Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology:

Nontargeted Therapy for Lung Cancer

Tuesday, January 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Matthew Gubens, MD, MS
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

YiR Nontargeted Therapy for Lung Cancer Faculty

Matthew Gubens, MD, MS
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Commercial Support

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Dr Love — Disclosures

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Dr Gubens — Disclosures

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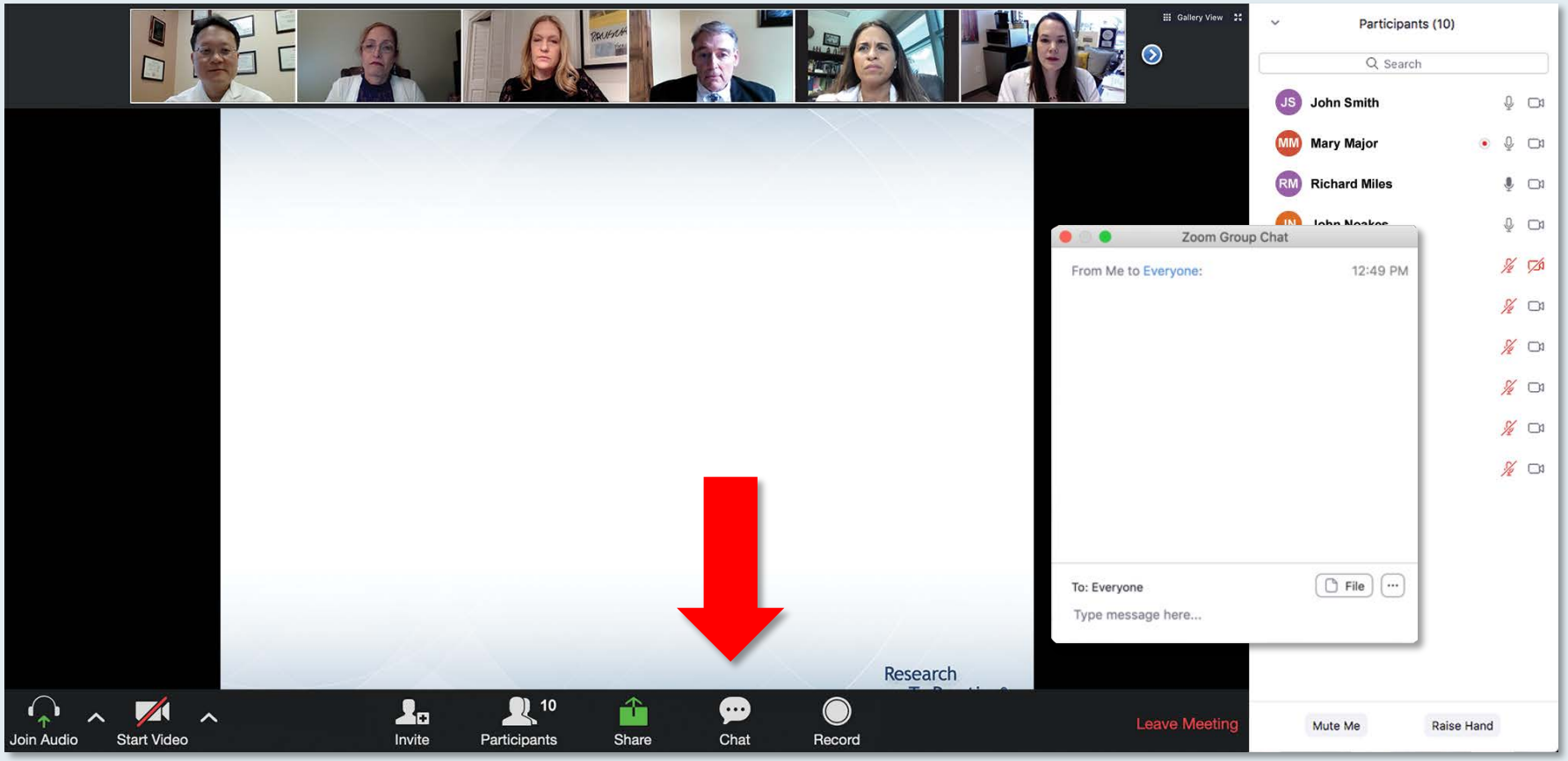
We Encourage Clinicians in Practice to Submit Questions



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Familiarizing Yourself with the Zoom Interface

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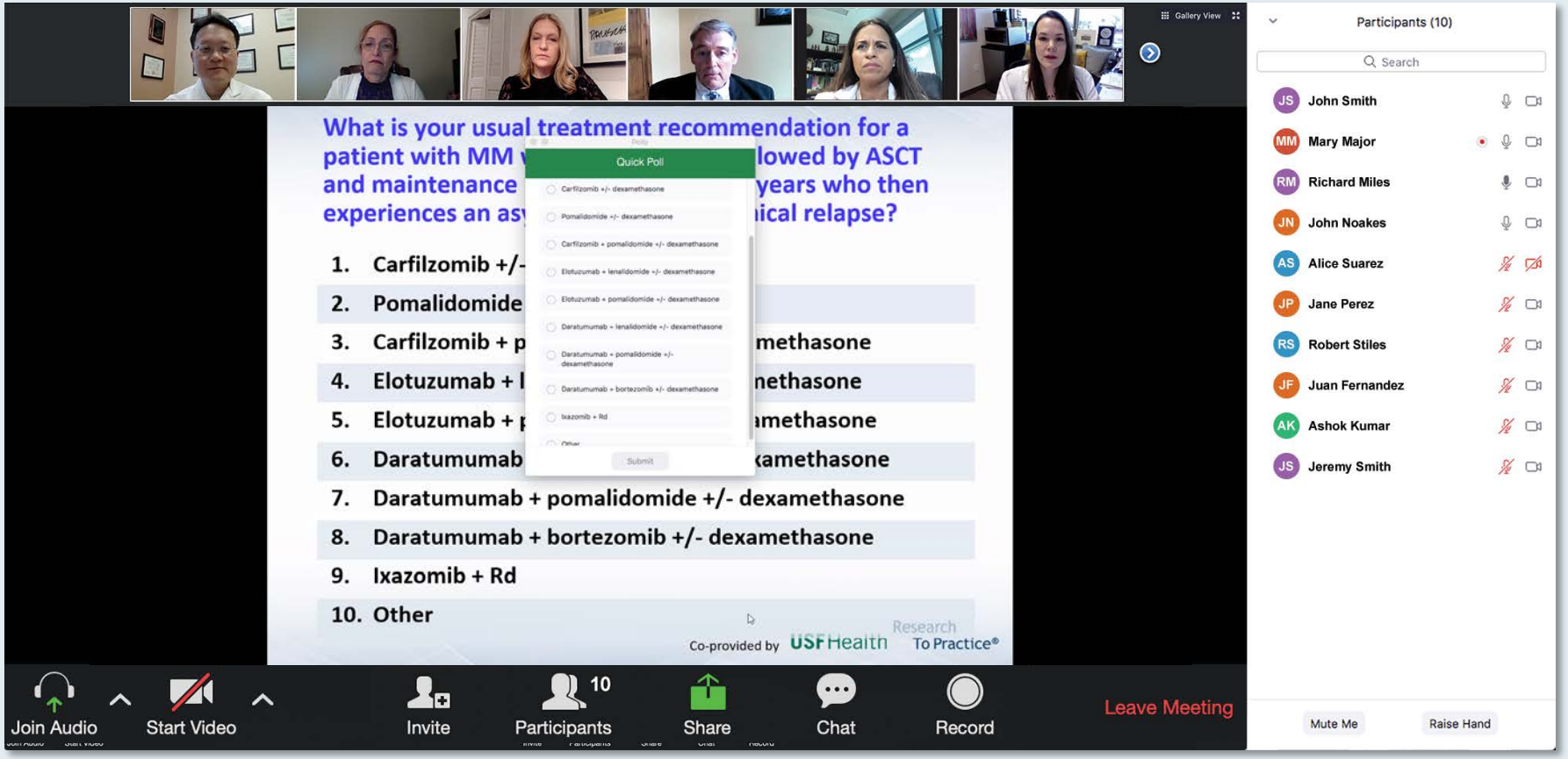

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ONCOLOGY TODAY

WITH DR NEIL LOVE

CURRENT MANAGEMENT OF AND FUTURE DIRECTIONS IN MESOTHELIOMA

DR MARJORIE ZAUDERER

MEMORIAL SLOAN KETTERING CANCER CENTER

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Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 1 — Acute Myeloid Leukemia

Wednesday, January 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Daniel A Pollyea, MD, MS
Eytan M Stein, MD
Andrew H Wei, MBBS, PhD

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Meet The Professor
Management of Ovarian Cancer

Friday, January 22, 2021
1:15 PM – 2:15 PM ET

Faculty

Professor Jonathan A Ledermann, MD

Moderator

Neil Love, MD

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Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Management of HER2-Positive Breast Cancer

Monday, January 25, 2021
5:00 PM – 6:00 PM ET

Faculty

Erika Hamilton, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology:

Targeted Therapy for Lung Cancer

Tuesday, January 26, 2021
5:00 PM – 6:00 PM ET

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Joel W Neal, MD, PhD
Paul K Paik, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Hepatocellular Carcinoma (Part 1 of a 3-Part Series)

Wednesday, January 27, 2021
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Tim Greten, MD
James J Harding, MD
Ahmed Omar Kaseb, MD, CMQ

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RTP RESEARCH TO PRACTICE

Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology:

Multiple Myeloma

Thursday, January 28, 2021
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Rafael Fonseca, MD
Jonathan L Kaufman, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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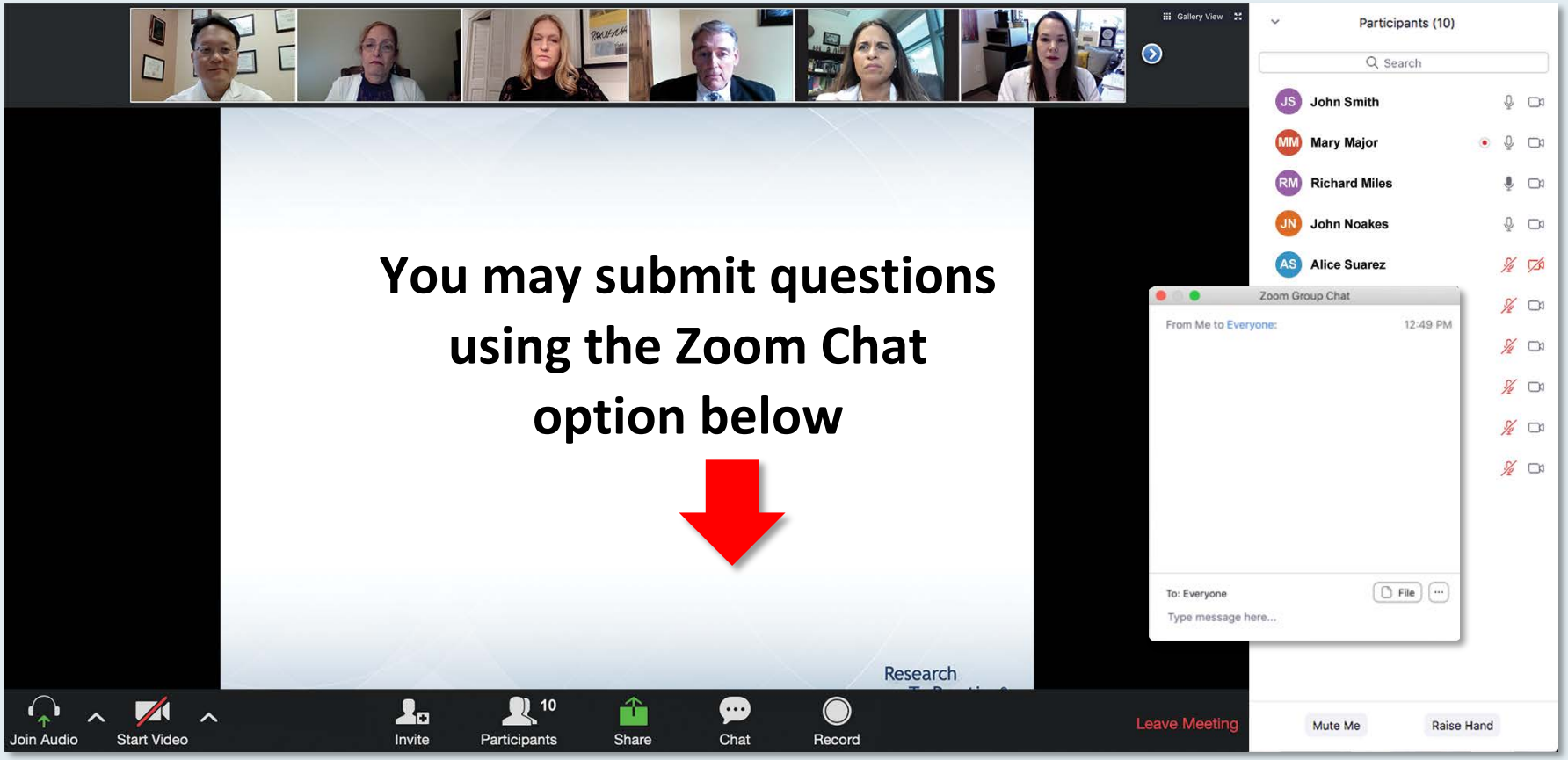

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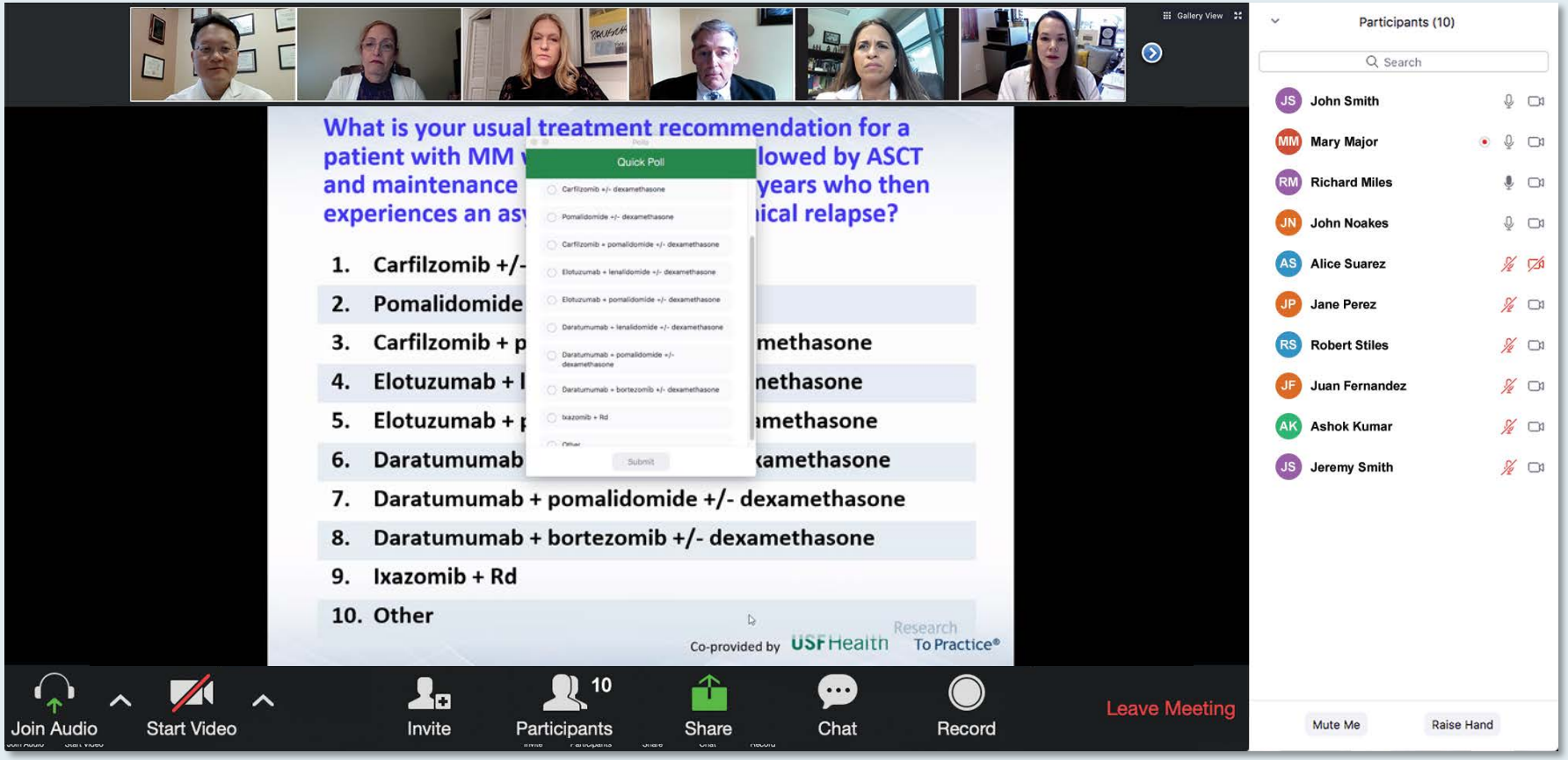

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Agenda

Module 1: Non-Small Cell Lung Cancer

Module 2: Malignant Pleural Mesothelioma

Module 3: Small Cell Lung Cancer

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Module 1: Non-Small Cell Lung Cancer

Module 2: Malignant Pleural Mesothelioma

Module 3: Small Cell Lung Cancer

Module 1: Non-Small Cell Lung Cancer (NSCLC)

- **Key Relevant Data Sets**
  - CheckMate 9LA: Nivolumab + ipilimumab + platinum-doublet chemotherapy
  - CheckMate 227 Part 1: Three-year update
  - KEYNOTE-189: Updated analysis
  - IMpower110: First-line atezolizumab
  - KEYNOTE-024: Five-year overall survival update
  - EMPOWER-Lung 1: Cemiplimab monotherapy vs platinum-doublet chemotherapy
  - PACIFIC: Three-year overall survival with durvalumab

FDA-Approved Immunotherapy Options for the First-Line Treatment of Metastatic NSCLC

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab + Platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.49
Pembrolizumab + Carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.64
Atezolizumab + Carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.78
Atezolizumab + Carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab + Ipilimumab[5]	5/15/20	CheckMate-227	PD-L1 TPS≥1%, EGFR and/or ALK *wt*	0.62
Nivolumab + Ipilimumab and chemotherapy[6]	5/26/20	CheckMate-9LA	EGFR and/or ALK *wt*	0.69
Monotherapy	**FDA approval**	**Pivotal study**	**Histologic type**	**HR (OS)**
Pembrolizumab[7,8]	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS≥1%	0.63
Atezolizumab[9]	5/18/20	IMpower110	PD-L1 TPS≥50%, EGFR and/or ALK *wt*	0.59

