Year in Review in Urothelial Bladder Cancer

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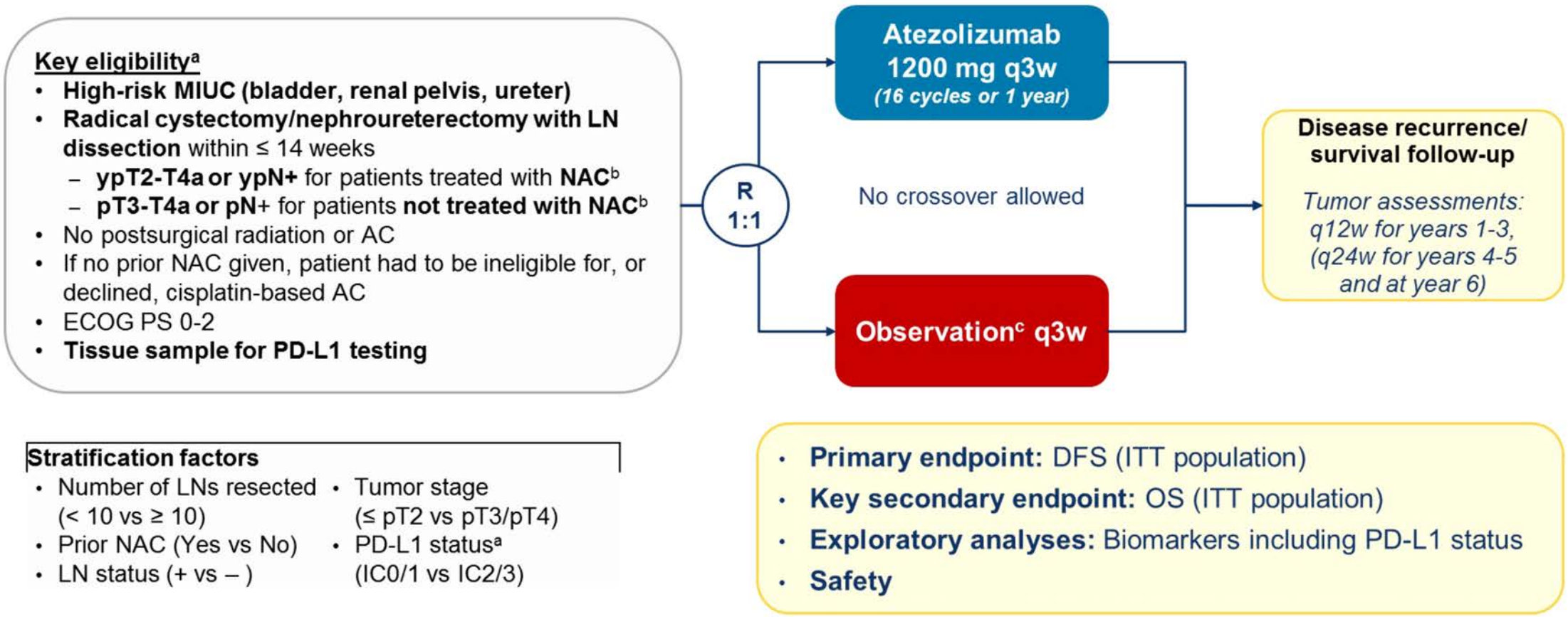
Earlier-Stage Disease: IMvigor010

IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC)

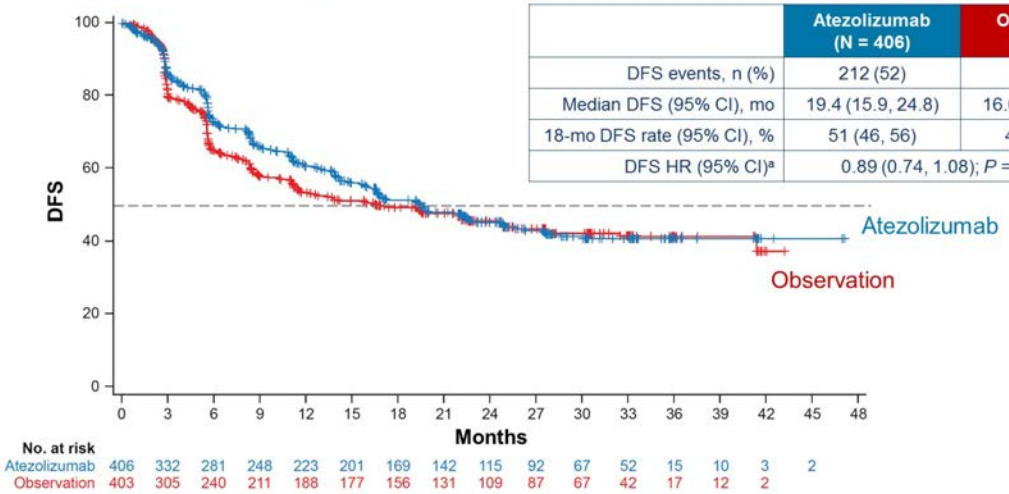


AC, adjuvant chemotherapy; DFS, disease-free survival; ITT, intention to treat; LN, lymph node; MIUC, muscle-invasive UC. [a] Protocol amendments broadened eligibility to "all-comers" (initially, only PD-L1–selected patients were enrolled [IC2/3: PD-L1 expression on tumor-infiltrating immune cells (IC) ≥ 5% of tumor area [VENTANA SP142 IHC assay]) and to patients with MIUC (initially, only patients with muscle-invasive bladder cancer were enrolled). [b] Upper-tract UC staging: ypT2-4 or ypN+ (with NAC) and pT3-4 or pN+ (without NAC). [c] Alternating clinic visits and phone calls.

Hussain MHA et al. Presented at ASCO Annual Meeting 2020 (Abstract 5000)

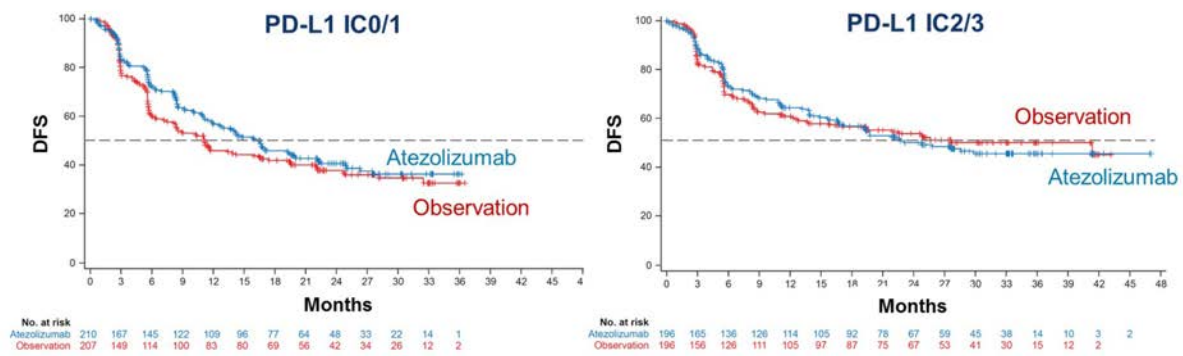
Earlier-Stage Disease: IMvigor010

DFS in ITT Population



	Atezolizumab (N = 406)	Observation (N = 403)
DFS events, n (%)	212 (52)	208 (52)
Median DFS (95% CI), mo	19.4 (15.9, 24.8)	16.6 (11.2, 24.8)
18-mo DFS rate (95% CI), %	51 (46, 56)	49 (44, 54)
DFS HR (95% CI)[a]	0.89 (0.74, 1.08); *P* = 0.2446[b]	

DFS by PD-L1 Status



	Atezolizumab (n = 210)	Observation (n = 207)
DFS events, n (%)	118 (56)	120 (58)
HR (95% CI)[a]	0.81 (0.63, 1.05)	

