 → docetaxel x 3
  - Patient desires discontinuation of IV chemotherapy
- Switched to abiraterone/prednisone, with PSA decline to < 10 → PD after 1 year
- Docetaxel, with PD after 2 cycles → cabazitaxel, with PD after 4-5 cycles
- NGS: Somatic BRCA2 mutation (BRCA1/2 negative for germline)
- Olaparib, with response x 6 months → PD and hospice

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 59-year-old man with metastatic hormone-sensitive prostate cancer
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Module 2: Highlights of ASCO 2021 – Dr Dreicer

Module 3: Cases from the Community

- Dr Patel: A 63-year-old man with metastatic ccRCC
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Module 4: Highlights of ASCO 2021 – Dr Balar

RTP RESEARCH TO PRACTICE

Morris MJ et al. Phase III study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION). ASCO 2021;Abstract LBA4.

Dr Robert Dreicer

1. For which clinical situations is this data clinically relevant?

- Patients with metastatic castration-resistant prostate cancer (mCRPC) following 1 or 2 taxane regimens and at least 1 androgen receptor pathway inhibitor (and potentially a positive PSMA PET/CT)

2. What are the key findings that are most relevant to patients in these clinical situations?

- Radiographic progression-free survival (rPFS) HR=0.063 (14.6 vs 10.4 months)
- Overall survival HR 0.63 (15.3 vs 11.3 months)
- Toxicity was relatively modest (8% grade 3-5)

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Use of PSMA targeted lutetium-177-PSMA-617 in patients with mCRPC post taxane/ARI
- Evolving role/indication for PSMA PET/CT both Ga and F based

Fizazi K et al. A phase 3 trial with a 2x2 factorial design of abiraterone acetate plus prednisone and/or local radiotherapy in men with de novo metastatic castration-sensitive prostate cancer (mCSPC): First results of PEACE-1. ASCO 2021;Abstract 5000.

Dr Robert Dreicer

1. For which clinical situations is this data clinically relevant?

- De novo metastatic castration-sensitive prostate cancer (mCSPC) with ≥ 1 lesion on bone scan or CT, ECOG 0-2

2. What are the key findings that are most relevant to patients in these clinical situations?

- Radiographic progression-free survival HR 0.50 (4.5 vs 2.0) P < 0.0001
- Some increase in hypertension and liver toxicity and less fatigue in combo arm

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Evolution of “ADT intensification” in De novo mCSPC
- Additional data regarding local intensification with RT

Agarwal N et al. Health-related quality of life (HRQoL) and patient-reported outcomes at final analysis of the TITAN study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT). ASCO 2021;Abstract 5068.

Dr Robert Dreicer

1. For which clinical situations is this data clinically relevant?

- Metastatic castration-sensitive prostate cancer

2. What are the key findings that are most relevant to patients in these clinical situations?

- With 4 years follow-up survival benefit of addition of apalutamide to ADT confirmed without major impact on quality of life

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Long-term benefit from ADT intensification
- Role of quality of life assessment in mCSPC

Graff JN et al. Pembrolizumab plus enzalutamide for enzalutamide-resistant metastatic castration-resistant prostate cancer (mCRPC): Updated analyses after one additional year of follow-up from cohorts 4 and 5 of the KEYNOTE-199 study. ASCO 2021;Abstract 5042.

Dr Robert Dreicer

1. For which clinical situations is this data clinically relevant?

- Patients with metastatic castration resistant prostate cancer

2. What are the key findings that are most relevant to patients in these clinical situations?

- With additional follow-up (30 months) modest activity of enzalatmide/pembrolizumab observed
- No new safety signals

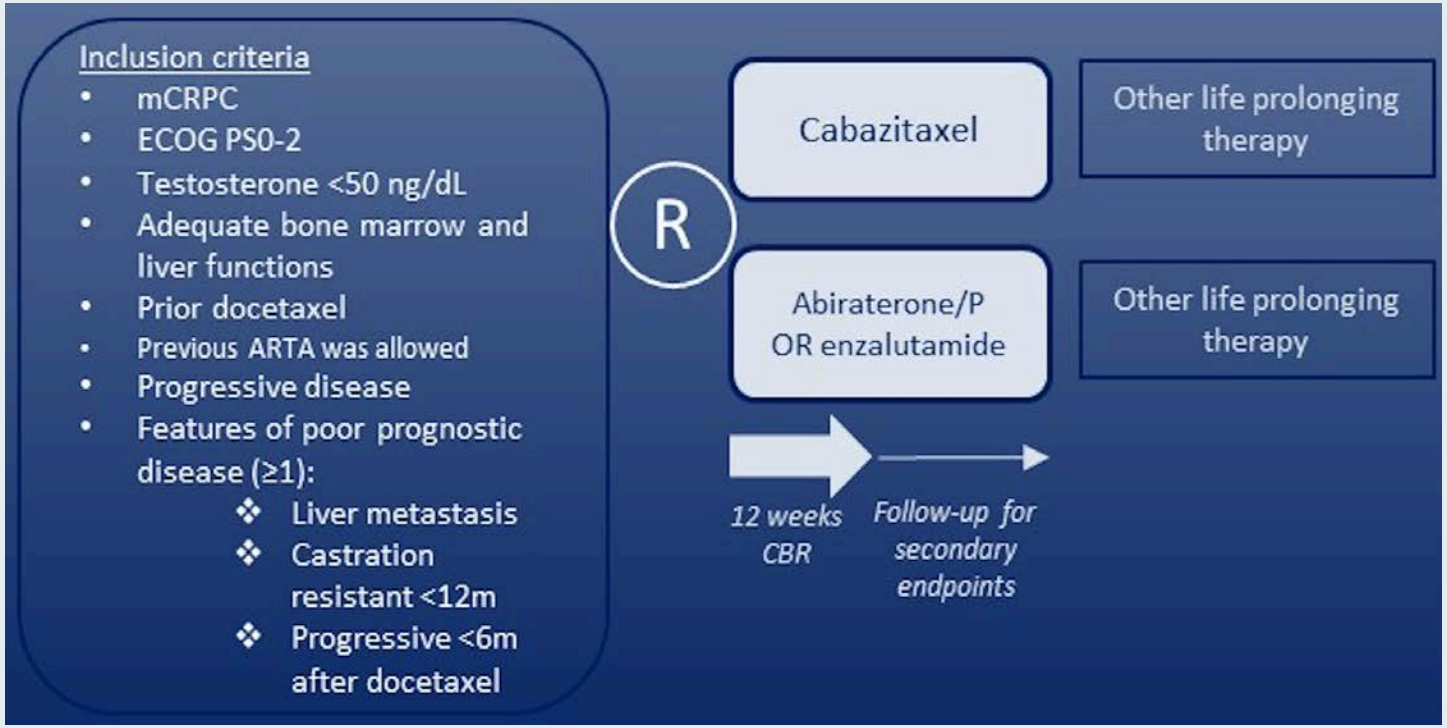
3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Immune checkpoint plus androgen receptor pathway inhibitor ongoing phase III studies

First Results from a Randomized Phase II Study of Cabazitaxel (CBZ) versus an Androgen Receptor Targeted Agent (ARTA) in Patients with Poor-Prognosis Castration-Resistant Prostate Cancer (mCRPC)

van der Zande K et al.
ASCO 2021;Abstract 5059.

OSTRICh: First results with CBZ versus an ARTA in patients with poor-prognosis mCRPC



- No significant difference in CBR between CBZ and ARTA treated patients at 12 weeks
- Visceral metastases were more frequent in CBZ patients
- Radiological response and stable disease at 12 weeks was significantly higher in patients treated with CBZ than with ARTA
- Time to clinical progression was significantly prolonged in patients treated with ARTA
- Overall survival and rPFS was similar in both groups

van der Zande K et al. ASCO 2021;Abstract 5059.

Gillessen S et al. Decreased fracture rate by mandating bone protecting agents in the EORTC 1333/PEACEIII trial combining Ra223 with enzalutamide versus enzalutamide alone: An updated safety analysis. ASCO 2021;Abstract 5002.

Dr Robert Dreicer

1. For which clinical situations is this data clinically relevant?

- Metastatic castration resistant prostate cancer with bone predominant disease treated with radium 223 and an androgen receptor pathway inhibitor

2. What are the key findings that are most relevant to patients in these clinical situations?

- Risk of fractures significantly decreased in patients receiving bone protective agents in men receiving enzalutamide alone or in combination with radium-223
- Fracture risk without bone proactive agent (BPA) enzalutamide 15.6% with BPA 2.6%
- Fracture risk without bone proactive agent (BPA) enzalutamide + radium 223 37.1.% with BPA 2.7%

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Attention to bone events in the setting of agents with positive impact on symptomatic skeletal events.
- Intensification of BPA in mCRPC

Agenda

Module 1: Cases from the Community

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Module 4: Highlights of ASCO 2021 – Dr Balar

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with a history of nephrectomy for clear cell renal cell carcinoma (RCC) who on routine follow-up 3 years later is found to have asymptomatic bilateral lung metastases (PS 0)?

- Nivolumab/ipilimumab
- Avelumab/axitinib
- Pembrolizumab/axitinib
- Nivolumab/cabozantinib
- Pembrolizumab/lenvatinib
- Tyrosine kinase inhibitor monotherapy
- Anti-PD-1/PD-L1 monotherapy
- Other (please specify)

What is your usual second-line treatment for a patient with metastatic clear cell RCC who responds to first-line nivolumab/ipilimumab but then experiences disease progression while receiving maintenance nivolumab?

- Continue nivolumab and add back ipilimumab
- Continue nivolumab and add cabozantinib
- Cabozantinib
- Axitinib
- Sunitinib
- Pazopanib
- Tivozanib
- Other (please specify)

Case Presentation – Dr Patel: A 63-year-old man with metastatic ccRCC

Dr Ina Patel

- 2/2019: Clear cell RCC, with clinical lung metastases, s/p radical nephrectomy
  - Biopsy attempt x 3 of lung nodules unsuccessful
- 5/2020: Ipilimumab/nivolumab x 1, with severe hepatic immunoreaction 6 days later
  - Steroids initiated

Date	AST	ALT	Notes
5/13/2020	23	23	
6/11/2020	**1164**	**2075**	**Steroids initiated at 2 mg/kg twice daily**
6/15/2020	113	843	
6/22/2020	22	154	Steroids changed to 1 mg/kg daily
6/25/2020	74	1818	Steroids increased to 1.5 mg/kg daily
6/29/2020	978	2437	***Admitted ICU with atrial fibrillation with rapid ventricular response***
6/30/2020	**2095**	**2849**	**2 grams IV solumedrol x 1 → 2 mg/kg iv bid and mycophenolate 1 gram po bid added**
7/1/2020	439	1959	
7/2/2020	266	1395	

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Case Presentation – Dr Patel: A 63-year-old man with metastatic ccRCC (continued)

Dr Ina Patel

Questions

- What is your next line of treatment recommendation in a patient with metastatic renal cell carcinoma if they don't tolerate immunotherapy?
- Do you ever rechallenge with immunotherapy once there are adverse effects?

Case Presentation – Dr Kodali: A 52-year-old woman with metastatic RCC who receives pembrolizumab/ axitinib

Dr Dhatri Kodali

- Presents to hospital with hematuria and work-up reveals large renal mass and lung and bone metastases
- Nephrectomy
- Pembrolizumab/axitinib
- Restaging scan at 3 months shows disease response in the lung and bone
- She has developed LFT abnormalities (ALT/AST in 300 range) → pembrolizumab on hold

Questions

- How often do you see LFT abnormalities with this treatment combination? Would you consider the IO or the TKI as the culprit?
- What are my options for this patient? Can I re-challenge?

RTP RESEARCH TO PRACTICE

Which of the following would you generally recommend first for a patient with metastatic urothelial bladder cancer who is eligible to receive all 3 agents?

- Enfortumab vedotin
- Erdafitinib
- Sacituzumab govitecan

Case Presentation – Dr Lamar: A 68-year-old man with metastatic urothelial carcinoma

Dr Zanetta Lamar

- 2014: Muscle-invasive high-grade urothelial carcinoma treated with TURBT → gemcitabine/cisplatin → PD
- Clinical trial with nivolumab/ipilimumab, with CR x 4 years → PD
- Enfortumab vedotin x 7 months (ongoing)
  - Mild neuropathy, dose reduction
- Pelvic adenopathy → referred for radiation therapy to site; disease stable elsewhere
- NGS: No actionable mutations

Questions

- If he had an FGFR mutation and had disease progression on immunotherapy, would you prefer an FGFR inhibitor over a drug like enfortumab vedotin?
- What is your standard approach for patients who are cisplatin ineligible?

Case Presentation – Dr Prakash: A 58-year-old man with metastatic transitional cell cancer of the bladder

Dr Chris Prakash

- Presents with hematuria
- Diagnosed with locally advanced muscle invasive transitional cell cancer of the bladder
- RT and cisplatin
- Metastases noted in lymph nodes and lung
- Carboplatin/gemcitabine → PD in lung, development of hydronephrosis
- Mutational analysis: FGFR1
- Erdafitinib x 1 year and ongoing, with resolution of lung metastases

Questions

- For patients with metastatic bladder cancer who have progressive disease on first-line chemotherapy, what is your usual second-line therapy? Do you check mutational status on all your patients?
- If you detect an FGFR mutation, is erdafitinib your drug of choice for second-line therapy, or do you still consider immunotherapy in that situation?
- In patients receiving erdafitinib, how do you enforce ophthalmologic exams and monitor visual changes?
- After a patient progresses on erdafitinib, do you consider immunotherapy or enfortumab vedotin?

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 59-year-old man with metastatic hormone-sensitive prostate cancer
- Dr Malik: A 55-year-old man with de novo metastatic prostate cancer

Module 2: Highlights of ASCO 2021 – Dr Dreicer

Module 3: Cases from the Community

- Dr Patel: A 63-year-old man with metastatic ccRCC
- Dr Kodali: A 52-year-old woman with metastatic RCC who receives pembrolizumab/axitinib
- Dr Lamar: A 68-year-old man with metastatic urothelial carcinoma
- Dr Prakash: A 58-year-old man with metastatic transitional cell cancer of the bladder

Module 4: Highlights of ASCO 2021 – Dr Balar

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Choueiri TK et al. Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for patients with renal cell carcinoma: Randomized, double-blind, phase III KEYNOTE-564 study. ASCO 2021;Abstract LBA5.

Dr Arjun Balar

1. For which clinical situations is this data clinically relevant?

- High-risk clear cell RCC after nephrectomy in the adjuvant setting, including those with resected oligometastatic disease.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Adjuvant immunotherapy with pembrolizumab improved DFS versus placebo, with a HR of 0.68. Clear trend in OS, but statistical significance not yet met.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This is the first adjuvant immunotherapy study in RCC, and is also the first positive study to demonstrate a DFS benefit. OS is not yet mature, but suggestion of benefit is there. The prior track record of adjuvant VEGFR TKI in this setting has tempered enthusiasm for this data, however IO is unique in its MOA and these data are stronger. The future could be adjuvant ipi/nivo, which could further improve DFS above single agent PD-1 alone.

Rini BI et al. Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426. ASCO 2021;Abstract 4500.

Dr Arjun Balar

1. For which clinical situations is this data clinically relevant?

- First-line untreated metastatic clear cell RCC. These data are updated long-term follow up for patients treated with axitinib/pembrolizumab, and provided important context/comparison to other, previously more mature studies such as CheckMate 214.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The ORR for axitinib/pembro improved slightly to just above 60%.
- Most importantly long-term follow up for PFS does not demonstrate the same “tail” we observe for CM214, implying that the ~35% that have long-term durable disease control > 4 year with ipi/nivo is not observed with axitinib/pembrolizumab.
- The median DoR for Axitinib/Pembro is just short of 2 years.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Axitinib/pembro remains a highly active first-line option in clear-cell RCC with high upfront responses, but long-term follow up puts these responses in context against those observed with ipi/nivo which appear to be more durable.

Galsky MD et al. Phase 2 trial of gemcitabine, cisplatin, plus nivolumab with selective bladder sparing in patients with muscle- invasive bladder cancer (MIBC): HCRN GU 16-257. ASCO 2021;Abstract 4503.

Dr Arjun Balar

1. For which clinical situations is this data clinically relevant?

- Patients with muscle-invasive bladder cancer who are interested in a risk-adapted approach to avoiding cystectomy after neoadjuvant chemotherapy and immunotherapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- NAC+PD-1 can achieve clinical CRs in close to 50% of patients in this investigator initiated study. Amongst these patients, a subgroup can be safely followed without any definitive local therapy for the bladder, however there is a small risk for occult invasive disease that will ultimately manifest as recurrence and pose a higher subsequent risk for metastases.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Subsequent correlative analyses linking clinical CR and baseline tumor genomics with long-term recurrence-free survival will be needed to better identify which amongst those with a clinical CR can be safely observed without definitive local bladder therapy versus those who should still undergo RC or ChemoRT.

Balar AJ et al. Pembrolizumab (pembro) in combination with gemcitabine (Gem) and concurrent hypofractionated radiation therapy (RT) as bladder sparing treatment for muscle-invasive urothelial cancer of the bladder (MIBC): A multicenter phase 2 trial. ASCO 2021;Abstract 4504.

Dr Arjun Balar

1. For which clinical situations is this data clinically relevant?

- Patients with muscle-invasive bladder cancer who are opting for bladder preservation chemoradiation, rather than radical cystectomy, or those who are not surgical candidates.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The estimated 1-year BIDFS rate is 88% in the efficacy cohort in this early analysis, suggesting a high-rate of bladder preservation. Therapy is well-tolerated, with manageable safety profile.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This trial is supporting the randomized phase III studies S1806 and KN992 which are testing chemoradiation with and without immunotherapy, to fully define the contribution of immunotherapy added to chemoradiation in MIBC.

Friedlander TW et al. Study EV-103: Update on durability results and long term outcome of enfortumab vedotin + pembrolizumab in first line locally advanced or metastatic urothelial carcinoma (la/mUC). ASCO 2021;Abstract 4528.

Dr Arjun Balar

1. For which clinical situations is this data clinically relevant?

- First-line cisplatin-ineligible patients with metastatic urothelial cancer. These are updated response, durability of response and safety for EV/pembro in the first-line setting

2. What are the key findings that are most relevant to patients in these clinical situations?

- The regimen is highly active, 73% ORR, with robust durability, now with median DoR of 25 months. 93% of patients have some decrease in baseline SLDs. Median survival of 26 months could be a preview of things to come in future randomized studies. No new safety signals.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Continued strong data to support enrollment to Cohort K of EV-103 and EV-302, which are both randomized studies and both poised to establish EV/pembro as a potential new standard of care in first-line metastatic urothelial cancer.

FDA Grants Accelerated Approval to Sacituzumab Govitecan for Advanced Urothelial Cancer

Press Release – April 13, 2021

"The Food and Drug Administration granted accelerated approval to sacituzumab govitecan for patients with locally advanced or metastatic urothelial cancer (mUC) who previously received a platinum-containing chemotherapy and either a programmed death receptor-1 (PD-1) or a programmed death-ligand 1 (PD-L1) inhibitor.

Efficacy and safety were evaluated in TROPHY (IMMU-132-06; NCT03547973), a single-arm, multicenter trial that enrolled 112 patients with locally advanced or mUC who received prior treatment with a platinum-containing chemotherapy and either a PD-1 or PD-L1 inhibitor. Patients received sacituzumab govitecan, 10 mg/kg intravenously, on days 1 and 8 of a 21-day treatment cycle."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sacituzumab-govitecan-advanced-urothelial-cancer

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TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors

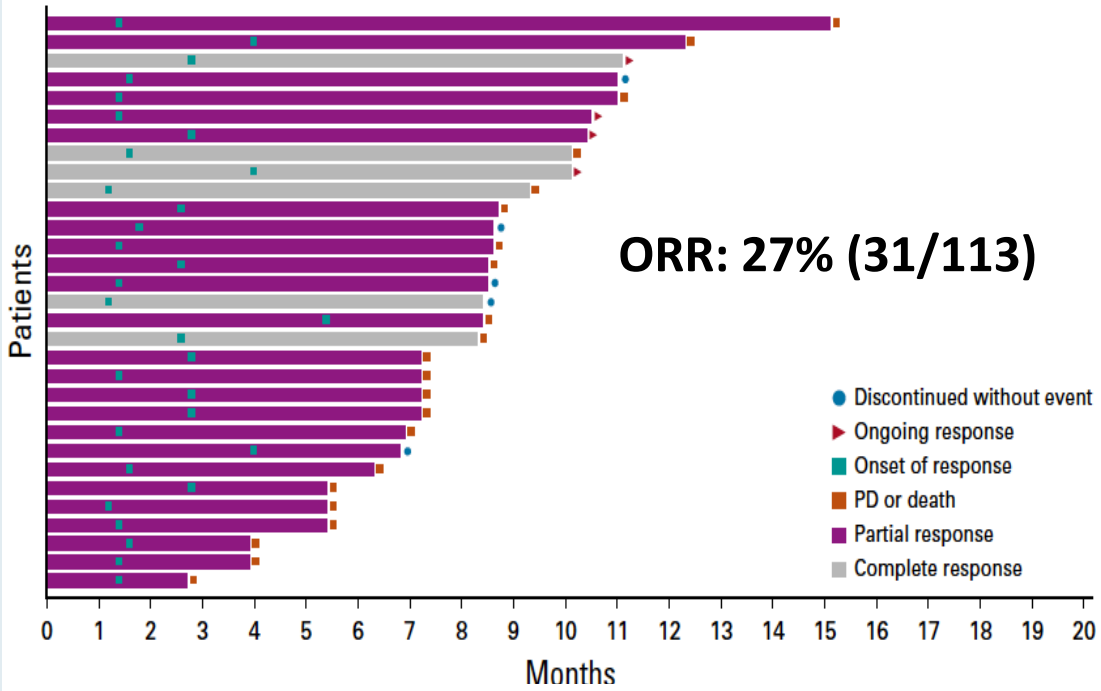
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11]; Phillip Palmbos, MD, PhD[12]; Christos E. Kyriakopoulos, MD[13]; Damien Pouessel, MD, PhD[14]; Cora N. Sternberg, MD[1]; Quan Hong, MD[15]; Trishna Goswami, MD[15]; Loretta M. Itri, MD[15]; and Petros Grivas, MD, PhD[16]

J Clin Oncol 2021;[Online ahead of print].

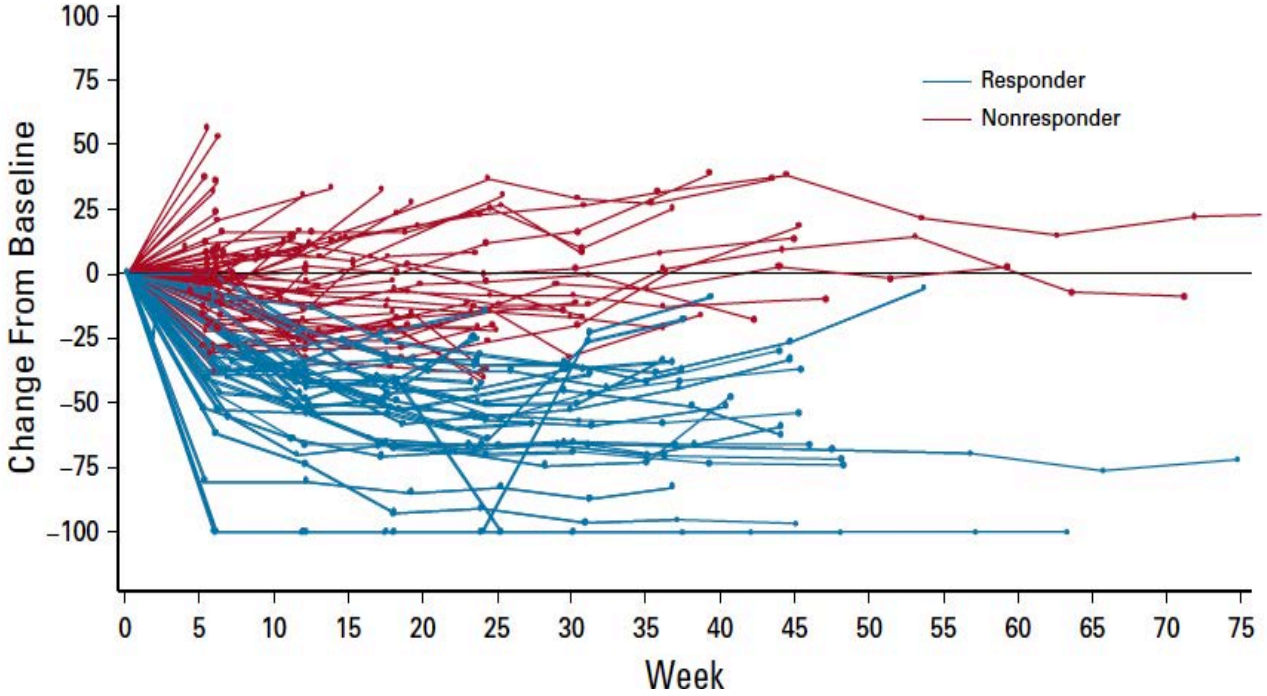
TROPHY-U-01 (Cohort 1): ORR, Duration of Response and Survival

Median DOR: 7.2 mo

Median time to onset of response: 1.6 mo



ORR: 27% (31/113)



Median PFS: 5.4 mo

Median OS: 10.9 mo

Tagawa ST et al. *J Clin Oncol* 2021;[Online ahead of print]; Loriot Y et al. ESMO 2020;Abstract LBA24.