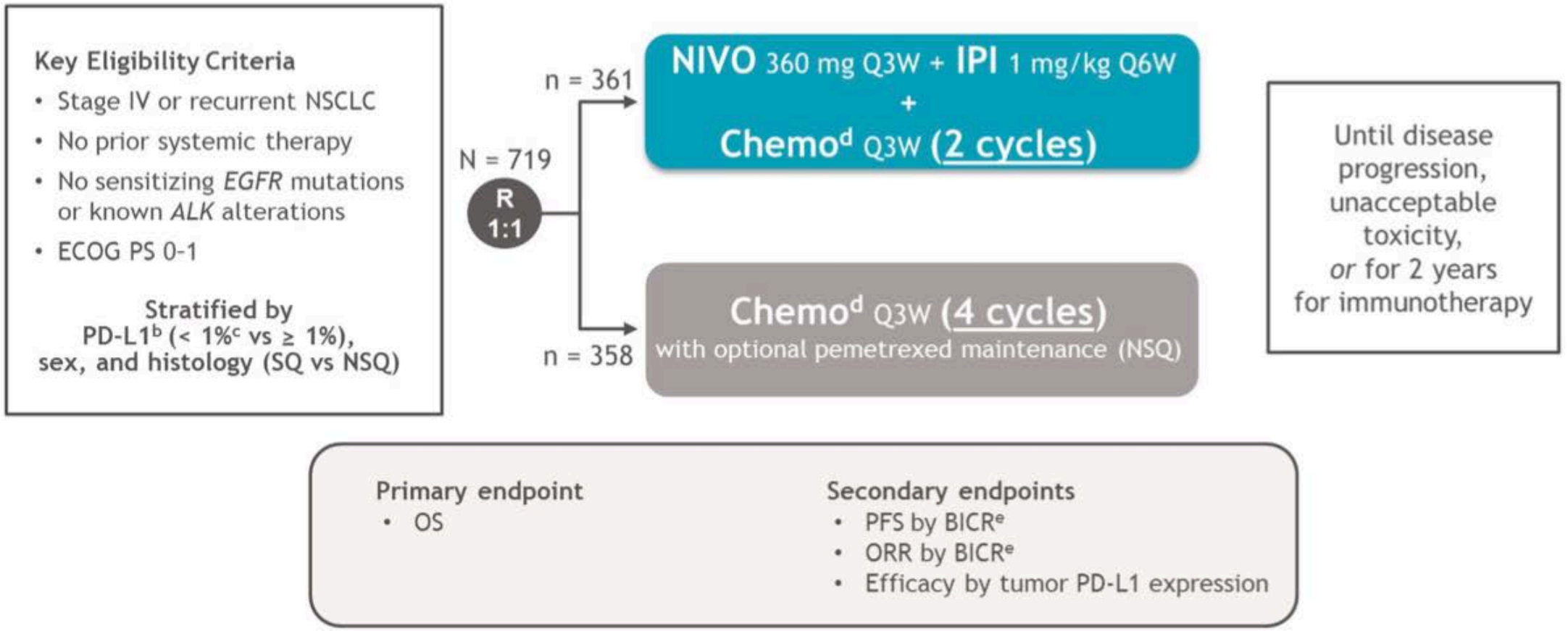
[1] Gandhi L et al. *NEJM* 2018;378(22):2078-92. [2] Paz-Ares L et al. *NEJM* 2018;379(21):2040-51.
[3] Socinski MA et al. *NEJM* 2018;378(24):2288-301. [4] West H et al. *Lancet Oncol* 2019;20(7):924-37.
[5] Hellmann MD et al. *N Engl J Med* 2019;381(21):2020-31. [6] Reck M et al. ASCO 2020;Abstract 9501.
[7] Mok TSK et al. *Lancet* 2019;393(10183):1819-30. [8] Reck M et al. *J Clin Oncol* 2019;37(7):537-46.
[9] Spigel DR et al. ESMO 2019;Abstract LBA78

Selection of First-Line Therapy for Metastatic NSCLC

What is the optimal treatment for a patient with newly diagnosed metastatic NSCLC and the following tumor proportion score (TPS)?

- **PD-L1 TPS of 0%**
- **PD-L1 TPS of 1% to 49%**
- **PD-L1 TPS of 50%**
- **PD-L1 TPS of 95%**

Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA)

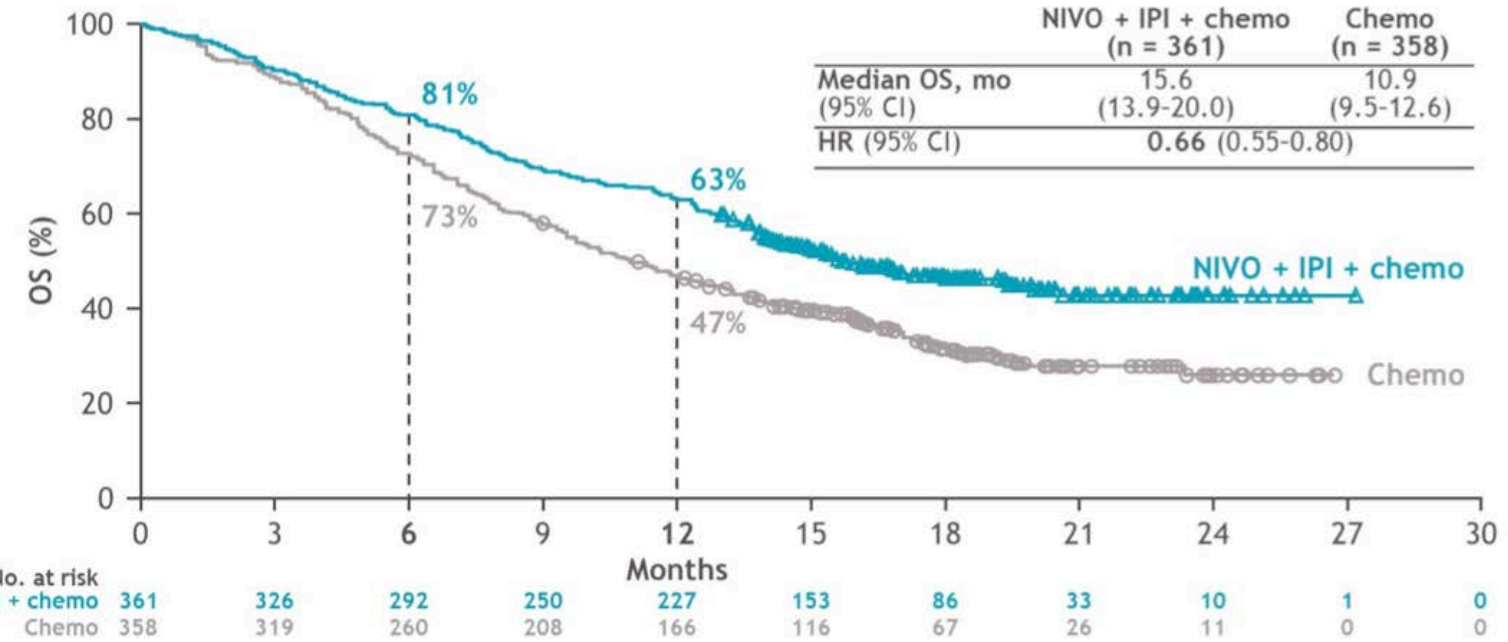


Reck M et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. Proc ASCO 2020; Abstract 9501. Oral, HoD

Courtesy of Matthew Gubens, MD, MS

Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA)

Primary endpoint (updated): Overall survival[a]



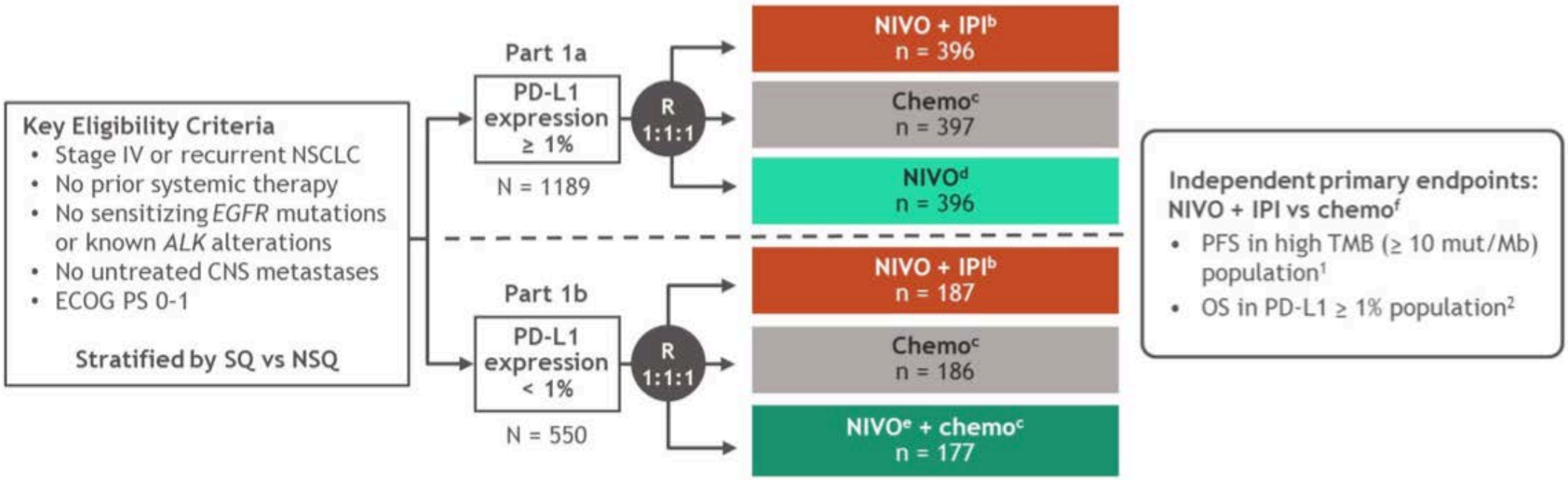
Minimum follow-up: 12.7 months.

[a]Patients remaining in follow-up were censored on the last date they were known to be alive; 47% of patients in the NIVO + IPI + chemo arm and 32% of patients in the chemo arm were censored. Subsequent systemic therapy was received by 31% of patients in the NIVO + IPI + chemo arm and 40% in the chemo arm; subsequent immunotherapy was received by 5% and 30%, and subsequent chemotherapy by 29% and 22%, respectively. Among patients with BICR-confirmed disease progression on study, subsequent systemic therapy was received by 40% in the NIVO + IPI + chemo arm and 44% in the chemo arm; subsequent immunotherapy was received by 7% and 34%, and subsequent chemotherapy by 38% and 24%, respectively

Reck M et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. Proc ASCO 2020; Abstract 9501. Oral, HoD

Courtesy of Matthew Gubens, MD, MS

Nivolumab/ipilimumab (Checkmate 227 3-year OS)

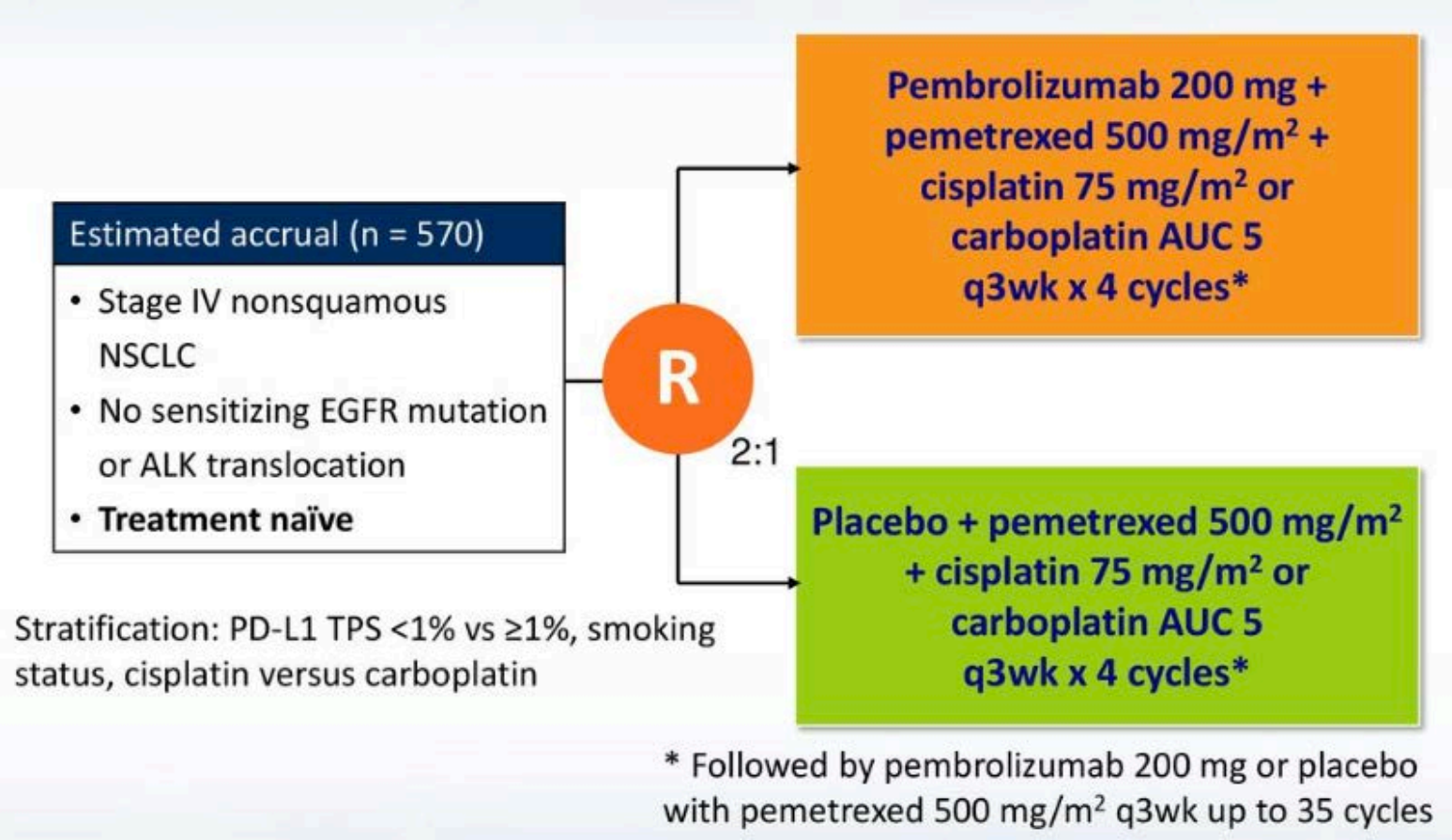


Ramalingam SS et al. Nivolumab + ipilimumab versus platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: Three-year update from CheckMate 227 Part 1. ASCO 2020; Abstract 9500. Oral, HoD

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)

- Median follow-up 23.1 mos



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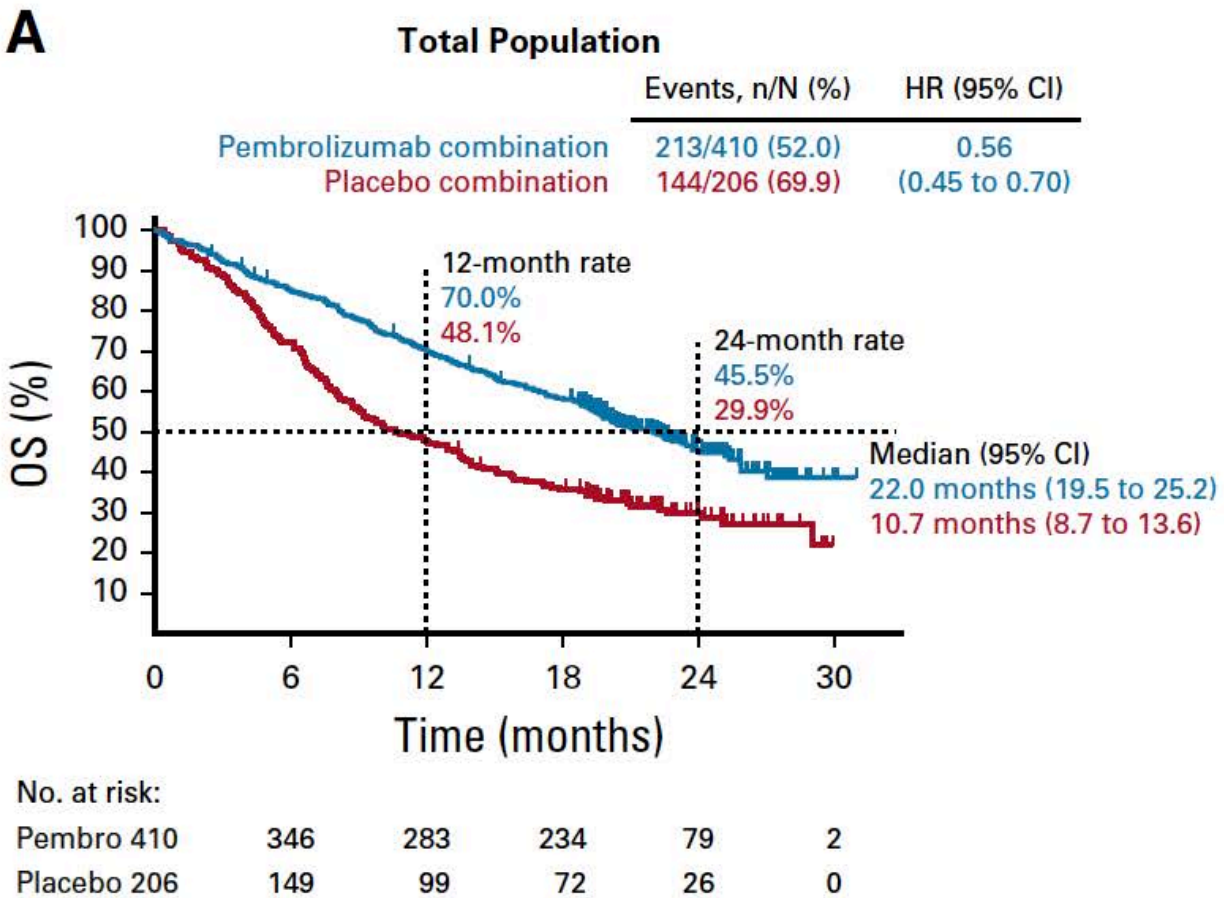
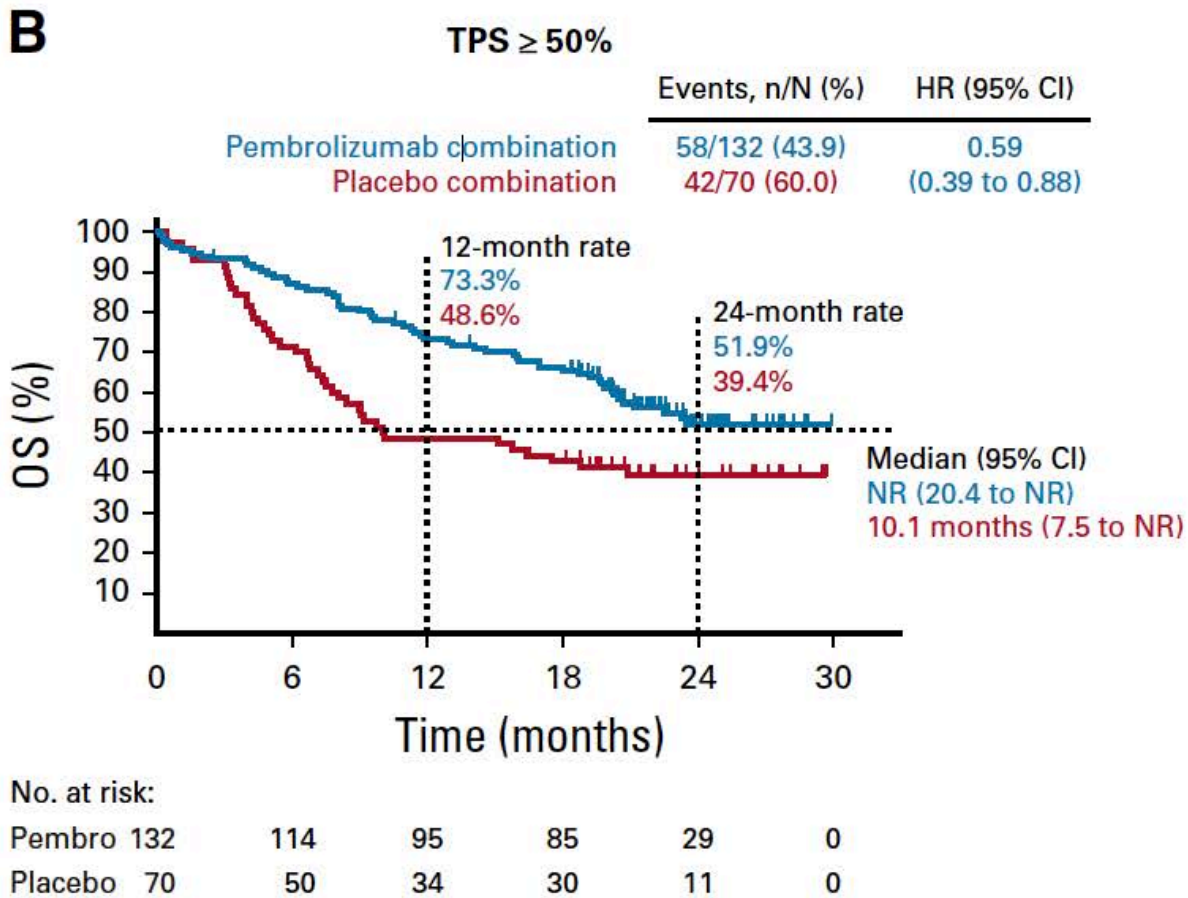
Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)