Atezolizumab (n = 196)	Observation (n = 196)
94 (48)	88 (45)
1.01 (0.75, 1.35)	

	Atezolizumab (n = 390)	Observation (n = 397)
AE, any cause	368 (94)	313 (79)
Treatment-related AE[a]	**276 (71)**	—
Grade 3-4 AE, any cause	145 (37)	80 (20)
Treatment-related Grade 3-4 AEs	**63 (16)**	—
Grade 5 AE	7 (2)	8 (2)
Treatment-related Grade 5 AE	**1 (< 1)[b]**	—
Serious AE[c]	122 (31)	71 (18)
Treatment-related serious AE	**41 (11)**	—
AE leading to discontinuation of atezolizumab	**61 (16)**	—
AE leading to dose interruption of atezolizumab	127 (33)	—

Hussain MHA et al. Presented at ASCO Annual Meeting 2020 (Abstract 5000)

Earlier-Stage Disease: IMvigor010

Impact on Patient Care and Treatment Algorithm

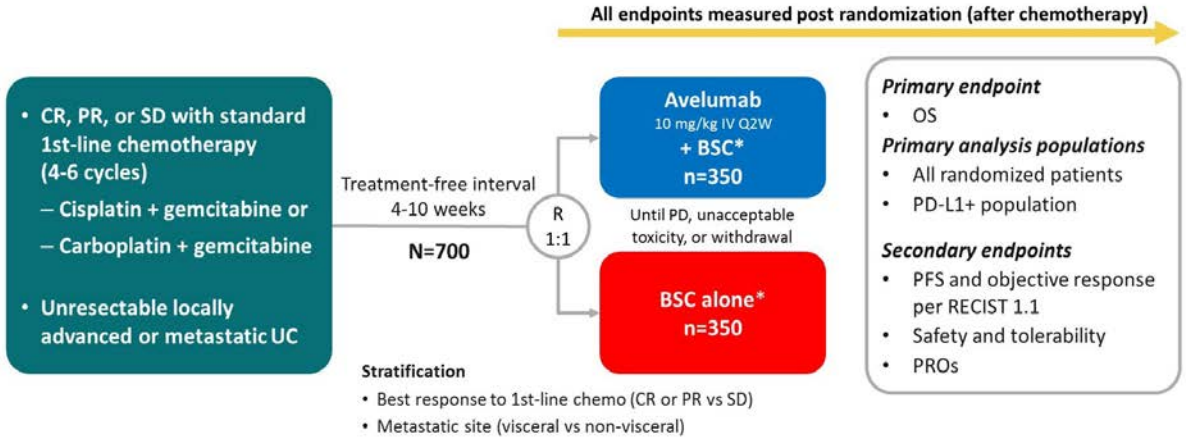
- Adjuvant atezolizumab for high-risk MIBC does not improve disease-free survival
- Clinical subgroup analysis similarly did not show benefit
- Biomarker analysis from ctDNA (Powles *et al* ESMO Asia) shows profound difference in outcome based on ctDNA status

Implications for Future Research

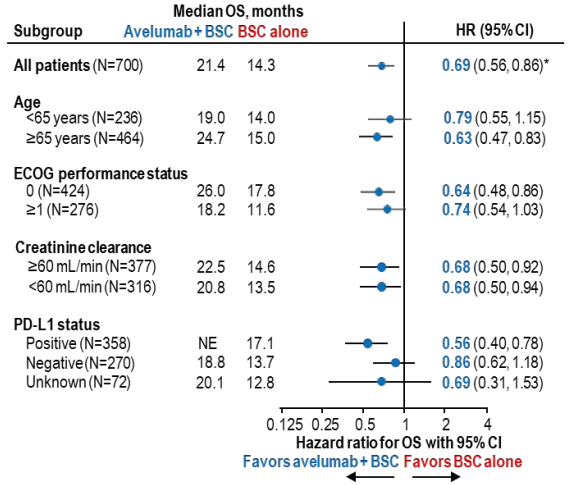
- Observation remains the current standard for adjuvant therapy
- Data from CheckMate274 (adjuvant nivolumab) on the horizon – press release positive!
- PROOF302 study is ongoing, exploring adjuvant FGFR3 inhibition with infigratinib

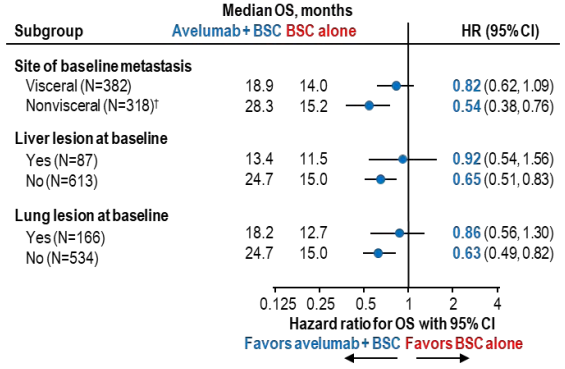
Advanced Disease: JAVELIN Bladder 100

Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma



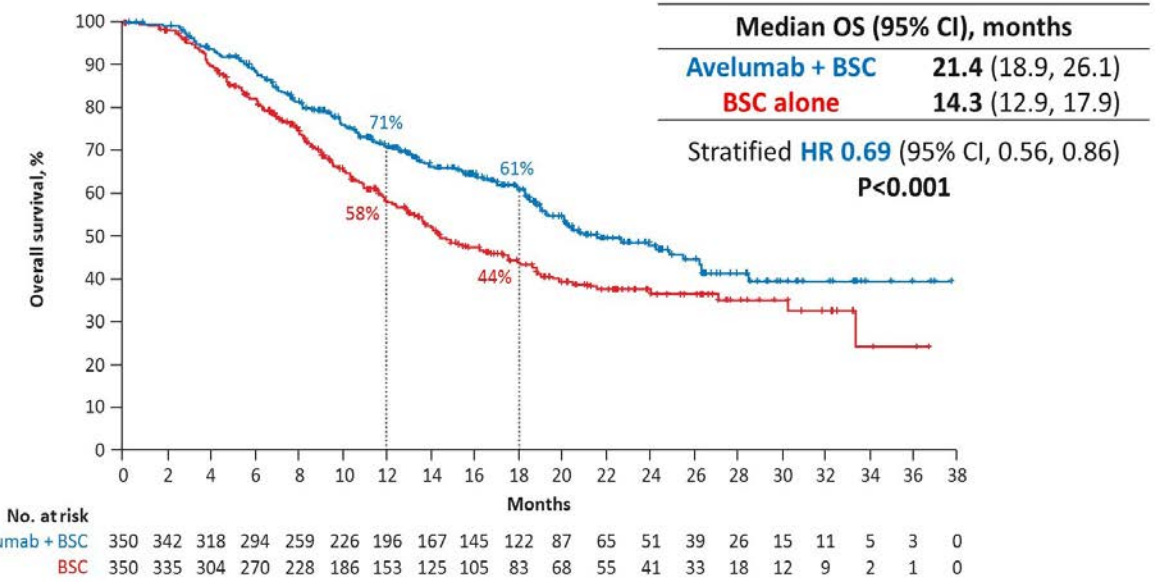
PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively, using the Ventana SP263 assay; 358 patients (51%) had a PD-L1–positive tumor





No significant treatment-by-subgroup interaction (at 0.05 level) was observed for any subgroup variable

OS in the overall population



Median OS (95% CI), months	
Avelumab + BSC	**21.4** (18.9, 26.1)
BSC alone	**14.3** (12.9, 17.9)