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Contributing Oncologists

Uday Dandamudi, MD
Florida Cancer Specialists and Research Institute
New Port Richey, Florida

Zanetta S Lamar, MD
Florida Cancer Specialists and Research Institute
Naples, Florida

Margaret Deutsch, MD
Duke Raleigh Cancer Center Raleigh
Raleigh, North Carolina

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Ina J Patel, DO
Assistant Professor of Internal Medicine
Division of Hematology/Oncology
Moncrief Cancer Institute
Fort Worth, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

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CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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We are taking a short break!

The program will resume at 10:30 AM CT (11:30 AM ET)

Up Next…

Drs John Allan and Sonali Smith discuss the management of chronic lymphocytic leukemia and lymphomas

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ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

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Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Chronic Lymphocytic Leukemia and Lymphomas Faculty

John N Allan, MD
Assistant Professor of Medicine
Weill Cornell Medicine
New York, New York

Sonali M Smith, MD
Elwood V Jensen Professor of Medicine
Chief, Section of Hematology/Oncology
Co-Leader, Cancer Service Line
Co-Director, Lymphoma Program
The University of Chicago
Chicago, Illinois

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Contributing Oncologists

Amanda Blackmon, DO, MS
Chief Fellow
Hematology/Oncology
University of California, Irvine
Irvine, California

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Anthony Nguyen, MD
Fellow, Loma Linda
University Health
Loma Linda, California

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

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Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Highlights of ASCO and EHA 2021
John N Allan, MD

1. Byrd JC et al. **First results of a head-to-head trial of acalabrutinib versus ibrutinib in previously treated chronic lymphocytic leukemia.** ASCO 2021;Abstract 7500.
2. Ghia P et al. **Fixed-duration (FD) first-line treatment (tx) with ibrutinib (I) plus venetoclax (V) for chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL): Primary analysis of the FD cohort of the phase 2 CAPTIVATE study.** ASCO 2021;Abstract 7501.
3. Hillman P et al. **First interim analysis of ALPINE study: Results of a Phase 3 randomized study of zanubrutinib vs ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma.** EHA 2021;Abstract LB1900.
4. Kater A et al. **Fixed-duration ibrutinib and venetoclax (I+V) versus chlorambucil plus obinutuzumab (CLB+O) for first-line (1L) chronic lymphocytic leukemia (CLL): Primary analysis of the Phase 3 GLOW study.** EHA 2021;Abstract LB1902.
5. Gribben J et al. **A comparison of updated clinical outcomes from ZUMA-5 (axicabtagene ciloleucel) and the international SCHOLAR-5 external control cohort in relapsed/refractory follicular lymphoma (R/R FL).** EHA 2021;Abstract LB1904.
6. Schuster SJ et al. **Efficacy and safety of tisagenlecleucel (Tisa-cel) in adult patients (Pts) with relapsed/refractory follicular lymphoma (r/r FL): Primary analysis of the phase 2 Elara trial.** ASCO 2021;Abstract 7508.

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Highlights of ASCO and EHA 2021
Sonali M Smith, MD

1. Smith MR et al. **ECOG-ACRIN E1411 randomized phase 2 trial of bendamustine-rituximab (BR)-based induction followed by rituximab (R) ± lenalidomide (L) consolidation for Mantle cell lymphoma: Effect of adding bortezomib to front-line BR induction on PFS.** ASCO 2021;Abstract 7503.
2. Phillips T et al. **The combination of venetoclax, lenalidomide, and rituximab in patients with newly diagnosed mantle cell lymphoma induces high response rates and MRD undetectability.** ASCO 2021; Abstract 7505.
3. Martin P et al. **Real-world (RW) treatment (tx) patterns and outcomes of 3,455 previously untreated mantle cell lymphoma (MCL) patients (pts) in U.S. routine clinical practice.** ASCO 2021;Abstract 7504.
4. LaCasce AS et al. **CALGB 50801 (Alliance): PET adapted therapy in bulky stage I/II classic Hodgkin lymphoma (cHL).** ASCO 2021;Abstract 7507.
5. Le Gouill S et al. **First results of DLBCL patients treated with CAR-T cells and enrolled in DESCAR-T registry, a French real-life database for CAR-T cells in hematologic malignancies.** EHA 2021;Abstract S216.

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Agenda

Module 1: Cases from the Community

- Dr Jasani: A 60-year-old man with newly diagnosed CLL
- Dr Blackmon: A 50-year-old man with Stage III, Grade I-II follicular lymphoma

Module 2: Highlights of ASCO and EHA 2021 – Dr Allan

Module 3: Cases from the Community

- Dr Prakash: A 66-year-old man with mantle cell lymphoma
- Dr Levin: A 70-year-old man with relapsed gastric mantle cell lymphoma
- Dr Nguyen: A 26-year-old woman with classical Hodgkin lymphoma
- Dr Meerasahib: An 84-year-old woman with relapsed, EBV-positive DLBCL

Module 4: Highlights of ASCO and EHA 2021 – Dr Smith

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 60-year-old man with newly diagnosed CLL
- Dr Blackmon: A 50-year-old man with Stage III, Grade I-II follicular lymphoma

Module 2: Highlights of ASCO and EHA 2021 – Dr Allan

Module 3: Cases from the Community

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Module 4: Highlights of ASCO and EHA 2021 – Dr Smith

Regulatory and reimbursement issues aside, what is your preferred initial regimen for a 65-year-old patient with IGHV-unmutated chronic lymphocytic leukemia without del(17p) or TP53 mutation who requires treatment?

- FCR
- BR
- Ibrutinib
- Ibrutinib + rituximab
- Ibrutinib + obinutuzumab
- Acalabrutinib
- Acalabrutinib + obinutuzumab
- Zanubrutinib
- Venetoclax + obinutuzumab
- Venetoclax + ibrutinib
- Other (please specify)

Case Presentation – Dr Jasani: A 60-year-old man with newly diagnosed CLL

Dr Nikesh Jasani

- Presents with newly diagnosed CLL with bulky LAD, night sweats, fatigue, other symptoms
- Patient desires time-limited treatment
- Venetoclax/obinutuzumab

Questions

- What are your thoughts about the newer efficacy and safety data with acalabrutinib versus ibrutinib?
- How are you incorporating venetoclax/obinutuzumab into upfront treatment and how do you monitor these patients for TLS in an outpatient setting?
- How are you using MRD status, and how do you measure it – NGS, next generation flow? How does MRD status affect your decision making? Do you stop therapy based on MRD?

What is your usual third-line treatment for a patient with follicular lymphoma with an EZH2 mutation who received first-line BR, second-line lenalidomide/rituximab and then develops disease progression?

- Idelalisib
- Copanlisib
- Duvelisib
- Umbralisib
- Tazemetostat
- R-CHOP
- Obinutuzumab +/- chemotherapy
- Other (please specify)

Case Presentation – Dr Blackmon: A 50-year-old man with newly diagnosed Stage III, Grade I-II FL

Dr Amanda Blackmon

- 2018: Presented with diffuse adenopathy and diagnosed with Stage III, Grade I-II FL
  - Observed until fatigue worsened and patient desired treatment
  - Discussion of R-chemotherapy and lenalidomide/rituximab (R^2) as treatment options
- R^2 → rituximab maintenance
- Patient remains in CR 2.5 years after completing maintenance therapy
- Agammaglobulinemia and COVID-19 vaccine

Questions

- What is your opinion regarding R-chemotherapy and R^2 as front-line treatment options?
- Does the extent of this patient's disease have any influence on which regimen you would choose?

Agenda

Module 1: Cases from the Community

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Module 2: Highlights of ASCO and EHA 2021 – Dr Allan

Module 3: Cases from the Community

- Dr Prakash: A 66-year-old man with mantle cell lymphoma
- Dr Levin: A 70-year-old man with relapsed gastric mantle cell lymphoma
- Dr Nguyen: A 26-year-old woman with classical Hodgkin lymphoma
- Dr Meerasahib: An 84-year-old woman with relapsed, EBV-positive DLBCL

Module 4: Highlights of ASCO and EHA 2021 – Dr Smith

Byrd JC et al. First results of a head-to-head trial of acalabrutinib versus ibrutinib in previously treated chronic lymphocytic leukemia. ASCO 2021;Abstract 7500.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- Patients with CLL who are being considered for treatment with BTKi whether in relapsed or frontline settings

2. What are the key findings that are most relevant to patients in these clinical situations?

- Acalabrutinib appears noninferior in terms of efficacy and with improved outcomes based on cardiovascular outcomes such as atrial fibrillation or hypertension.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This data provides the first head to head efficacy and safety data between acalabrutinib and ibrutinib in high risk relapsed refractory CLL. Acalabrutinib was equally effective with less cardiovascular toxicity and thus becomes an important study to consider when devising a treatment plan for patients with CLL

Hillman P et al. First interim analysis of ALPINE study: Results of a Phase 3 randomized study of zanubrutinib vs ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. EHA 2021;Abstract LB1900.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- All patients with CLL for whom a BTKi may be indicated. (Caveat Zanubrutinib is currently only FDA approved for MCL)

2. What are the key findings that are most relevant to patients in these clinical situations?

- This study demonstrates improved response rates with suggestion of improved PFS with improved toxicity profile in regards to cardiovascular outcomes.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Zanubrutinib has potential to establish itself as best in class in terms of efficacy and safety if ongoing trends continue over time. Currently only interim analysis.

Ghia P et al. Fixed-duration (FD) first-line treatment (tx) with ibrutinib (I) plus venetoclax (V) for chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL): Primary analysis of the FD cohort of the phase 2 captivate study. ASCO 2021;Abstract 7501.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- This data is relevant for younger fit patients with CLL

2. What are the key findings that are most relevant to patients in these clinical situations?

- This study demonstrates high rates of CR and uMRD negativity in patients with CLL in the frontline setting with excellent 2 year PFS data demonstrating the potential for an all oral once daily fixed duration regimen for patients with CLL

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- The treatment regime was safe tolerable and effective with 92% of patients completing the assigned treatment and demonstrates the potential of an all oral fixed duration treatment approach.

Kater A et al. Fixed-duration ibrutinib and venetoclax (I+V) versus chlorambucil plus obinutuzumab (CLB+O) for first-line (1L) chronic lymphocytic leukemia (CLL): Primary analysis of the Phase 3 GLOW study. EHA 2021;Abstract LB1902.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- For older patients with CLL who have treatment indications in the frontline.

2. What are the key findings that are most relevant to patients in these clinical situations?

- This all oral fixed duration regimen achieved high rates of response, uMRD negativity and PFS in older patients with comorbidities. Safety was tolerable and the majority of these older patients were able to complete therapy and stop treatment.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This data showed that this regimen can be given safely to older patients with comorbidities and thus extending this treatment strategy not only to young fit patients but to older patients with comorbidities in the frontline setting.

Gribben J et al. A comparison of updated clinical outcomes from ZUMA-5 (axicabtagene ciloleucel) and the international SCHOLAR-5 external control cohort in relapsed/refractory follicular lymphoma (R/R FL). EHA 2021;Abstract LB1904.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- Patients with FL and needing a 3rd line or later treatment for their relapsed disease

2. What are the key findings that are most relevant to patients in these clinical situations?

- When compared to historical controls in this high risk setting response rates, PFS and OS favored CART with axi-cel vs standard treaetments including those with targeted treatment like PI3K.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Axi Cel CART therapy for patients with multiply relapsed refractory FL have a new treatment option with promising early survival outcome data bringing in a new effective therapy for these patients

Schuster SJ et al. Efficacy and safety of tisagenlecleucel (Tisa-cel) in adult patients (Pts) with relapsed/refractory follicular lymphoma (r/r FL): Primary analysis of the phase 2 Elara trial. ASCO 2021;Abstract 7508.

Dr John Allan

1. For which clinical situations is this data clinically relevant?

- Patients with relapsed FL.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Tisa-cel offers high response rates CR rates and encouraging early PFS and OS data. The treatment was administered as an outpatient in ~20% of patients and had very low rates of Grade3/4 CRS or ICAN toxicities.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This option has demonstrated the potential to offer CART therapy as an outpatient and demonstrated a new option with relatively low toxicity compared to other CART clinical trials.

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 60-year-old man with newly diagnosed CLL
- Dr Blackmon: A 50-year-old man with Stage III, Grade I-II follicular lymphoma

Module 2: Highlights of ASCO and EHA 2021 – Dr Allan

Module 3: Cases from the Community

- Dr Prakash: A 66-year-old man with mantle cell lymphoma
- Dr Levin: A 70-year-old man with relapsed gastric mantle cell lymphoma
- Dr Nguyen: A 26-year-old woman with classical Hodgkin lymphoma
- Dr Meerasahib: An 84-year-old woman with relapsed, EBV-positive DLBCL

Module 4: Highlights of ASCO and EHA 2021 – Dr Smith

A 78-year-old patient with mantle cell lymphoma initially treated with BR followed by 2 years of maintenance rituximab experiences disease relapse 3 years later. The patient is otherwise healthy. What would you recommend?

- Ibrutinib
- Acalabrutinib
- Zanubrutinib
- Lenalidomide
- Lenalidomide + rituximab
- Venetoclax
- Venetoclax + rituximab
- Other (please specify)

Case Presentation – Dr Prakash: A 66-year-old man with mantle cell lymphoma

Dr Chris Prakash

- Presents with partial splenic rupture associated with trauma
  - Pancytopenia, with WBC 30,000 and lymphocytosis
- Bone marrow aspirate and biopsy: MCL, with no lymphadenopathy

Questions

- In a patient with MCL and significant symptoms, would you treat with ibrutinib upfront or initiate bendamustine/rituximab?
- Which BTK inhibitor do you prefer – ibrutinib, zanubrutinib or acalabrutinib?
- In refractory MCL, do you consider transplant – either autologous or allogeneic? What is the role of CAR T-cell therapy in that situation?

Case Presentation – Dr Levin: A 70-year-old man with relapsed gastric mantle cell lymphoma

Dr Pavel Levin

- Presented to the ICU with GI bleeding and massive splenomegaly
- GI ulcerations biopsy-confirmed gastric MCL
- Bendamustine/rituximab, with response and significant improvement in symptoms
- Recently, PD with GI bleeding
- Acalabrutinib

Questions

- What tends to be the second-line treatment for MCL?
- How often do you consider acalabrutinib as first-line therapy instead of bendamustine/rituximab?
- What are your preferred first-line regimens for patients in their 70s with borderline performance status?
- Is there are role for venetoclax in MCL?
- What criteria would you use to determine if he might be a candidate for CAR T-cell therapy?

What initial treatment would you recommend for a 26-year-old patient with classical Hodgkin lymphoma with anemia, diffuse adenopathy, hepatosplenomegaly and diffuse bone marrow involvement?

- ABVD
- PET-adapted ABVD
- Brentuximab vedotin + AVD
- AVD
- Other chemotherapy
- Other (please specify)

Case Presentation – Dr Nguyen: A 26-year-old woman with classical Hodgkin lymphoma

Dr Anthony Nguyen

- Presents with enlarging neck mass, profound anemia, double-vision, headache
  - PET/CT: Diffuse cervical, intrathoracic, and intrabdominal adenopathy; hepatosplenomegaly and diffuse bone marrow involvement
  - MRI: 1.4-cm avidly enhancing pituitary mass (prolactinoma)
  - Biopsy of axillary node: Classical Hodgkin lymphoma
- AVD + brentuximab vedotin x 6
  - End of treatment PET: Deauville 2 and 3, except of anterior mediastinum → Biopsy: Thymus
- Currently, patient is pregnant and undergoing surveillance every 6 months

Questions

- For this patient, would you consider using BV plus AVD, or ABVD?
- Is there any data on the fertility rates for BV plus AVD versus ABVD?

RTP RESEARCH TO PRACTICE

Which of the following would you generally recommend first for a patient with diffuse large B-cell lymphoma who experiences disease progression on front-line R-CHOP and is fit for high-dose therapy?

- Chemotherapy → autologous stem cell transplant
- Polatuzumab vedotin/BR
- Tafasitamab/lenalidomide
- Selinexor
- CAR T-cell therapy
- Loncastuximab tesirine
- I don’t know

Case Presentation – Dr Meerasahib: An 84-year-old woman with relapsed, EBV-positive DLBCL

Dr Anish Meerasahib

- 12/2019: Presents with dysphagia from an 8-cm paratracheal soft tissue mass with LAD to base of neck
  - Stage IIB DLBCL, with normal LDH, negative bone marrow
- Mini-R-CHOP, with CR → 6/2020: Consolidative RT
- 1/2021: New 8-mm hypermetabolic left lung nodule; unable to biopsy
- 3/2021: Multiple liver and lung lesions, all hypermetabolic, biopsy-proven DLBCL, EBV-positive
- Polatuzumab vedotin/rituximab/bendamustine

Questions

- How do we treat EBV-positive DLBCL? Do we treat differently? How do we approach treatment in an elderly population with aggressive disease?
- What would your approach be if she progressed – lenalidomide/rituximab, CAR T?
- In the relapsed/refractory setting, would you use tafasitamab/lenalidomide rather than R-squared in the second- or third-line setting?

Agenda

Module 1: Cases from the Community

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- Dr Meerasahib: An 84-year-old woman with relapsed, EBV-positive DLBCL

Module 4: Highlights of ASCO and EHA 2021 – Dr Smith

Smith MR et al. ECOG-ACRIN E1411 randomized phase 2 trial of bendamustine-rituximab (BR)-based induction followed by rituximab (R) ± lenalidomide (L) consolidation for Mantle cell lymphoma: Effect of adding bortezomib to front-line BR induction on PFS. ASCO 2021;Abstract 7503.

Dr Sonali Smith

1. For which clinical situations is this data clinically relevant?

- Newly diagnosed mantle cell lymphoma patients (all ages)

2. What are the key findings that are most relevant to patients in these clinical situations?

- This was a large study (154 vs. 156 pts in BR vs. BVR)
- Addition of bortezomib is well-tolerated (low rates of grade 3-4 neuropathy)
- Addition of bortezomib to BR backbone does not improve CR, ORR, or PFS
- No difference by age
- No difference by MIPI
- B(V)R plus maintenance rituximab has median PFS over 5 years

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Maintenance rituximab should continue to be evaluated in frontline regimens
- Should BR remain the backbone for future trials?

Phillips T et al. The combination of venetoclax, lenalidomide, and rituximab in patients with newly diagnosed mantle cell lymphoma induces high response rates and MRD undetectability. ASCO 2021;Abstract 7505.

Dr Sonali Smith

1. For which clinical situations is this data clinically relevant?

- This abstract is relevant to practicing physicians who take care of patients with MCL who do not want a chemotherapy-based regimen. It is important to note that this is a small, single arm phase 2 trial that is still ongoing and not yet ready for clinical practice.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Triplet is well-tolerated without unexpected toxicity
- High CR rate of 67% at 3m and 100% by 12m
- High MRD neg rate of 63% at 3m and 92% by 12m
- Time limited approach
- Note: med age 65y and all pts under age 70y
- Note: 4 deaths, including 2 from lymphoma; also, 2 secondary cancers

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Should this be compared to LenR? Or against chemoimmunotherapy and transplant?
- Can a chemo-free regimen become a standard front-line option?

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Martin P et al. Real-world (RW) treatment (tx) patterns and outcomes of 3,455 previously untreated mantle cell lymphoma (MCL) patients (pts) in U.S. routine clinical practice. ASCO 2021; Abstract 7504.

Dr Sonali Smith

1. For which clinical situations is this data clinically relevant?

- This analysis is relevant for providers who care for patients of all ages with MCL. It is a descriptive analysis of practice patterns in the United States using the Flatiron database and includes 3600 pts.

2. What are the key findings that are most relevant to patients in these clinical situations?

- This was one of the more sobering abstracts: large gap between academia and the real world
- The main findings are that only one-third of younger patients receive cytarabine-based regimens (despite evidence that this is the most active chemo agent for MCL)
- only 11% had a transplant
- only 25% had maintenance rituximab (which has a survival advantage after transplant).
- outcomes in terms of median time to next treatment are inferior compared to clinical trials (roughly 2y for both older and younger patients)

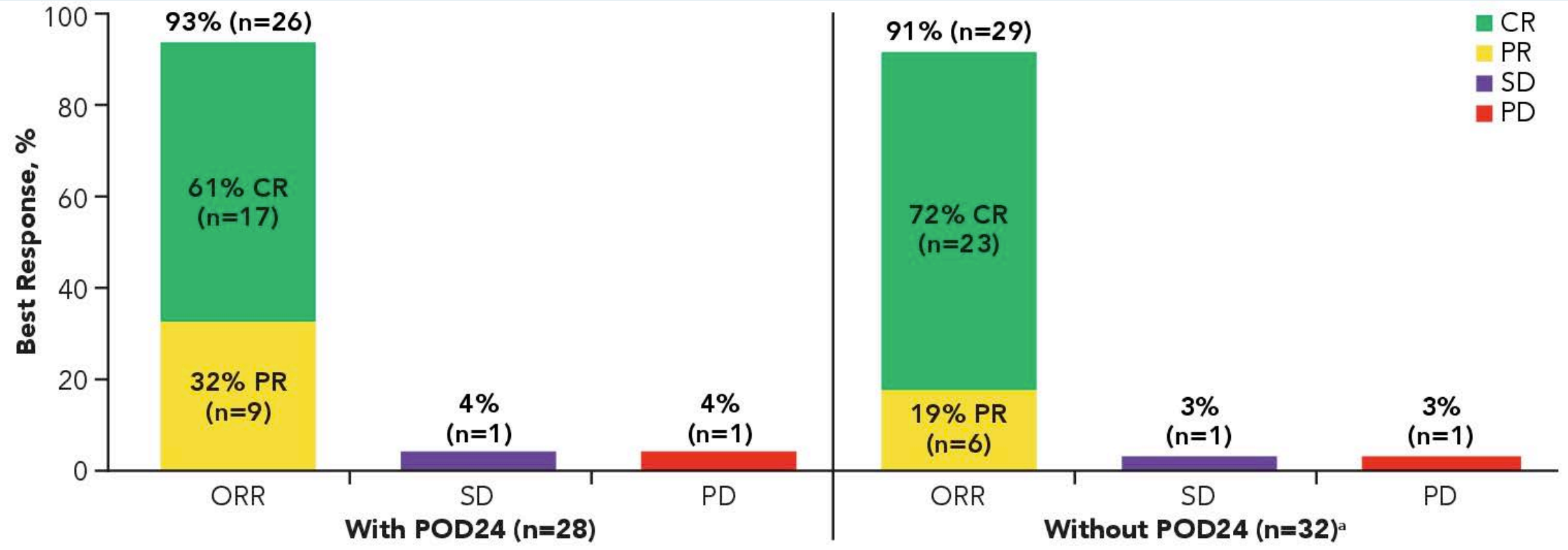
3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This trial will likely influence the development of trials perhaps from a communication perspective. If most patients are not benefiting from what we find in trials or at academic medical centers, then we need to rethink how we do these trials.

Outcomes with KTE-X19 in Patients (pts) with Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL) in ZUMA-2 who had Progression of Disease within 24 months of Diagnosis (POD24)

Wang M et al.
ASCO 2021;Abstract 7547.

ZUMA-2: ORR by IRRC Assessment in Patients with and without Progressive Disease within 24-months (POD24) of Diagnosis



- The ORR was similar among patients with and without POD24, slightly higher in patients without POD24
- Similar rates of MRD-negativity were also observed among patients with (82%; n=9/11) and without (79%; n = 15/19) POD24

Wang M et al. ASCO 2021;Abstract 7547.

RTP RESEARCH TO PRACTICE

LaCasce AS et al. CALGB 50801 (Alliance): PET adapted therapy in bulky stage I/II classic Hodgkin lymphoma (cHL). ASCO 2021;Abstract 7507.