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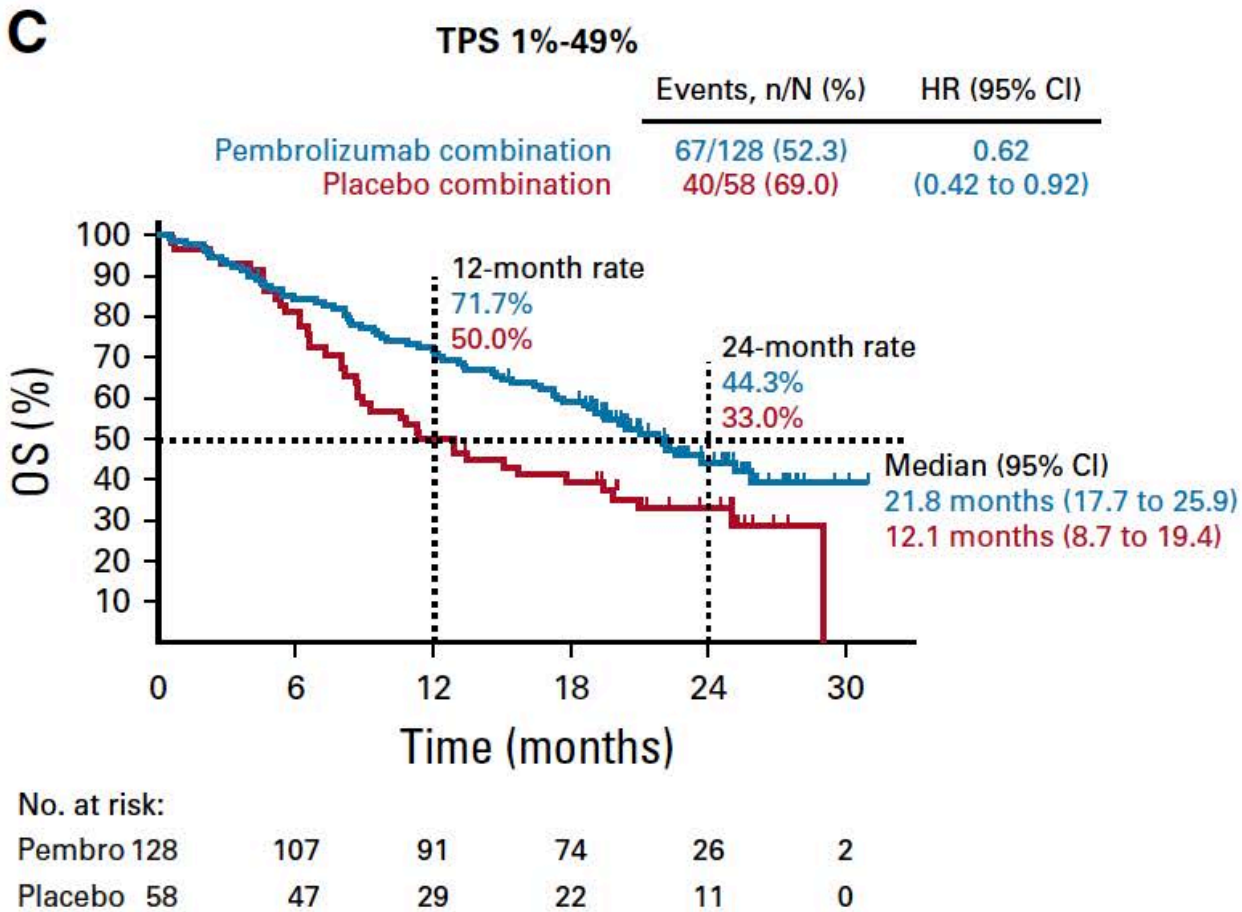
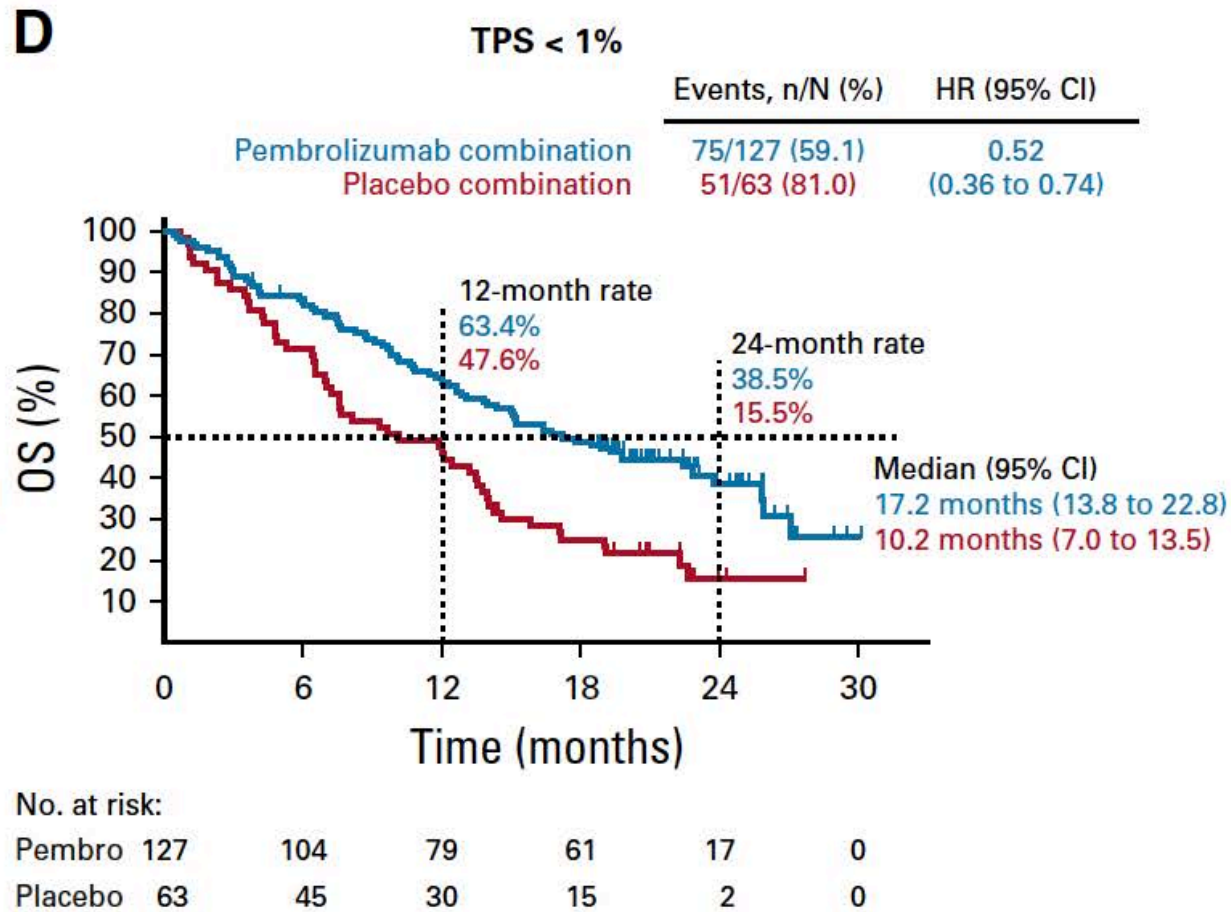




Courtesy of Matthew Gubens, MD, MS

Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)

- Liver metastases
  - OS with liver mets HR 0.62, OS without HR 0.58
- Brain metastases
  - OS with brain mets HR 0.41, OS without 0.59
- Though both show poorer OS overall as expected

- PFS2 analysis also shows clear benefit for pembro in first line

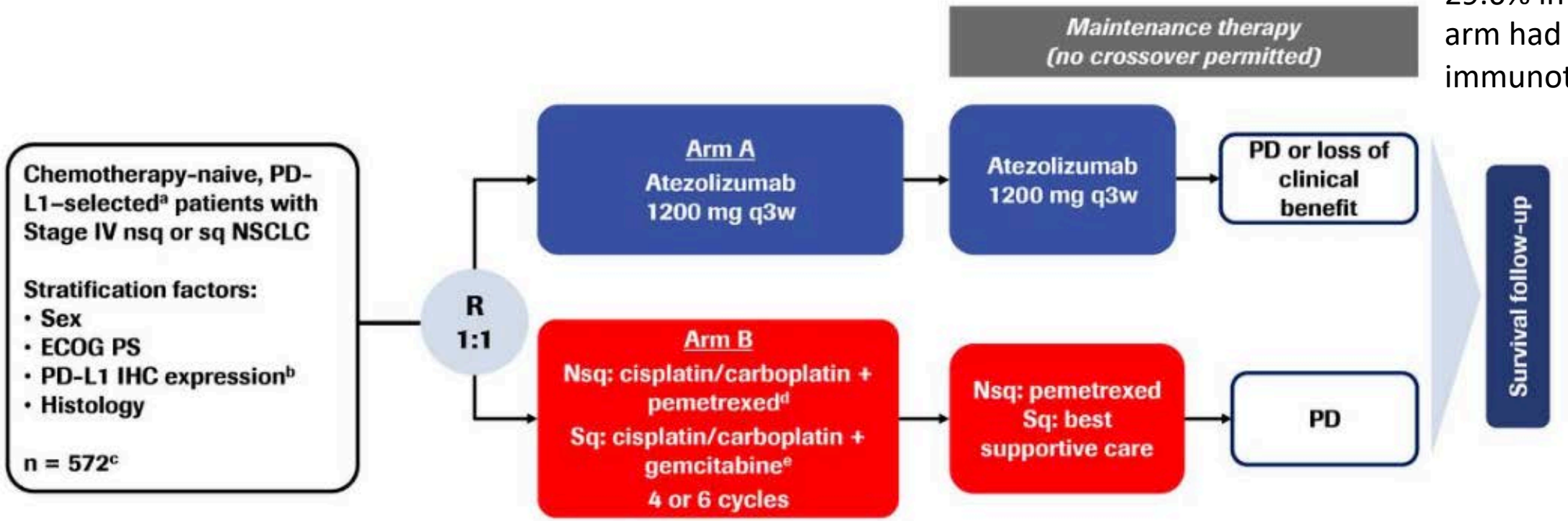
- Safety as expected
  - Grade 3-5 adverse events 72% with pembro, 67% without

Gadgeel S et al. Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. J Clin Oncol. 2020 May 10;38(14):1505-1517.

Courtesy of Matthew Gubens, MD, MS

Atezolizumab (IMpower110)

29.6% in chemo arm had later immunotherapy

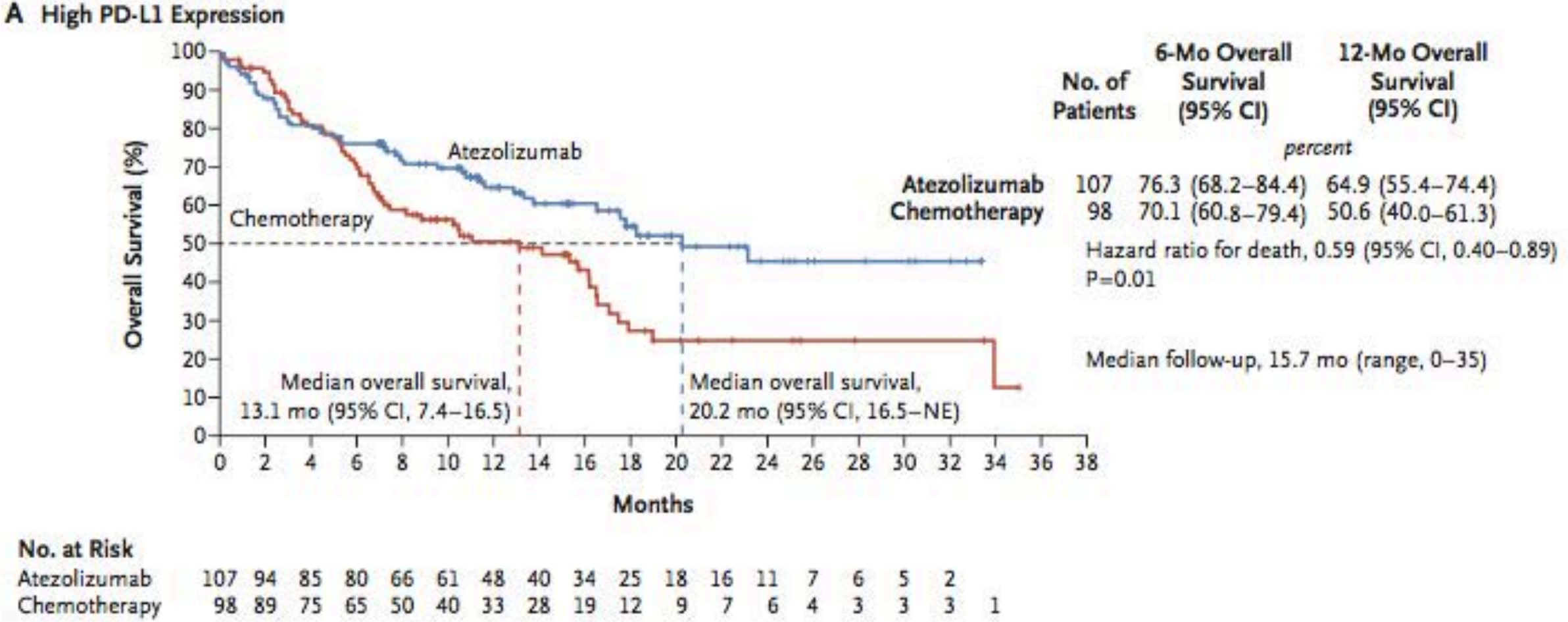


- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST 1.1)

Herbst RS et al; IMpower110 investigators. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020 Oct 1;383(14):1328-1339.