Stratified HR 0.69 (95% CI, 0.56, 0.86)
P<0.001

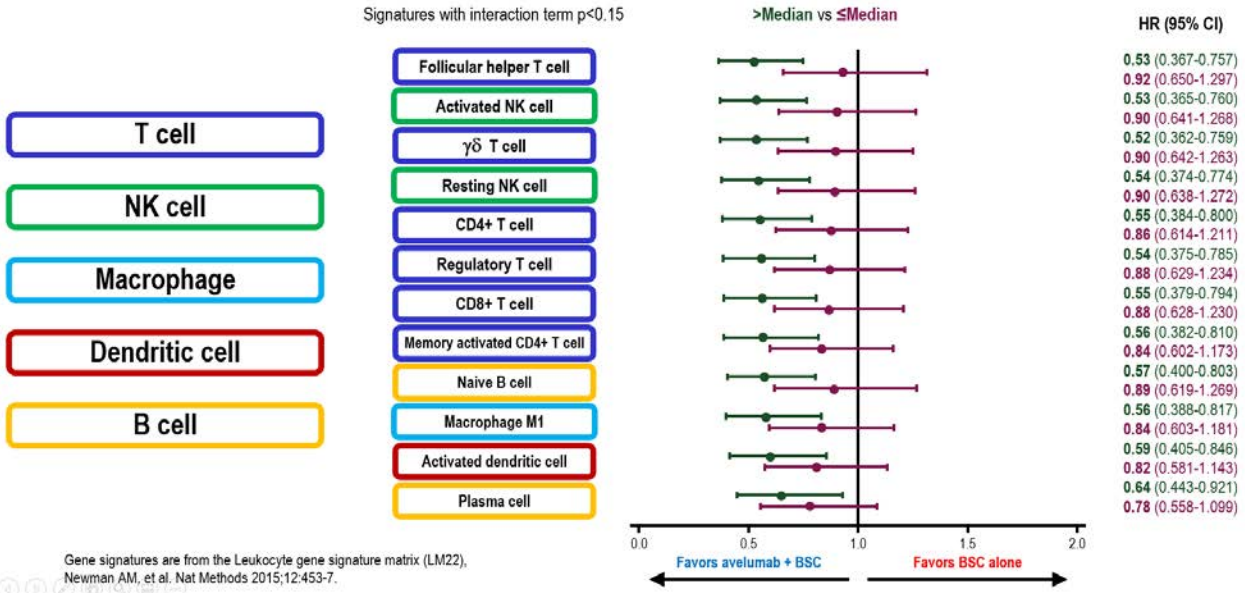
Powles T et al. N Engl J Med 2020 Sep 4;383 (13): 1218-1230; Presented at ASCO Annual Meeting 2020 (Abstract LBA1)

Advanced Disease: JAVELIN Bladder 100

Avelumab first-line (1L) maintenance + best supportive care (BSC) vs BSC alone for advanced urothelial carcinoma (UC): association between clinical outcomes and exploratory biomarkers

Relationship between immune cell gene expression signatures and OS with avelumab

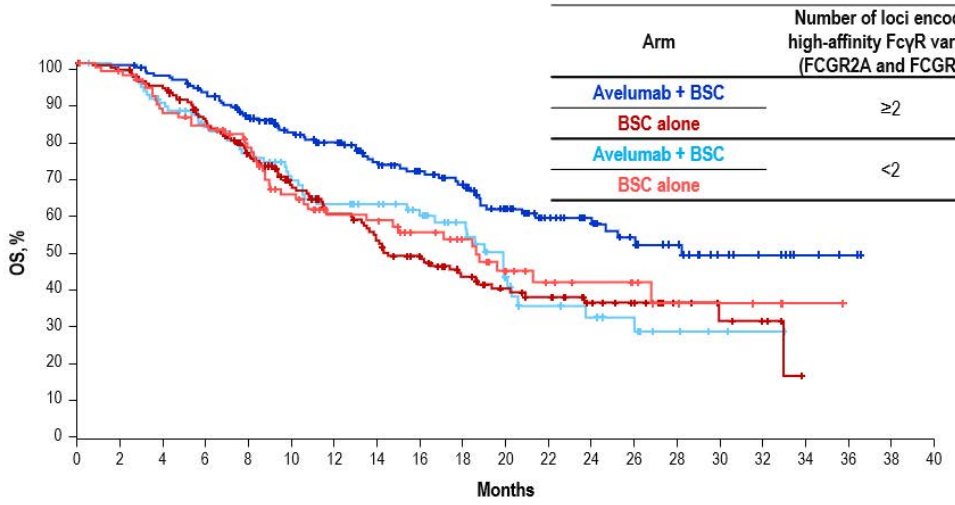
Multiple immune cell signatures may predict OS benefit with avelumab



Gene signatures are from the Leukocyte gene signature matrix (LM22), Newman AM, et al. Nat Methods 2015;12:453-7.

Correlation between number of high-affinity FcγR variants and outcomes with avelumab

May indicate contribution of FcR-mediated antitumor mechanisms



Arm	Number of loci encoding high-affinity FcγR variants (FCGR2A and FCGR3A)	HR (95% CI)
Avelumab + BSC BSC alone	≥2	**0.53** (0.384-0.732)
Avelumab + BSC BSC alone	<2	**1.03** (0.682-1.548)

c receptor

Sridhar S et al. Presented at the ESMO 2020 Virtual Congress (Abstract 699O)

Advanced Disease: JAVELIN Bladder 100

Impact on Patient Care and Treatment Algorithm

- Maintenance therapy with avelumab should represent a standard for patients with metastatic urothelial cancer who have a response or stabilization following 4-6 cycles of platinum-based chemotherapy
- Benefit exists irrespective of PD-L1 status

Implications for Future Research

- Fc gamma receptors may be involved in anti-tumor mechanisms and may identify patients who respond to avelumab
- Could other PD-1/PD-L1 inhibitors be substituted in the maintenance space?
- People may be tempted to use other PD-1/PD-L1 inhibitors in this space; appropriate?

Advanced Disease: IMvigor130

Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomised, placebo-controlled phase 3 trial

- Locally advanced or mUC
- No prior systemic therapy in the metastatic setting
- ECOG PS ≤ 2
- 1L platinum-eligible
- N = 1200
- Randomised 1:1:1

→ **Arm A** Atezo + plt/gem

→ **Arm B** Atezo monotherapy

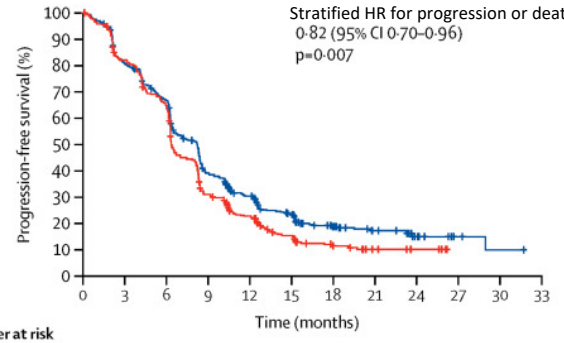
→ **Arm C** Placebo + plt/gem

Stratification factors:
- PD-L1 IC status (IC0 vs IC1 vs IC2/3)
- Bajorin risk factor score including KPS < 80% vs ≥ 80% and presence of visceral metastases (0 vs 1 vs 2 and/or patients with liver metastases)
- Investigator choice of plt/gem (cisplatin + gem or carboplatin + gem)

Co-primary endpoints:
- INV-assessed PFS[a] and OS (Arm A vs C)
- OS (Arm B vs C, hierarchical approach)

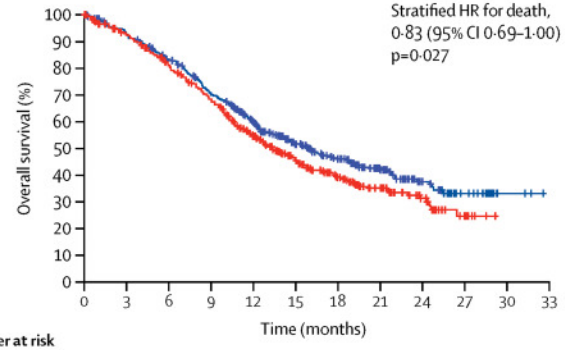
Key secondary endpoints:
- INV-ORR[a] and DOR
- PFS[a] and OS (Arm B vs C; PD-L1 IC2/3 subgroup)
- Safety