Dr Sonali Smith

1. For which clinical situations is this data clinically relevant?

- Hodgkin lymphoma patients with bulky disease

2. What are the key findings that are most relevant to patients in these clinical situations?

- This is a single arm, multicenter, PET-adapted trial
- 78% of patients had a Deauville 1-3 (neg)
- Excellent outcomes despite the omission of RT with PFS 93% and OS 99%
- Even PET positive patients had a good outcome with escBEACOPP plus RT
- PRACTICE CHANGING and can avoid RT for many patients with bulky cHL

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Is there a better treatment for the few patients who have PET positive disease?
- Can we reduce treatment further?
- Should new agents be introduced?

Le Gouill S et al. First results of DLBCL patients treated with CAR-T cells and enrolled in DESCAR-T registry, a French real-life database for CAR-T cells in hematologic malignancies. EHA 2021;Abstract S216.

Dr Sonali Smith

1. For which clinical situations is this data clinically relevant?

- Relapsed/refractory DLBCL patients undergoing CAR-T cell therapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- This is the first report of a national French registry with likely many to follow
- This is a real-world analysis and reports med age 63y but 41% over age 65y
- Data is consistent with findings from the trials and from US RWE
- Median survival from CAR-T is 12m

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Will be interesting to see shifts over time (i.e. which product, survival rates, toxicity)
- Can CAR-T be delivered in outpatient and/or community setting?

Positive Top-Line Results Announced from Phase III TRANSFORM Trial: Lisocabtagene Maraleucel versus Chemotherapy → ASCT

Press Release – June 10, 2021

" Today positive topline results [were announced] from TRANSFORM, a global, randomized, multicenter Phase 3 study evaluating lisocabtagene maraleucel as a second-line treatment in adults with relapsed or refractory large B-cell lymphoma (LBCL) compared to salvage therapy followed by high-dose chemotherapy and hematopoietic stem cell transplant, which is currently considered a gold standard treatment for these patients. Results of a pre-specified interim analysis conducted by an independent review committee showed the study met its primary endpoint of demonstrating a clinically meaningful and highly statistically significant improvement in event-free survival, as well as key secondary endpoints of complete response rate and progression-free survival compared to standard of care. Overall survival data were immature at the time of this interim analysis. Safety results were consistent with the known safety profile of lisocabtagene maraleucel for the treatment of LBCL in the third-line setting, and no new safety concerns were identified in this second-line setting.

The results represent the first time a therapy has shown a benefit over standard of care high-dose chemotherapy and stem cell transplant in relapsed or refractory LBCL, and the first time a CD19-directed CAR T cell therapy has demonstrated potential as a second-line therapy in this patient population. The company will complete an evaluation of the TRANSFORM data and looks forward to sharing the results at an upcoming medical conference, as well as with health authorities. "

https://www.businesswire.com/news/home/20210610005259/en/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-from-Phase-3-TRANSFORM-Trial-Evaluating-Breyanzi-lisocabtagene-maraleucel-Versus-Chemotherapy-Followed-by-Stem-Cell-Transplant-in-Second-line-Relapsed-or-Refractory-Large-B-cell-Lymphoma

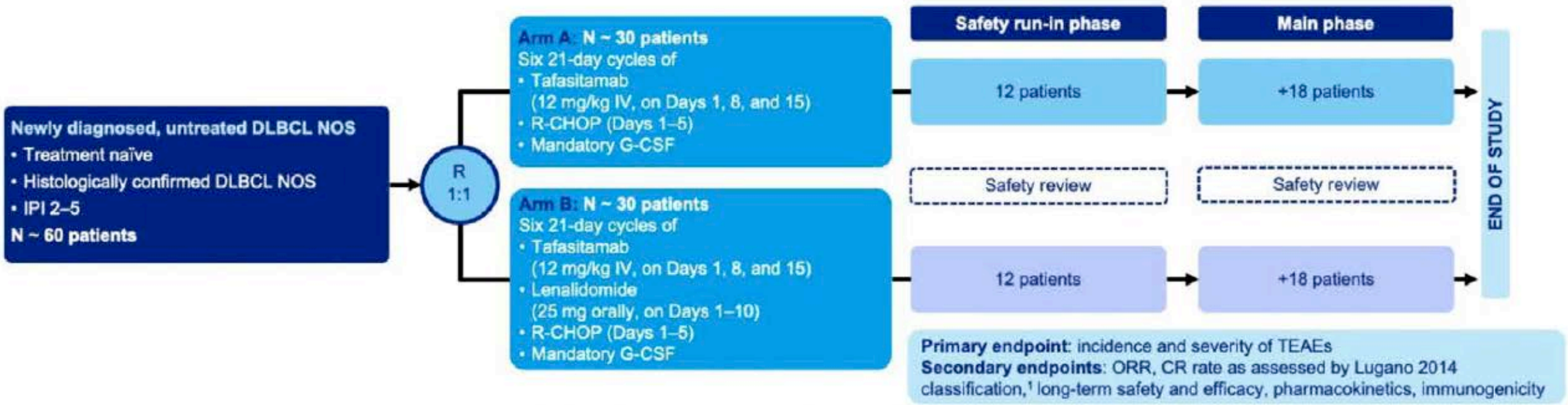
A Phase Ib, Open-Label, Randomized Study to Assess Safety and Preliminary Efficacy of Tafasitamab (MOR208) or Tafasitamab + Lenalidomide in Addition to R-CHOP in Patients with Newly Diagnosed Diffuse Large B-Cell Lymphoma: Analysis of the Safety Run-in Phase

Belada D et al.

ASH 2020;Abstract 3028.

First-MIND: Study Design

- An open-label, prospective, randomized, Phase Ib study designed to evaluate the safety and preliminary efficacy of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL

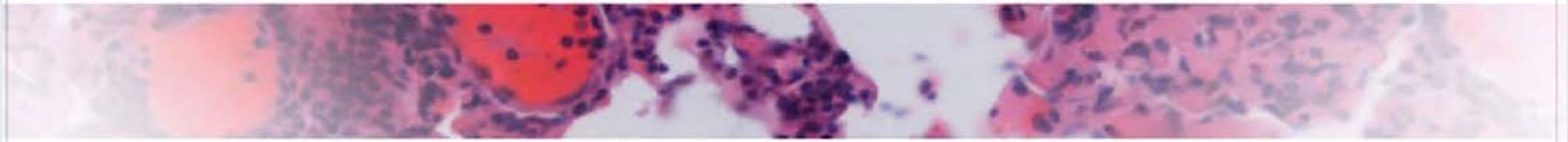


In the lenalidomide arm, prophylaxis with either low-molecular weight heparins or aspirin is mandatory.

Belada D et al. ASH 2020;Abstract 3028.

American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide



Selinexor in Combination with R-CHOP for Frontline Treatment of Non-Hodgkin Lymphoma: Results of a Phase 1b Study

Erlene K. Seymour[1], Li Yi[1], Mahmoud Chaker[1], Amro Aboukameel[1], Radhakrishanan Ramchandren[2], Golbon Sterbis[1], Jay Yang[1], Divaya Bhutani[3], Ramzi M. Mohammad[1], Asfar S. Azmi[1*], Jeffrey A. Zonder[1*]

[1]Department of Oncology, Wayne State University School of Medicine and Karmanos Cancer Institute, Detroit, MI; [2]Department of Oncology, University of Tennessee, Knoxville, TN; [3]Department of Oncology, Columbia University, New York, NY

Presenting Author: Erlene K. Seymour, MD

Abstract #2109

December 6, 2020

Front-Line Selinexor with R-CHOP: Efficacy

	Patient	Diagnosis	Days on Selinexor	Best Response
Selinexor 60 mg weekly	KCI-01	Transformed DLBCL	514	CR
	KCI-02	Transformed DLBCL	134	CR
	KCI-03	DLBCL (non-GCB)	371	CR
	KCI-05	DLBCL (non-GCB)	88	PR
	KCI-06	DLBCL (non-GCB)	152	CR
	KCI-07	DLBCL (non-GCB)	461	CR
Selinexor 80 mg weekly	KCI-12	FL	258	CR
	KCI-14	DLBCL (GCB)	164	CR
	KCI-15	Transformed DLBCL	84	CR
	KCI-18	DLBCL (non-GCB)	443	CR

ORR: 100%
CR rate: 90%

All CRs ongoing
Median F/U: 476 days

Seymour E et al. ASH 2020;Abstract 2109.

Polatuzumab Vedotin (Pola) + Rituximab (R) + Lenalidomide (Len) in Patients (pts) with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): Primary Analysis of a Phase 1b/2 trial

Diefenbach CS et al.

ASCO 2021;Abstract 7512.

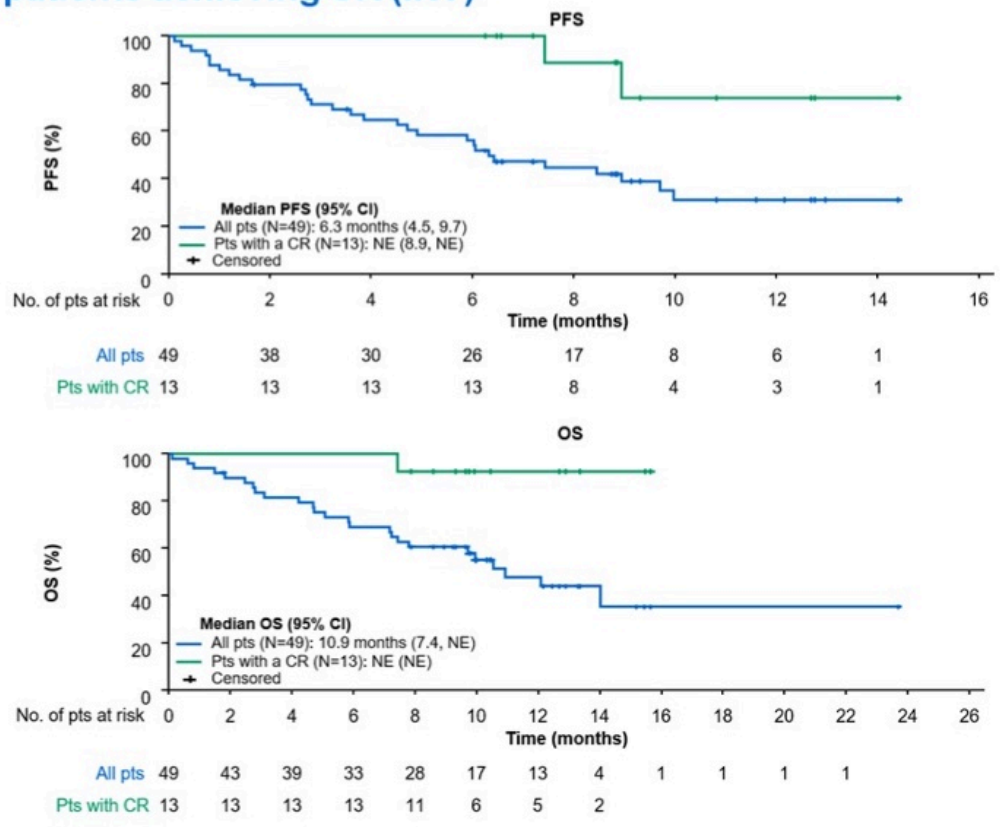
Polatuzumab Vedotin + Rituximab + Lenalidomide in R/R DLBCL

Response rates at EOI and time-to-event outcomes

Response, n (%)	Efficacy evaluable (N=49)			
	Modified Lugano 2014*		Lugano 2014	
	IRC	INV	IRC	INV
Objective response	17 (35)	19 (39)	19 (39)	19 (39)
Complete response	14 (29)	13 (27)	14 (29)	13 (27)
Partial response	3 (6)	6 (12)	5 (10)	6 (12)
Stable disease	2 (4)†	0	0	0
Disease progression	15 (31)	21 (43)	15 (31)	21 (43)
Missing/NE	15 (31)‡¶	9 (18)¶	15 (31)‡¶	9 (18)¶
INV				
Median DOR, months (95% CI)	8.1 (4.7–NE)			
Median PFS, months (95% CI)	6.3 (4.5–9.7)			
Median OS, months (95% CI)	10.9 (7.4–NE)			

*Modified Lugano requires a negative bone marrow biopsy to confirm PET-CR and PET-PR must also meet CT-PR criteria; †Two cases of PET-PR were downgraded to SD by IRC due to Modified Lugano criteria; ‡One patient was assessed as CR by INV and was considered not evaluable by IRC; ¶Two patients had CT-based CR but were unable to have PET scans due to COVID-19 restrictions; No responses were downgraded due to missing bone marrow biopsies.
CI, confidence interval; CR, complete response; CT, computer tomography; DOR, duration of response; EOI, end of induction; INV, Investigator assessed; IRC, Independent review committee assessed; NE, not evaluated; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PR, partial response; pts, patients; SD, stable disease.

PFS and OS in all efficacy-evaluable patients and in patients achieving CR (INV)



Diefenbach CS et al. ASCO 2021;Abstract 7512.

RTP RESEARCH TO PRACTICE

Contributing Oncologists

Amanda Blackmon, DO, MS
Chief Fellow
Hematology/Oncology
University of California, Irvine
Irvine, California

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Anthony Nguyen, MD
Fellow, Loma Linda
University Health
Loma Linda, California

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

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CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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We are taking a short break!

The program will resume at 11:45 AM CT (12:45 AM ET)

Up Next…

Drs Thomas Abrams and Randolph Hecht discuss the management of gastrointestinal cancers

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TO PRACTICE

ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

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RESEARCH
TO PRACTICE

Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Gastrointestinal Cancers Faculty

Thomas A Abrams, MD
Senior Physician
Dana-Farber Cancer Institute
Assistant Professor of Medicine
Harvard Medical School
Director, Liver Tumor Center
Boston, Massachusetts

J Randolph Hecht, MD
Professor of Clinical Medicine
Director, UCLA GI Oncology Program
Carol and Saul Rosenzweig Chair in Cancer Therapies Development
Santa Monica, California

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RESEARCH TO PRACTICE

Contributing Oncologists

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

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Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Highlights of ASCO 2021 – Colon and Gastric Cancers
J Randolph Hecht, MD

- Andre T et al. **Final overall survival for the phase III KN177 study: Pembrolizumab versus chemotherapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC).** ASCO 2021;Abstract 3500.
- Kaboki Y et al. **The TRUSTY study: A randomized phase 2/3 study of trifluridine/tipiracil plus bevacizumab versus irinotecan and fluoropyrimidine plus bevacizumab as second-line treatment in patients with metastatic colorectal cancer.** ASCO 2021;Abstract 3507.
- Yoshino T et al. **Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): Final results from a phase 2, multicenter, open-label study (DESTINY-CRC01).** ASCO 2021;Abstract 3505.
- Chau I et al. **Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study.** ASCO 2021;Abstract LBA4001.
- Janjigian YY et al. **Pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction (G/GEJ) cancer: Initial findings of the global phase 3 KEYNOTE-811 study.** ASCO 2021;Abstract 4013.
- Catenacci DV et al. **FIGHT: A randomized, double-blind, placebo-controlled, phase II study of bemarituzumab (bema) combined with modified FOLFOX6 in 1L FGFR2b+ advanced gastric/gastroesophageal junction adenocarcinoma (GC).** ASCO 2021;Abstract 4010.

Highlights of ASCO 2021 – Hepatocellular and Pancreatic Cancers
Thomas A Abrams, MD

- Li S et al. **Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial.** ASCO 2021;Abstract 4008.
- Lyu N et al. **Hepatic arterial infusion chemotherapy of oxaliplatin plus fluorouracil versus sorafenib in advanced hepatocellular carcinoma: A biomolecular exploratory, randomized, phase 3 trial (The FOHAIC-1 study).** ASCO 2021;Abstract 4007.
- Yoo C et al. **Liposomal irinotecan (nal-IRI) in combination with fluorouracil (5-FU) and leucovorin (LV) for patients with metastatic biliary tract cancer (BTC) after progression on gemcitabine plus cisplatin (GemCis): Multicenter comparative randomized phase 2b study (NIFTY).** ASCO 2021;Abstract 4006.
- Makawita S et al. **IDH1 and IDH2 Driven Intrahepatic Cholangiocarcinoma (IHCC): A comprehensive genomic and immune profiling study.** ASCO 2021;Abstract 4009.
- Perera S et al. **hENT1 gene expression as a predictor of response to gemcitabine and nab-paclitaxel in advanced pancreatic cancer.** ASCO 2021;Abstract 4011.

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 40-year-old man with MSI-H metastatic colon cancer – KRAS and somatic BRCA1 mutation-positive
- Dr Meerasahib: A 53-year-old woman with MSS metastatic CRC – KRAS mutation
- Dr Levin: A 92-year-old man with BRAF V600E-mutant, metastatic colon cancer
- Dr Kodali: A 59-year-old woman with signet cell diffuse gastric cancer
- Dr Martins: A 48-year-old man with recurrent metastatic GEJ adenocarcinoma – HER2-positive

Module 2: Highlights of ASCO 2021 – Dr Hecht

Module 3: Cases from the Community

- Dr Levin: A 63-year-old woman and liver transplant recipient presents with metastatic hepatocellular carcinoma
- Dr Malik: A 63-year-old woman with cholangiocarcinoma

Module 4: Highlights of ASCO 2021 – Dr Abrams

Agenda

Module 1: Cases from the Community

- Dr Jasani: A 40-year-old man with MSI-H metastatic colon cancer – KRAS and somatic BRCA1 mutation-positive
- Dr Meerasahib: A 53-year-old woman with MSS metastatic CRC – KRAS mutation
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Module 2: Highlights of ASCO 2021 – Dr Hecht

Module 3: Cases from the Community

- Dr Levin: A 63-year-old woman and liver transplant recipient presents with metastatic hepatocellular carcinoma
- Dr Malik: A 63-year-old woman with cholangiocarcinoma

Module 4: Highlights of ASCO 2021 – Dr Abrams

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your most likely first-line treatment for a younger patient with microsatellite instability (MSI)-high metastatic colorectal cancer?

- Pembrolizumab
- Ipilimumab/nivolumab
- Nivolumab
- Chemotherapy + immunotherapy
- Chemotherapy + biologic agent
- Chemotherapy
- Other (please specify)

Case Presentation – Dr Jasani: A 40-year-old man with MSI-H metastatic colon cancer – KRAS and somatic BRCA1 mutation-positive

Dr Nikesh Jasani

- 7/2018: Presented with weight loss and abdominal pain; found to have stage IV signet ring, poorly differentiated adenocarcinoma of the colon at the hepatic flexure
- FOLFOX x 4 cycles → mixed response → ipilimumab/nivolumab x 3 cycles → severe grade 3 colitis
  - Steroids, vedolizumab for over a year and fecal transplant
- Rechallenged with nivolumab → recurrent colitis; all treatment stopped 11/2019.
- Remains off treatment with no progression

Questions

- What is the ideal upfront regimen for the treatment of MSI-H colon cancer? Is it dual checkpoint inhibitors with nivolumab/ipilimumab?
- After colitis, what is the appropriate amount of time to wait before rechallenge with a checkpoint inhibitor? Have you observed the phenomena of immune response in CPI but persistent mass on imaging, which is likely acellular in terms of malignant cells?
- Is there are role for PARP inhibitors in colon cancer that is positive for somatic BRCA mutations?

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Case Presentation – Dr Meerasahib: A 53-year-old woman with MSS metastatic CRC – KRAS mutation

Dr Anish Meerasahib

- Summer 2019: Metastatic sigmoid cancer, with obstructive symptoms s/p diversion colostomy
- FOLFIRI/bevacizumab x 12 → resection of primary (T4N1bM1 disease) → FOLFIRI/bevacizumab
- Summer 2020: CEA increased to 370, with imaging showing PD in the liver
- 6/2020: Switched to FOLFOX/bevacizumab, with excellent response after 3 months
- Resection of liver metastases → FOLFOX/bevacizumab x 10 (CEA: 4)
  - TMB-low, PIK3CA mutation
- 3/2021: CEA increases to 23, new liver lesions and periportal lymph nodes
- Insurance did not cover clinical trial of PI3K inhibitor + immunotherapy → regorafenib + RT to liver lesions
  - Regorafenib: 40 mg → 80 mg → 120 mg → 80 mg

Questions

- What treatment would you have recommended for this patient? Should we add bevacizumab if we are using TAS-102? What is the ideal starting dose for regorafenib?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Levin: A 92-year-old man with BRAF V600E-mutant, metastatic colon cancer

Dr Pavel Levin

- 2008: Diagnosed with Stage IIA mucinous adenocarcinoma of the transverse colon
- Resected, no adjuvant chemotherapy
- 2015: T4 small bowel mass with lymphovascular invasion → resection
- 2016: PET RUL nodule → capecitabine → FOLFIRI and maintenance 5-FU, with brief response
- 2018: PET PD in the lung → SBRT to lung nodule
- 1/2019: New rectosigmoid primary, BRAF V600E mutation
- FOLFOX → 5-FU/RT, with PD in the rectum → patient declines surgery → FOLFIRI, with PD
- LAR and surgery
- 9/2020: Lung nodules → encorafenib/cetuximab, with response but significant blepharitis

Questions

- What would you recommend as his next therapy upon disease progression? Would you completely stop BRAF inhibition, and just switch him to another line of therapy?

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what is your usual initial treatment for a 65-year-old patient with MSS adenocarcinoma of the esophagus with a PD-L1 CPS of 0?

- FOLFOX or other chemotherapy
- Pembrolizumab + chemotherapy
- Nivolumab + chemotherapy
- Pembrolizumab
- Nivolumab
- Other chemotherapy
- Other (please specify)

Case Presentation – Dr Kodali: A 59-year-old woman with signet cell diffuse gastric cancer

Dr Dhatri Kodali

- Presented with epigastric pain and GERD symptoms → endoscopy showed diffuse ulcerations
- Biopsy reveals signet cell diffuse gastric cancer
- Neoadjuvant FOLFOX initiated
- Tolerating therapy well after 3 cycles

Questions

- What are our options for preoperative chemotherapy versus chemo-XRT?
- What are the options for anti-PD-L1 therapy in the adjuvant setting? In the neoadjuvant setting for a patient with high-risk disease?
- Do you consider the CPS score in the adjuvant setting?

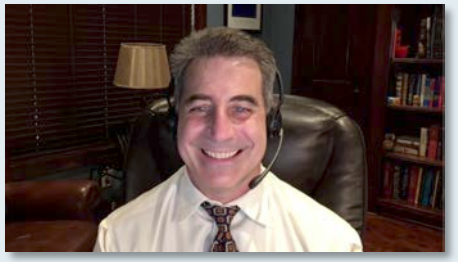
Regulatory and reimbursement issues aside, what is your usual initial treatment for a 65-year-old patient with metastatic HER2-positive, microsatellite-stable (MSS) adenocarcinoma of the gastroesophageal junction (GEJ) (combined positive score [CPS] <1)?

- FOLFOX/trastuzumab
- Pembrolizumab + chemotherapy + trastuzumab
- Nivolumab + chemotherapy + trastuzumab
- Other anti-HER2 regimen
- Other (please specify)

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ (CPS <1) with disease progression on FOLFOX/trastuzumab?

- Ramucirumab
- Ramucirumab/paclitaxel
- Continue trastuzumab and switch chemotherapy
- Pembrolizumab
- Nivolumab
- Trastuzumab deruxtecan
- Other (please specify)

Case Presentation – Dr Martins: A 48-year-old man with recurrent metastatic GEJ adenocarcinoma – HER2-positive



Dr Joseph Martins

- 4/2018: Presented GE junction tumor, positive celiac node
- Neoadjuvant FOLFOX/trastuzumab with response on PET
- Surgery → residual disease and one suspicious node found
- TC-XRT + trastuzumab → trastuzumab
- 2/2020: Solitary brain metastasis found → Surgery and RT
- Trastuzumab continued
- Remains in remission

Questions

- Do you agree with the decision to continue trastuzumab therapy, or would you have recommended something different?
- Is there a role for immunotherapy in his case? Any role for any of the newer HER2-targeted agents?
- What treatment would you recommend if his disease progresses?