Courtesy of Matthew Gubens, MD, MS

Atezolizumab (IMpower110)



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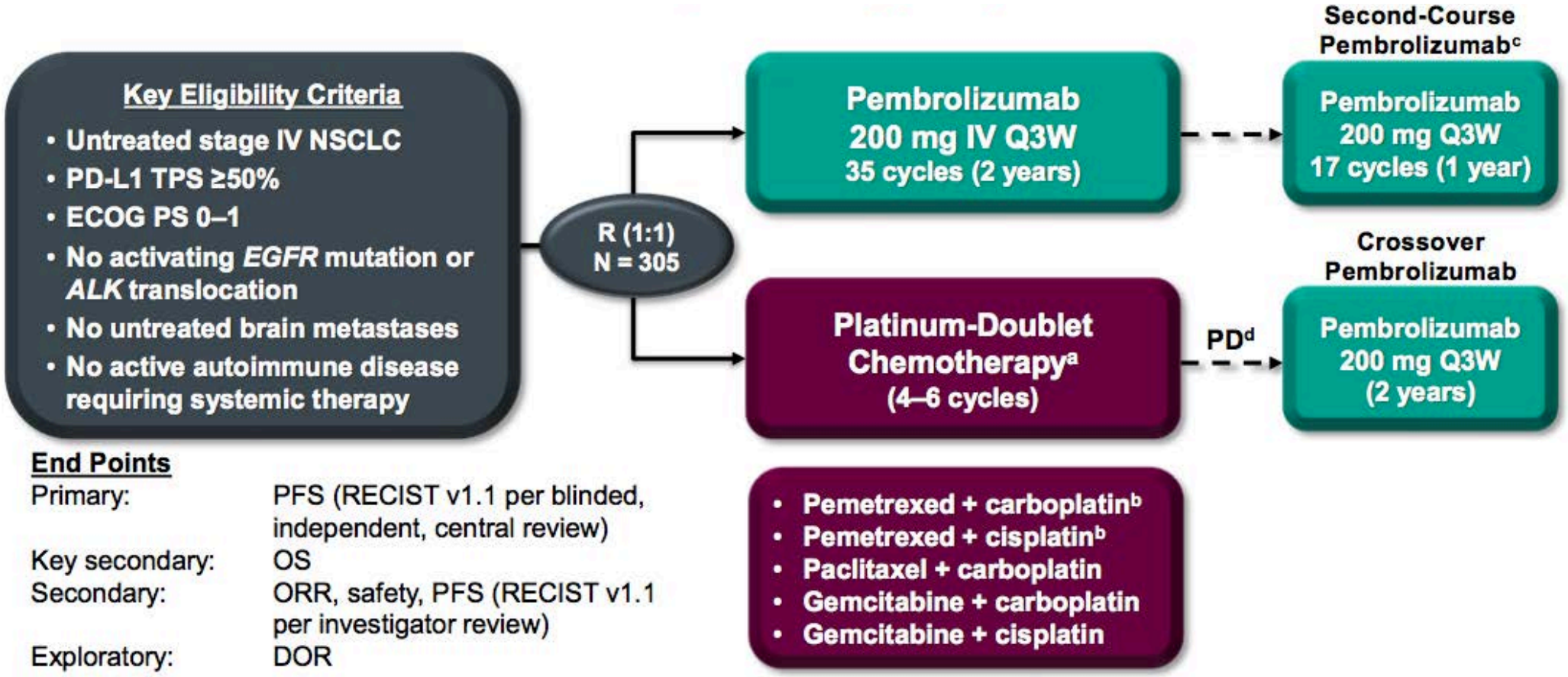
Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)



Brahmer J et al. KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab(pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS) ≥50%. ESMO 2020; Abstract LBA51. Oral

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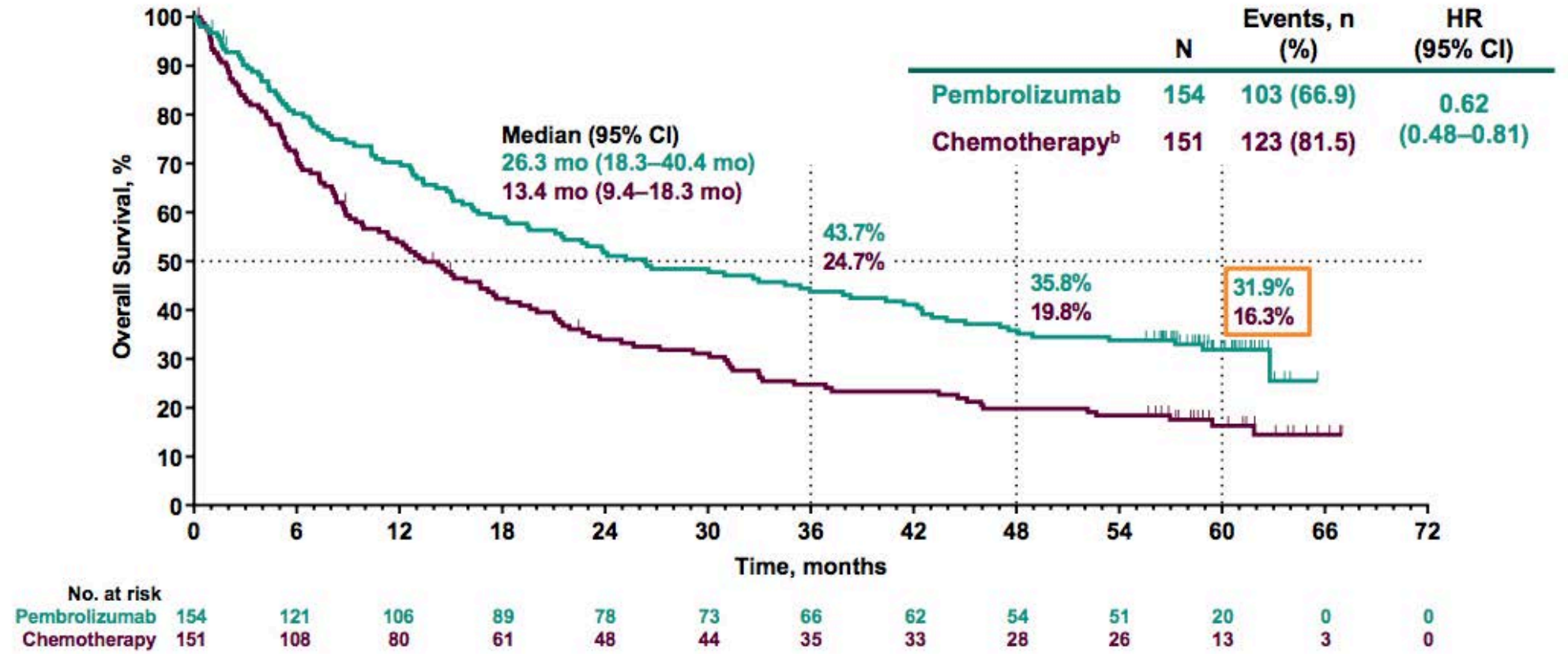

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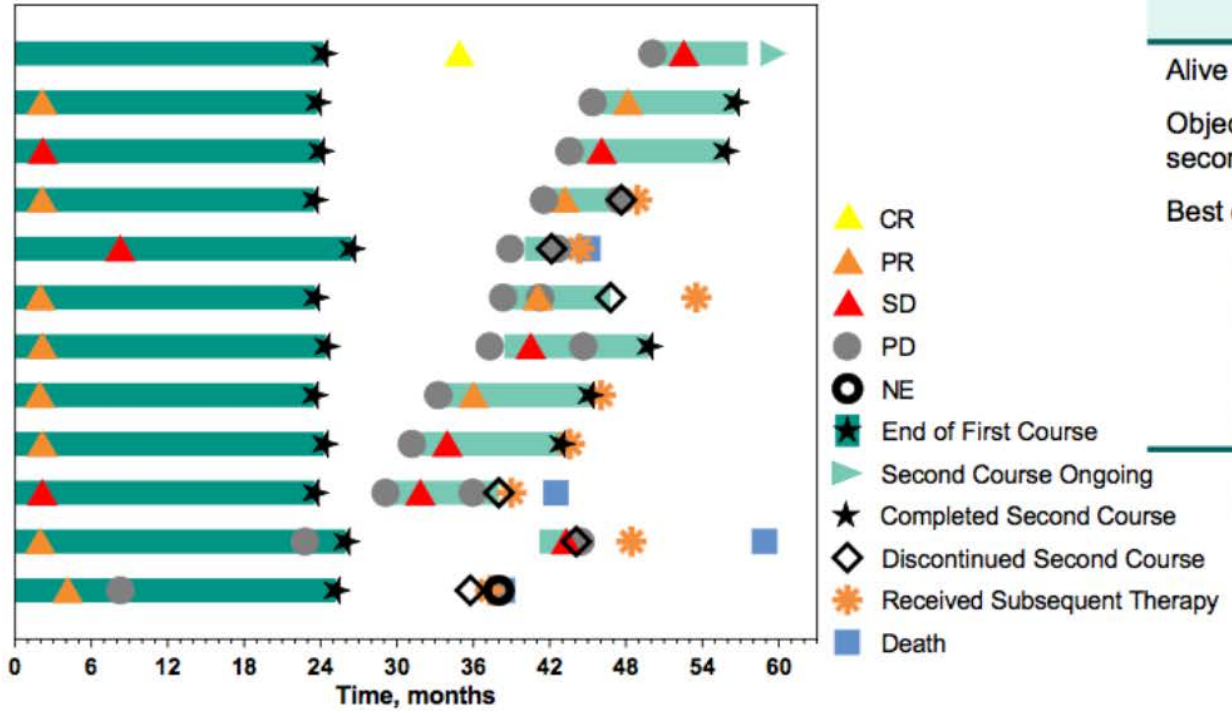
Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)

Treatment Duration and Time to Response

Second Course of Pembrolizumab



	N = 12
Alive at data cutoff, n (%)	8 (67)
Objective response during second course, n (%)	4 (33)
Best objective response, n (%)	
Complete response	0
Partial response	4 (33)
Stable disease	6 (50)
Progressive disease	1 (8)

- **At data cutoff, 5/12 patients (42%) were alive without PD per investigator assessment**
  - **3 (25%) did not receive subsequent therapy**

Brahmer J et al. KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab(pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS) ≥50%. ESMO 2020; Abstract LBA51. Oral

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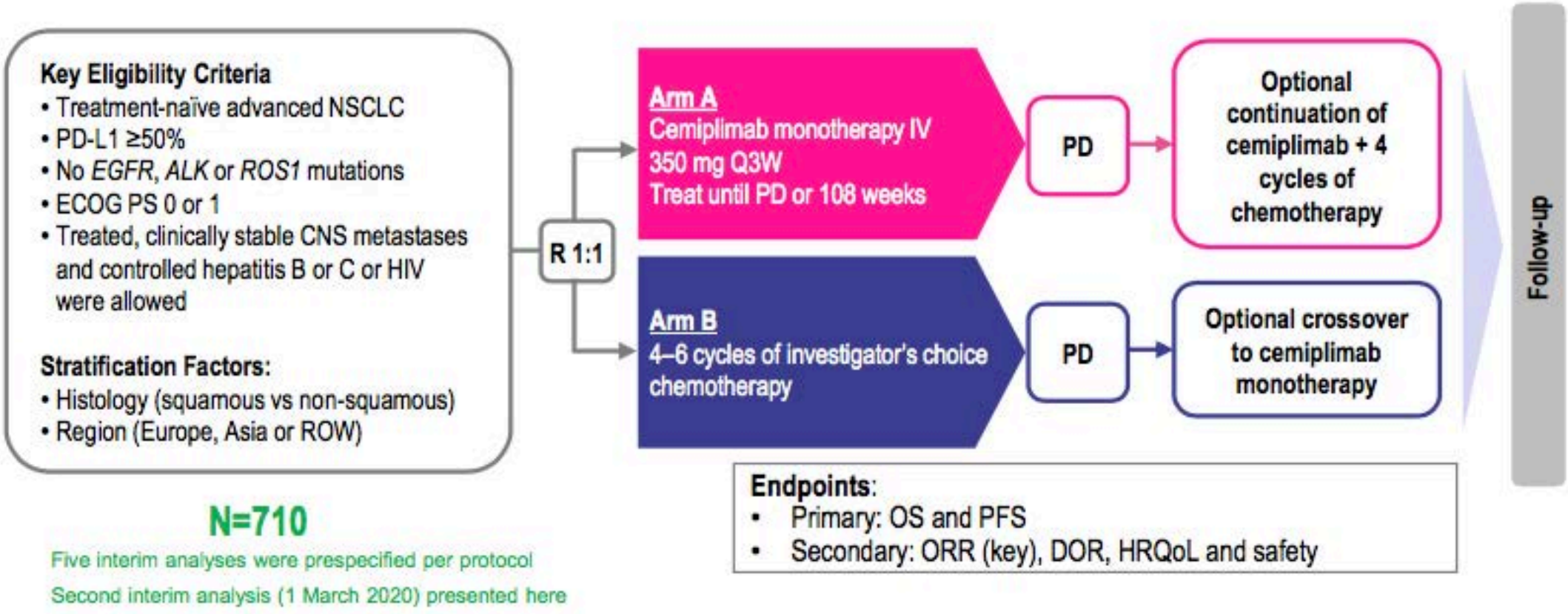
Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)

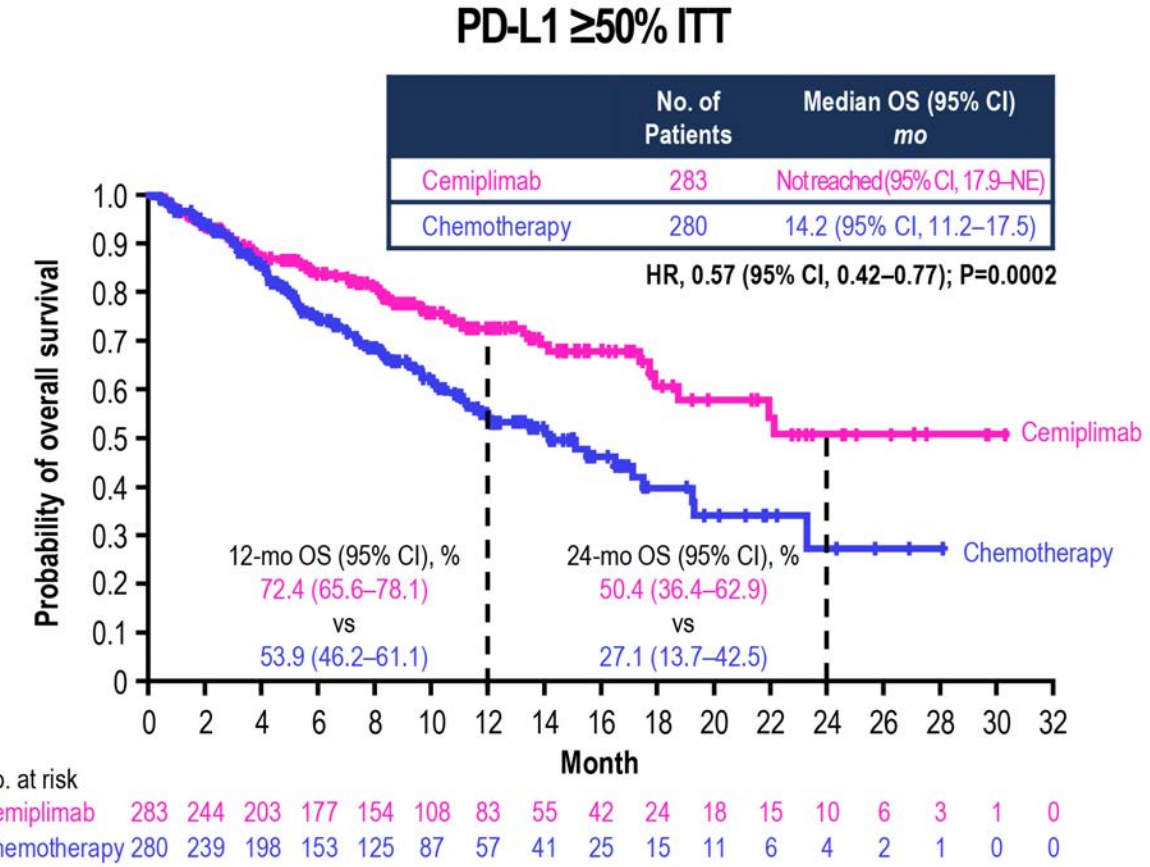


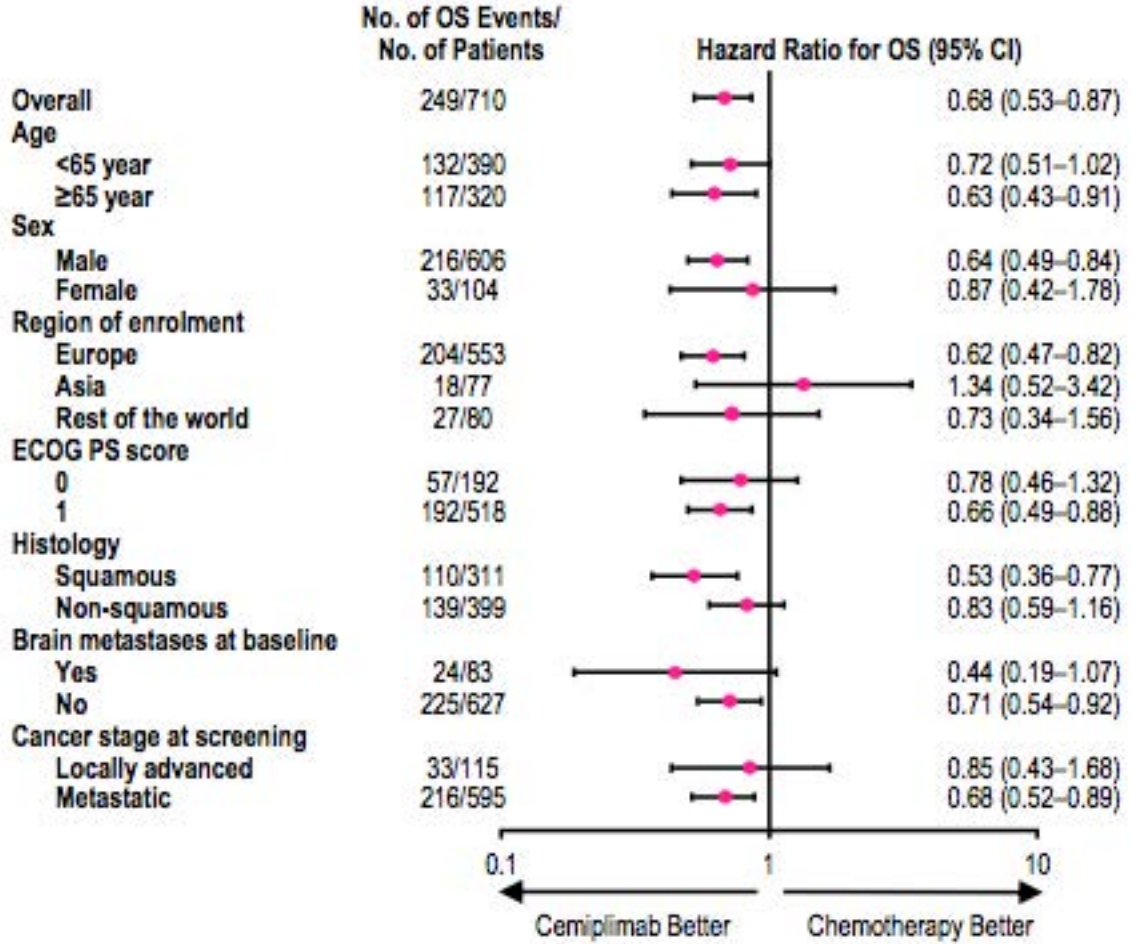
Sezer A et al. EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%. ESMO 2020; Abstract LBA52. Oral

Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)