	Number of events/ number of patients	Median progression-free survival (95% CI), months
Atezolizumab + platinum-based chemotherapy (group A)	334/451	8·2 (6·5–8·3)
Placebo + platinum-based chemotherapy (group C)	326/400	6·3 (6·2–7·0)



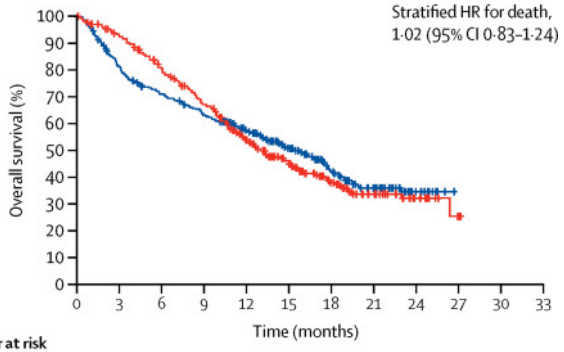
Number at risk (number censored)												
Atezolizumab + platinum-based chemotherapy (group A)	451 (0)	345 (22)	282 (27)	160 (34)	111 (49)	74 (62)	42 (81)	22 (98)	10 (108)	4 (114)	2 (115)	NE
Placebo + platinum-based chemotherapy (group C)	400 (0)	317 (13)	246 (14)	116 (19)	73 (31)	40 (45)	18 (58)	11 (63)	4 (70)	NE	NE	NE

	Number of events/ number of patients	Median overall survival (95% CI), months
Atezolizumab + platinum-based chemotherapy (group A)	235/451	16·0 (13·9–18·9)
Placebo + platinum-based chemotherapy (group C)	228/400	13·4 (12·0–15·2)



Number at risk (number censored)												
Atezolizumab + platinum-based chemotherapy (group A)	451 (0)	408 (11)	360 (17)	301 (23)	229 (51)	163 (88)	117 (118)	72 (154)	36 (184)	16 (200)	3 (213)	NE
Placebo + platinum-based chemotherapy (group C)	400 (0)	359 (13)	308 (19)	255 (24)	182 (48)	123 (79)	79 (108)	49 (131)	25 (151)	8 (164)	NE	NE

	Number of events/ number of patients	Median overall survival (95% CI), months
Atezolizumab monotherapy (group B)	191/360	15·7 (13·1–17·8)
Placebo + platinum-based chemotherapy (group C)	198/359	13·1 (11·7–15·1)



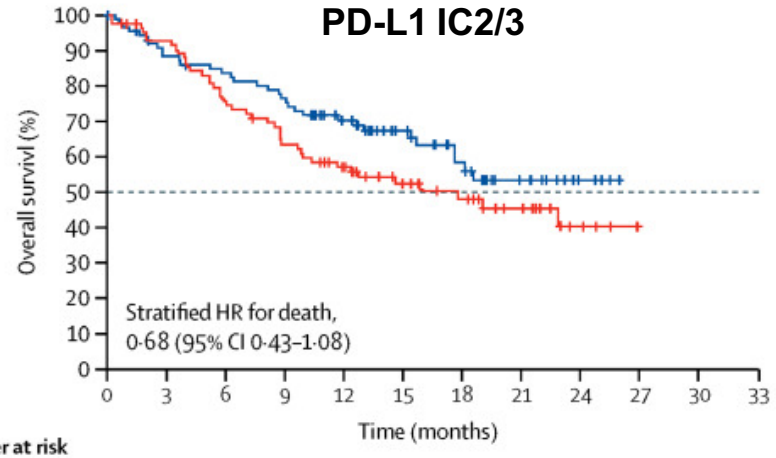
Number at risk (number censored)												
Atezolizumab monotherapy (group B)	360 (0)	285 (10)	245 (14)	216 (16)	173 (41)	120 (75)	72 (107)	42 (128)	16 (153)	NE	NE	NE
Placebo + platinum-based chemotherapy (group C)	359 (0)	322 (13)	274 (19)	224 (24)	158 (48)	103 (79)	62 (107)	35 (128)	15 (147)	3 (158)	NE	NE

Galsky MD et al; IMvigor130 Study Group. Lancet. 2020 May 16;395(10236):1547-1557

Advanced Disease: IMvigor130

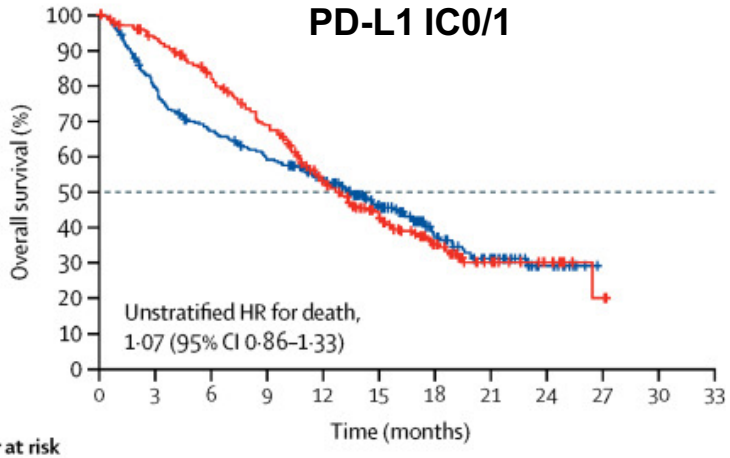
Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomised, placebo-controlled phase 3 trial

	Number of events/ number of patients	Median overall survival (95% CI), months
Atezolizumab monotherapy (group B)	33/88	NE (17·7–NE)
Placebo + platinum-based chemotherapy (group C)	42/85	17·8 (10·0–NE)



Number at risk (number censored)												
Atezolizumab monotherapy (group B)	88 (0)	75 (3)	70 (4)	64 (4)	49 (14)	35 (26)	24 (33)	14 (41)	5 (50)	NE	NE	NE
Placebo + platinum-based chemotherapy (group C)	85 (0)	76 (3)	62 (3)	51 (4)	42 (8)	30 (17)	21 (24)	14 (30)	5 (38)	1 (42)	NE	NE

	Number of events/ number of patients	Median overall survival (95% CI), months
Atezolizumab monotherapy (group B)	158/272	13·5 (11·1–16·4)
Placebo + platinum-based chemotherapy (group C)	156/274	12·9 (11·3–15·0)



Number at risk (number censored)												
Atezolizumab monotherapy (group B)	272 (0)	210 (7)	175 (10)	152 (12)	124 (27)	85 (49)	48 (74)	28 (87)	11 (103)	NE	NE	NE
Placebo + platinum-based chemotherapy (group C)	274 (0)	246 (10)	212 (16)	173 (20)	116 (40)	73 (62)	41 (83)	21 (98)	10 (109)	2 (116)	NE	NE

Galsky MD et al; IMvigor130 Study Group. Lancet. 2020 May 16;395(10236):1547-1557