RTP RESEARCH TO PRACTICE

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Module 2: Highlights of ASCO 2021 – Dr Hecht

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- Dr Malik: A 63-year-old woman with cholangiocarcinoma

Module 4: Highlights of ASCO 2021 – Dr Abrams

RTP RESEARCH TO PRACTICE

Andre T et al. Final overall survival for the phase III KN177 study: Pembrolizumab versus chemotherapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC). ASCO 2021;Abstract 3500.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- First-line therapy of the 3-5% of metastatic colorectal cancer patients who are MSI-H/dMMR

2. What are the key findings that are most relevant to patients in these clinical situations?

- RR 45.1 vs 33.1%
- PFS HR = 0.59; median 16.5 vs 8.2 m
- Overall survival HR = 0.74 NR vs 36.7 p=0.0359 NS, but crossover
- Better outcome, less toxicity with PD-1 alone
- 40% didn't crossover

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- PD-1 alone superior to standard therapy in MSI-H/dMMR CRC, a new SOC
- Many 1st line patients don't make it to 2nd line, patient selection, combinations
- Some early fall-off in IO alone
- ?Nivolumab, nivo+ipi

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Yoshino T et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): Final results from a phase 2, multicenter, open-label study (DESTINY-CRC01). ASCO 2021;Abstract 3505.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- The 2-3% of patients who are HER2-positive, especially 3+ by IHC

2. What are the key findings that are most relevant to patients in these clinical situations?

- RR 45.3% Cohort A (IHC 3+ 57.5% or IHC 2+/ISH+ 7.7%); 0% Cohort B (IHC 2+/ISH-) and Cohort C (IHC 1+).
- DOR 7.0m, 30% had prior trastuzumab, 44% RR
- Disappointing lack of efficacy in 2+ and 1+ ISH-
- 9% ILD, 4% G5!

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Another future choice for HER2+ mCRC patients
- Need for close follow-up for ILD and possible markers of susceptibility
- Use in earlier lines of therapy?
- Can you combine with other agents?

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Kaboki Y et al. The TRUSTY study: A randomized phase 2/3 study of trifluridine/tipiracil plus bevacizumab versus irinotecan and fluoropyrimidine plus bevacizumab as second-line treatment in patients with metastatic colorectal cancer. ASCO 2021;Abstract 3507.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- Second-line metastatic colorectal cancer

2. What are the key findings that are most relevant to patients in these clinical situations?

- PFS 4.5 vs 6.0m; HR 1.45, trifluridine/tipiracil+bev worse!
- OS 14.8 vs 18.1; HR 1.38 trifluridine/tipiracil+bev worse!
- ≥G3 AE 77.6 vs 66.5% trifluridine/tipiracil+bev worse!

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Even with low RR, FOLFIRI/bev still SOC
- Doesn’t mean trifluridine/tipiracil+bev couldn’t find a place in salvage

Catenacci DV et al. FIGHT: A randomized, double-blind, placebo-controlled, phase II study of bemarituzumab (bema) combined with modified FOLFOX6 in 1L FGFR2b+ advanced gastric/gastroesophageal junction adenocarcinoma (GC). ASCO 2021;Abstract 4010.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- For up to 30% of UGI adenocarcinomas that overexpress FGFR2b or have ctDNA amplification.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improves PFS 9.4 v 7.4m HR=0.68 and OS 19.2 v 13.5 HR=0.6
- Even better outcomes with IHC 2+/3+ >10% (62% of IHC+) PFS HR= 0.44 OS 25.4 v 11.1m HR=0.41!
- Even better outcomes in 13% +ctDNA/+IHC (PFS HR=0.15 OS HR=0.10) but small numbers (20)
- Corneal toxicity manageable, other toxicities except stomatitis similar

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Await phase III trial
- What about IHC+ but <5%, ctDNA-?
- Further segmentation of UGI adenocarcinoma
- How does this fit with immunotherapy, just approved? Combinations like KN-811?

Janjigian YY et al. Pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction (G/GEJ) cancer: Initial findings of the global phase 3 KEYNOTE-811 study. ASCO 2021;Abstract 4013.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- 1st line treatment of ~10% of advanced adenocarcinomas of stomach/GEJ that are HER2+

2. What are the key findings that are most relevant to patients in these clinical situations?

- Increased RR adding pembro (74.4 vs 51.9%) similar to single arm studies.
- AEs not significantly increased

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Await more mature data, but early time on treatment data encouraging
- If positive, will be new SOC
- What about chemotherapy free regimens**?**

Chau I et al. Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study. ASCO 2021; Abstract LBA4001.

Dr Randolph Hecht

1. For which clinical situations is this data clinically relevant?

- 1st line advanced (recurrent or unresectable) squamous cell carcinoma of the esophagus.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Chemotherapy+nivo was superior for OS to chemotherapy alone both in PD-L1>1% (15.4 vs 9.1m HR=0.54) and all comers (13.2 vs 10.7m HR=0.74)
- Nivo+ipi (3mg/kg q2w/1mg/kg q6w) was superior for OS to chemotherapy alone both in PD-L1>1% (13.7 vs 9.1m HR=0.64) and all comers (12.8 vs 10.7m HR=0.78) and looks very similar to chemo+nivo.
- mDOR nivo+ipi 11m!!!
- Very similar to KN-590 and ESCORT-1st

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Either chemo/PD-1 or nivo/ipi are now SOC 1st line ESCC
- How do we identify patients who may need chemotherapy upfront?
- Should there be trials of hybrid regimens such as maintenance after induction?

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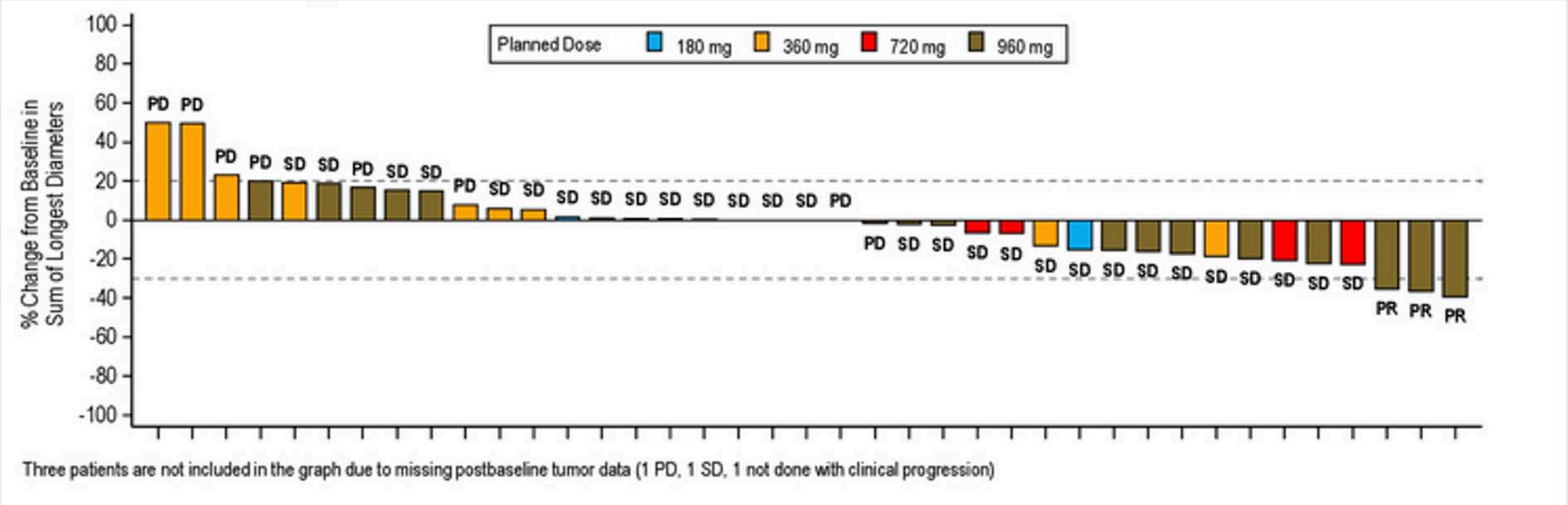
CodeBreak 100: Activity of AMG 510, A Novel Small Molecule Inhibitor of KRAS^{G12C}, in Patients with Advanced Colorectal Cancer

Fakih MF et al.

ASCO 2020;Abstract 4018.

CodeBreak100: Tumor Change From Baseline with Sotorasib (AMG 510) in Patients with Advanced Colorectal Cancer



Three patients are not included in the graph due to missing postbaseline tumor data (1 PD, 1 SD, 1 not done with clinical progression)

Fakih MG et al. ASCO 2020;Abstract 4018.

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What would be your preferred second-line therapy for a 65-year-old patient with hepatocellular carcinoma, a Child-Pugh A score and PS 0 who received first-line atezolizumab/bevacizumab and experienced disease progression after 18 months (AFP 2,500 ng/mL)?

- Sorafenib
- Lenvatinib
- Regorafenib
- Cabozantinib
- Ramucirumab
- Anti-PD-1 antibody monotherapy
- Nivolumab/ipilimumab
- Other (please specify)

Case Presentation – Dr Levin: A 63-year-old woman and liver transplant recipient presents with metastatic hepatocellular carcinoma

Dr Pavel Levin

- HCC s/p liver transplant presents 12 years later with mediastinal LAD biopsy-proven HCC who is receiving tacrolimus immunosuppression
  - NASH cirrhosis
- Sorafenib without response
- 2018: Reduced tacrolimus dose, initiated nivolumab with response and improvement in QoL x 4 months

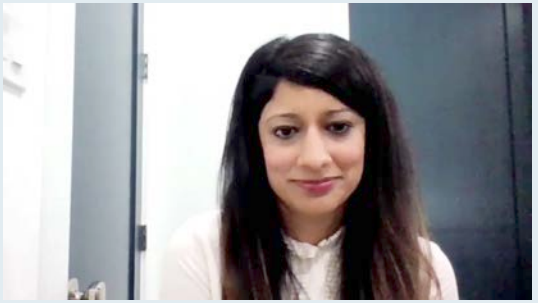
Questions

- How often have you successfully treated posttransplant patients with immunotherapy? And in which transplanted organs have you tried immunotherapy?

Patients with advanced cholangiocarcinoma should have…

- NGS or panel somatic testing
- Germline panel testing
- Both
- Neither

Case Presentation – Dr Malik: A 63-year-old woman with cholangiocarcinoma



Dr Henna Malik

- Presented with abdominal pain, n/v diarrhea, weakness and jaundice
- 4 cm mass in the right lobe of the liver and 2 other liver lesions
- ERCP: Adenocarcinoma consistent with cholangiocarcinoma
- Next generation sequencing: Negative for any actionable mutation
- Cisplatin/gemcitabine x 2 → Y-90, with significant response → Cisplatin/gemcitabine x 2
  - Poor tolerability to chemotherapy, with neuropathy, pancytopenia, fatigue and weakness
- Oral capecitabine, with PD after 6 months
- Currently on gemcitabine/oxaliplatin and has been responding x 5 months

Questions

- What is the role of FGFR inhibitors, possibly combined with immunotherapy or chemotherapy?
- Should Y-90 be used in earlier treatment lines instead of chemotherapy?

RTP RESEARCH TO PRACTICE

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Module 4: Highlights of ASCO 2021 – Dr Abrams

Li S et al. Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial. ASCO 2021;Abstract 4008.

Dr Thomas Abrams

1. For which clinical situations is this data clinically relevant?

- Patients with potentially resectable HCC (BCLC A/B) who would ordinarily be considered for up-front hepatectomy

2. What are the key findings that are most relevant to patients in these clinical situations?

- 1-, 2- and 3-year OS and 6-, 12- and 18-month PFS significantly improved in the HAI arm vs upfront surgery
- 10% pCR rate
- Subgroup analysis shows benefit most concentrated in patients with AFP >400 and those who have solitary tumors

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Shows that HAIC is feasible as neoadjuvant treatment
- Unclear to me whether the benefit seen owes more to the general effect of HAIC on HCC or was limited to those with biologically unfavorable disease
- Would be very interesting to run a prospective trial in patients with AFP >400

Lyu N et al. Hepatic arterial infusion chemotherapy of oxaliplatin plus fluorouracil versus sorafenib in advanced hepatocellular carcinoma: A biomolecular exploratory, randomized, phase 3 trial (The FOHAIC-1 study). ASCO 2021;Abstract 4007.

Dr Thomas Abrams

1. For which clinical situations is this data clinically relevant?

- Patients with advanced HCC and “heavy” intrahepatic tumor burden characterized by large average sized tumors and high rates of macrovascular invasion. These patients were ineligible for curative treatments and would otherwise be considered for systemic therapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- Patients with >50% tumor volume involvement of the liver was 41.5% and 39.4%, respectively (P = 0.724).
- Patients receiving HAIC-FO had a median OS of 13.9 months (95%CI 10.6-17.2), compared with 8.2 months (7.5-9.0) for those receiving sorafenib (HR 0.408 [95%CI 0.301-0.552], P < 0.001).
- Tumor downstaging occurred in 16 (12.3% of 130) patients of the HAIC-FO group, and 15 (93.8%) received curative surgery or ablation with median OS 20.8 mos and PFS of 16.4 mos for this select group.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Shows even more clearly than in the first abstract that HAIC with FOLFOX can be safely used for patients with biologically aggressive HCC
- These patients do not do well with sorafenib
- Magnitude of benefit might not have been as great if atezo/bev had been the control arm

Makawita S et al. IDH1 and IDH2 Driven Intrahepatic Cholangiocarcinoma (IHCC): A comprehensive genomic and immune profiling study. ASCO 2021;Abstract 4009.

Dr Thomas Abrams

1. For which clinical situations is this data clinically relevant?

- This is a genomic analysis of intrahepatic cholangiocarcinomas with IDH1/2 mutations in comparison to IDHwt tumors.

2. What are the key findings that are most relevant to patients in these clinical situations?

- biIDH1 and IDH2 mutations were mutually exclusive.
- All IDH1 mutations occurred at the R132 locus and IDH2 GA at R172 (94.4%) and R140 (6.6%).
- IDH1+ and IDH2+ IHCC had fewer co-occurring targetable GA than IDHwt cases including FGFR2 rearrangements (RE) (P<.0001), ERBB2 (P =.0009) and BRAF (P =.04).
- Potential biomarkers of immune checkpoint inhibition (ICI) response including MSI High, TMB > 10 mut/Mb, and PD-L1 positivity were more frequent in IDHwt IHCC than IDH1+ IHCC.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- These results strongly suggest that both IDH1/2 mutations are critical to carcinogenesis when present

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Yoo C et al. Liposomal irinotecan (nal-IRI) in combination with fluorouracil (5-FU) and leucovorin (LV) for patients with metastatic biliary tract cancer (BTC) after progression on gemcitabine plus cisplatin (GemCis): Multicenter comparative randomized phase 2b study (NIFTY). ASCO 2021;Abstract 4006.

Dr Thomas Abrams

1. For which clinical situations is this data clinically relevant?

- Patients with advanced BTC who have progressed on 1L gem/cis. In the sudy these patients were randomized to receive 5-FU +/- nal-IRI. Primary endpoint was PFS by BICR.

2. What are the key findings that are most relevant to patients in these clinical situations?

- mPFS per BICR in nal-IRI plus 5-FU/LV group and 5-FU/LV group was 7.1 mo (95% CI, 3.6-8.8) and 1.4 mo (1.2-1.5), respectively (HR=0.56 [0.39-0.81], p=0.0019)
- mPFS per investigator review was 3.9 mo (2.7-5.2) and 1.6 mo (1.3-2.2), respectively (HR=0.48 [0.34-0.69], p<0.0001).
- mOS was 8.6 mo (5.4-10.5) and 5.5 mo (4.7-7.2), respectively (HR=0.68 [0.48-0.98], p=0.0349).
- ORR was 14.8% and 5.8% per BICR, respectively (p=0.0684) and 19.3% and 2.3% per investigator review, respectively (p=0.0002).
- Most common grade ≥3 AEs in nal-IRI plus 5-FU/LV group were neutropenia (n=21, 23.9%), fatigue (7, 8.0%), and nausea (5, 5.7%)

Yoo C et al. Liposomal irinotecan (nal-IRI) in combination with fluorouracil (5-FU) and leucovorin (LV) for patients with metastatic biliary tract cancer (BTC) after progression on gemcitabine plus cisplatin (GemCis): Multicenter comparative randomized phase 2b study (NIFTY). ASCO 2021;Abstract 4006. (continued)

Dr Thomas Abrams

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Control arm of 5-FU alone makes data difficult to interpret in the context of the current SOC of FOLFOX, but the nal-IRI/5-FU regimen has clear-cut activity with reasonable tolerance
- Lack of QoL benefit is a red flag
- No mention of NGS testing for common driver mutations/fusions

Perera S et al. hENT1 gene expression as a predictor of response to gemcitabine and nab-paclitaxel in advanced pancreatic cancer. ASCO 2021;Abstract 4011.

Dr Thomas Abrams

1. For which clinical situations is this data clinically relevant?

- This study examined the potential utility of hENT1 expression to predict response to gemcitabine-based treatments in metastatic pancreatic cancer as hENT1 is critical to cellular uptake of gemcitabine. Patients were treated with either FFX or GA (provider choice) and testing for hENT1 was done in parallel.

2. What are the key findings that are most relevant to patients in these clinical situations?

- No differences were found in OS (10.6 vs 10.6 mos) or RR (32 vs 31%) in patients treated with FFX with respect to hENT1 expression
- OS (9.8 vs 6.1 mos) and RR (45 vs 21%) were significantly higher for hENT1 high patients treated with GA

3. What is the relevance of this data to clinical research for patients in these clinical settings?

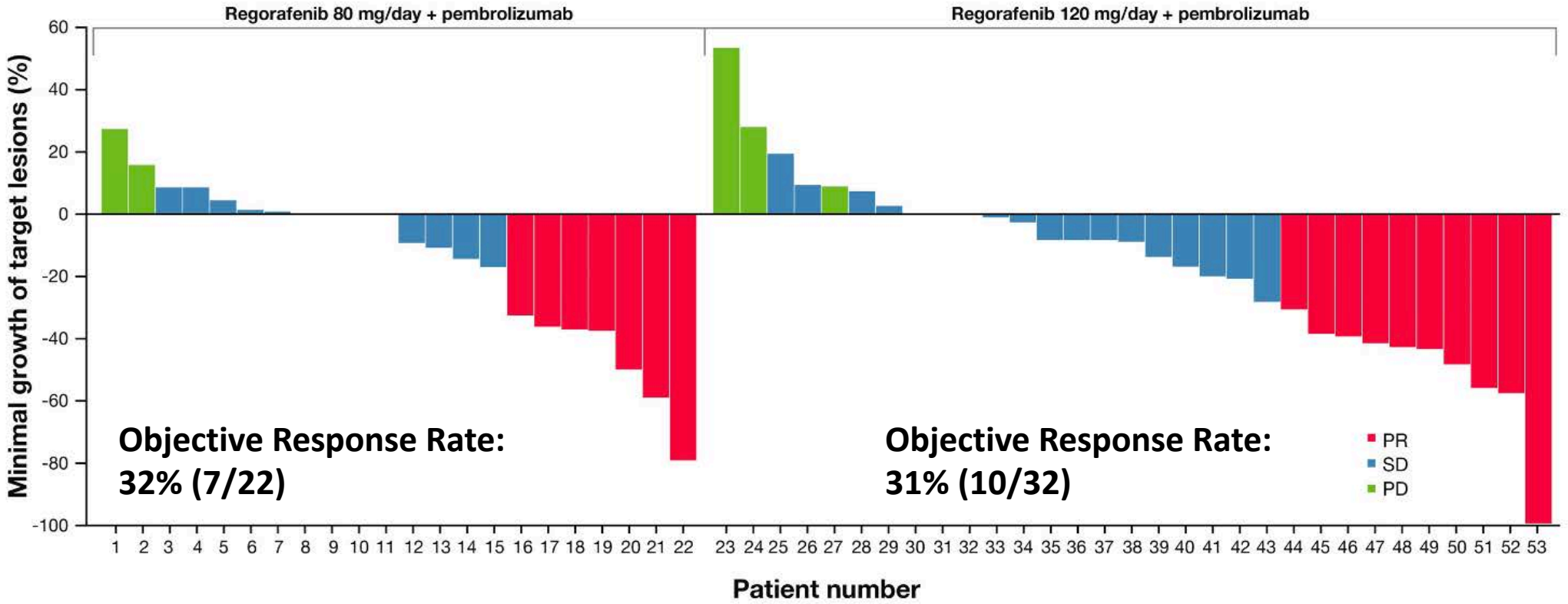
- Not sure there is much in 1L since FFX was superior to GA irrespective of hENT1 status
- But this could provide some guidance in 2L treatment decision making

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Updated Results of a Phase 1b Study of Regorafenib (REG) 80 mg/day or 120 mg/day plus Pembrolizumab (PEMBRO) for First-Line Treatment of Advanced Hepatocellular Carcinoma (HCC)

El-Khoueiry AB et al.
ASCO 2021;Abstract 4078.

Efficacy of Regorafenib (80 mg or 120 mg) with Pembrolizumab as First-Line Therapy for HCC

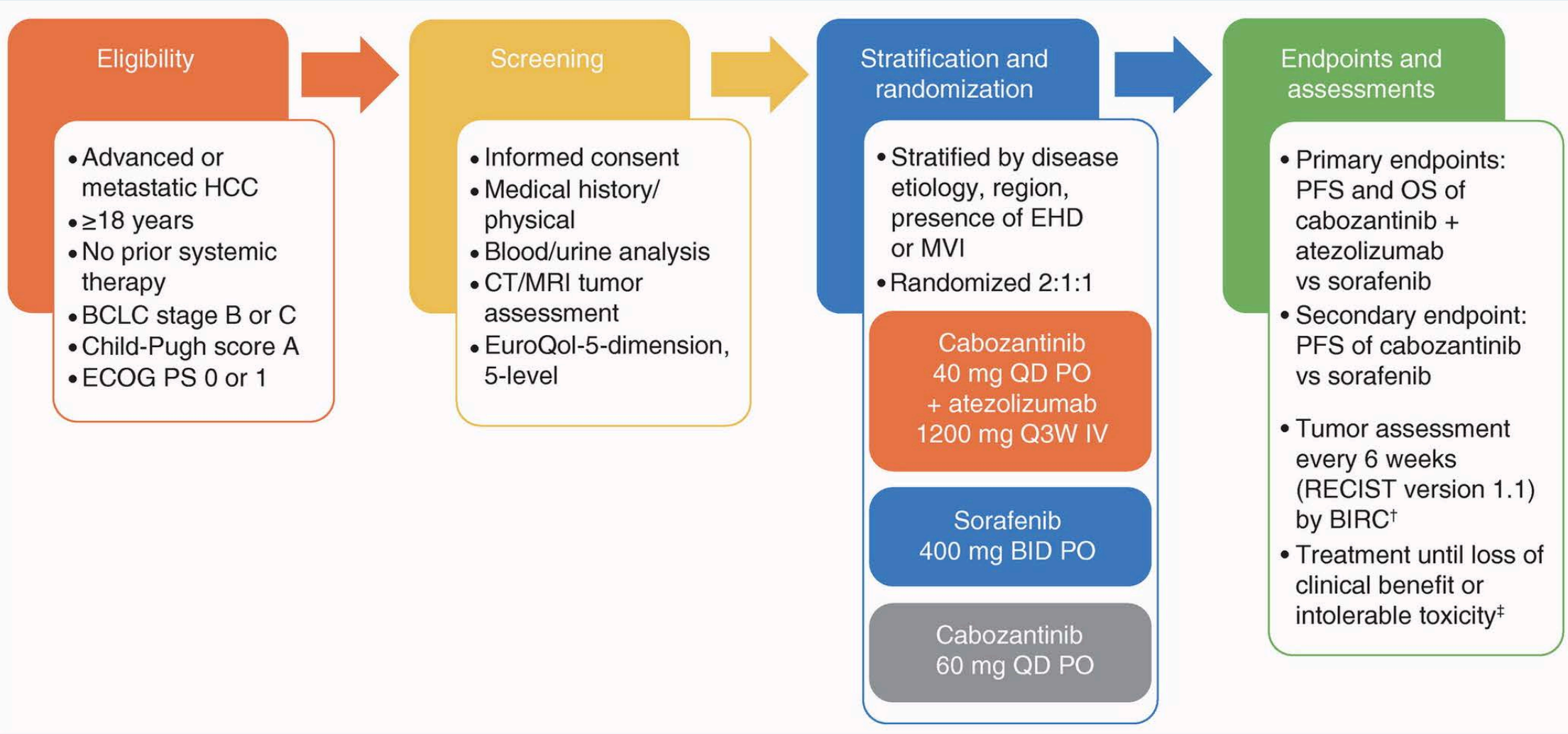


Tumor response according to RECIST v1.1. Response data are derived from the updated efficacy analysis (April 9, 2021).
PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

El-Khoueiry AB et al. ASCO 2021;Abstract 4078.