74% crossover

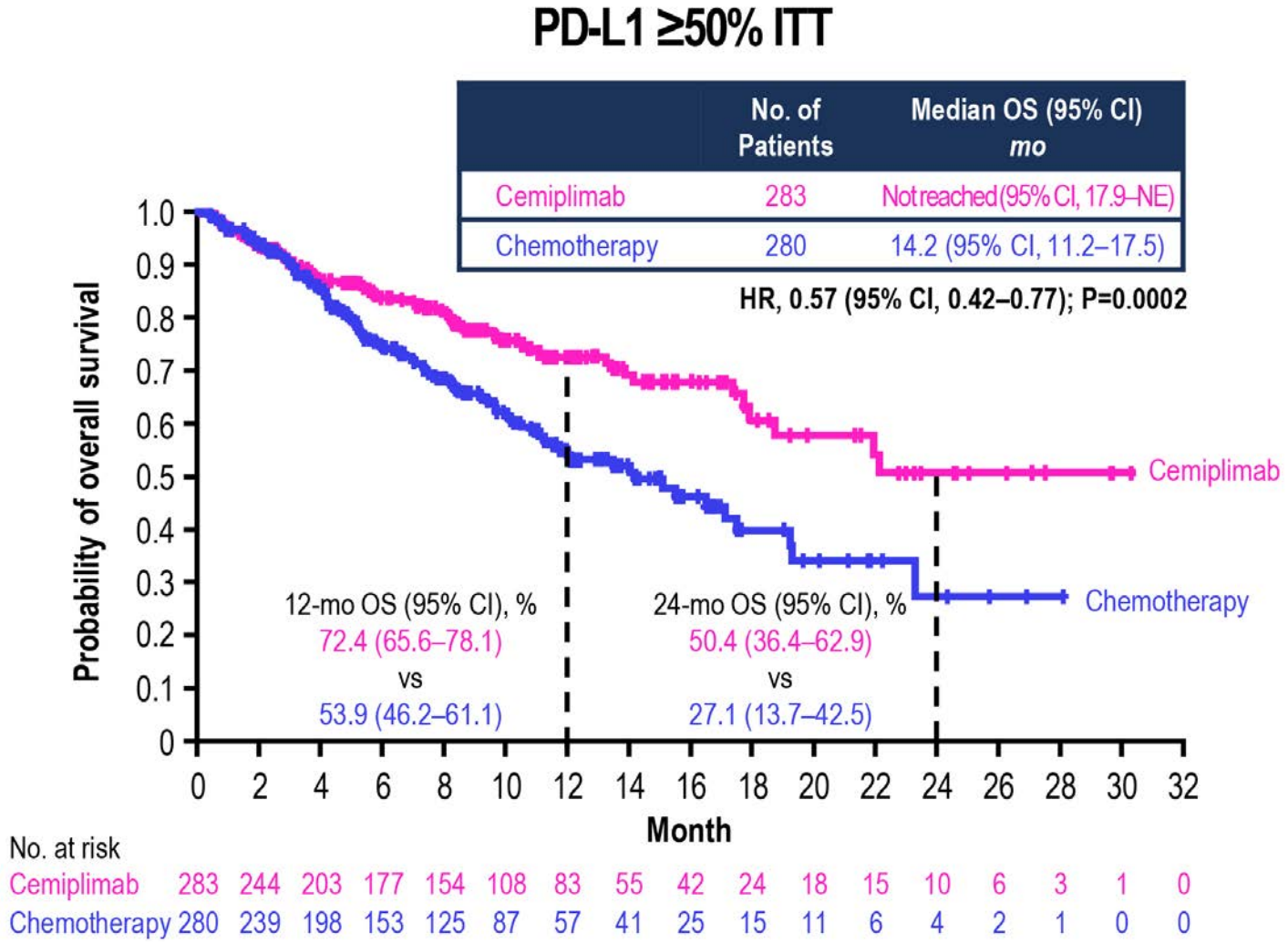




Sezer A et al. EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%. ESMO 2020; Abstract LBA52. Oral

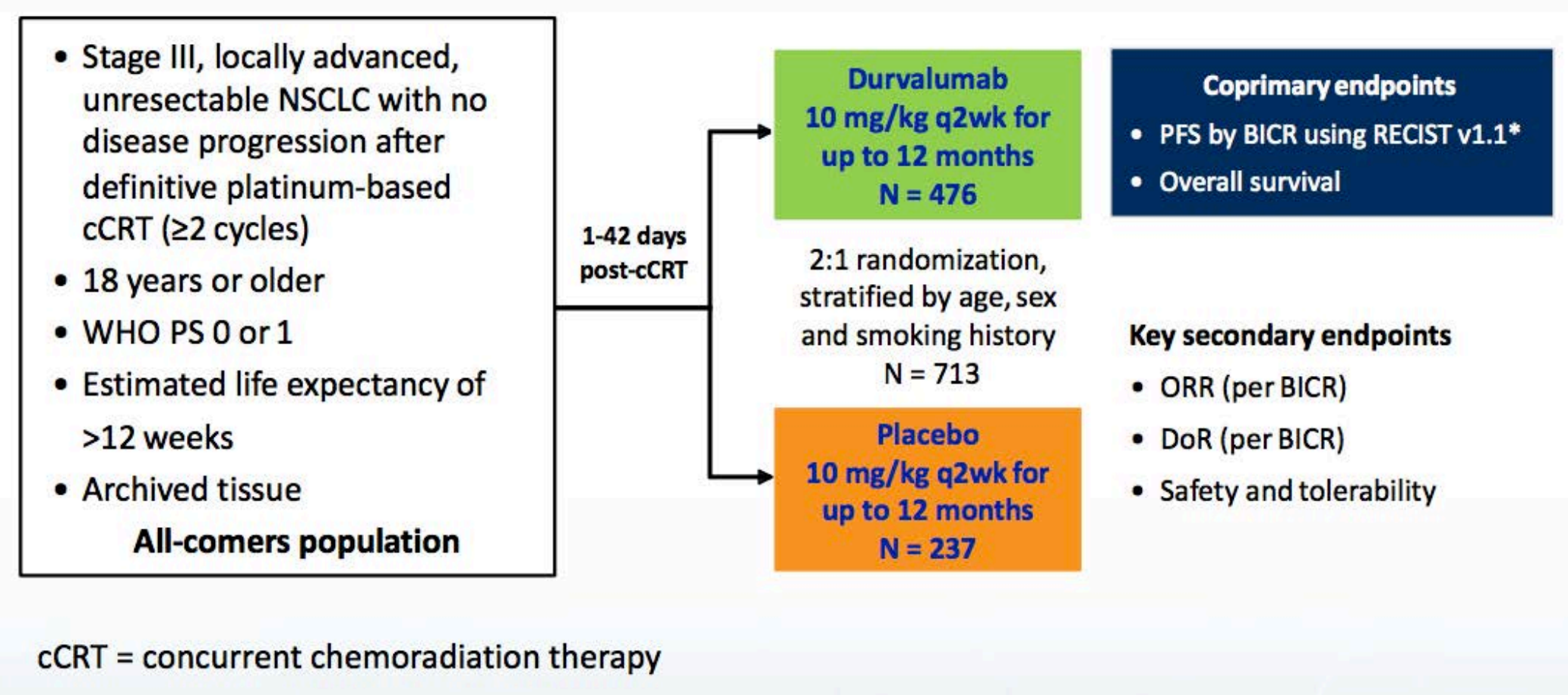
Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)



Courtesy of Matthew Gubens, MD, MS

Durvalumab consolidation in stage III (PACIFIC 3-year OS)

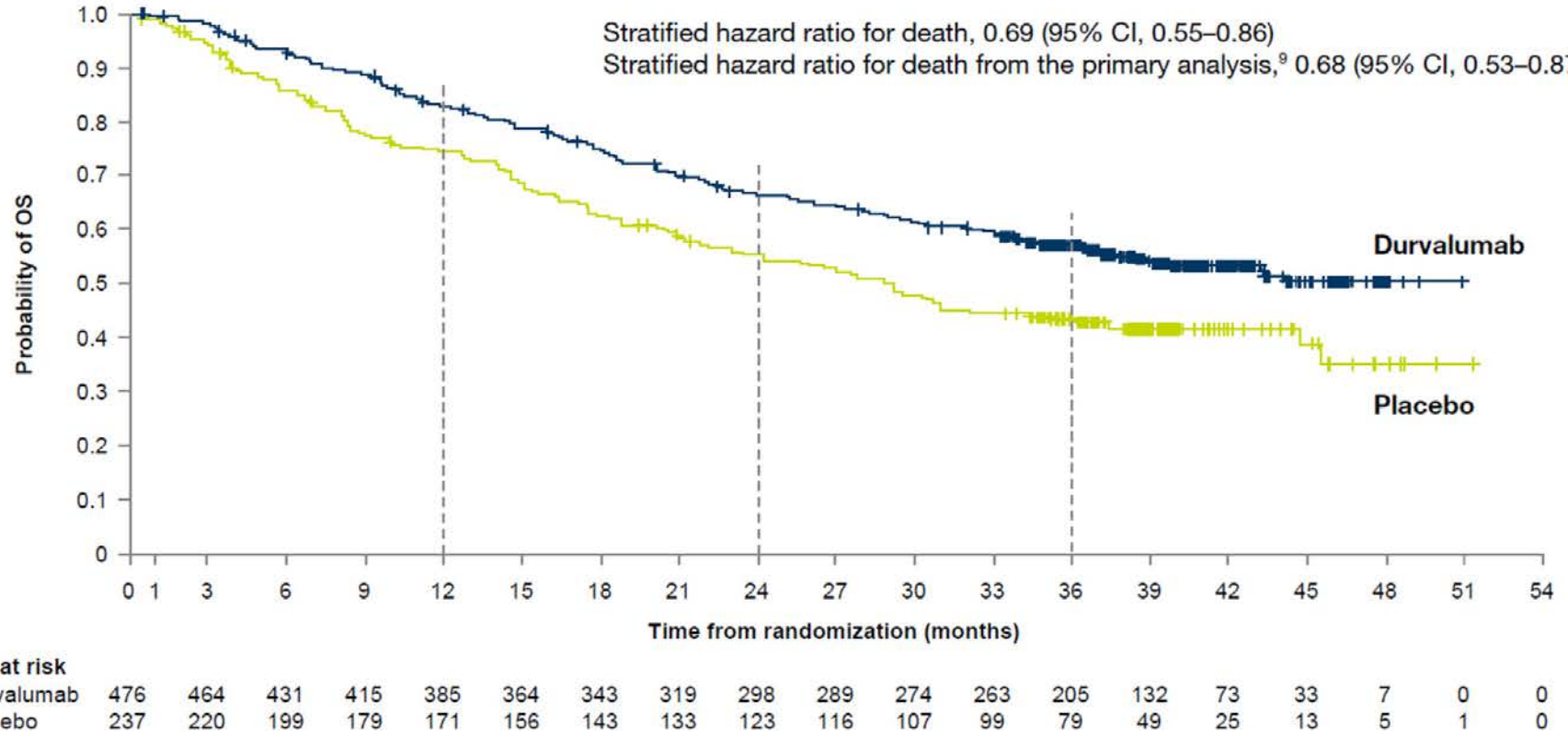


Gray JE et al. Three-year overall survival with durvalumab after chemoradiotherapy in Stage III NSCLC — Update from PACIFIC. J Thorac Oncol 2020;15(2):288-93.
Paz-Ares LG et al. Outcomes with durvalumab by tumour PD-L1 expression in unresectable, Stage III NSCLC in the PACIFIC trial. Ann Oncol 2020; [Epub ahead of print].

Courtesy of Matthew Gubens, MD, MS

Durvalumab consolidation in stage III (PACIFIC 3-year OS)

	No. of events/ total no. of patients (%)	Median OS (95% CI) months	12-month OS rate (95% CI) %	24-month OS rate (95% CI) %	36-month OS rate (95% CI) %
Durvalumab	210/476 (44.1)	NR (38.4–NR)	83.1 (79.4–86.2)	66.3 (61.8–70.4)	57.0 (52.3–61.4)
Placebo	134/237 (56.5)	29.1 (22.1–35.1)	74.6 (68.5–79.7)	55.3 (48.6–61.4)	43.5 (37.0–49.9)



Gray JE et al. Three-year overall survival with durvalumab after chemoradiotherapy in Stage III NSCLC — Update from PACIFIC. J Thorac Oncol 2020;15(2):288-93.
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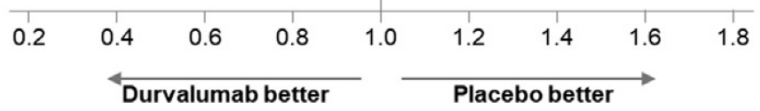
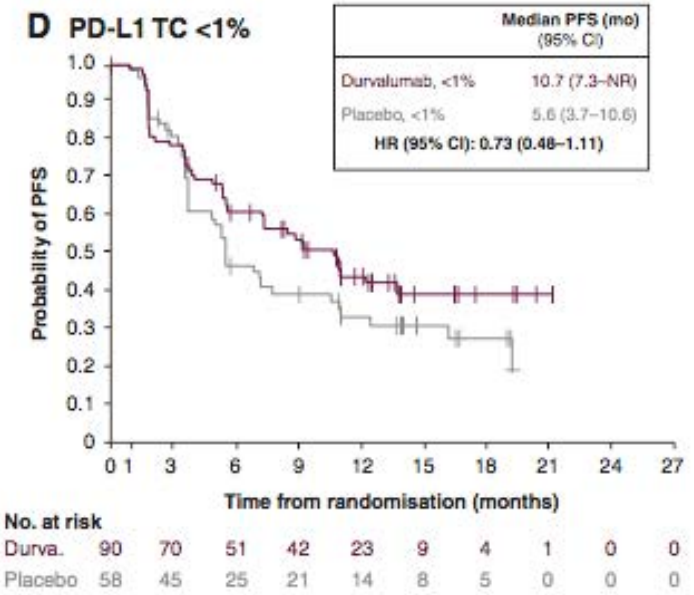
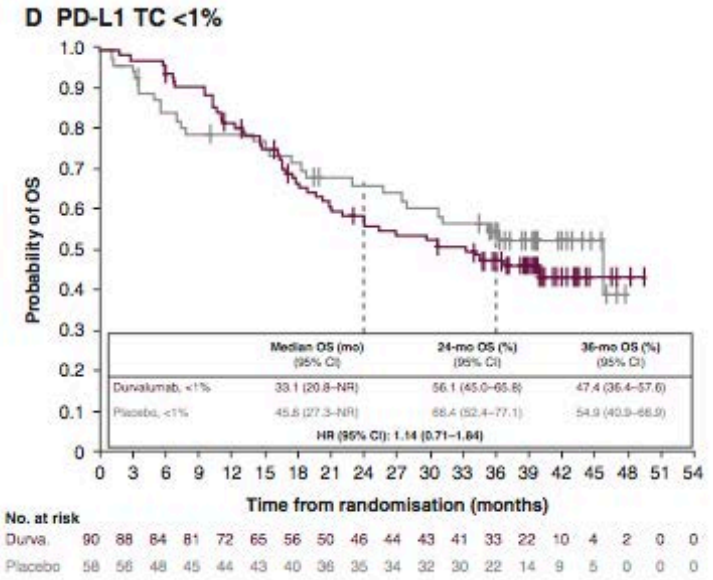
Courtesy of Matthew Gubens, MD, MS

Durvalumab consolidation in stage III (PACIFIC 3-year OS)

***EGFR* mutation**			
Positive	13/29 (44.8)	6/14 (42.9)	
Negative	136/317 (42.9)	95/165 (57.6)	0.63 (0.49–0.82)
Unknown	61/130 (46.9)	33/58 (56.9)	0.75 (0.49–1.15)
PD-L1 status			
≥25%	41/115 (35.7)	23/44 (52.3)	0.50 (0.30–0.83)
<25%	90/187 (48.1)	53/105 (50.5)	0.89 (0.63–1.25)
Unknown	79/174 (45.4)	58/88 (65.9)	0.60 (0.43–0.84)
1–24% (posthoc analysis)	43/97 (44.3)	26/47 (55.3)	0.67 (0.41–1.10)
≥1% (posthoc analysis)	84/212 (39.6)	49/91 (53.8)	0.59 (0.41–0.83)
<1% (posthoc analysis)	47/90 (52.2)	27/58 (46.6)	1.14 (0.71–1.84)







PD-L1 <1%: a post-hoc analysis, small subgroup of 148 pts

- ?Pre-CRT samples, whereas hypothesis is that CRT may alter PD-L1
- ?37% samples unevaluable, perhaps not missing at random

Courtesy of Matthew Gubens, MD, MS

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%?

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

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 10%?

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

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 50%?

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

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 95%?

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

What would you most likely recommend as consolidation treatment for a patient with locally advanced NSCLC who has completed chemoradiation therapy and is found to have an EGFR activating mutation?