Advanced Disease: IMvigor130

Impact on Patient Care and Treatment Algorithm

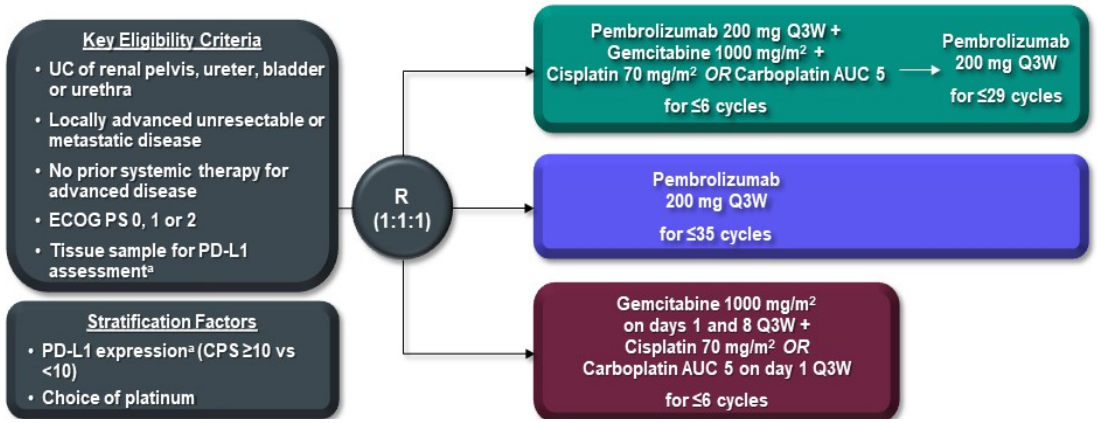
- Platinum chemotherapy with atezolizumab offers a modest PFS advantage compared to chemotherapy alone
- OS data immature
- Versus chemotherapy, no advantage for atezolizumab monotherapy in patients who are PD-L1 low

Implications for Future Research

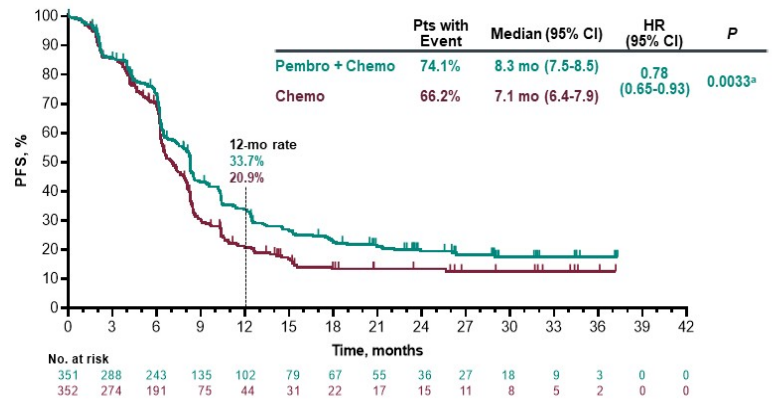
- The KEYNOTE-361 carries a nearly identical design …
- Why does maintenance work, but not combination therapy?
- Will OS migrate over time?

Advanced Disease: First-Line Pembrolizumab

Pembrolizumab (P) combined with chemotherapy (C) vs C alone as firstline(1L) therapy for advanced urothelial carcinoma (UC): KEYNOTE-361

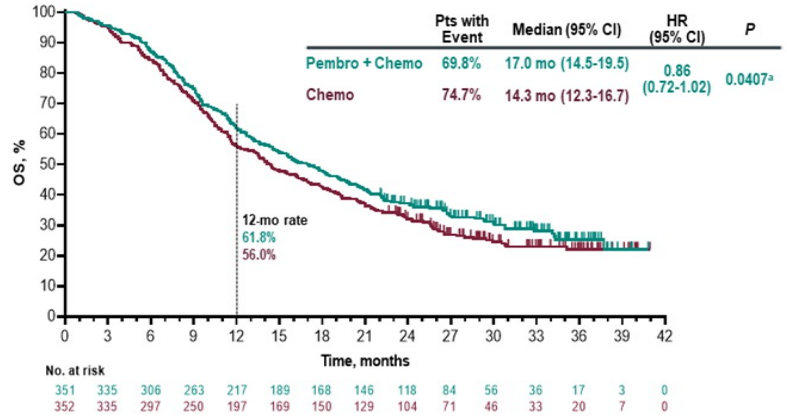


PFS by BICR: Pembro + Chemo vs Chemo, ITT Population (Primary Endpoint)



[a]*P*-value boundary of significance at final analysis ≤0.0019.
PFS assessed per RECIST v1.1. Data cutoff date: April 29, 2020.

OS: Pembro + Chemo vs Chemo, ITT Population



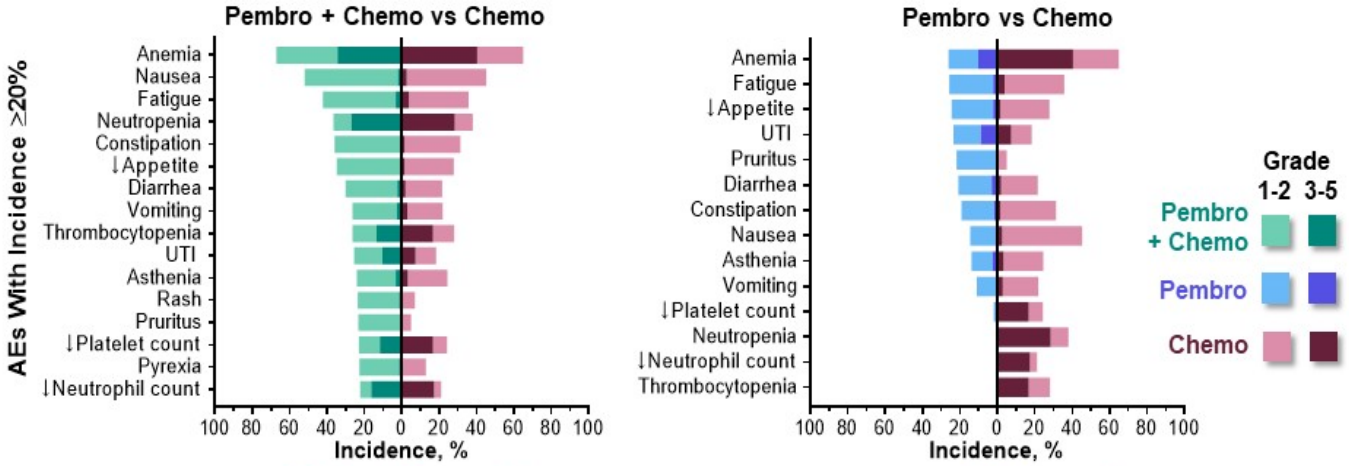
[a]*P*-value boundary of significance at final analysis ≤0.0142. Per the statistical analysis plan, no further formal statistical testing was performed.
Data cutoff date: April 29, 2020.

Alva A et al. Presented at the ESMO 2020 Virtual Congress (Abstract LBA23)

Advanced Disease: First-Line Pembrolizumab

Pembrolizumab (P) combined with chemotherapy (C) vs C alone as firstline(1L) therapy for advanced urothelial carcinoma (UC): KEYNOTE-361

All-Cause AEs, As-Treated Population

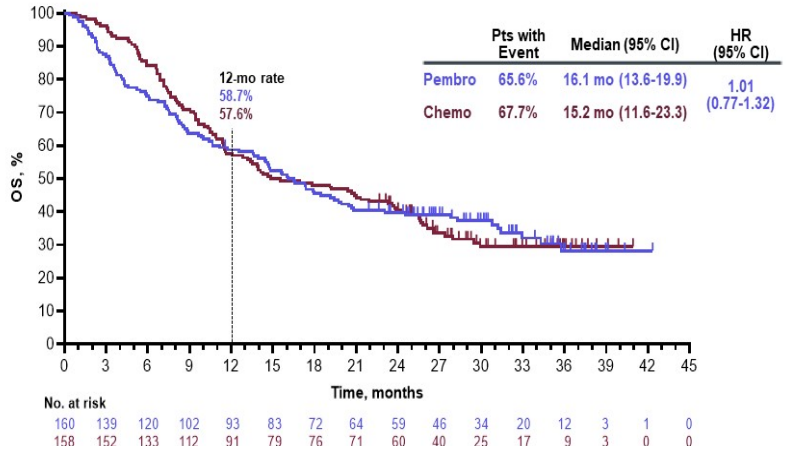


All AEs	Pembro + Chemo	Chemo
Any grade	99.7%	99.7%
Grade 3-5	87.4%	81.9%
Led to death	9.2%	2.6%
Led to discontinuation	30.9%	18.1%