RTP RESEARCH TO PRACTICE

COSMIC-312: Ongoing Phase III Trial of Cabozantinib in Combination with Atezolizumab Versus Sorafenib in Treatment-Naïve Advanced HCC



Kelley RK et al. *ESMO Open* 2020;5(4):e000714.

Pemigatinib for Previously Treated Locally Advanced/Metastatic Cholangiocarcinoma (CCA): Update of FIGHT-202

Abou-Alfa GK et al.
ASCO 2021;Abstract 4086.

FIGHT-202: Updated Efficacy with Pemigatinib in Patients with HCC and FGFR2 Fusions or Rearrangements (Cohort A)

Variable	Primary Analysis[1] (n = 107)	Current Analysis (n = 108)*
ORR (95% CI), %	35.5 (26.5–45.4)	**37.0 (27.9–46.9)**
Best OR, † n (%)		
CR	3 (2.8)	4 (3.7)
PR	35 (32.7)	36 (33.3)
SD	50 (46.7)	49 (45.4)
PD	16 (14.9)	16 (14.8)
Not evaluable‡	3 (2.8)	3 (2.8)
DCR (95% CI), %	82 (74–89)	82.4 (73.9–89.1)
mDOR (95% CI), mo	7.5 (5.7–14.5)	8.1 (5.7–13.1)
mPFS (95% CI), mo	6.9 (6.2–9.6)	7.0 (6.1–10.5)
mOS (95% CI), mo	21.1 (14·8–NE)§	17.5 (14.4–23.0)
Responders	–	30.1 (21.5–NE)
Nonresponders	–	13.7 (9.6–16.2)

[1]Abou-Alfa GK et al. Lancet Oncol 2020;21:671-84.

Abou-Alfa GK et al. ASCO 2021;Abstract 4086.

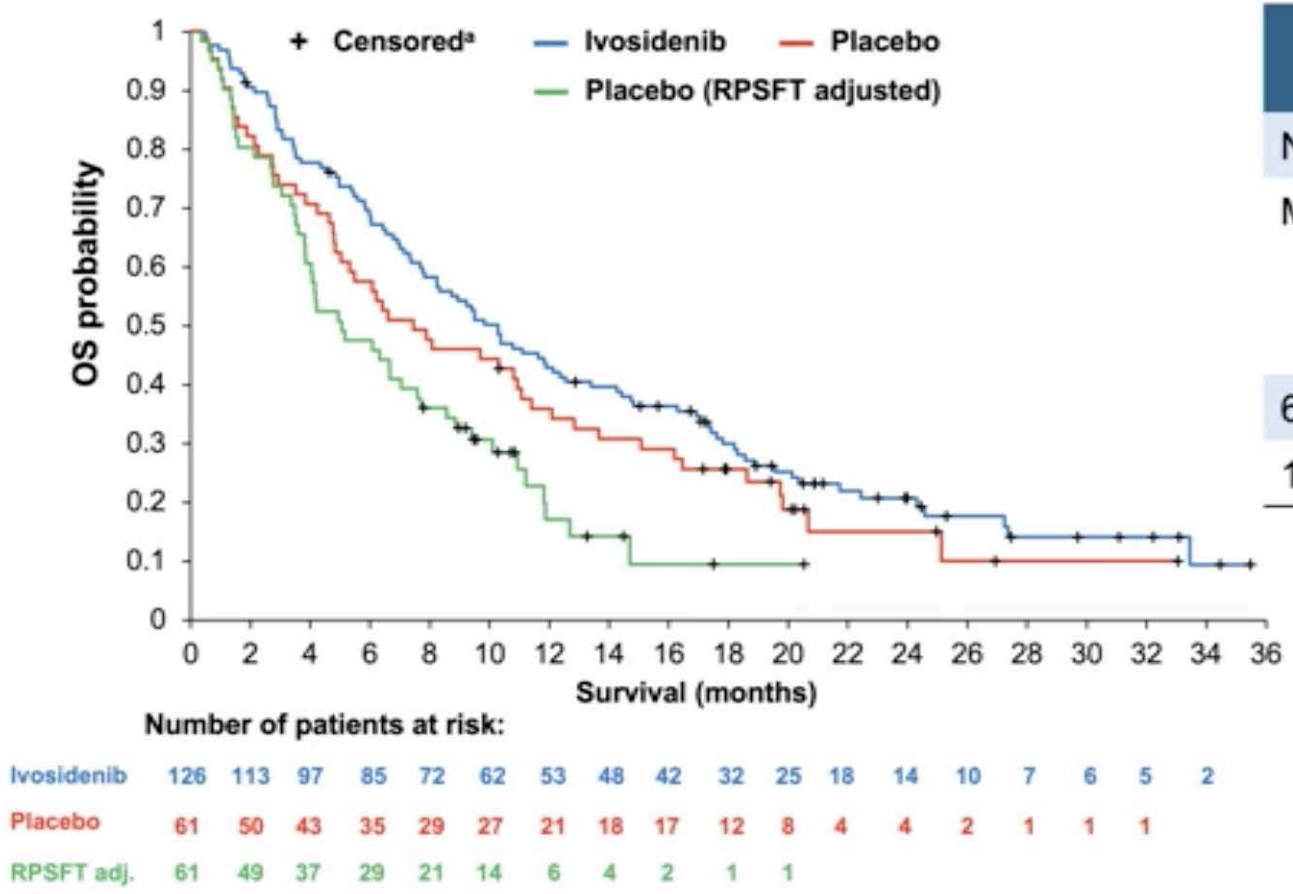
Final Results from ClarIDHy, a Global, Phase 3, Randomized, Double-Blind Study of Ivosidenib (IVO) versus Placebo (PBO) in Patients (pts) with Previously Treated Cholangiocarcinoma (CCA) and an Isocitrate Dehydrogenase 1 (IDH1) Mutation

Abou-Alfa GK et al.

ASCO 2021;Abstract 4069.

ClariDHy: Overall Survival

The planned crossover-adjusted OS was derived using the rank-preserving structural failure time (RPSFT) model



	Ivosidenib n = 126	Placebo n = 61
Number of events (%)	100 (79.4)	50 (82.0)
Median OS, months	10.3	7.5
HR (95% CI)	0.79 (0.56, 1.12)	
1-sided p-value	0.093	
6-month OS rate, %	69	57
12-month OS rate, %	43	36

- The median OS in the placebo arm after adjustment for crossover was 5.1 months (HR = 0.49 [95% CI 0.34, 0.70]; 1-sided $p < 0.0001$)

Abou-Alfa GK et al. ASCO 2021;Abstract 4069.

Contributing Oncologists

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Anish Meerasahib, MD
Texas Oncology
Houston, Texas

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CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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We are taking a short break!

The program will resume at 1:00 PM CT (2:00 PM ET)

Up Next…

Drs Deborah Armstrong and Krishnansu Tewari discuss the management of gynecologic cancers

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ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

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Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Gynecologic Cancers Faculty

Deborah K Armstrong, MD
Professor of Oncology
Professor of Gynecology and Obstetrics
Skip Viragh Outpatient Cancer Building
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Krishnansu S Tewari, MD
Professor and Division Director
Division of Gynecologic Oncology
University of California, Irvine
Irvine, California

Contributing Oncologists

Sulfi Ibrahim, MD
Hematology/Oncology
Reid Health
Richmond, Indiana

Ina J Patel, DO
Assistant Professor of Internal Medicine
Division of Hematology/Oncology
Moncrief Cancer Institute
Fort Worth, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

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Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Highlights of ASCO 2021 – Ovarian Cancer
Deborah K Armstrong, MD

- Ray-Coquard IL et al. **Efficacy and safety results from neopembrov study, a randomized phase II trial of neoadjuvant chemotherapy (CT) with or without pembrolizumab (P) followed by interval debulking surgery and standard systemic therapy ± P for advanced high-grade serous carcinoma (HGSC): A GINECO study.** ASCO 2021;Abstract 5500.
- Pfisterer J et al. **Optimal treatment duration of bevacizumab (BEV) combined with carboplatin and paclitaxel in patients (pts) with primary epithelial ovarian (EOC), fallopian tube (FTC) or peritoneal cancer (PPC): A multicenter open-label randomized 2-arm phase 3 ENGOT/GCIG trial of the AGO Study Group, GINECO, and NSGO (AGO-OVAR 17/BOOST, GINECO OV118, ENGOT Ov-15, NCT01462890).** ASCO 2021;Abstract 5501.
- O'Malley DM T et al. **Mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients (pts) with platinum-agnostic ovarian cancer: Final analysis**. ASCO 2021;Abstract 5504.
- Westin SN et al. **EFFORT: EFFicacy Of adavosertib in parp ResisTance: A randomized two-arm non-comparative phase II study of adavosertib with or without olaparib in women with PARP-resistant ovarian cancer.** ASCO 2021;Abstract 5505.
- Rocconi RP et al. **Maintenance Vigil immunotherapy in newly diagnosed advanced ovarian cancer: Efficacy assessment of homologous recombination proficient (HRP) patients in the phase IIb VITAL trial.** ASCO 2021;Abstract 5502.

RTP RESEARCH TO PRACTICE

Highlights of ASCO and ESMO 2021 – Endometrial and Cervical Cancers
Krishnansu S Tewari, MD

1. Tewari KS et al. **EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Interim analysis of phase III trial of cemiplimab vs investigator's choice (IC) chemotherapy (chemo) in recurrent/metastatic (R/M) cervical carcinoma.** ESMO 2021;Abstract VP4-2021

2. Mileshkin LR et al. **Adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone: The randomized phase III OUTBACK Trial (ANZGOG 0902, RTOG 1174, NRG 0274)**. ASCO 2021;Abstract LBA3.

3. Park JS et al. **Efficacy and safety results of GX-188E, a therapeutic DNA vaccine, combined with pembrolizumab administration in patients with HPV 16- and/or 18- positive advanced cervical cancer: Phase II interim analysis results (KEYNOTE-567).** ASCO 2021;Abstract 5511.

4. Ali-Ahmad HM et al. **Pertuzumab plus trastuzumab (P+T) in patients (Pts) with uterine cancer (UC) with ERBB2 or ERBB3 amplification, overexpression or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.** ASCO 2021;Abstract 5508.

5. Zola P et al. **Intensive versus minimalist follow-up in patients treated for endometrial cancer: A multicentric randomized controlled trial (The TOTEM study — NCT00916708).** ASCO 2021;Abstract 5506.

6. Heudel PE et al. **Victoria: A multicentric, randomized, open-label, phase I/II of mTOR inhibitor (VISTUSERTIB) combined with anastrozole in patients with hormone receptor-positive advanced/metastatic endometrial cancer — A CLIPP program INCA in collaboration with GINECO group.** ASCO 2021;Abstract 5507.

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Agenda

Module 1: Cases from the Community

- Dr Prakash: A 65-year-old woman with germline and somatic BRCA wild-type, HRD-positive ovarian cancer
- Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Module 2: Highlights of ASCO 2021 – Dr Armstrong

Module 3: Cases from the Community

- Dr Malik: A 71-year-old woman with advanced MSI-high endometrial cancer
- Dr Patel: A 64-year-old woman with metastatic endometrial cancer
- Dr Patel: A 39-year-old woman with recurrent cervical cancer – PD-L1 positive
- Dr Levin: A 46-year-old woman with metastatic small cell carcinoma of the cervix

Module 4: Highlights of ASCO 2021 – Dr Tewari

Agenda

Module 1: Cases from the Community

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Module 4: Highlights of ASCO 2021 – Dr Tewari

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel
- Carboplatin/paclitaxel → olaparib
- Carboplatin/paclitaxel + bevacizumab → olaparib
- Carboplatin/paclitaxel → niraparib
- Carboplatin/paclitaxel + bevacizumab → niraparib
- Carboplatin/paclitaxel + bevacizumab → bevacizumab
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + niraparib
- Other (please specify)

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-negative) is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

- Carboplatin/paclitaxel
- Carboplatin/paclitaxel → olaparib
- Carboplatin/paclitaxel + bevacizumab → olaparib
- Carboplatin/paclitaxel → niraparib
- Carboplatin/paclitaxel + bevacizumab → niraparib
- Carboplatin/paclitaxel + bevacizumab → bevacizumab
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
- Carboplatin/paclitaxel + bevacizumab → bevacizumab + niraparib
- Other (please specify)

Case Presentation – Dr Prakash: A 65-year-old woman with germline and somatic BRCA wild-type, HRD-positive ovarian cancer

Dr Chris Prakash

- Presents with ascites and abdominal pain
- Imaging: omental caking, ascites, mesenteric LAD and right adnexal mass
  - Baseline CA 125: 350
  - Somatic and germline BRCA testing: Negative, HRD-positive
- Optimal cytoreduction surgery → carboplatin/paclitaxel/bevacizumab x 6
  - CA 125: Normal
- Olaparib

Questions

- What is the role of PARP inhibitor in a woman who does not have a BRCA mutation but does have HRD on somatic testing?
- How much do you worry about the development of MDS in patients receiving long-term PARP inhibitor therapy? How long do you continue maintenance with a PARP inhibitor?
- Since niraparib is approved as maintenance therapy regardless of HRD status, would you even test women for HRD? If they are BRCA and HRD negative, would you give them a PARP inhibitor?

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Case Presentation – Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Dr Sulfi Ibrahim

- Diagnosed with Stage IIIC ovarian cancer
- Neoadjuvant carboplatin/paclitaxel x 3 cycles → optimal debulking surgery → adjuvant carboplatin/paclitaxel x 3 cycles
- Olaparib maintenance therapy is initiated, but the patient develops significant anemia (Hb 5 g/dL)
- Blood transfusion accompanied by olaparib dose reduction from 300 mg BID to 300 mg in the morning and 150 mg in the evening
- Repeat CBC shows Hb at 7 g/dL → second blood transfusion

Question

- What would be the best way to manage this patient who is extremely motivated to stay on the olaparib and complete the 2 years of adjuvant therapy but obviously does have significant anemia with the olaparib? Should I dose reduce the olaparib further, or would you advocate for the use of erythropoietin-stimulating agents to manage her anemia and keep her on a higher dose of olaparib?

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Prakash: A 65-year-old woman with germline and somatic BRCA wild-type, HRD-positive ovarian cancer
- Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Module 2: Highlights of ASCO 2021 – Dr Armstrong

Module 3: Cases from the Community

- Dr Malik: A 71-year-old woman with advanced MSI-high endometrial cancer
- Dr Patel: A 64-year-old woman with metastatic endometrial cancer
- Dr Patel: A 39-year-old woman with recurrent cervical cancer – PD-L1 positive
- Dr Levin: A 46-year-old woman with metastatic small cell carcinoma of the cervix

Module 4: Highlights of ASCO 2021 – Dr Tewari

Ray-Coquard IL et al. Efficacy and safety results from neopembrov study, a randomized phase II trial of neoadjuvant chemotherapy (CT) with or without pembrolizumab (P) followed by interval debulking surgery and standard systemic therapy ± P for advanced high-grade serous carcinoma (HGSC): A GINECO study. ASCO 2021;Abstract 5500.

Dr Deborah Armstrong

1. For which clinical situations is this data clinically relevant?

- Subjects undergoing NACT for initial treatment of ovarian cancer

2. What are the key findings that are most relevant to patients in these clinical situations?

- In this small randomized phase II study, the addition of pembrolizumab to NACT +\- bevacizumab did not improve complete resection rate or PFS

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This is one of a large number of trials looking at the addition of IO to initial chemotherapy for ovarian cancer. IO therapy has not demonstrated great activity in ovarian cancer in general, perhaps with the exception of clear cell carcinoma, and it is yet to be seen whether in larger RP3 studies the addition of IO is beneficial

Pfisterer J et al. Optimal treatment duration of bevacizumab (BEV) combined with carboplatin and paclitaxel in patients (pts) with primary epithelial ovarian (EOC), fallopian tube (FTC) or peritoneal cancer (PPC): A multicenter open-label randomized 2-arm phase 3 ENGOT/GCIG trial of the AGO Study Group, GINECO, and NSGO (AGO-OVAR 17/BOOST, GINECO OV118, ENGOT Ov-15, NCT01462890). ASCO 2021;Abstract 5501.

Dr Deborah Armstrong

1. For which clinical situations is this data clinically relevant?

- This is applicable to patients with advanced disease who will be treated with bevacizumab in the upfront setting

2. What are the key findings that are most relevant to patients in these clinical situations?

- The extension of maintenance bevacizumab from 15 to 30 months did not improve PFS or OS

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- There were significant questions about the duration of bev maintenance since ICON7 and GOG 218 used different durations of therapy. I look at this somewhat like adjuvant trastuzumab. We now know that using bev maintenance longer is tolerable but doesn't improve clinical outcomes. This study was done before PARP inhibitor maintenance but it is still applicable to many of our patients.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Westin SN et al. EFFORT: EFFicacy Of adavosertib in parp ResisTance: A randomized two-arm non-comparative phase II study of adavosertib with or without olaparib in women with PARP-resistant ovarian cancer. ASCO 2021; Abstract 5505.

Dr Deborah Armstrong

1. For which clinical situations is this data clinically relevant?

- For the increasingly large group of patients with recurrent ovarian cancer who have previously received a PARP inhibitor and progressed, a real area of need

2. What are the key findings that are most relevant to patients in these clinical situations?

- This was a pretty heavily pretreated group, 4-5 prior on average, about half with a BRCA mutation. 90% had had prior benefit from prior PARP inhibitor therapy so these data may not be applicable to those who never had any benefit from prior PARPi. Adavosertib has a very reasonable ORR of 23% while the combination was 29%. There was longer DOR, PFS and clinical benefit rate in the combination arm as well. Interestingly, the ORR was the same to adavo alone or adavo/olaparib in BRCA mutated disease (~20%) but was higher in non-BRCA mutation (ORR of 31% and 39% respectively) in BRCA non-mutated disease

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- There is synergistic toxicity between the two agents. Shorter duration and lower dosing of adavosertib is needed when it is given with olaparib. Both adavosertib and the combination are worthy of further clinical investigation.

O'Malley DM T et al. Mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients (pts) with platinum-agnostic ovarian cancer: Final analysis. ASCO 2021;Abstract 5504.

Dr Deborah Armstrong

1. For which clinical situations is this data clinically relevant?

- Either platinum sensitive or platinum resistant ovarian cancers with median or high tumor FR-alpha expression

2. What are the key findings that are most relevant to patients in these clinical situations?

- There were very high ORR and DOR in both sensitive and resistant patient groups. The ORR of 59% in the PROC FR-alpha high group is really unprecedented.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- It would be good to know what percentage of screened patients didn't meet the FR-alpha criteria for the trial. It would also be good to know if the 40% of patients who had previously received BEV did similarly or worse than those who were bev naïve. Nonetheless, this looks like a very promising combination.

Rocconi RP et al. Maintenance Vigil immunotherapy in newly diagnosed advanced ovarian cancer: Efficacy assessment of homologous recombination proficient (HRP) patients in the phase IIb VITAL trial. ASCO 2021;Abstract 5502.

Dr Deborah Armstrong

1. For which clinical situations is this data clinically relevant?

- This trial was using an autologous vaccine as maintenance after initial chemo in responding patients

2. What are the key findings that are most relevant to patients in these clinical situations?

- The PFS in the overall population was not statistically significantly improved for the GEM arm but there were very significant improvements in PFS and OS in the HRP group

3. What is the relevance of this data to clinical research for patients in these clinical settings?

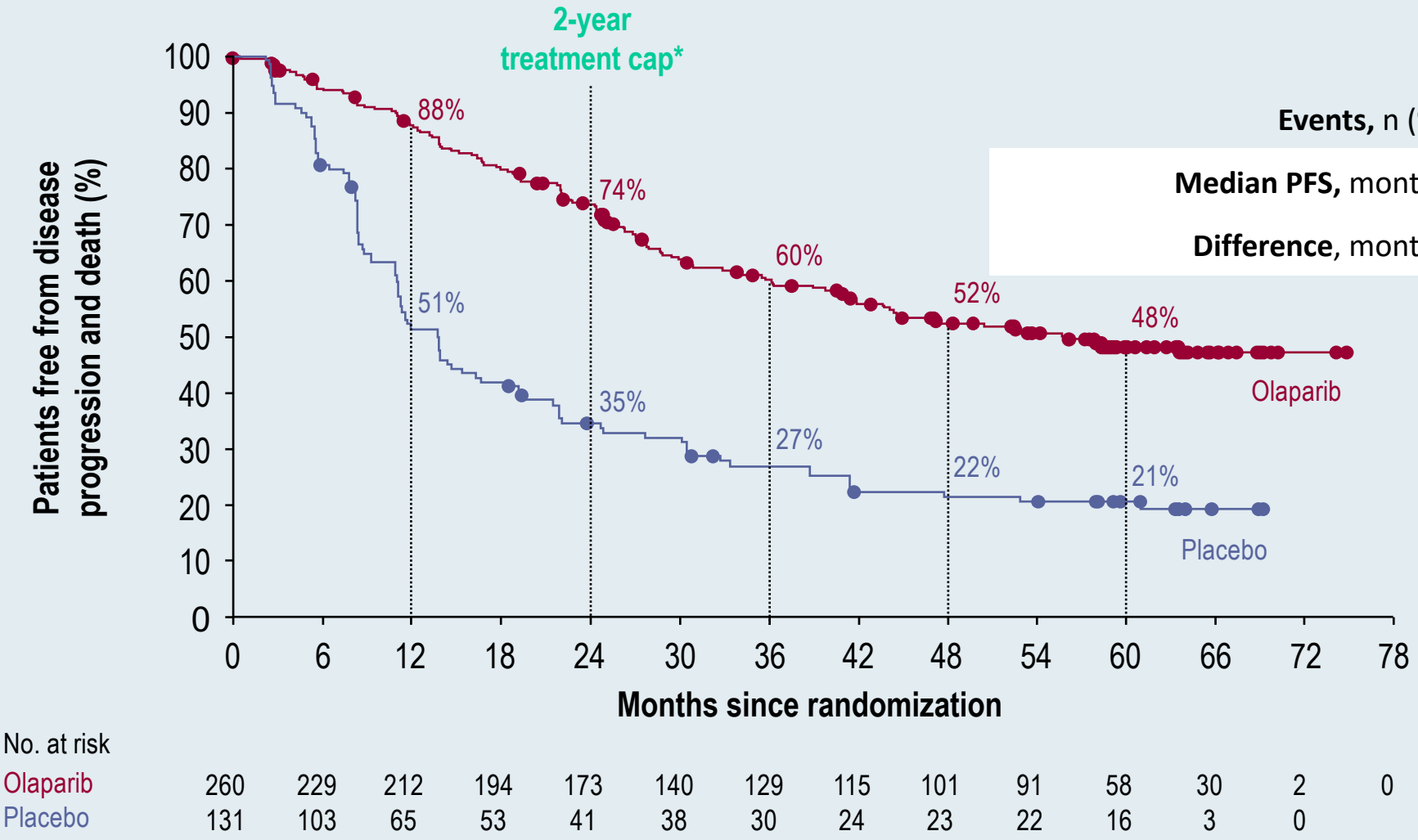
- Given the very minimal benefits of PARP inhibitor maintenance in HRP disease, this could be a very valuable approach for that group of patients if the data hold up

Maintenance Olaparib for Patients (pts) with Newly Diagnosed, Advanced Ovarian Cancer and a BRCA Mutation: 5-year Follow-Up from SOLO1

Bradley WH et al.

SGO 2021;Abstract 10520.

SOLO-1: Updated PFS (60 Months Follow-Up)



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	

HR 0.33 (95% CI 0.25–0.43)

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

Bradley WH et al. SGO 2021;Abstract 10520.