1. Durvalumab
2. Osimertinib
3. Durvalumab + osimertinib
4. Durvalumab followed by osimertinib
5. Other

Agenda

Module 1: Non-Small Cell Lung Cancer

Module 2: Malignant Pleural Mesothelioma

Module 3: Small Cell Lung Cancer

Module 2: Malignant Pleural Mesothelioma

- **Key Relevant Data Sets**
  - CheckMate 743: First-line nivolumab + ipilimumab vs chemotherapy
  - STELLAR: Tumor Treating Fields (TTF) + pemetrexed/platinum as first-line therapy
  - Evaluation of TTF in combination with pembrolizumab

IPILIMUMAB + NIVOLUMAB FOR PLEURAL MESOTHELIOMA (CM 743 STUDY)

Key Eligibility Criteria
- Unresectable pleural mesothelioma
- No prior systemic therapy
- ECOG performance status 0-1

Stratified by:
histology (epithelioid vs non-epithelioid) and gender

N = 605
R
1:1

n = 303
NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W (for up to 2 years)

n = 302
Cisplatin or carboplatin + pemetrexed Q3W[b] (6 cycles)

Until disease progression, unacceptable toxicity *or* for 2 years for immunotherapy arm

Primary Endpoint
- OS

Secondary Endpoints
- ORR, DCR, and PFS by BICR
- PD-L1[c] expression as a predictive biomarker

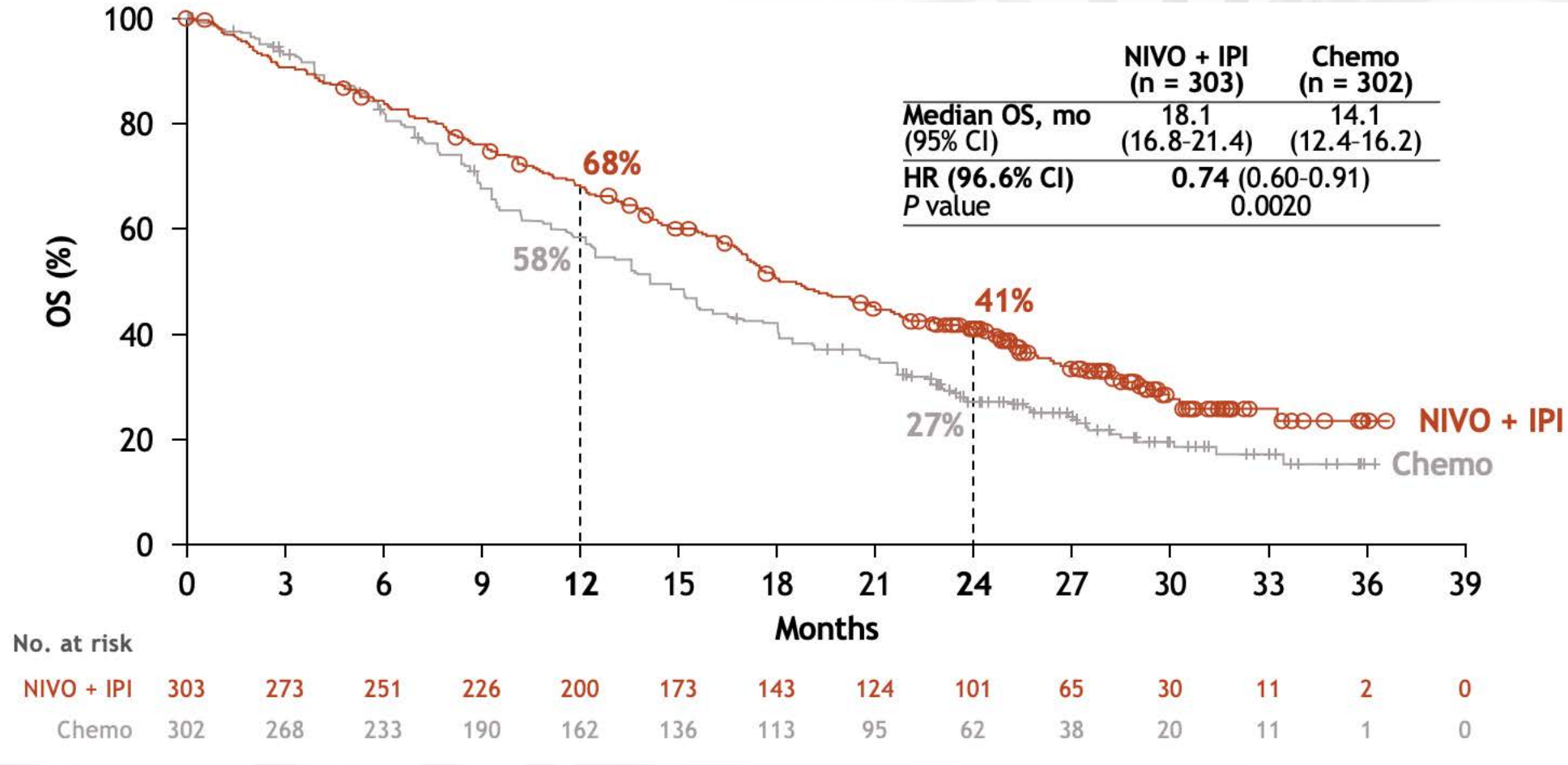
Database lock: April 3, 2020; minimum follow-up for OS: 22.1 months; median follow-up: 29.7 months.

[a]NCT02899299; [b]Cisplatin (75 mg/m^2) or carboplatin (AUC 5) + pemetrexed (500 mg/m^2), Q3W for 6 cycles; [c]Determined by PD-L1 IHC 28-8 pharmDx assay from Dako.

Baas P et al, IASLC 2020.

Courtesy of Suresh S Ramalingam, MD

CM743: OVERALL SURVIVAL

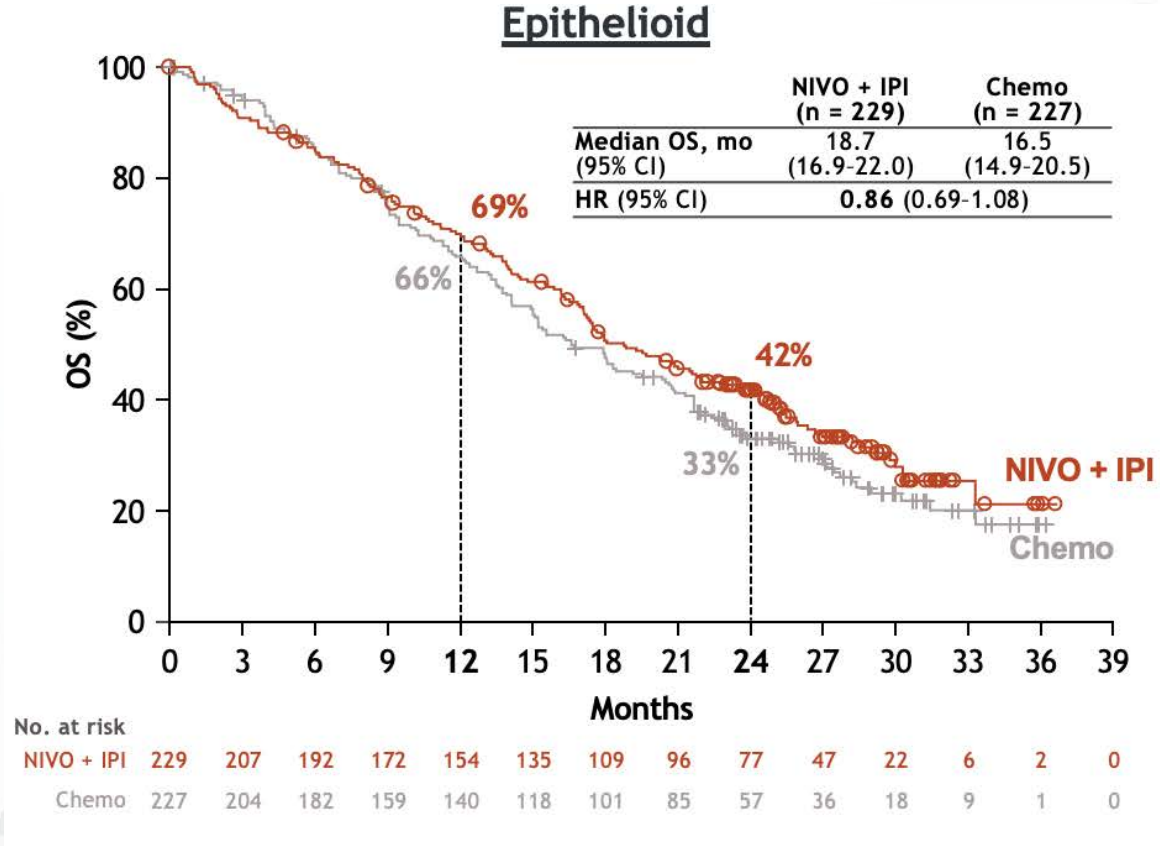


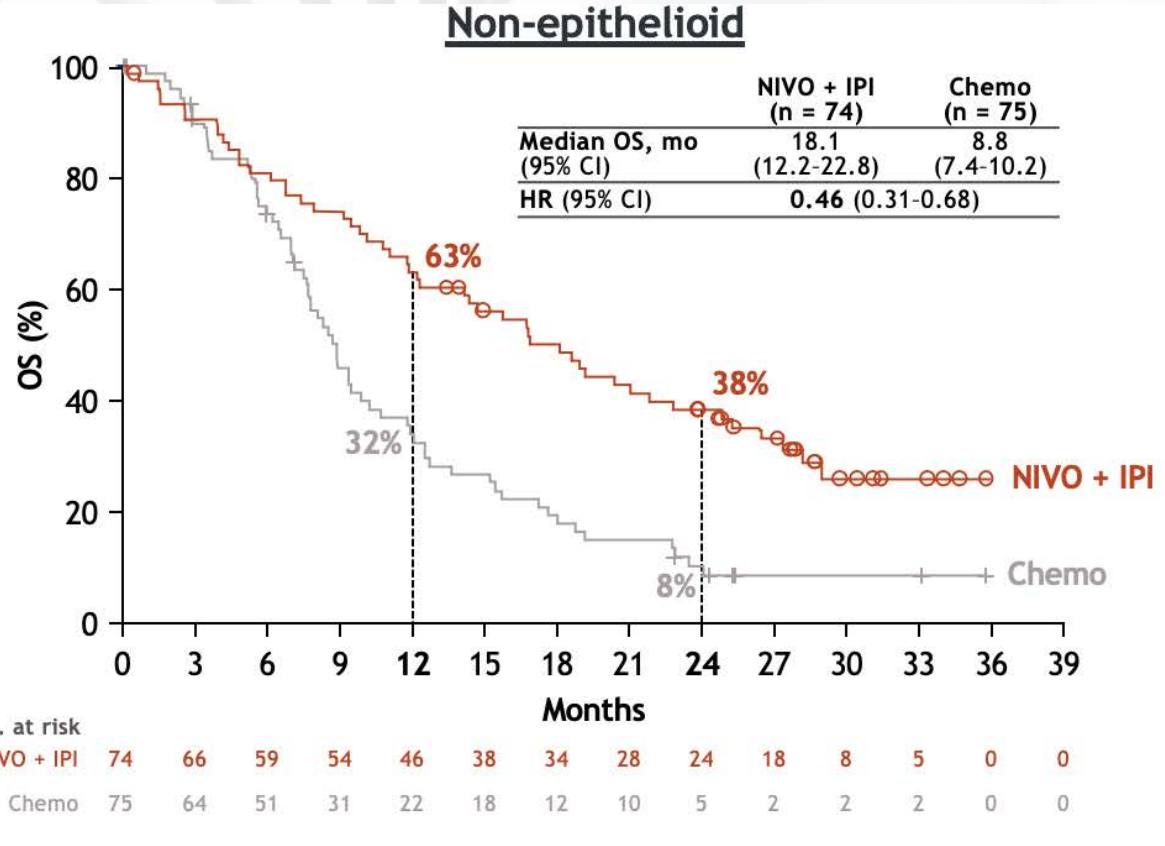
	NIVO + IPI (n = 303)	Chemo (n = 302)
Median OS, mo (95% CI)	18.1 (16.8-21.4)	14.1 (12.4-16.2)
HR (96.6% CI)	0.74 (0.60-0.91)	
P value	0.0020	

Baas P et al, IASLC 2020.

Courtesy of Suresh S Ramalingam, MD

CM743: SURVIVAL BASED ON HISTOLOGY

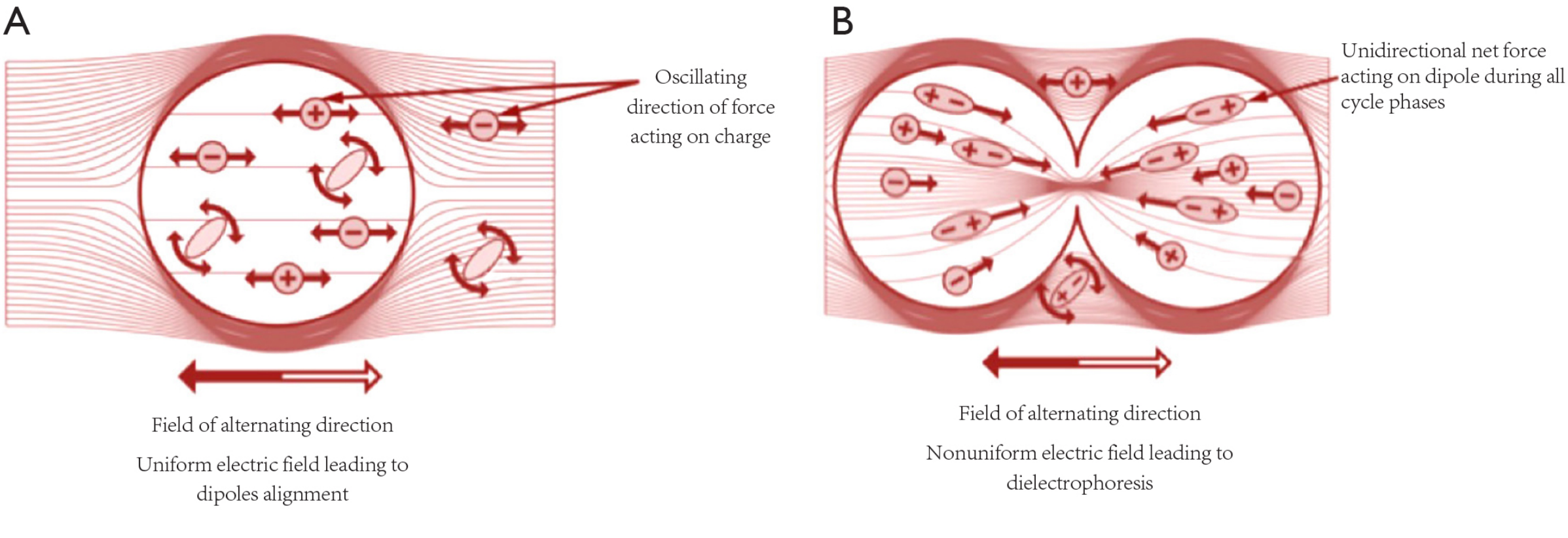




Baas P et al, IASLC 2020.

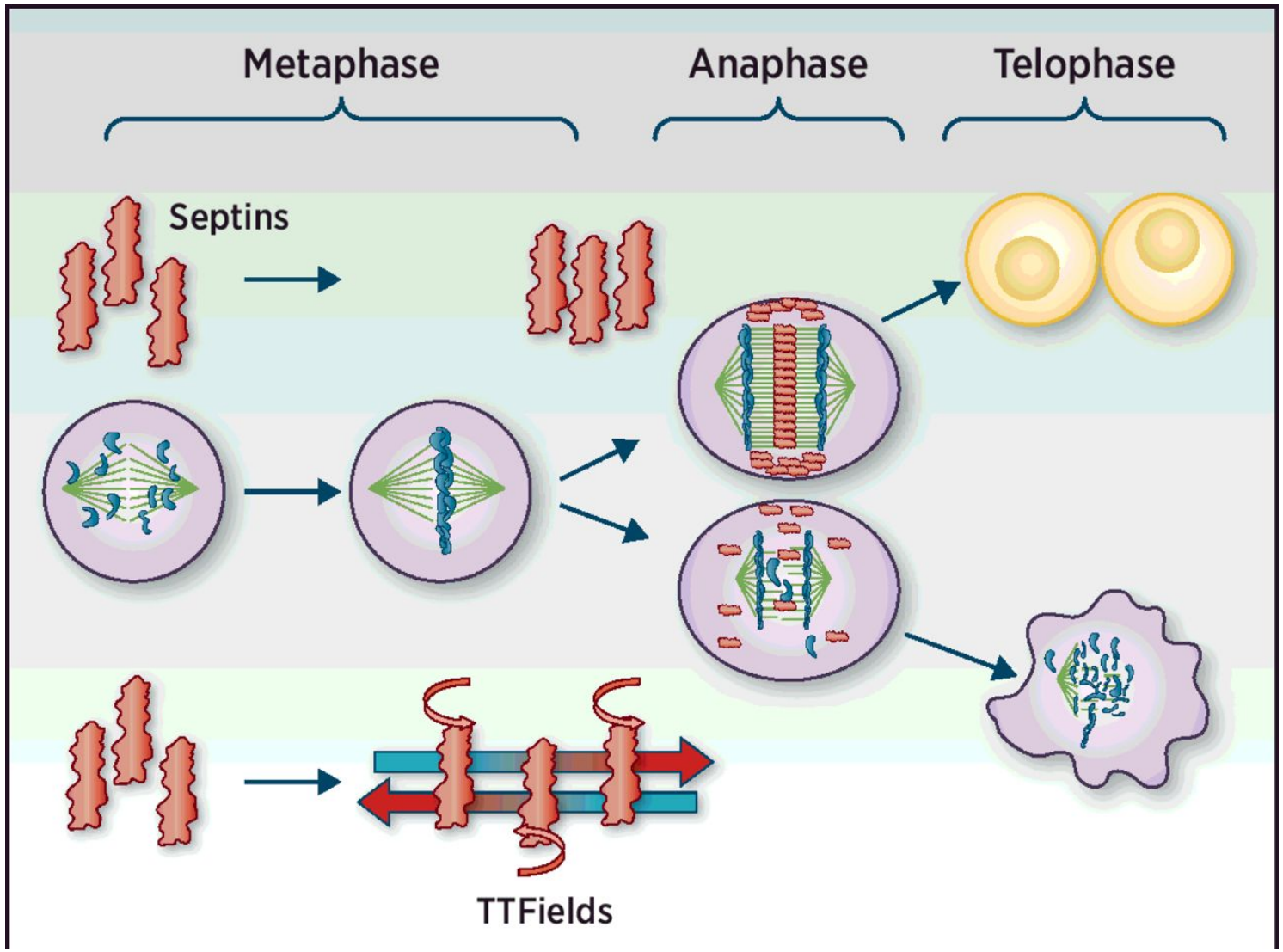
Courtesy of Suresh S Ramalingam, MD

Mechanisms of Action of Tumor Treating Fields



Zhu P et al, *Chin Clin Oncol*, 2017; 6(4). 41-55

Tumor treating fields (TTF) cause mitotic disruption



Courtesy of Marjorie Zauderer, MD

Memorial Sloan Kettering Cancer Center

FDA Approves TTF Delivery System in Combination with Chemotherapy for the Treatment of Malignant Pleural Mesothelioma

Press Release: May 23, 2019

"The FDA approval is based on the results of the STELLAR trial. STELLAR was a prospective, single-arm trial designed to study the safety and efficacy of NovoTTF-100L plus chemotherapy first-line in patients with unresectable MPM. The trial included 80 patients with unresectable and previously untreated MPM who were candidates for treatment with pemetrexed and cisplatin or carboplatin. The trial was powered to prospectively determine the overall survival in patients treated with NovoTTF-100L plus chemotherapy. Secondary endpoints included overall response rate (per mRECIST criteria), progression free survival and safety.

The median overall survival was 18.2 months across all patients treated with NovoTTF-100L plus chemotherapy. The median overall survival was 21.2 months for patients with epithelioid MPM (n=53) and 12.1 months for patients with non-epithelioid MPM (n=21). More than half, 62 percent, of patients (n=80) enrolled in the STELLAR trial who used NovoTTF-100L plus chemotherapy were still alive at one year. The disease control rate in patients with at least one follow-up CT scan performed (n=72) was 97 percent. 40 percent of patients had a partial response, 57 percent had stable disease, and 3 percent had progressive disease. The median progression free survival was 7.6 months. . . There was no increase in serious systemic adverse events when NovoTTF-100L was added to chemotherapy. Mild-to-moderate skin irritation was the most common device-related side effect with NovoTTF-100L."