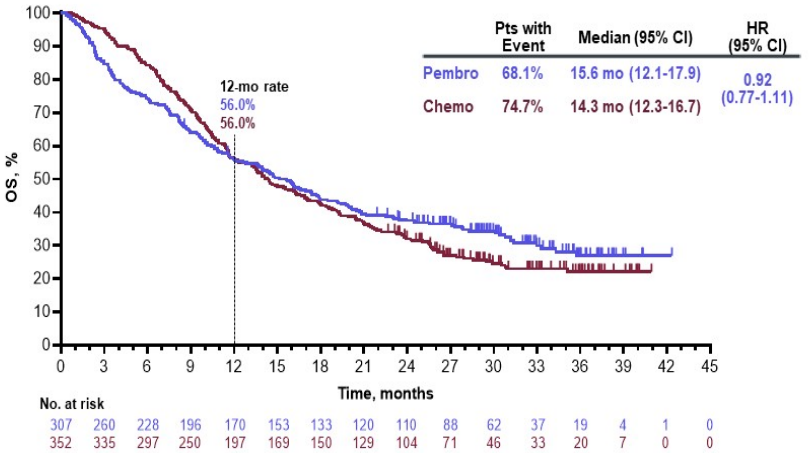
All AEs	Pembro	Chemo
Any grade	95.7%	99.7%
Grade 3-5	62.9%	81.9%
Led to death	8.6%	2.6%
Led to discontinuation	15.9%	18.1%

Median (range) duration of treatment was 7.7 (0-27.8) months for pembro + chemo, 4.2 (0-28.1) months for pembro, and 3.7 (0-7.2) months for chemo. As-treated population includes all patients who received ≥1 dose of trial treatment. Data cutoff date: April 29, 2020.

OS: Pembro vs Chemo, Patients With CPS≥10 Tumors



OS: Pembro vs Chemo, ITT Population

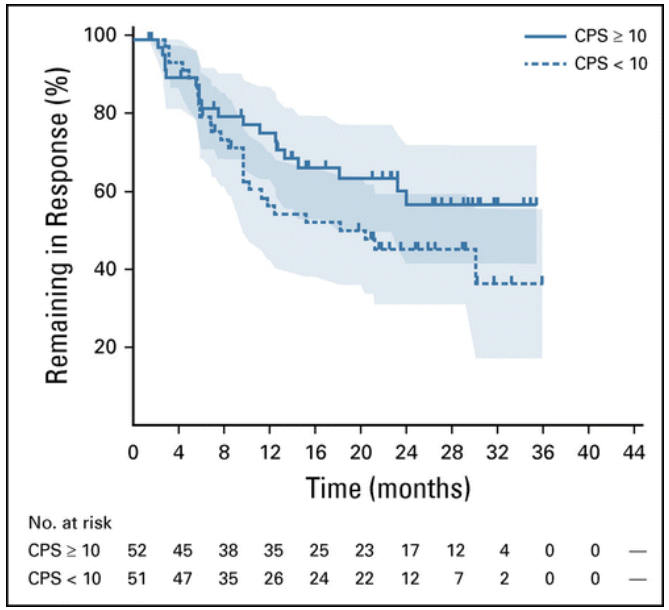


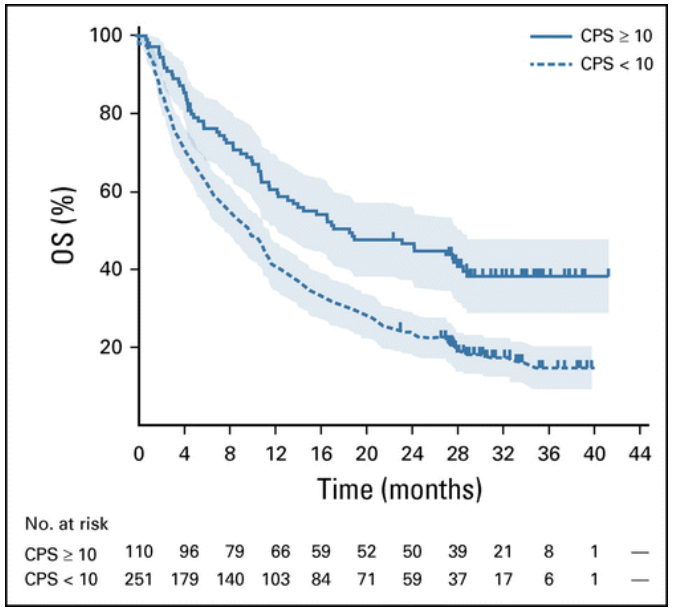
Data cutoff date: April 29, 2020.

Alva A et al. Presented at the ESMO 2020 Virtual Congress (Abstract LBA23)

Advanced Disease: First-Line Pembrolizumab

Long-Term Outcomes in KEYNOTE-052: Phase II Study Investigating First-Line Pembrolizumab in Cisplatin-Ineligible Patients With Locally Advanced or Metastatic Urothelial Cancer





Kaplan-Meier estimates and 95% CIs of duration of response and overall survival (OS) in relation to programmed death ligand 1 expression combined positive score (CPS) ≥ 10 or CPS < 10

AE	No. (%)
Any-grade treatment-related AE	249 (67.3)
Treatment-related AEs in ≥ 3%	
Fatigue	67 (18.1)
Pruritus	66 (17.8)
Rash	43 (11.6)
Decreased appetite	40 (10.8)
Hypothyroidism	37 (10.0)
Diarrhea	34 (9.2)
Nausea	32 (8.6)
Asthenia	15 (4.1)
Maculopapular rash	15 (4.1)
Pneumonitis	15 (4.1)
AST increased	14 (3.8)
Pyrexia	14 (3.8)
ALT increased	13 (3.5)
Dysgeusia	13 (3.5)
Vomiting	13 (3.5)
Cough	12 (3.2)
Constipation	11 (3.0)
Dry mouth	11 (3.0)
Influenza-like illness	11 (3.0)
Peripheral edema	11 (3.0)

Abbreviations: AE, adverse event ALT; alanine aminotransferase; AST, aspartate aminotransferase.

Vuky J et al. J Clin Oncol. 2020 Aug 10;38(23):2658-2666.