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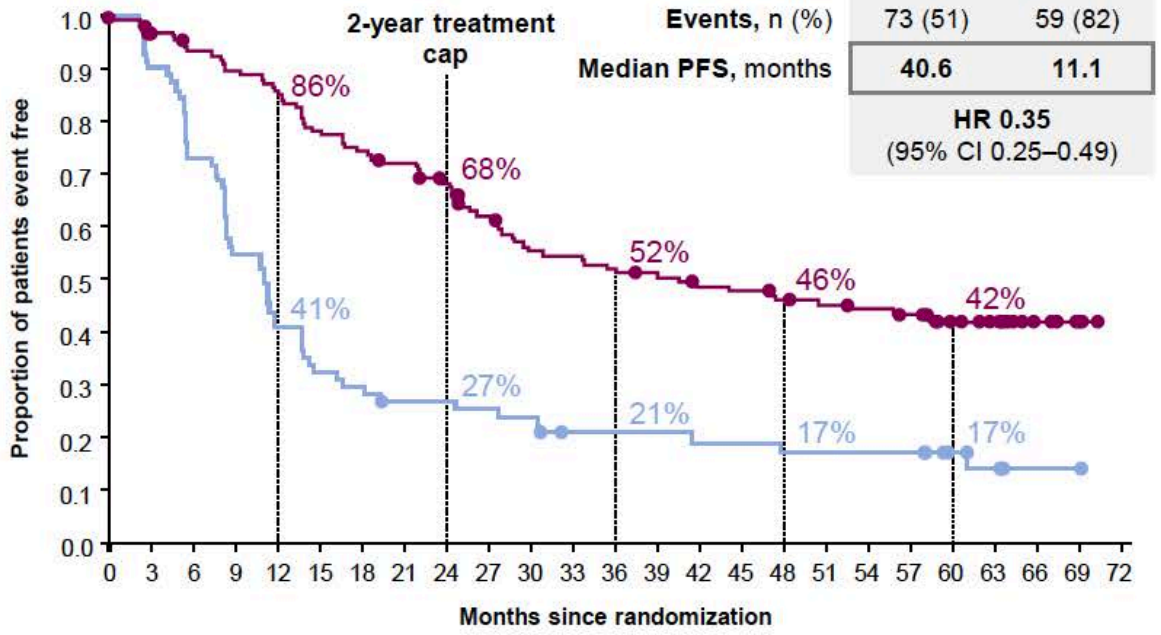
SOLO-1: Updated PFS by Risk Group

Higher-risk

Baseline characteristic, n (%)	Olaparib (N=146)	Placebo (N=73)
Interval debulking surgery	94 (64)	43 (59)
CR to prior chemotherapy*	107 (73)	54 (74)
*BRCA1*m	109 (75)	43 (59)
*BRCA2*m	36 (25)	30 (41)
*BRCA1*m and *BRCA2*m	1 (1)	0

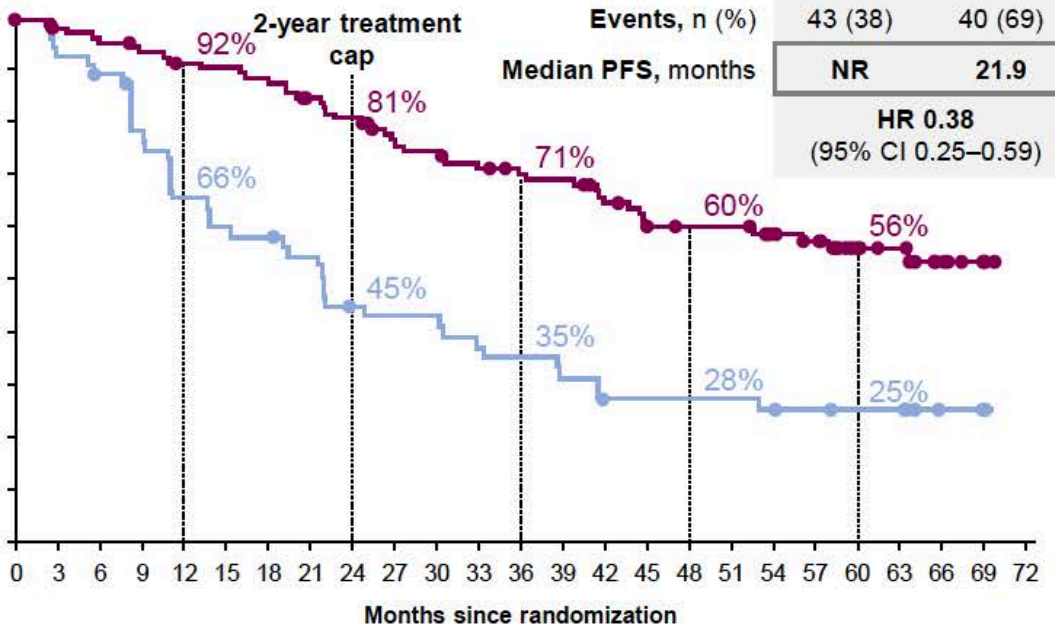
	(N=142)†	(N=72)†
Events, n (%)	73 (51)	59 (82)
Median PFS, months	**40.6**	**11.1**
	HR 0.35 (95% CI 0.25–0.49)	



Lower-risk

Baseline characteristic, n (%)	Olaparib (N=114)	Placebo (N=58)
Interval debulking surgery	0	0
CR to prior chemotherapy*	106 (93)	53 (91)
*BRCA1*m	82 (72)	48 (83)
*BRCA2*m	30 (26)	10 (17)
*BRCA1*m and *BRCA2*m	2 (2)	0

	(N=114)	(N=58)
Events, n (%)	43 (38)	40 (69)
Median PFS, months	**NR**	**21.9**
	HR 0.38 (95% CI 0.25–0.59)	



Bradley WH et al. SGO 2021;Abstract 10520.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Prakash: A 65-year-old woman with germline and somatic BRCA wild-type, HRD-positive ovarian cancer
- Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Module 2: Highlights of ASCO 2021 – Dr Armstrong

Module 3: Cases from the Community

- Dr Malik: A 71-year-old woman with advanced MSI-high endometrial cancer
- Dr Patel: A 64-year-old woman with metastatic endometrial cancer
- Dr Patel: A 39-year-old woman with recurrent cervical cancer – PD-L1 positive
- Dr Levin: A 46-year-old woman with metastatic small cell carcinoma of the cervix

Module 4: Highlights of ASCO 2021 – Dr Tewari

In general, what treatment would you recommend for a patient with MSS metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

- Cisplatin/doxorubicin
- Carboplatin/docetaxel
- Lenvatinib/pembrolizumab
- Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
- Pembrolizumab
- Other chemotherapy
- Other (please specify)

In general, what treatment would you recommend for a patient with MSI-high metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

- Cisplatin/doxorubicin
- Carboplatin/docetaxel
- Lenvatinib/pembrolizumab
- Pembrolizumab
- Dostarlimab
- Other chemotherapy
- Other (please specify)

Case Presentation – Dr Malik: A 71-year-old woman with advanced MSI-high endometrial cancer

Dr Henna Malik

- Endometrial cancer s/p surgery → adjuvant carboplatin/paclitaxel x 5 and radiation therapy
- Recurrence of endometrial cancer 8 months after completing treatment
- Restarted on carboplatin/paclitaxel, with PD after 6 months
  - Pelvic tumor grew from 6 to 11 cm
- NGS: MSI-high, TP53 mutation
- Pembrolizumab 200 mg IV q3 weeks, with excellent response, Grade 2 diarrhea
  - Pelvic tumor decreased to 4 cm
- Presented recently to hospital with rectal urethral fistula

Question

- Do we need to use pembrolizumab in the upfront setting for certain mutations or tumor types?

When initiating lenvatinib and pembrolizumab for a woman with endometrial cancer, what is your typical starting dose of lenvatinib?

- 20 mg daily
- 14 mg daily
- 10 mg daily
- 8 mg daily
- Other (please specify)

Case Presentation – Dr Patel: A 64-year-old woman with metastatic endometrial cancer

Dr Ina Patel

- 2016: Diagnosed with endometrial cancer after hysterectomy for heavy periods
  - Declined bilateral oophorectomy, RT to the pelvic cuff
- 2019: PCP noted vaginal lesion, workup reveals lung metastasis of endometrioid origin
  - Carboplatin/paclitaxel with poor response and development of neuropathy
- 5/2020: Pembrolizumab/lenvatinib (20 mg)
- 7/2020: Lenvatinib discontinued due to hypertension; pembrolizumab continued

Questions

- What are your recommendations for how to dose-reduce lenvatinib when it is being administered with pembrolizumab?
- For patients experiencing a good response with immunotherapy, how long do you continue treatment?

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Regulatory and reimbursement issues aside, in general, assuming all agents below are available, what would be your preferred second-line therapy for a patient with MSS metastatic cervical cancer who experiences disease progression on carboplatin/paclitaxel/bevacizumab?

- Other chemotherapy
- Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
- Cemiplimab
- Pembrolizumab
- Tisotumab vedotin
- Other (please specify)

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in general, assuming all agents below are available, what would be your preferred second-line therapy for a patient with MSS metastatic cervical cancer who experiences symptomatic disease progression on carboplatin/paclitaxel/bevacizumab and has a PD-L1 CPS of 10%?

- Other chemotherapy
- Cemiplimab
- Pembrolizumab
- Tisotumab vedotin
- Other (please specify)

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Case Presentation – Dr Patel: A 39-year-old woman with recurrent cervical cancer – PD-L1 positive

Dr Ina Patel

- 2018: Diagnosed with Stage IIB squamous cell carcinoma of the cervix
  - Chemoradiation with weekly cisplatin → NED
- 2019: Recurrence in inguinal node
  - Paclitaxel/carboplatin/bevacizumab x 8 cycles → surveillance
  - Poor quality of life on chemotherapy
- 3/2020: recurrent visits to ER for abdominal pain and recto-vaginal fistula
  - Imaging confirmed progression and multi focal nodal metastases
  - PD-L1-positive
- 7/2020: Pembrolizumab with great response

Questions

- Given her great response, how long would you continue immunotherapy for her?
- What would you recommend as her next line of therapy, given that she has already received immunotherapy and chemotherapy?
- Would you recommend immunotherapy for patients with PD-L1-negative disease?

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Case Presentation – Dr Levin: A 46-year-old woman with metastatic small cell carcinoma of the cervix

Dr Pavel Levin

- Cervical cancer, lost to follow up x 1 year
- Presents with cough, SOB, diffuse lung metastases
  - Pathology: Small cell carcinoma
- Carboplatin/paclitaxel x 6, with significant symptomatic improvement
- Monitoring the patient past 2-3 years

Question

- What treatment regimens would you have recommended for this patient?

Agenda

Module 1: Cases from the Community

- Dr Prakash: A 65-year-old woman with germline and somatic BRCA wild-type, HRD-positive ovarian cancer
- Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Module 2: Highlights of ASCO 2021 – Dr Armstrong

Module 3: Cases from the Community

- Dr Malik: A 71-year-old woman with advanced MSI-high endometrial cancer
- Dr Patel: A 64-year-old woman with metastatic endometrial cancer
- Dr Patel: A 39-year-old woman with recurrent cervical cancer – PD-L1 positive
- Dr Levin: A 46-year-old woman with metastatic small cell carcinoma of the cervix

Module 4: Highlights of ASCO 2021 – Dr Tewari

Tewari KS et al. EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Interim analysis of phase III trial of cemiplimab vs investigator's choice (IC) chemotherapy (chemo) in recurrent/metastatic (R/M) cervical carcinoma. ESMO 2021;Abstract VP4-2021.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- The data from the EMPOWER trial are relevant clinically to women with recurrent cervical cancer who have progressed following treatment of recurrence with at least one cycle of platinum-containing therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The key findings are that cemiplimab (compared to chemotherapy in this randomized phase 3 trial) significantly improved overall survival in this very poor prognostic population. This survival benefit was seen in the overall population and in the squamous cell population and was not accompanied by any deterioration in quality of life - in fact, some patients treated with cemiplimab experienced improved quality of life. This contrasts with the physician's choice single-agent chemotherapy arm where patients experienced deterioration in quality of life.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- The most important clinical ramification is whether this anti-PD-1 inhibitor will be as active (or even superior) in earlier lines of therapy for recurrent cervical cancer.

Mileshkin LR et al. Adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone: The randomized phase III OUTBACK Trial (ANZGOG 0902, RTOG 1174, NRG 0274). ASCO 2021;Abstract LBA3.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- Locally advanced cervical cancer i.e., stages IB3 to IVA

2. What are the key findings that are most relevant to patients in these clinical situations?

- The unfortunate finding is that there is no survival benefit with consolidation chemoRx after primary chemoradiation plus high-dose-rate intracavitary brachytherapy

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- The relevance to clinical research is that we need to study novel agents in the consolidation setting – eg, durvalumab in the CALLA trial

Park JS et al. Efficacy and safety results of GX-188E, a therapeutic DNA vaccine, combined with pembrolizumab administration in patients with HPV 16- and/or 18- positive advanced cervical cancer: Phase II interim analysis results (KEYNOTE-567). ASCO 2021;Abstract 5511.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- This study applies to patients with recurrent cervical cancer in need of 2nd line or greater therapy following progression/failure of platinum-containing therapy with or without bevacizumab.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The key finding for me is that when this therapeutic vaccine is combined with pembrolizumab in patients whose tumors express PD-L1, the ORR is increased to 40% compared to pembro alone (14%). The combination also appears to be tolerable.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- With respect to ongoing research, this definitely has important potential implications for many other 2nd line medicines currently under investigation (anti-PD-1 monotherapy, anti-PD-1+anti-CTLA-4, anti-TIGIT, etc.)

Ali-Ahmad HM et al. Pertuzumab plus trastuzumab (P+T) in patients (Pts) with uterine cancer (UC) with ERBB2 or ERBB3 amplification, overexpression or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study. ASCO 2021;Abstract 5508.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- Heavily pre-treated uterine cancer patients with ERBB2 and ERBB3 alterations. It is not clear to me from the presentation if these are uterine cervical cancer patients or uterine endometrial cancer patients.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Unfortunately, this is dual intravenous targeted therapy with not very encouraging ORR. I understand these are heavily pre-treated patients. The median PFS of 28 wks is notable, however

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- There are some clinical implications but further research needs to be done to clarify them further. Specifically are the responses observed in patients with amplification of HER2 (as observed with neratinib in HER2+ cervix) or specific genomic alterations?

Heudel PE et al. Victoria: A multicentric, randomized, open-label, phase I/II of mTOR inhibitor (VISTUSERTIB) combined with anastrozole in patients with hormone receptor-positive advanced/metastatic endometrial cancer — A CLIPP program INCA in collaboration with GINECO group. ASCO 2021; Abstract 5507.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- Patients with recurrent ER/PR+ endometrial cancer who may have received one line of prior systemic therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The 24% ORR with the combination including 1 CR is encouraging.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- This study is encouraging – 5 years ago there were a number of large trials studying at least 3 different mTOR inhibitors but we got nowhere with those studies because the patient populations were unselected. In this study the ER/PR expression may be a soft biomarker. Further research should look for PI3K/Akt/mTOR pathway genomic aberrations as possible predictive biomarkers to be validated with these drugs.

Zola P et al. Intensive versus minimalist follow-up in patients treated for endometrial cancer: A multicentric randomized controlled trial (The TOTEM study — NCT00916708). ASCO 2021;Abstract 5506.

Dr Krishnansu Tewari

1. For which clinical situations is this data clinically relevant?

- It is not clear which patients should be considered the relevant study population b/c patients with stage I-IV were included. I think this study mainly can be used to counsel patients with early stage disease that has been placed into remission with surgery with or without adjuvant therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The use of serial imaging and laboratory tests does not have an impact on OS or QoL, even among patients considered to be high-risk for recurrence.

3. What is the relevance of this data to clinical research for patients in these clinical settings

- While I agree that imaging and lab evaluation is not likely to impact OS, I hope that the results are not misinterpreted and that clinicians stop performing pelvic exams. Patients with isolated vaginal vault recurrences of endometrial cancer can be detected relatively early by pelvic exam and treated effectively with radiotherapy. Until additional research is done in that space the results from TOTEM should be cautiously interpreted.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Contributing Oncologists

Sulfi Ibrahim, MD
Hematology/Oncology
Reid Health
Richmond, Indiana

Ina J Patel, DO
Assistant Professor of Internal Medicine
Division of Hematology/Oncology
Moncrief Cancer Institute
Fort Worth, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

Chris Prakash, MD
Medical Director, Texas Oncology
Board of Directors, Texas Oncology
Board of Directors, TxSCO
Paris, Texas

Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

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CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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We are taking a short break!

The program will resume at 2:15 PM CT (3:15 PM ET)

Up Next…

Drs Virginia Borges and Harold Burstein discuss the management of breast cancer

RTP
RESEARCH TO PRACTICE

ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:15 PM Central Time
(9:00 AM – 4:15 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Saturday, June 26, 2021

9:00 AM ET — Lung Cancer

Justin F Gainor, Corey J Langer

10:15 AM ET — Genitourinary Cancers

Arjun Balar, Robert Dreicer

11:30 AM ET — Chronic Lymphocytic Leukemia and Lymphomas

John N Allan, Sonali M Smith

12:45 PM ET — Gastrointestinal Cancers

Thomas A Abrams, J Randolph Hecht

2:00 PM ET — Gynecologic Cancers

Deborah K Armstrong, Krishnansu S Tewari

3:15 PM ET — Breast Cancer

Virginia F Borges, Harold J Burstein

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Lung Cancer: *Drs Gainor and Langer*

Module 2 — Genitourinary Cancers: *Drs Balar and Dreicer*

Module 3 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Allan and Smith*

Module 4 — Gastrointestinal Cancers: *Drs Abrams and Hecht*

Module 5 — Gynecologic Cancers: *Drs Armstrong and Tewari*

Module 6 — Breast Cancer: *Drs Borges and Burstein*

Breast Cancer Faculty

Virginia F Borges, MD, MMSc
Professor of Medicine with Tenure
John C and Patricia Young-Connor Endowed Chair
in Young Women's Breast Cancer
Deputy Head, Division of Medical Oncology
Director, Breast Cancer Research Program and
Young Women's Breast Cancer Translational Program
University of Colorado Cancer Center
Aurora, Colorado

Harold J Burstein, MD, PhD
Institute Physician, Dana-Farber Cancer Institute
Professor of Medicine, Harvard Medical School
Boston, Massachusetts

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RESEARCH
TO PRACTICE

Contributing Oncologists

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Debra Patt, MD, PhD, MBA
Executive Vice President, Policy and Strategic Initiatives
Texas Oncology
President, Texas Society of Clinical Oncology
Austin, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

RTP
RESEARCH TO PRACTICE

Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Highlights of ASCO 2021 – Early Breast Cancer
Harold J Burstein, MD, PhD

- Tutt A et al. **OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer.** ASCO 2021;Abstract LBA1.
- Litton K et al. **Neoadjuvant talazoparib in patients with germline BRCA1/2 (gBRCA1/2) mutation-positive, early HER2-negative breast cancer (BC): Results of a phase 2 study.** ASCO 2021;Abstract 505.
- Harbeck N et al. **De-escalated neoadjuvant pertuzumab + trastuzumab with or without paclitaxel weekly in HR-/HER2+ early breast cancer: ADAPT-HR-/HER2+ biomarker and survival results.** ASCO 2021;Abstract 503.
- Mamounas EP et al. **Breast Cancer Index (BCI) and prediction of benefit from extended aromatase inhibitor (AI) therapy (tx) in HR+ breast cancer: NRG oncology/NSABP B-42.** ASCO 2021;Abstract 501.
- Loibl S et al. **Durvalumab improves long-term outcome in TNBC: Results from the phase II randomized GeparNUEVO study investigating neodjuvant durvalumab in addition to an anthracycline/taxane based neoadjuvant chemotherapy in early triple-negative breast cancer (TNBC).** ASCO 2021;Abstract 506.

Highlights of ASCO 2021 – Metastatic Breast Cancer
Virginia F Borges, MD, MMSc

- Cristofanilli M et al. **Overall survival (OS) with palbociclib (PAL) + fulvestrant (FUL) in women with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced breast cancer (ABC): Updated analyses from PALOMA-3.** ASCO 2021;Abstract 1000.
- Slamon DJ et al. **Updated overall survival (OS) results from the phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2- advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB).** ASCO 2021;Abstract 1001.
- Yuan Z et al. **Trastuzumab plus endocrine therapy or chemotherapy as first-line treatment for metastatic breast cancer with hormone receptor-positive and HER2-positive: The sysucc-002 randomized clinical trial.** ASCO 2021;Abstract 1003.
- Emans LA et al. **The tumor microenvironment (TME) and atezolizumab + nab-paclitaxel (A + nP) activity in metastatic triple-negative breast cancer (mTNBC): IMpassion130.** ASCO 2021; Abstract 1006.
- Chen L et al. **Combination of famitinib with camrelizumab plus nab-paclitaxel as first-line treatment for patients with immunomodulatory advanced triple-negative breast cancer (FUTURE-C-PLUS): A prospective, single-arm, phase 2 study.** ASCO 2021;Abstract 1007.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Patt: A 73-year-old woman with ER-negative, HER2-positive metastatic breast cancer (mBC) and brain metastases
- Dr Martins: A frail 58-year-old woman with metastatic triple-positive BC and a germline CHEK2 mutation
- Dr Jasani: A 55-year-old woman with a 4.5-cm ER-positive, HER2-positive localized breast cancer

Module 2: Highlights of ASCO 2021 – Drs Borges and Burstein

Module 3: Cases from the Community

- Dr Levin: A 48-year-old woman with metastatic triple-negative breast cancer (TNBC)
- Dr Kodali: A 40-year-old woman with left-sided, node-positive TNBC and a germline BRCA1 mutation
- Dr Patt: A 52-year-old woman with ER-positive, HER2-negative BC
- Dr Kodali: A 62-year-old woman with ER-positive mBC and a PIK3CA mutation

Module 4: Highlights of ASCO 2021 – Drs Borges and Burstein

Agenda

Module 1: Cases from the Community

- Dr Patt: A 73-year-old woman with ER-negative, HER2-positive metastatic breast cancer (mBC) and brain metastases
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Module 2: Highlights of ASCO 2021 – Drs Borges and Burstein

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Module 4: Highlights of ASCO 2021 – Drs Borges and Burstein

A 65-year-old woman with ER-negative, HER2-positive metastatic breast cancer with bone and soft tissue metastases receives first-line THP and second-line T-DM1 but then experiences symptomatic disease progression. Which systemic treatment would you most likely recommend next?

- Trastuzumab/lapatinib
- Neratinib/capecitabine
- Tucatinib/trastuzumab/capecitabine
- Trastuzumab deruxtecan
- Margetuximab/chemotherapy
- Other (please specify)

Case Presentation – Dr Patt: A 73-year-old woman with ER-negative, HER2-positive mBC and brain metastases

Dr Debra Patt

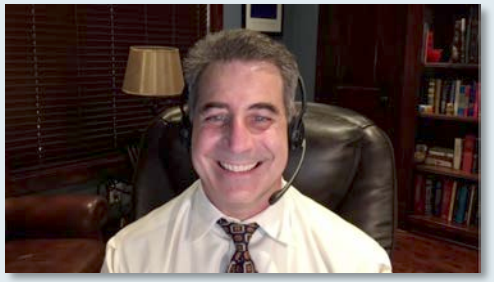
- 2014: ER/PR-negative, HER2-positive right inflammatory breast cancer s/p neoadjuvant TCHP and mastectomy, with CR
- 2018: Recurrence in liver
- THP → HP → Brain metastases
- 2019: SBRT and T-DM1 → NED extracranial, PD in brain

Questions

- What would you be thinking in terms of next lines of therapy?
- If she had previously received capecitabine, is there still a role for capecitabine/tucatinib/trastuzumab?
- What is the role of trastuzumab deruxtecan in this patient population? Margetuximb?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Martins: A frail 58-year-old woman with metastatic triple-positive BC and a germline CHEK2 mutation



Dr Joseph Martins

- 2/2018: Presented with bone pain and weakness
  - Bone scan and workup: Spinal cord compression and hypercalcemia
  - Diagnosed with ER/PR-positive, HER2-positive metastatic breast cancer, with a CHEK2 mutation
  - Extensive family history of breast cancer
- Surgery and radiation therapy
- Trastuzumab/anastrozole/denosumab, with CR
  - Previously healthy but currently frail

Questions

- Do we have any treatments for patients with CHEK2 mutations? Do PARP inhibitors have a role?
- Is there a survival advantage for chemotherapy/HER2-directed therapy versus hormonal therapy and HER2-directed therapy in patients with triple-positive breast cancer?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Jasani: A 55-year-old woman with a 4.5-cm ER-positive, HER2-positive localized breast cancer

Dr Nikesh Jasani

- 3/2020: Presents with palpable right breast mass
  - Imaging: 4.5-cm mass, prominent axillary nodes
  - Biopsy: right breast mass and node IDC, grade 3, ER95%, HER2 3+
- Genetic testing: NGS negative
- Neoadjuvant TCHP → surgery → residual low grade IDC

Questions

- What is your threshold to add pertuzumab to your neoadjuvant HER2 regimens? What about the "classic" T2N0 patient?
- Would you offer this patient extended adjuvant therapy with neratinib?