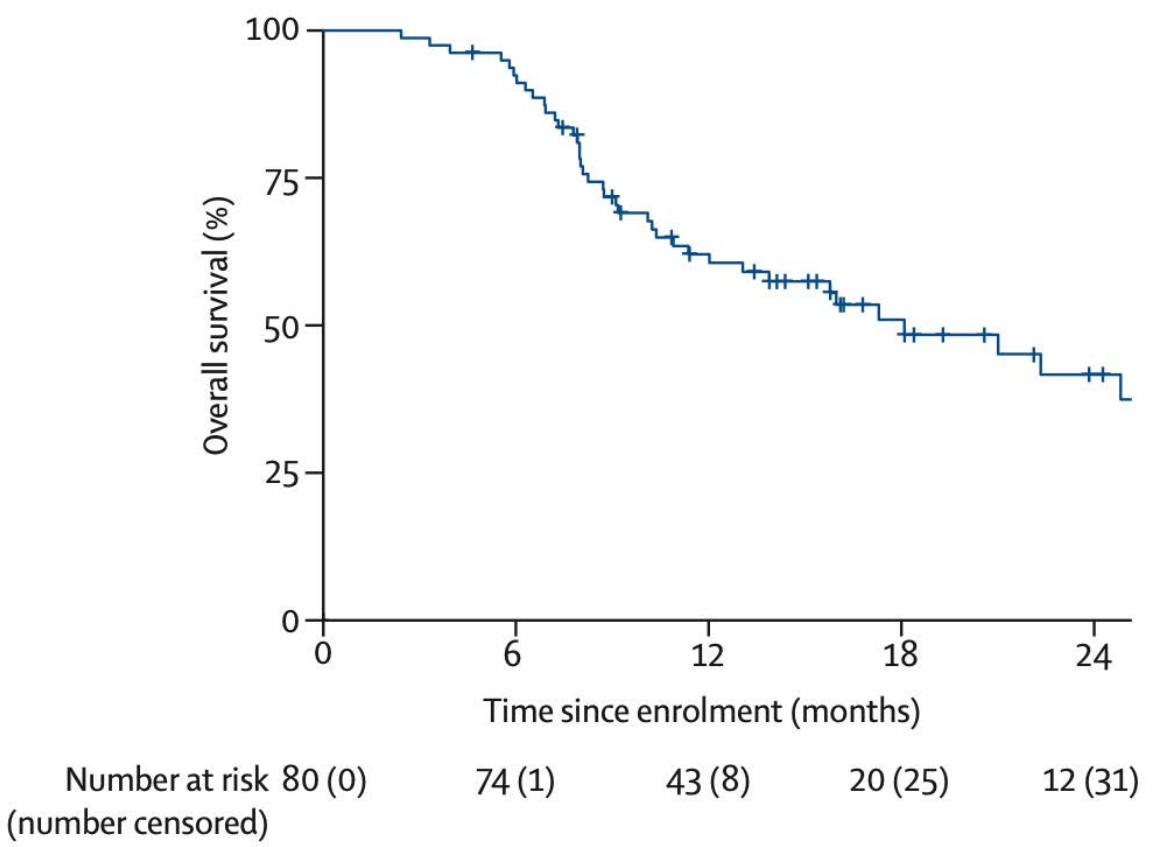
https://www.novocure.com/fda-approves-the-novottf-100ltm-system-in-combination-with-chemotherapy-for-the-treatment-of-malignant-pleural-mesothelioma/

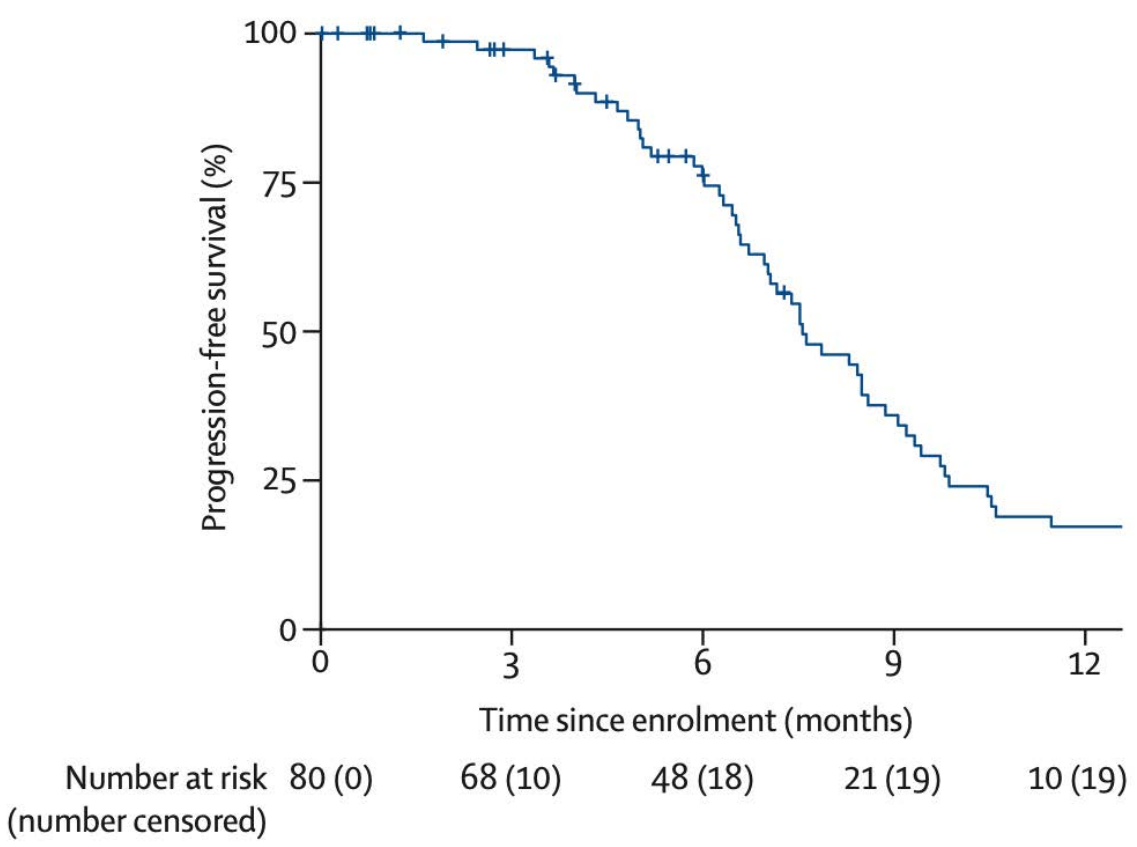
Tumour Treating Fields in combination with pemetrexed and cisplatin or carboplatin as first-line treatment for unresectable malignant pleural mesothelioma (STELLAR): a multicentre, single-arm phase 2 trial

Giovanni L Ceresoli, Joachim G Aerts, Rafal Dziadziuszko, Rodryg Ramlau, Susana Cedres, Jan P van Meerbeeck, Manlio Mencoboni, David Planchard, Antonio Chella, Lucio Crinò, Maciej Krzakowski, Jörn Rüssel, Antonio Maconi, Letizia Gianoncelli, Federica Grosso

***Lancet Oncol* 2019;20:1702-9.**

STELLAR: CHEMOTHERAPY PLUS TUMOR-TREATING FIELDS (TTF) FOR MESOTHELIOMA





Adverse event of interest: skin toxicity grade 1-2: 66%; grade 3: 5%.

Ceresoli et al, Lancet Oncol, 2019.

Courtesy of Suresh S Ramalingam, MD

STELLAR: OS comparable to historical controls

TTFields + Pemetrexed + Platinum as First-Line Therapy

- DCR in pts with ≥1 follow-up CT scan: 70/72 (97%)
- PR: 41/72 (57%)
- PD: 2/72 (3%)

- Median PFS = 7.6 months

- Median OS 18.2 months (95% CI 12.1-25.8)

- The most common Grade ≥3 AEs:
  - o Anemia, 9 (11%)
  - o Neutropenia, 7 (9%)
  - o Thrombocytopenia, 4 (5%)

- Skin reaction was the only AE associated with TTFields (N = 80)
  - o Grade 1 or 2: 53 (66%)
  - o Grade 3: 4 (5%)

- No treatment-related deaths were observed

Conclusion: TTFields (150 kHz) to the thorax concomitant with pemetrexed and platinum was a safe option for front-line treatment of unresectable MPM.

Ceresoli GL et al. *Lancet Oncol* 2019;20(12):1702-9.

Courtesy of Marjorie Zauderer, MD

Memorial Sloan Kettering Cancer Center

Phase II Pilot Study Initiated to Evaluate Tumor Treating Fields plus Pembrolizumab in NSCLC

Press Release: July 15, 2020

"Tumor Treating Fields (TTF) is a cancer therapy that uses electric fields tuned to specific frequencies to disrupt cell division, inhibiting tumor growth and causing cancer cells to die. TTF does not stimulate or heat tissue and targets dividing cancer cells of a specific size and causes minimal damage to healthy cells. Mild to moderate skin irritation is the most common side effect reported. TTF is approved in certain countries for the treatment of adults with glioblastoma and in the US for mesothelioma, two of the most difficult cancer types to treat."

This Phase 2 pilot study will evaluate TTF concomitant with pembrolizumab as first-line treatment of intrathoracic advanced or metastatic, PD-L1 positive NSCLC. The study is designed to enroll approximately 66 patients in the US and is expected to begin in the second half of 2020. Objective response rate (ORR) is the primary endpoint of the study. Secondary endpoints include overall survival, progression-free survival (PFS), PFS at six months, one-year survival rate, duration of response, disease control rate at 18 weeks and safety.

https://www.businesswire.com/news/home/20200715005430/en/

What is your preferred first-line treatment for a patient with malignant pleural mesothelioma (MPM)?

1. Chemotherapy
2. Chemotherapy + bevacizumab → maintenance bevacizumab
3. Chemotherapy + TTF
4. Nivolumab/ipilimumab
5. Pembrolizumab
6. Nivolumab
7. Other

Regulatory and reimbursement issues aside, what is your most likely second-line treatment for a patient with MPM who receives cisplatin/pemetrexed/bevacizumab → maintenance pemetrexed/ bevacizumab and experiences disease progression?

1. Chemotherapy
2. Chemotherapy + TTF
3. Lurbinectedin
4. Nivolumab/ipilimumab
5. Pembrolizumab
6. Nivolumab
7. Other

Agenda

Module 1: Non-Small Cell Lung Cancer

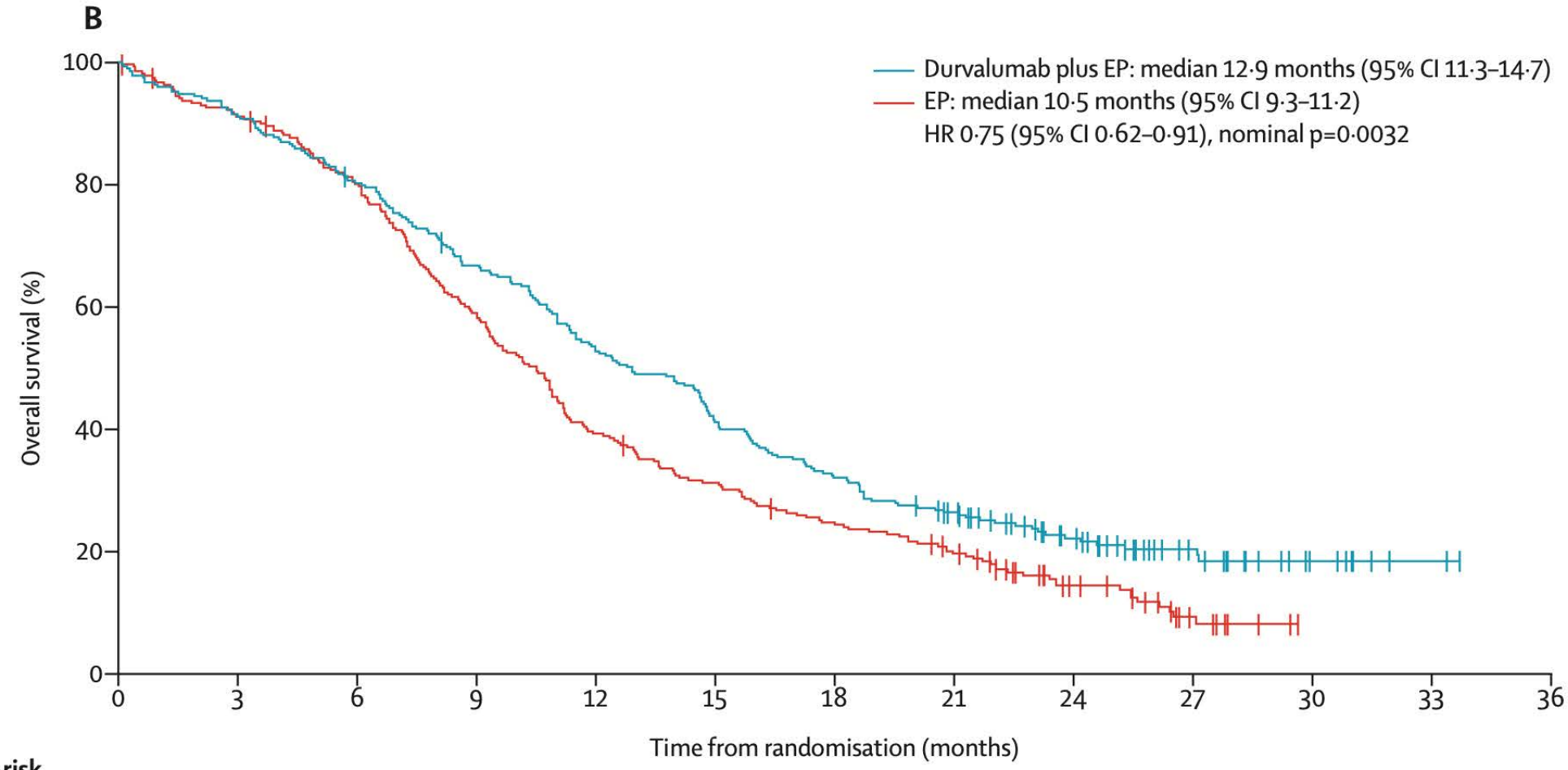
Module 2: Malignant Pleural Mesothelioma

Module 3: Small Cell Lung Cancer

Module 3: Small Cell Lung Cancer (SCLC)

- **Key Relevant Data Sets**
  - CASPIAN: Durvalumab +/- tremelimumab + platinum/etoposide
  - IMpower133: Updated overall survival and exploratory analyses
  - KEYNOTE-604: Pembrolizumab + platinum/etoposide
  - Lurbinectedin as second-line therapy

PLATINUM-ETOPOSIDE +/- DURVALUMAB (CASPIAN STUDY)
OVERALL SURVIVAL



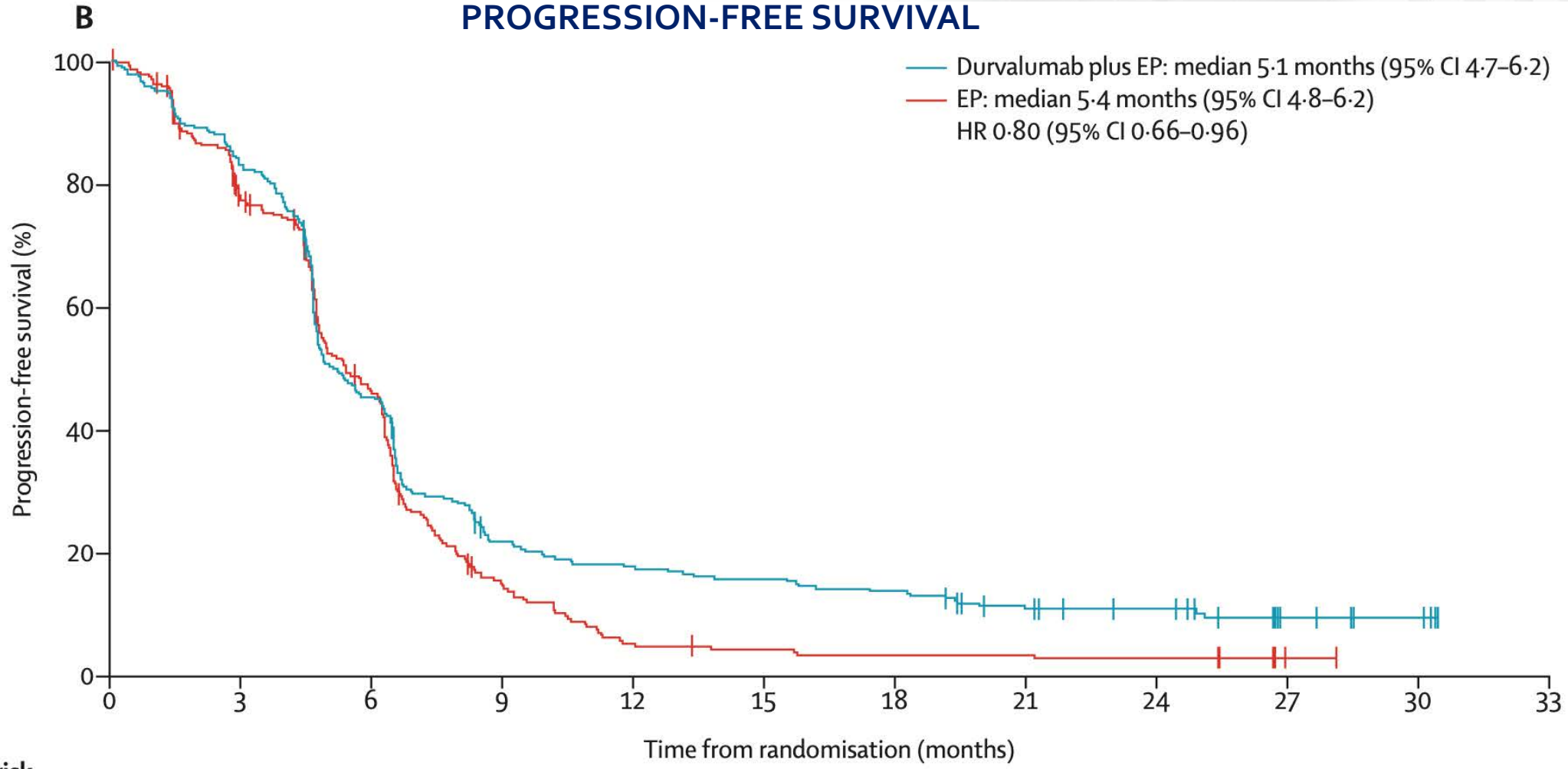
Number at risk (number censored)													
Durvalumab plus EP	268 (0)	244 (0)	214 (1)	177 (2)	140 (2)	109 (2)	85 (2)	66 (6)	41 (22)	21 (39)	8 (50)	2 (56)	0 (58)
EP	269 (0)	243 (2)	212 (4)	156 (4)	104 (4)	82 (5)	64 (6)	48 (9)	24 (22)	8 (31)	0 (38)	0 (38)	0 (38)

Goldman J et al, Lancet Oncol, 2020.