Advanced Disease: First-Line Pembrolizumab

Impact on Patient Care and Treatment Algorithm

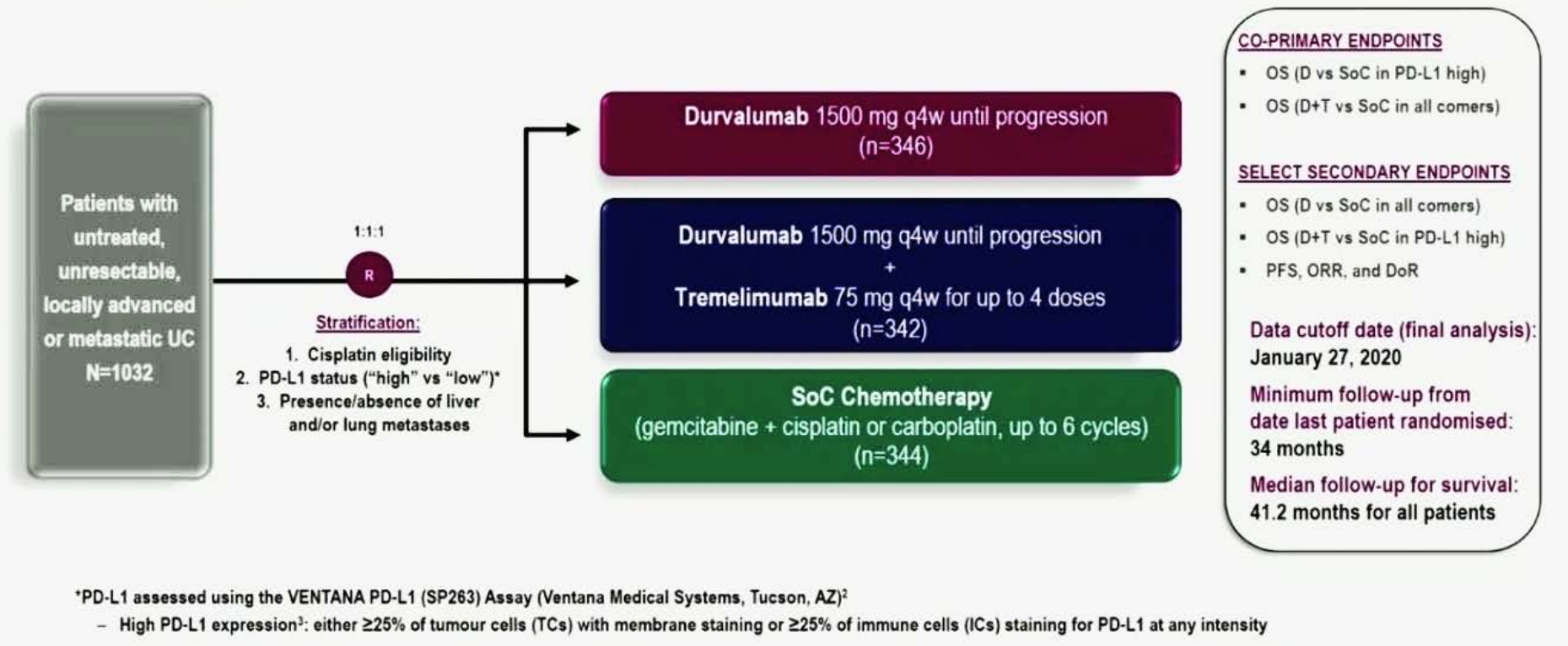
- PFS and OS did not reach pre-specified statistical cutoffs for significance
- Therefore, chemotherapy with pembrolizumab does not appear to offer an advantage to chemotherapy alone
- No difference between pembrolizumab monotherapy and chemotherapy, even in those with high CPS scores – consider chemo upfront across the board (especially given opportunity for maintenance treatment)?

Implications for Future Research

- If adjuvant therapy is utilized upfront, how will this impact use of chemotherapy and IO?
- Again, will enfortumab plus IO potentially slide up in our algorithm?

Advanced Disease: DANUBE

Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): a randomised, open-label, multicentre, phase 3 trial



Powles T et al; DANUBE study investigators Lancet Oncol. 2020 Dec;21(12):1574-1588; Presented at the ESMO 2020 Virtual Congress (Abstract 697O)

Advanced Disease: DANUBE

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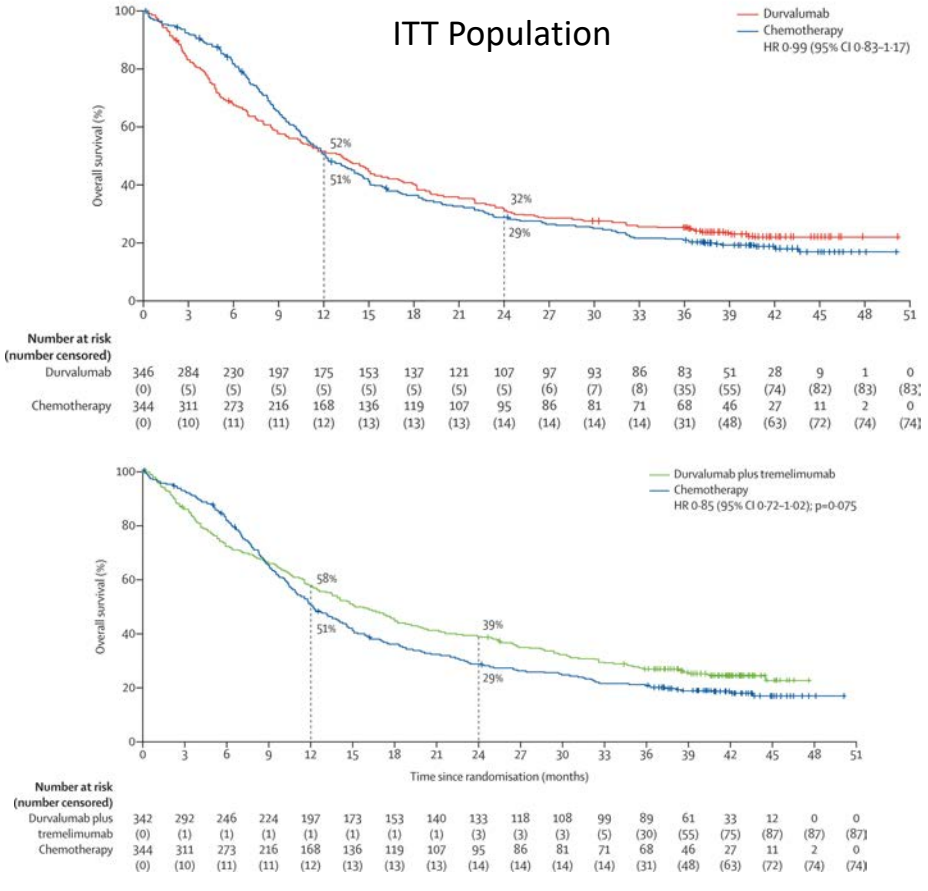
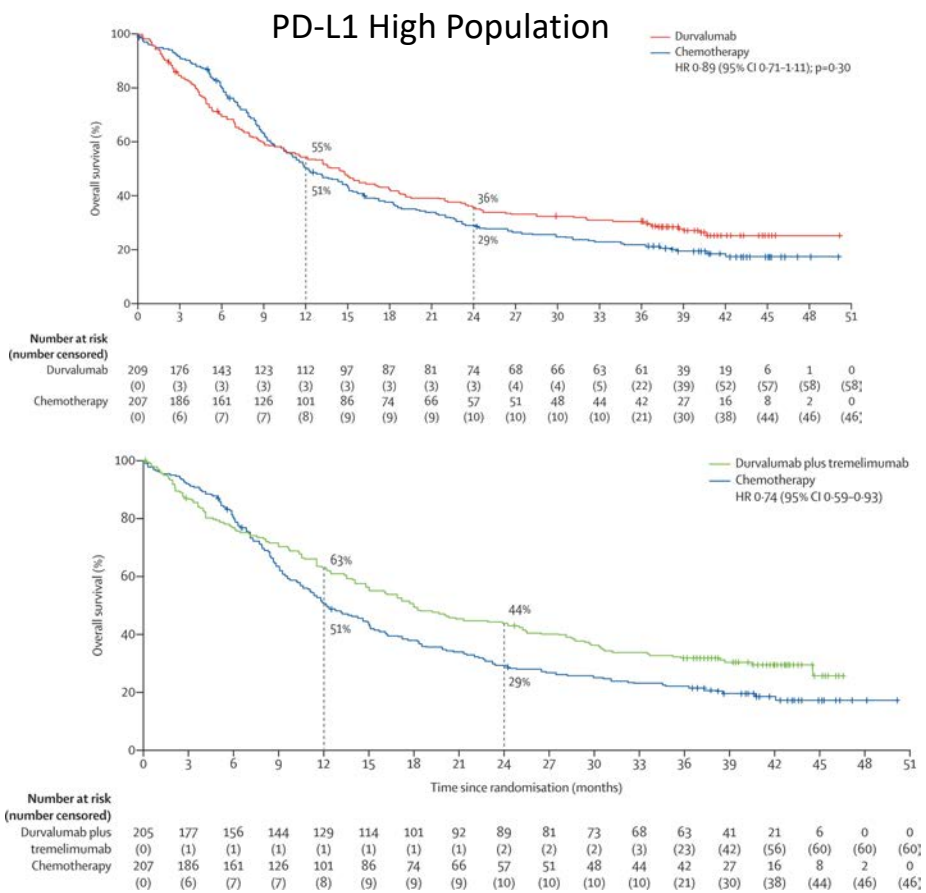
ITT Population