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

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- Dr Jasani: A 55-year-old woman with a 4.5-cm ER-positive, HER2-positive localized breast cancer

Module 2: Highlights of ASCO 2021 – Drs Borges and Burstein

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Module 4: Highlights of ASCO 2021 – Drs Borges and Burstein

Yuan Z et al. Trastuzumab plus endocrine therapy or chemotherapy as first-line treatment for metastatic breast cancer with hormone receptor-positive and HER2-positive: The sysucc-002 randomized clinical trial. ASCO 2021;Abstract 1003.

Dr Virginia Borges

1. For which clinical situations is this data clinically relevant?

- This presentation is relevant to women with metastatic hormone receptor positive and HER2-positive metastatic breast cancer with de novo or recurrent disease more than 12 months from prior therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Women treated with trastuzumab and endocrine therapy had similar progression free survival and overall survival as compared with women treated with chemotherapy and trastuzumab.
- Side effect profiles favored the ET and trastuzumab regimen.
- There appeared to be a benefit to chemotherapy and trastuzumab for women who were less than 24 months from prior adjuvant treatment.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- For women who do not have access to or could not tolerate the addition of other HER2 targeted agents and are either de novo metastatic or >24 months from adjuvant therapy, ET plus trastuzumab is a reasonable first line therapy in comparison to chemotherapy plus trastuzumab.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Harbeck N et al. De-escalated neoadjuvant pertuzumab+trastuzumab with or without paclitaxel weekly in HR-/HER2+ early breast cancer: ADAPT-HR-/HER2+ biomarker and survival results. ASCO 2021; Abstract 503.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with ER-/HER2+ and largely stage 2 breast cancer

2. What are the key findings that are most relevant to patients in these clinical situations?

- HP → pCR 30%; THP pCR = 80%
- Trends favor better longer term outcome with inclusion of taxanes

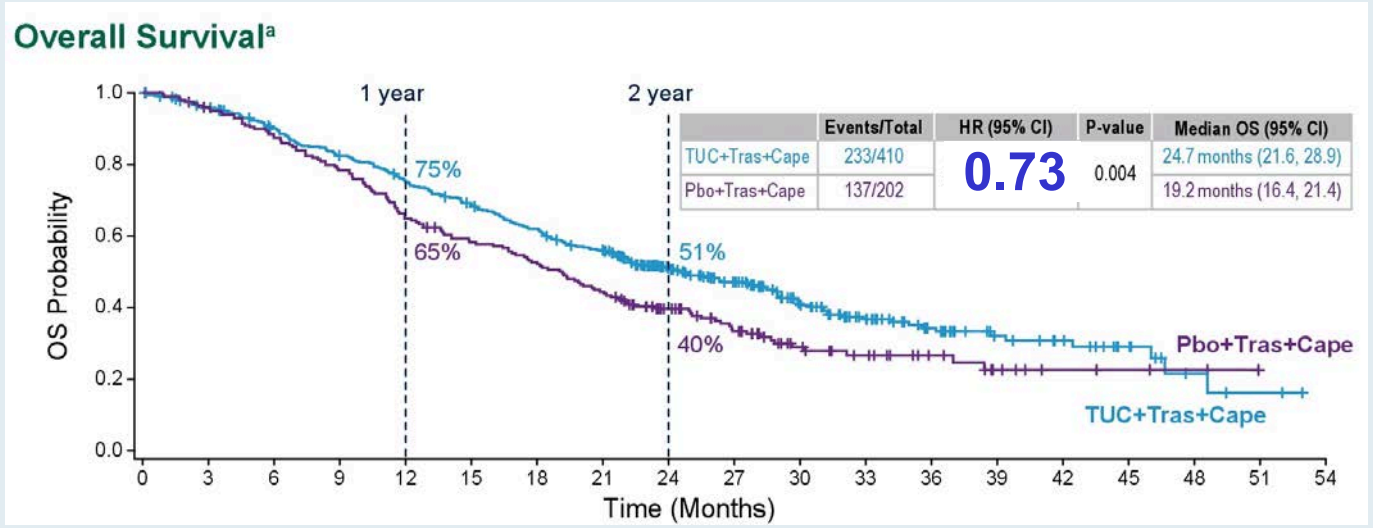
3. What is the relevance of this data to clinical research for patients in these clinical settings?

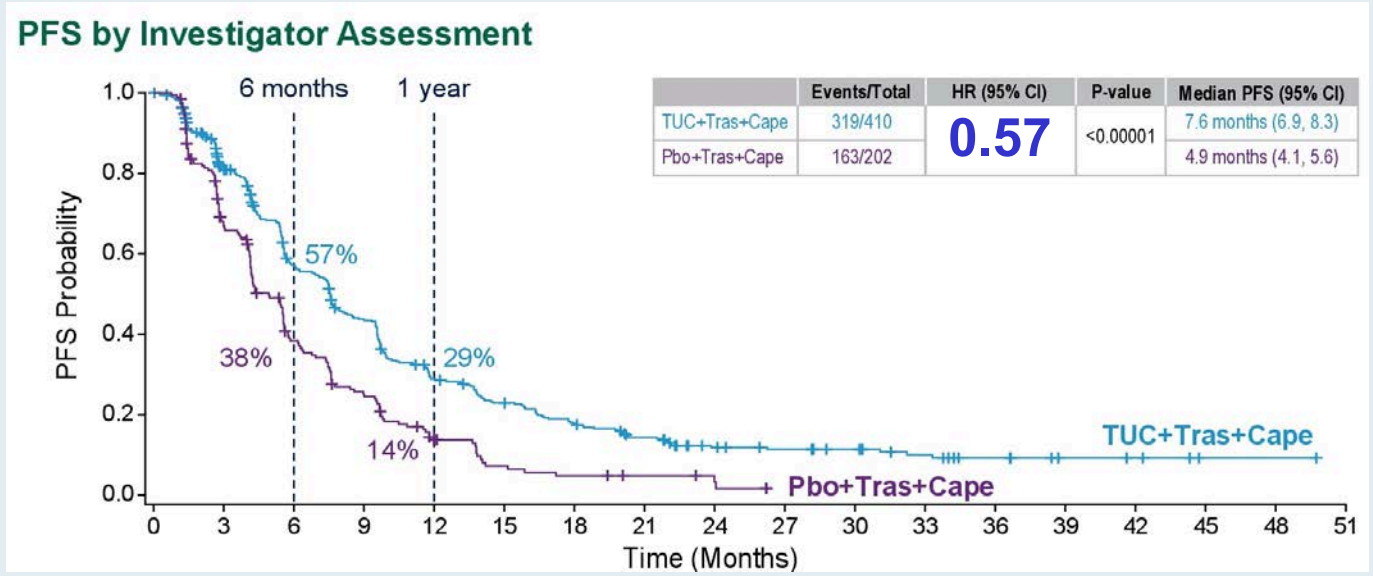
- THP is a very active regimen in ER-/HER2+ breast cancer
- Likley means we can omit carboplatin in many such patients but might need more data
- Can some patients get 'only' HP? Not clear yet.

Updated Results of Tucatinib versus Placebo Added to Trastuzumab and Capecitabine for Patients with Pretreated HER2+ Metastatic Breast Cancer with and Without Brain Metastases (HER2CLIMB)

Curigliano G et al.
ASCO 2021;Abstract 1043.

Updated HER2CLIMB Survival Analyses Two Years After the Last Patient Randomized





Curigliano G et al. ASCO 2021;Abstract 1043.

RTP RESEARCH TO PRACTICE

Trastuzumab Deruxtecan (T-DXd) in Patients with HER2+ Metastatic Breast Cancer with Brain Metastases: A Subgroup Analysis of the DESTINY-Breast01 Trial

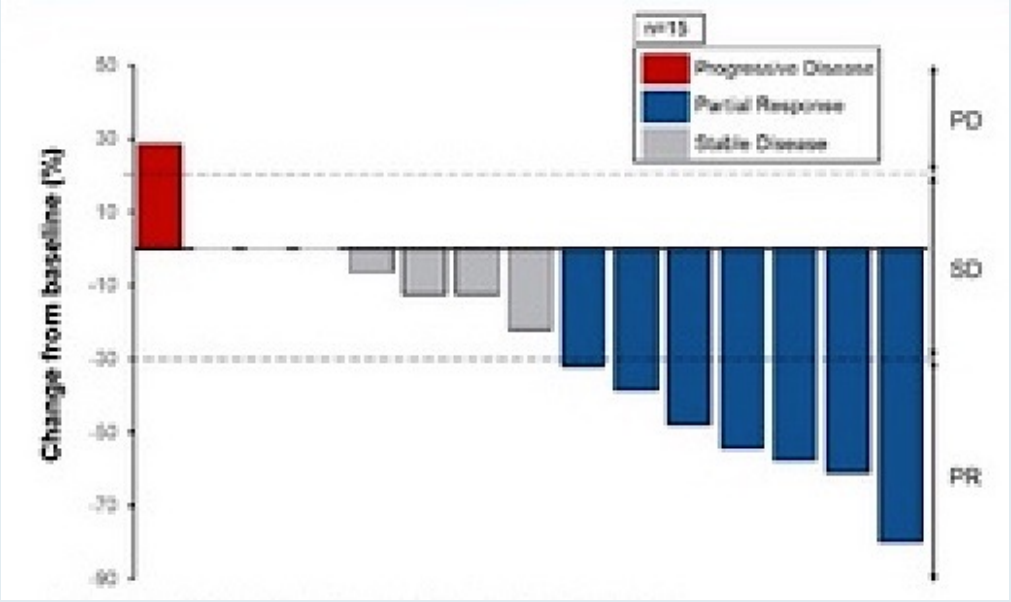
Jerusalem GHM et al.

ASCO 2021;Abstract 526.

DESTINY-Breast01: Clinical Activity Outcomes of Trastuzumab Deruxtecan

Endpoint	CNS Subgroup (n = 24)	All Patients (N = 184)
Confirmed ORR	58.3%	60.9%
Duration of response	16.9 mo	14.8 mo
Progression-free survival	18.1 mo	16.4 mo

Best Response in Brain Lesions in the CNS Subroup



Jerusalem GHM et al. ASCO 2021;Abstract 526.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Patt: A 73-year-old woman with ER-negative, HER2-positive metastatic breast cancer (mBC) and brain metastases
- Dr Martins: A frail 58-year-old woman with metastatic triple-positive BC and a germline CHEK2 mutation
- Dr Jasani: A 55-year-old woman with a 4.5-cm ER-positive, HER2-positive localized breast cancer

Module 2: Highlights of ASCO 2021 – Drs Borges and Burstein

Module 3: Cases from the Community

- Dr Levin: A 48-year-old woman with metastatic triple-negative breast cancer (TNBC)
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- Dr Patt: A 52-year-old woman with ER-positive, HER2-negative BC
- Dr Kodali: A 62-year-old woman with ER-positive mBC and a PIK3CA mutation

Module 4: Highlights of ASCO 2021 – Drs Borges and Burstein

A 35-year-old woman with triple-negative breast cancer (TNBC) receives neoadjuvant anthracycline/taxane therapy followed by surgery and capecitabine but 1 year later develops PD-L1-negative, BRCA-negative metastatic disease. What would be your next treatment?

- Chemotherapy
- Chemotherapy + anti-PD-1/PD-L1 antibody
- Sacituzumab govitecan
- Other (please specify)

Case Presentation – Dr Levin: A 48-year-old woman with metastatic TNBC

Dr Pavel Levin

- Stage IIIC right, inflammatory TNBC with extensive skin involvement, Ki-67: 90%
- Dose-dense AC x 4 → Carboplatin/paclitaxel x 4 → Modified mastectomy and ALND, with residual disease
- Adjuvant RT → Capecitabine, with rising tumor markers
- PET: Subcutaneous nodules throughout her body, no visceral disease
- Testing: PD-L1: 8%, BRCA1 SUV
- Nab-paclitaxel/atezolizumab, without response → Carboplatin/gemcitabine, with brief response
- 11/2020: Sacituzumab govitecan, with response and well tolerated

Questions

- At what point would you introduce sacituzumab govitecan into the management of metastatic TNBC?

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, to which of the following patients with breast cancer and a BRCA germline mutation would you offer adjuvant olaparib?

- A patient with TNBC and residual disease after neoadjuvant therapy
- A patient with ER-positive, HER2-negative, node-negative breast cancer and a high Recurrence Score
- Both
- Neither

Regulatory and reimbursement issues aside, to which of the following patients with ER-positive, HER2-negative breast cancer and 2 positive nodes would you offer adjuvant olaparib?

- A patient with a somatic BRCA mutation
- A patient with a PALB2 mutation
- Both
- Neither

Case Presentation – Dr Kodali: A 40-year-old woman with left-sided, node-positive TNBC and a germline BRCA1 mutation

Dr Dhatri Kodali

- Diagnosed with a 7-cm left-sided, node-positive (N3) TNBC
- Germline BRCA1 mutation

Questions

- What is the role of platinum agents in the neoadjuvant setting?
- What is the role of PD-L1 in the neoadjuvant setting?
- What the role of PARP inhibitors? After neoadjuvant therapy and surgery, should I be considering adjuvant olaparib?

A premenopausal woman presents with a 2.1-cm, Grade II, ER/PR-positive, HER2-negative infiltrating ductal carcinoma (IDC) with 2 positive sentinel lymph nodes. Would you order a genomic assay for this patient?

- No
- Yes, the 21-gene assay
- Yes, the 70-gene signature
- Yes, Prosigna PAM50
- Yes, Breast Cancer Index
- Yes, other

Which adjuvant therapy would you generally recommend for a 65-year-old postmenopausal woman with a 2.1-cm, Grade II, ER/PR-positive, HER2-negative IDC with 2 positive sentinel nodes and a 21-gene Recurrence Score® of 10?

- Tamoxifen
- Aromatase inhibitor (AI)
- AI + abemaciclib
- Chemotherapy → endocrine therapy
- Chemotherapy → AI + abemaciclib
- Other (please specify)

Case Presentation – Dr Patt: A 52-year-old woman with ER-positive, HER2-negative breast cancer

Dr Debra Patt

- Self palpated a left breast mass about a year ago in her periareolar nipple region
  - Mammogram one year ago was normal
  - Recent mammogram and ultrasound: Dense breasts and a 5 mm lesion just below her left nipple
- Biopsy: Low-grade ER-positive HER-2 negative breast cancer
- Oncotype Dx RS: Low

Questions

- How do you think about risk-reducing strategies in this patient who has — even though it's small and low grade — really a locally more advanced cancer because of the dermal invasion?
- What is the role of radiation therapy?
- What are your thoughts about extended adjuvant endocrine therapy (ie, 10 years) or adding in a CDK4/6 inhibitor, like abemaciclib?

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Case Presentation – Dr Kodali: A 62-year-old woman with ER-positive mBC and a PIK3CA mutation

Dr Dhatri Kodali

- ER-positive breast cancer with metastases to the liver and bone
- Disease progression on prior CDK4/6 inhibitor therapy
- Alpelisib with great response noted at 3-month restaging scan
- Blood sugar levels were uncontrolled despite management efforts with metformin, pioglitazone agents, and insulin; significant weight loss
- Alpelisib discontinued; capecitabine initiated

Question

- What supportive care and hypoglycemic measures do you administer for patients receiving PI3-kinase inhibitors?

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Cases from the Community

- Dr Patt: A 73-year-old woman with ER-negative, HER2-positive metastatic breast cancer (mBC) and brain metastases
- Dr Martins: A frail 58-year-old woman with metastatic triple-positive BC and a germline CHEK2 mutation
- Dr Jasani: A 55-year-old woman with a 4.5-cm ER-positive, HER2-positive localized breast cancer

Module 2: Highlights of ASCO 2021 – Drs Borges and Burstein

Module 3: Cases from the Community

- Dr Levin: A 48-year-old woman with metastatic triple-negative breast cancer (TNBC)
- Dr Kodali: A 40-year-old woman with left-sided, node-positive TNBC and a germline BRCA1 mutation
- Dr Patt: A 52-year-old woman with ER-positive, HER2-negative BC
- Dr Kodali: A 62-year-old woman with ER-positive mBC and a PIK3CA mutation

Module 4: Highlights of ASCO 2021 – Drs Borges and Burstein

RTP RESEARCH TO PRACTICE

Tutt A et al. OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. ASCO 2021;Abstract LBA1.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Patients with stage 2/3, HER2-negative breast cancers who have BRCA1/2 mutations

2. What are the key findings that are most relevant to patients in these clinical situations?

- Improvement in 3-year DFS (77% → 86%) and trend to improved OS.
- Treatment with acceptable toxicity

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Adjuvant olaparib is std for such cancers
- Women potentially as candidates warrant genetic testing
- Research Qs: lower risk patients; related mutations (such as PALB2), substitute for regular chemo? Will there be any increase in 2nd cancers in long run?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Litton K et al. Neoadjuvant talazoparib in patients with germline BRCA1/2 (gBRCA1/2) mutation-positive, early HER2-negative breast cancer (BC): Results of a phase 2 study. ASCO 2021;Abstract 505.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Women with TNBC and known BRCA1/2 mutations considering neoadjuvant therapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- Single agent talazoparib achieves pCR in 45 to 50%
- Probably lower pCR rate than std chemotherapy regimens (65+%) for similar patients

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Could this be a substitute for std chemo in the future?
- Are pCRs with talazoparib the ‘same’ as those with chemo in longer term outcomes

Loibl S et al. Durvalumab improves long-term outcome in TNBC: results from the phase II randomized GeparNUEVO study investigating neodjuvant durvalumab in addition to an anthracycline/taxane based neoadjuvant chemotherapy in early triple-negative breast cancer (TNBC). ASCO 2021; Abstract 506.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Women with TNBC considering neoadjuvant therapy

2. What are the key findings that are most relevant to patients in these clinical situations?

- Adding PDL1 targeting with durvalumab improves pCR and now with longer follow-up shows improvement in DFS and OS
- pCR after chemo did less well than pCR after chemo + IO

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Likely sets stage for FDA approval of related but different agent, pembrolizumab, in treatment of similar patients with chemotherapy
- Research questions: is adjuvant therapy with IO needed? Are all pCRs the same, or not?

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Emans LA et al. The tumor microenvironment (TME) and atezolizumab + nab-paclitaxel (A+nP) activity in metastatic triple-negative breast cancer (mTNBC): IMpassion130. ASCO 2021;Abstract 1006.

Dr Virginia Borges

1. For which clinical situations is this data clinically relevant?

- The data in this presentation is relevant for patient with metastatic triple negative breast cancer eligible for immunotherapy as part of their first line therapy in the metastatic setting.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The Impassion130 study previously showed the benefit of anti-PDL1 therapy with atezolizumab with nab-paclitaxel and that the benefit was most in patients with PDL1+ tumors with the presence of tumor-infiltrating immune cells [IC+]
- This study explores the immune subsets within the TNBC subsets for identifying groups with better benefit from IO therapy.
- PFS and OS was highest in the immune inflamed, followed by immune excluded phenotypes. The TNBC subsets of BLIA, and BLIS as well as tumors with increased proliferative /DNA repair pathways also had highest benefit.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Increased understanding of the genomic subtypes and the influence of the immune response and tumor:host environment within the tumor are providing deeper insights into how available treatments work or fail to work. These data emphasize the importance of supporting tissue collections and biopsies on clinical trials to move the field ahead for the betterment of our patients.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Chen L et al. Combination of famitinib with camrelizumab plus nab-paclitaxel as first-line treatment for patients with immunomodulatory advanced triple-negative breast cancer (FUTURE-C-PLUS): A prospective, single-arm, phase 2 study. ASCO 2021;Abstract 1007.

Dr Virginia Borges

1. For which clinical situations is this data clinically relevant?

- Patients with metastatic triple negative breast cancer with more than 10% CD8+ immune cell infiltrate by IHC, that have not received prior therapy in the metastatic setting and at least 6 months since (neo)adjuvant treatment.

2. What are the key findings that are most relevant to patients in these clinical situations?

- The data presented are a phase II triplet combination of the anti-VEGFR-2, PDGFR and c-kit TKI famitinib, the anti-PD-1 antibody camrelizumab and nab-paclitaxel for IM subtype of TNBC.
- ORR was 81% with 10% CR; Median progression free survival has not yet been reached and is 53.5% at 10-month follow up.
- Durable responses are reported and expected manageable toxicities.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Increasing understanding of subtyping of TNBC and selected therapy tailored to the subtypes [ie IO for IM subtype] will enhance benefit to appropriate patients and spare toxicity and absence of benefit in patients whose treatment should be directed elsewhere. Encouraging TNBC patients to enroll on clinical trials is of high importance to ultimately advance our standards of care.

Mamounas EP et al. Breast Cancer Index (BCI) and prediction of benefit from extended aromatase inhibitor (AI) therapy (tx) in HR+ breast cancer: NRG oncology/NSABP B-42. ASCO 2021;Abstract 501.

Dr Harold Burstein

1. For which clinical situations is this data clinically relevant?

- Postmenopausal women with ER+ breast cancer, finishing 5 years of endocrine therapy and considering extended duration treatment

2. What are the key findings that are most relevant to patients in these clinical situations?

- Neither BCI (nor Mammaprint, in related abstract) identified tumors that particularly benefit from extended endocrine therapy, or not

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- Clinical decision on extended therapy remains based on patient preferences and anatomic stage
- Still searching for marker to identify those who do / do not warrant ongoing treatment

Cristofanilli M et al. Overall survival (OS) with palbociclib (PAL) + fulvestrant (FUL) in women with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced breast cancer (ABC): Updated analyses from PALOMA-3. ASCO 2021;Abstract 1000.

Dr Virginia Borges

1. For which clinical situations is this data clinically relevant?

- This presentation is relevant to people with metastatic breast cancer that is ER positive, HER2-negative and had previously progressed on endocrine therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- With longer follow-up, the difference in mean overall survival continues to show an ~7-month improvement for the combination arm and excellent safety.
- Long term overall survival at >5 years is improved when palbociclib is added to fulvestrant [23.3% versus 16.8%] with the effect greatest in patients without prior chemo in the metastatic setting.
- Sub analysis of ESR1, p53, and PI3KCA mutations show they negatively influence prognosis/OS though benefit to addition of palbociclib is seen.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- The longer follow up confirms the importance of adding palbociclib to anti-endocrine therapy in the early lines of treatment for metastatic ER positive Her 2 negative breast cancer.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Slamon DJ et al. Updated overall survival (OS) results from the phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2- advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). ASCO 2021;Abstract 1001.

Dr Virginia Borges

1. For which clinical situations is this data clinically relevant?

- This presentation is relevant to men and postmenopausal women and with hormone receptor positive, HER2-negative advanced breast cancer who had previously received no more than 1 prior line of anti-endocrine therapy.

2. What are the key findings that are most relevant to patients in these clinical situations?

- Extended follow up shows significantly improved median OS of 53.7 versus 41.5 months, with 5 year OS 46% versus 31% significantly improved by the addition of ribociclib to fulvestrant.
- The magnitude of benefit is greatest for patients treated in the first line setting.
- The need to initiate chemotherapy as subsequent treatment was delays by 20 months for the combination and even after progression, the time to next progression was delayed for combination recipients.