Courtesy of Suresh S Ramalingam, MD

PLATINUM-ETOPOSIDE +/- DURVALUMAB (CASPIAN STUDY)

PROGRESSION-FREE SURVIVAL



Number at risk (number censored)												
Durvalumab plus EP	268 (0)	220 (3)	119 (5)	55 (8)	45 (8)	40 (8)	35 (8)	24 (12)	18 (18)	8 (26)	5 (29)	0 (34)
EP	269 (0)	195 (15)	110 (23)	33 (26)	12 (26)	9 (27)	7 (27)	7 (27)	6 (27)	1 (32)	0 (33)	0 (33)

Goldman J et al, Lancet Oncol, 2020.

Courtesy of Suresh S Ramalingam, MD

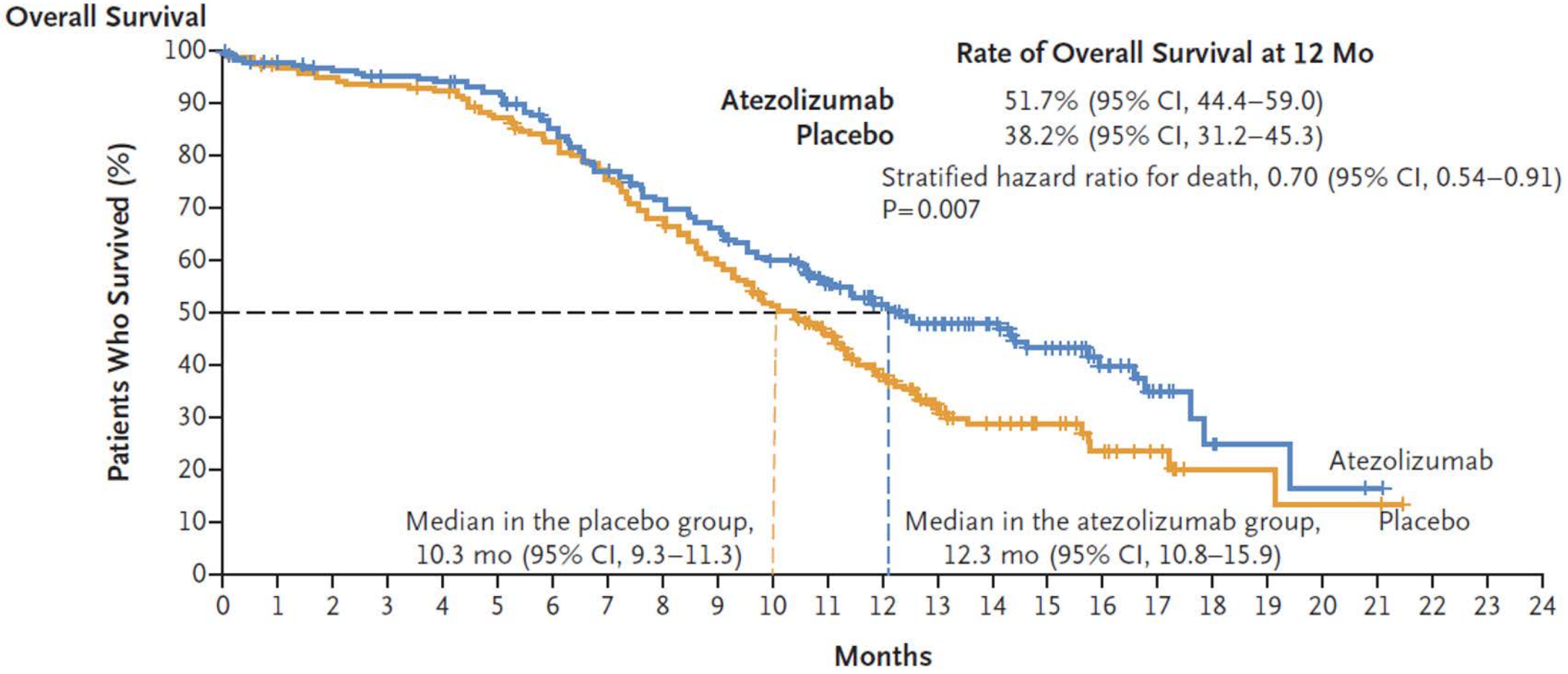
IMPOWER 133: UPDATED EFFICACY

Parameter	Chemo + Atezo	Chemo
Median OS	12.3 m (HR 0.76)	10. 3 m
18m- OS Rate	34%	21%
PD-L1 Expression		
<1% (n=72 pts)	10.2 m	8.3 m
< 5% (n=108 pts)	9.2 m	8.9 m
> 5% (n=29 pts)	21.6 m	9.2 m

Horn et al, AACR 2020.

Courtesy of Suresh S Ramalingam, MD

CARBOPLATIN-ETOPOSIDE +/- ATEZOLIZUMAB (IMPOWER 133 STUDY)
OVERALL SURVIVAL

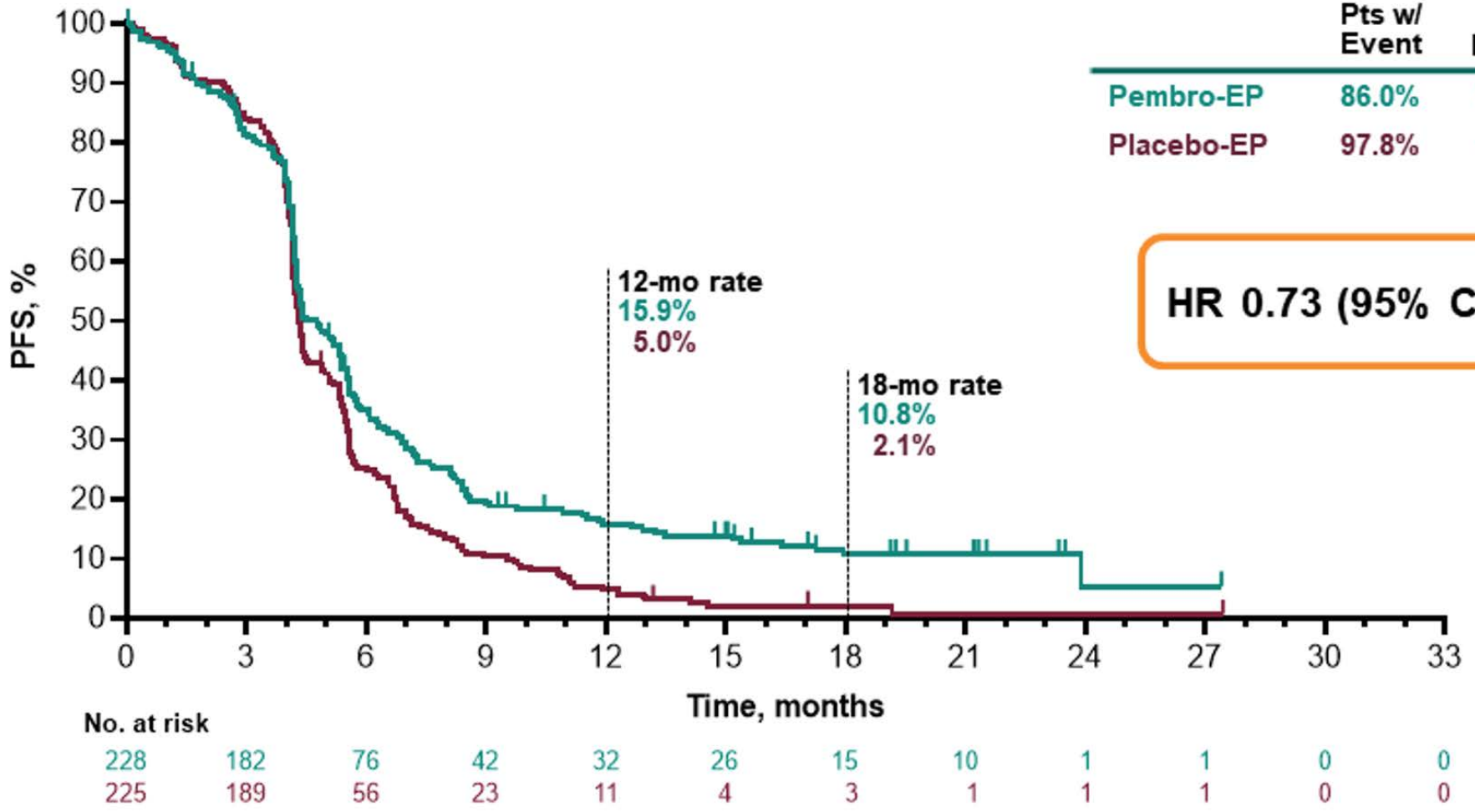


Horn et al, N Engl J Med, 2018.

Courtesy of Suresh S Ramalingam, MD

PLATINUM-ETOPOSIDE +/- PEMBROLIZUMAB (KN 604 STUDY)

PROGRESSION-FREE SURVIVAL



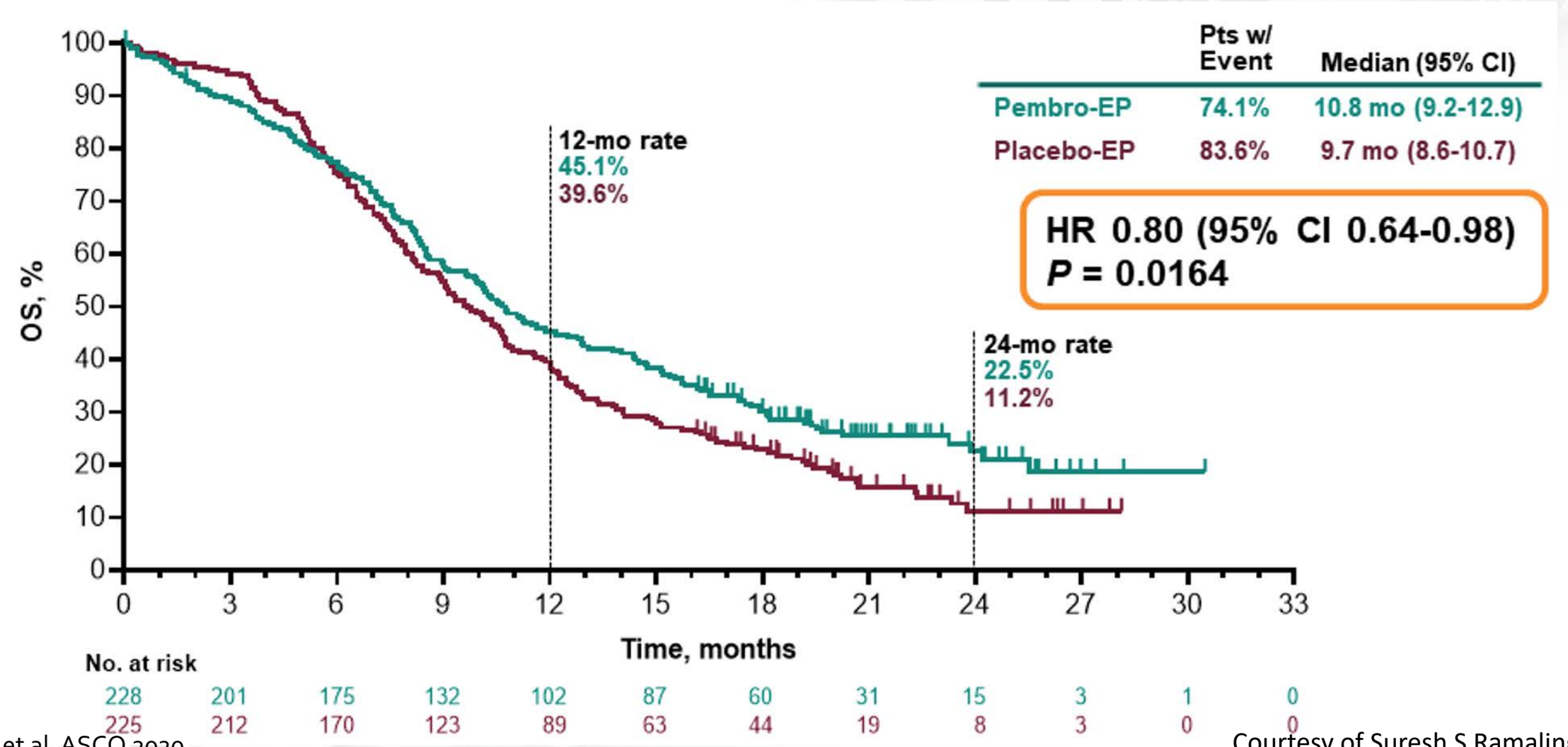
	Pts w/ Event	Median (95% CI)
Pembro-EP	86.0%	4.8 mo (4.3-5.4)
Placebo-EP	97.8%	4.3 mo (4.2-4.5)

HR 0.73 (95% CI 0.60-0.88)

Rudin C et al, ASCO 2020.

Courtesy of Suresh S Ramalingam, MD

PLATINUM-ETOPOSIDE +/- PEMBROLIZUMAB (KN 604 STUDY)
OVERALL SURVIVAL

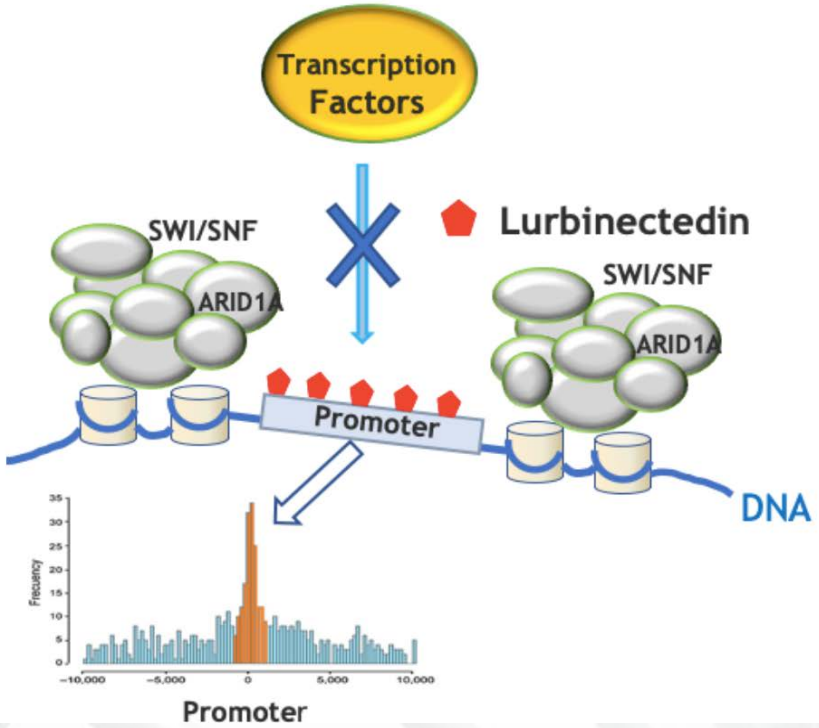


Rudin C et al, ASCO 2020.

Courtesy of Suresh S Ramalingam, MD

LURBINECTEDIN

- Synthetic derivative from a sea sponge
  - Inhibits gene expression
  - ? Other effects??



SCLC-ED

ECOG PS=0-2

No brain metastasis

Prior Chemotherapy

Lurbinectedin3.2 mg/m^2 Q 3 weeks

N=105 Pts

Primary endpoint: Response Rate

Courtesy of Suresh S Ramalingam, MD

LURBINECTEDIN: EFFICACY

	All patients (n=105)	Chemotherapy-free interval <90 days (n=45)	Chemotherapy-free interval ≥90 days (n=60)
RECIST responses			
Complete response	0	0	0
Partial response	37 (35%)	10 (22%)	27 (45%)
Stable disease*	35 (33%)	13 (29%)	22 (37%)
Progressive disease	28 (27%)	18 (40%)	10 (17%)
Not evaluable†	5 (5%)	4 (9%)	1 (2%)
Overall response, % (95% CI)	35·2% (26·2–45·2)	22·2% (11·2–37·1)	45·0% (32·1–58·4)
Disease control, % (95% CI)‡	68·6% (58·8–77·3)	51·1% (35·8–66·3)	81·7% (69·6–90·5)
mPFS	3.5 m	2.6 m	4.6 m
mOS:	9.3 m	5 m	11.9 m

Adverse events of interest:
Hematological: Anemia, neutropenia, thrombocytopenia
Non-hematological: Fatigue, nausea, vomiting, diarrhea, transaminitis

Trigo J et al, Lancet Oncol, 2020.

Courtesy of Suresh S Ramalingam, MD

Phase III ATLANTIS Study Evaluating Lurbinectedin in Combination with Doxorubicin as Second-Line Treatment for SCLC

Press Release: December 3, 2020

"The multicenter, randomized, controlled, phase 3 ATLANTIS study, which evaluated lurbinectedin in combination with doxorubicin versus physician's choice of topotecan or cyclophosphamide/doxorubicin/vincristine (CAV) for adult patients with small cell lung cancer (SCLC) whose disease progressed following 1 prior platinum-containing line of therapy, did not meet the pre-specified criteria of significance for the primary end point of overall survival (OS) in the intent-to-treat (ITT) population of patients.

The study compared lurbinectedin in combination with doxorubicin to the control arm, though there was no adverse effect on OS observed within the experimental arm. Trial participants received lurbinectedin at a dose of 2.0 mg/m^2 in the combination arm, which is lower than the FDA approved dose of 3.2 mg/m^2."

https://www.cancernetwork.com/view/phase-3-atlantis-study-fails-to-meet-primary-end-point-of-os-for-patients-with-sclc

Have you administered or would you administer at some point ipilimumab/nivolumab to a patient with extensive-stage SCLC that progresses after first-line treatment with combination chemotherapy/immunotherapy?

1. I have
2. I have not but would for the right patient
3. I have not and would not

What is your preferred second-line treatment for a patient with extensive-stage small cell cancer of the lung with metastases and disease progression on chemotherapy/atezolizumab?

1. Topotecan or irinotecan
2. Lurbinectedin
3. Nivolumab/ipilimumab
4. Pembrolizumab
5. Nivolumab
6. Other

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