3. What is the relevance of this data to clinical research for patients in these clinical settings?

- First line use of ribociclib with fulvestrant in HR positive/HER2-negative men and postmenopausal women prolongs median OS by a year and remains well tolerated with longer follow up. It also appears to offer prolonged benefit beyond progression regardless of next treatment type and delay onset to needing chemotherapy.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

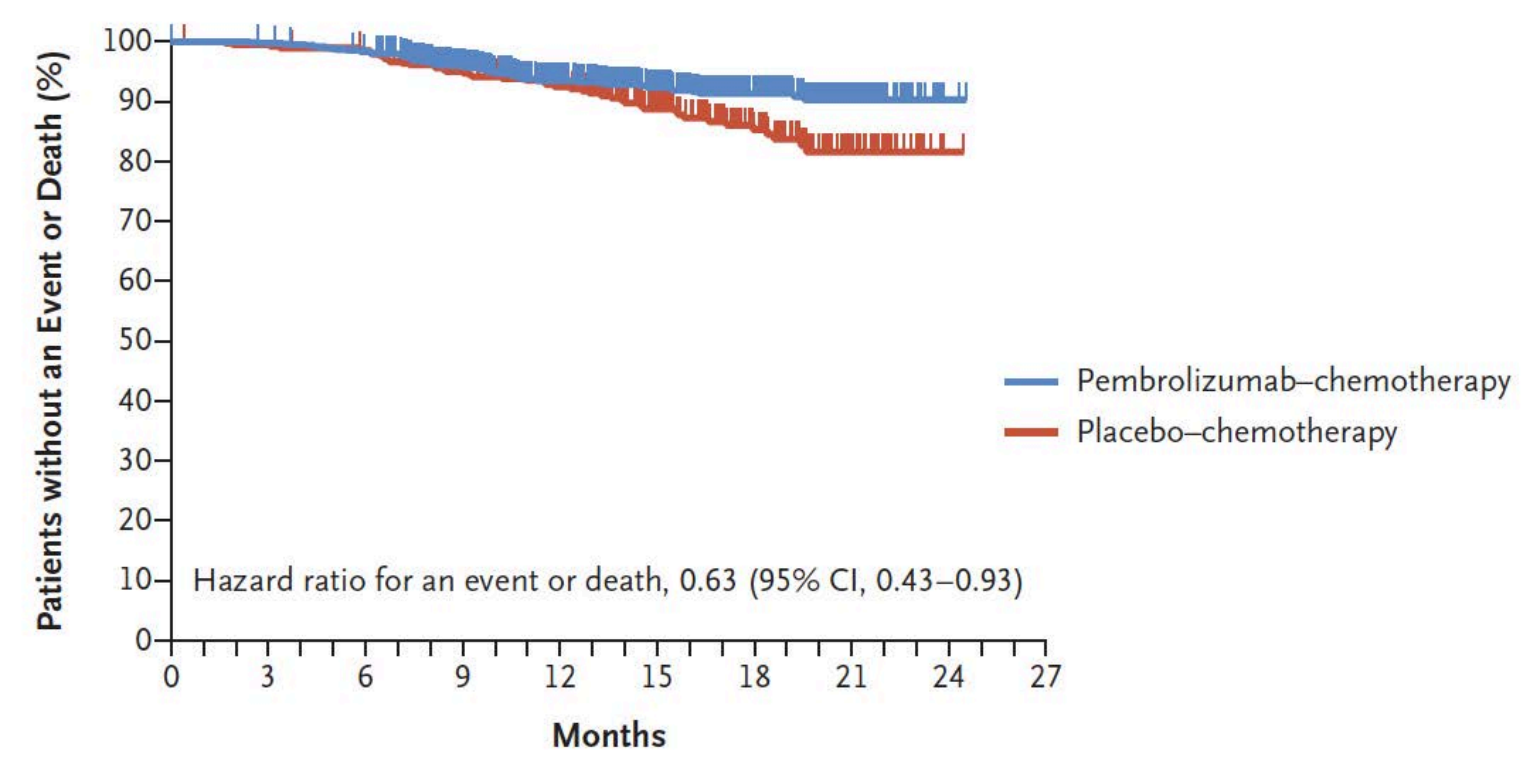
Pembrolizumab for Early Triple-Negative Breast Cancer

P. Schmid, J. Cortes, L. Pusztai, H. McArthur, S. Kümmel, J. Bergh, C. Denkert, Y.H. Park, R. Hui, N. Harbeck, M. Takahashi, T. Foukakis, P.A. Fasching, F. Cardoso, M. Untch, L. Jia, V. Karantza, J. Zhao, G. Aktan, R. Dent, and J. O'Shaughnessy, for the KEYNOTE-522 Investigators*

N Engl J Med 2020;382(9):810-21.

KEYNOTE-522 Primary Endpoints: pCR and EFS

Variable	Pembrolizumab + chemotherapy	Placebo + chemotherapy	Estimated Tx difference	*p*-value
Pathological stage ypT0/Tis ypN0	64.8%	51.2%	13.6%	< 0.001
Pathological stage ypT0 ypN0	59.9%	45.3%	14.5%	
Pathological stage ypT0/Tis	68.6%	53.7%	14.8%	



Schmid P et al. *N Engl J Med* 2020;382(9):810-21.

Outcomes in Patients (pts) Aged ≥65 Years in the Phase 3 ASCENT Study of Sacituzumab Govitecan (SG) in Metastatic Triple-Negative Breast Cancer (mTNBC)

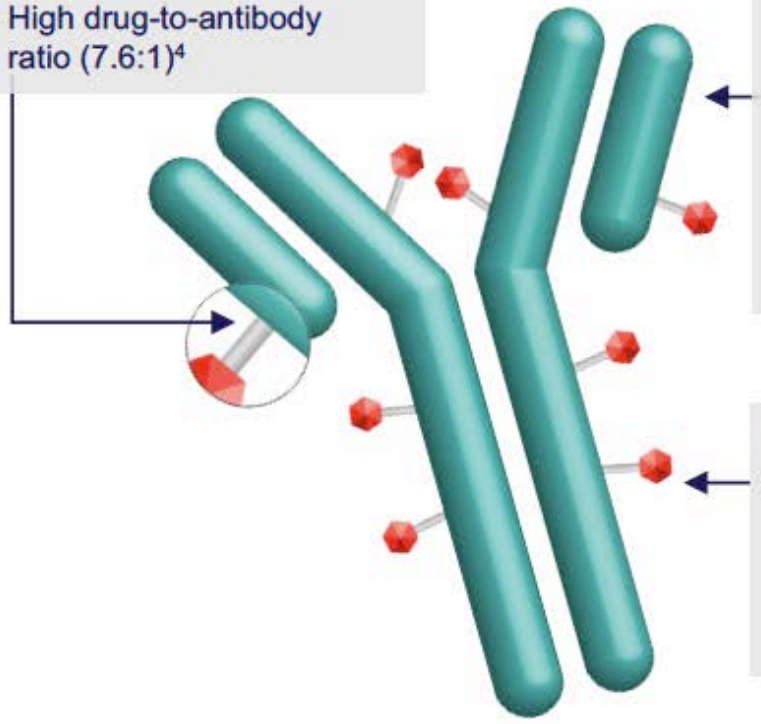
Kalinsky K et al.

ASCO 2021;Abstract 1011.

Sacituzumab Govitecan (SG) Is a First-in-Class Trop-2–Directed ADC

- SG is distinct from other ADCs[1-4]
  - Antibody highly specific for Trop-2
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and enzymatic cleavage by tumor cell not required for SN-38 liberation from antibody
  - Hydrolysis of the linker also releases SN-38 extracellularly in the tumor microenvironment (bystander effect)
- Granted FDA accelerated approval for mTNBC[5]
- Landmark ASCENT study demonstrated a significant survival improvement of SG over chemotherapy, with a tolerable safety profile in pretreated mTNBC[6]
  - Median PFS of 5.6 vs 1.7 months (HR 0.41, *P*<0.0001)
  - Median OS of 12.1 vs 6.7 months (HR 0.48, *P*<0.0001)

Linker for SN-38
- Hydrolyzable linker for payload release
- High drug-to-antibody ratio (7.6:1)[4]



Humanized anti–Trop-2 antibody
- Directed toward Trop-2, an epithelial antigen expressed on many solid cancers

SN-38 payload
- SN-38 more potent than parent compound, irinotecan

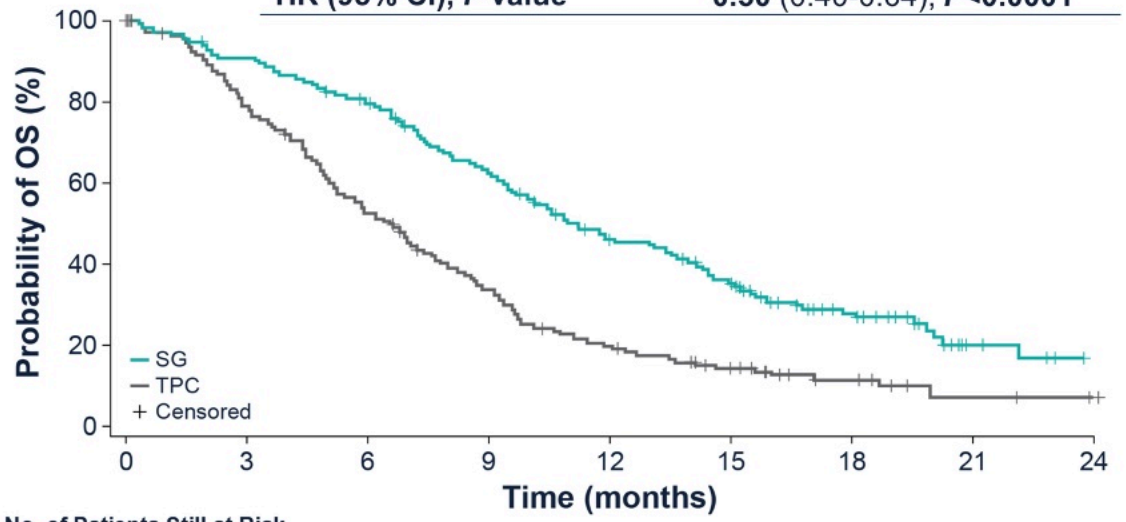
ADC, antibody-drug conjugate; FDA, US Food and Drug Administration; OS, overall survival; PFS, progression-free survival; TNBC, triple-negative breast cancer; Trop-2, trophoblast cell surface antigen 2.

1. Goldenberg DM, et al. *Expert Opin Biol Ther.* 2020;20:871-885. 2. Nagayama A, et al. *Ther Adv Med Oncol.* 2020;12:1758835920915980. 3. Cardillo TM, et al. *Bioconjugate Chem.* 2015;26:919-931. 4. Goldenberg DM, et al. *Oncotarget.* 2015;6:22496-224512. 5. Press Release. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer. Accessed August 26, 2020. 6. Bardia A, et al. ESMO 2020. Abstract LBA17.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

ASCENT: Overall Survival in Young and Older Patients with mTNBC Treated with Sacituzumab Govitecan

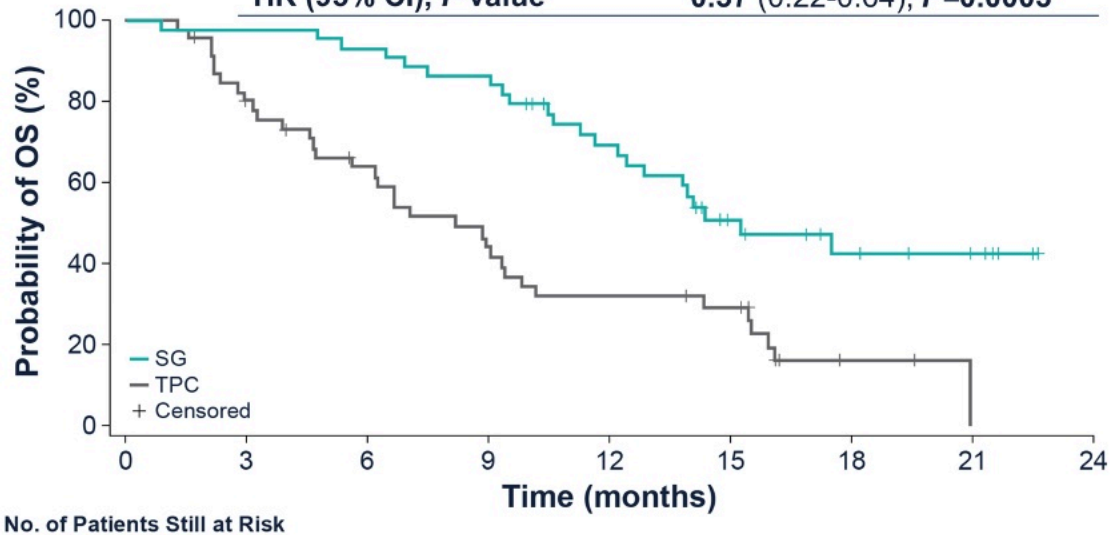
	<65 y	
	SG (n=191)	TPC (n=187)
No. of events	133	150
Median OS—mo (95% CI)	11.2 (9.9-13.4)	6.6 (5.3-7.4)
HR (95% CI), *P* value	**0.50** (0.40-0.64), ***P*<0.0001**	



No. of Patients Still at Risk

SG	191	185	177	171	163	155	149	135	123	115	102	89	80	77	68	56	40	32	28	22	14	7	6	1	0
TPC	187	168	157	138	125	106	91	77	66	56	42	37	32	28	25	19	14	11	9	5	3	3	3	2	1

	≥65 y	
	SG (n=44)	TPC (n=46)
No. of events	22	35
Median OS—mo (95% CI)	15.3 (12.4-NE)	8.2 (5.6-9.8)
HR (95% CI), *P* value	**0.37** (0.22-0.64), ***P*=0.0003**	



No. of Patients Still at Risk

SG	44	43	43	43	43	42	41	39	38	38	33	29	27	24	22	14	12	11	9	8	7	6	2	0
TPC	46	46	43	35	31	28	26	22	21	18	14	13	13	13	12	11	6	3	2	2	1	0	0	0

- In patients aged ≥65 years, improvement in median OS with SG vs TPC treatment was comparable with that of the overall population (12.1 vs 6.7 months)[1]

Kalinsky K et al. ASCO 2021;Abstract 1011.

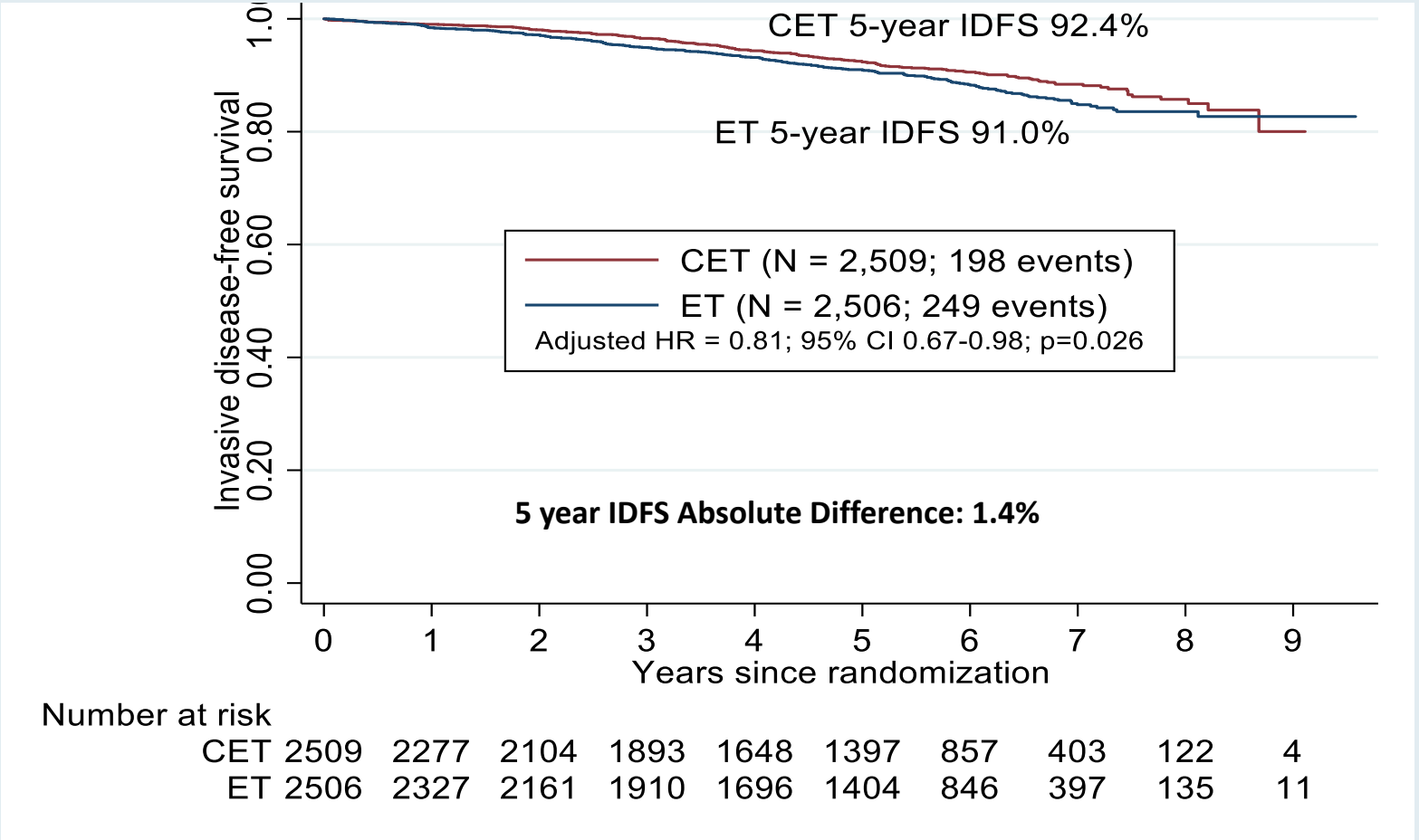
RTP RESEARCH TO PRACTICE

First Results from a Phase III Randomized Clinical Trial of Standard Adjuvant Endocrine Therapy (ET) +/- Chemotherapy (CT) in Patients (pts) with 1-3 Positive Nodes, Hormone Receptor-Positive (HR+) and HER2-Negative (HER2-) Breast Cancer (BC) with Recurrence Score (RS) ≤25: SWOG S1007 (RxPonder)

Kalinsky K et al.

SABCS 2020;Abstract GS3-00.

RxPONDER: Invasive Disease-Free Survival (IDFS) in Overall Population by Treatment Arm



CET = Chemotherapy + Endocrine Therapy; ET = Endocrine Therapy Alone

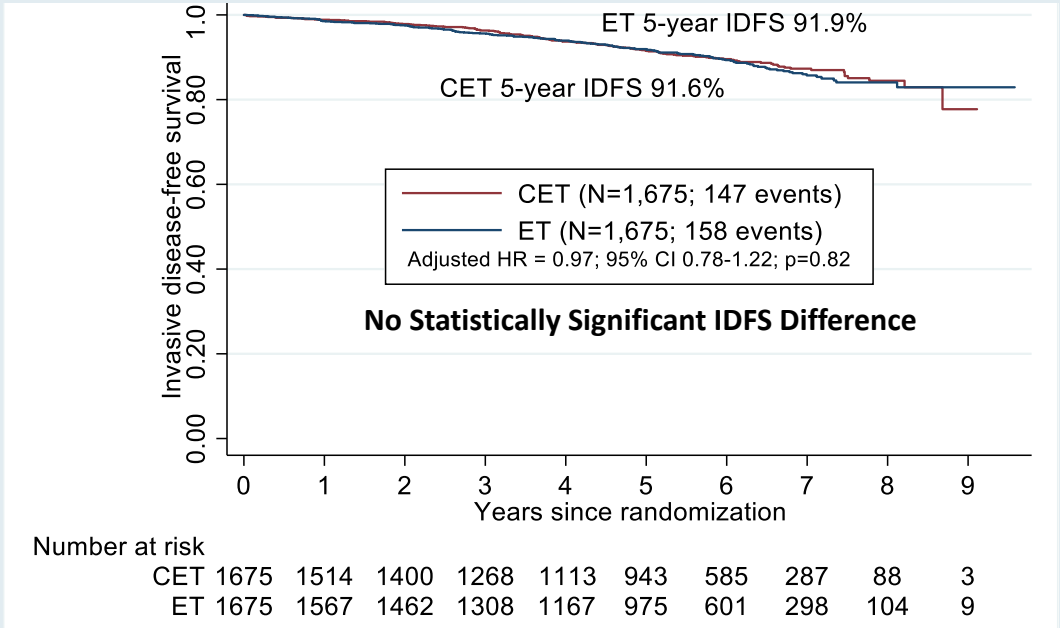
447 observed IDFS events (54% of expected at final analysis) at a median follow-up of 5.1 years

Kalinsky K et al. SABCS 2020;Abstract GS3-00.

RTP RESEARCH TO PRACTICE

RxPONDER: IDFS Stratified by Menopausal Status

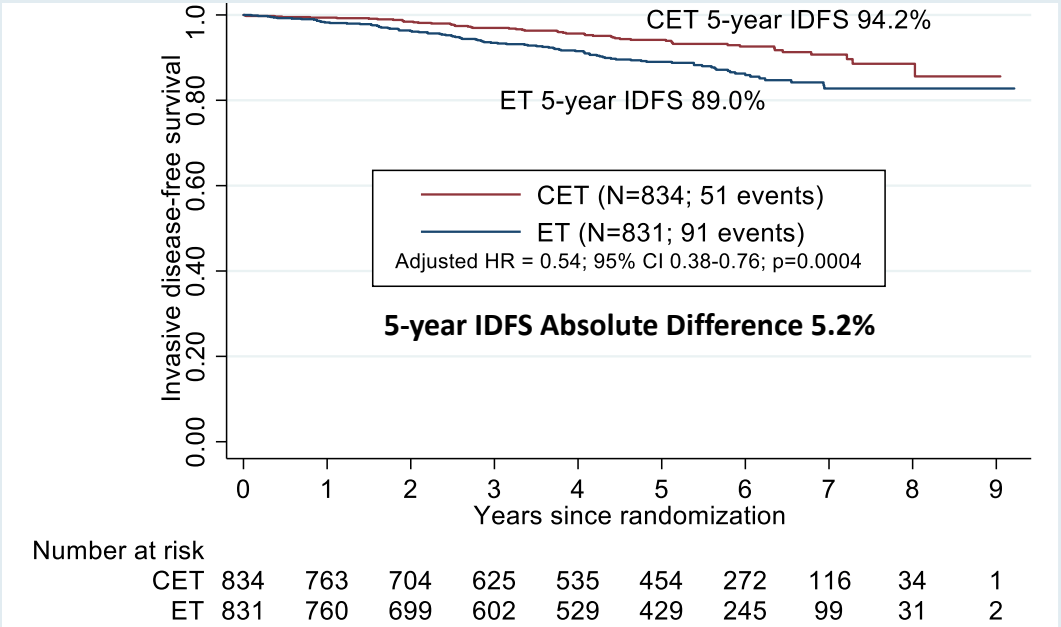
Postmenopausal



IDFS Event	CET	ET	Total (%)
Distant	39	44	83 (27%)
Local-Regional	10	14	24 (8%)
Contralateral	10	9	19 (6%)
Non-Breast Primary	44	47	91 (30%)
Recurrence Not Classified	9	7	16 (5%)
Death not due to Recurrence or Second Primary	35	37	72 (24%)

Absolute Difference in Distant Recurrence as 1st site: 0.3% (2.3% CET vs. 2.6% ET)

Premenopausal



IDFS Event	CET	ET	Total (%)
Distant	26	50	76 (54%)
Local-Regional	8	17	25 (18%)
Contralateral	4	8	12 (8%)
Non-Breast Primary	10	10	20 (14%)
Recurrence Not Classified	1	1	2 (1%)
Death not due to Recurrence or Second Primary	2	5	7 (5%)

Absolute Difference in Distant Recurrence as 1st site: 2.9% (3.1% CET vs. 6.0% ET)

Kalinsky K et al. SABCS 2020;Abstract GS3-00.

RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21:345-57

Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive breast cancer (FAKTION): a multicentre, randomised, controlled, phase 2 trial

Robert H Jones, Angela Casbard*, Margherita Carucci, Catrin Cox, Rachel Butler, Fouad Alchami, Tracie-Ann Madden, Catherine Bale, Pavel Bezecny, Johnathan Joffe, Sarah Moon, Chris Twelves, Ramachandran Venkitaraman, Simon Waters, Andrew Foxley, Sacha J Howell*

FAKTION: Capivasertib + Fulvestrant for AI-Resistant ER-Positive, HER2-Negative mBC

- **Phase II study of capivasertib + fulvestrant vs placebo + fulvestrant (N = 140)**
  - **Relapse or progression on an AI**
  - **Capivasertib (AZD5363): selective, oral AKT inhibitor**
- **Capivasertib + fulvestrant improved PFS in endocrine-resistant mBC vs placebo + fulvestrant**
  - **Primary endpoint met**
  - **Trend toward improvement in OS**
- **Ongoing Phase III CAPitello291 Trial**
- **IPATunit150: ipatasertib +/- palbociclib and fulvestrant**

Outcome	CAP + FULV (n = 69)	PBO + FULV (n = 71)
Median PFS, mos	10.3	4.8
	HR: 0.57 *P* = .0035	
Median OS, mos	26.0	20.0
	HR: 0.59 *P* = .071	

- **Similar benefit was observed in patients with PI3K/AKT/PTEN-activated and nonactivated tumors**
- **39% of patients in the capivasertib + fulvestrant arm required dose reductions, primarily due to diarrhea and rash, and 12% discontinued due to toxicity**

Jones RH et al. *Lancet Oncol* 2020;21:345-57.

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Contributing Oncologists

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas

Debra Patt, MD, PhD, MBA
Executive Vice President, Policy and Strategic Initiatives
Texas Oncology
President, Texas Society of Clinical Oncology
Austin, Texas

Pavel A Levin, MD, PhD
Hematology-Oncology
Texas Oncology-Pearland
Houston, Texas

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Thank you for joining us!

CME, MOC and NCPD credit information will be emailed to each participant in 1 to 2 business days.

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