PD-L1 High Population



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Advanced Disease: DANUBE

Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): a randomised, open-label, multicentre, phase 3 trial

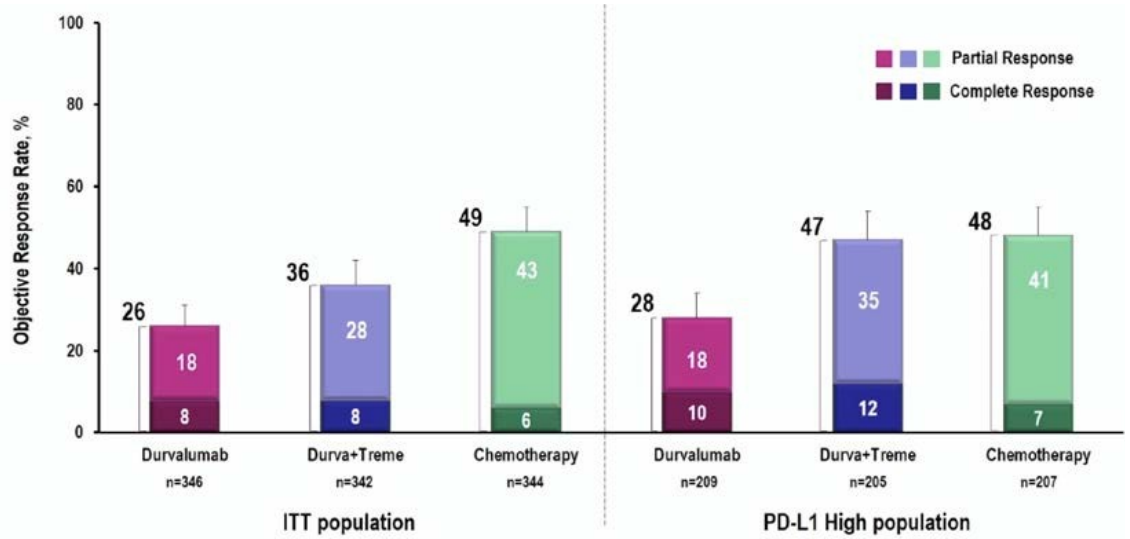
Safety Summary

	Durvalumab n=345	Durvalumab + Tremelimumab n=340	Chemotherapy n=313
Treatment-related AEs			
Any grade	56%	75%	90%
Grade 3 or 4	14%	28%	60%
Grade 5	1%	1%	<1%
Treatment-related serious AEs	9%	23%	16%
Treatment-related AEs leading to discontinuation	6%	16%	12%
Treatment-related AEs of special interest*			
Any grade	26%	49%	15%
Grade 3 or 4	6%	12%	2%
Systemic corticosteroid use	11%	26%	1%

*Excluding infusion/hypersensitivity reactions.

- Most common treatment-related AEs of grade 3 or 4 were increased lipase (in both the durvalumab and durvalumab + tremelimumab groups) and neutropenia and anemia (in the chemotherapy group)

Anti-tumour Activity: Objective Response Rate*



*Secondary endpoint; response was assessed by the investigators according to RECIST v1.1.

Powles T et al; DANUBE study investigators Lancet Oncol. 2020 Dec;21(12):1574-1588; Presented at the ESMO 2020 Virtual Congress (Abstract 697O)

Advanced Disease: DANUBE

Impact on Patient Care and Treatment Algorithm

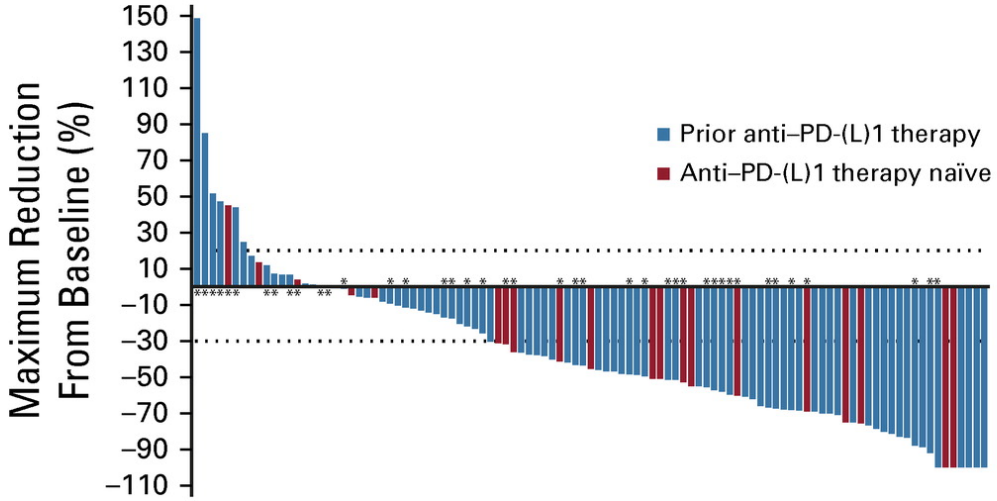
- Durvalumab with tremelimumab does not offer benefit over chemotherapy
- There is crossover on the survival curves – and a meaningful “tail”, particularly in those patients that are PD-L1 positive
- In some ways (adverse events leading to discontinuation, corticosteroid use), durvalumab/tremelimumab seems more tolling than chemotherapy

Implications for Future Research

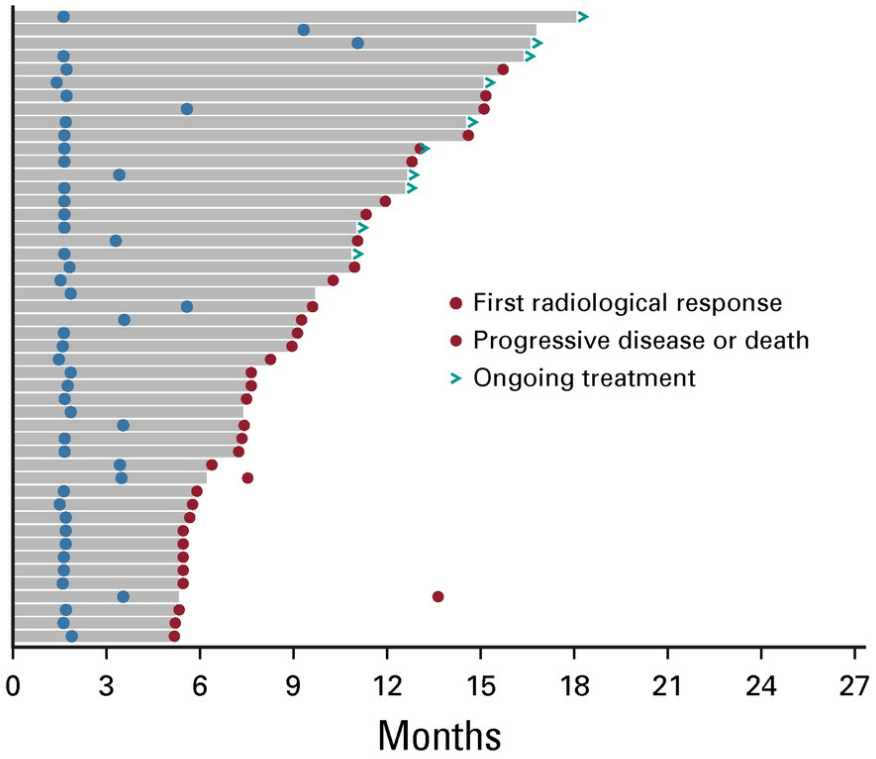
- Who are the patients on the tail of the curve?

Advanced Disease: Enfortumab Vedotin

EV-101: A Phase I Study of Single-Agent Enfortumab Vedotin in Patients With Nectin-4-Positive Solid Tumors, Including Metastatic Urothelial Carcinoma



Response	Overall mUC, No. (%)	Prior Anti–PD-(L)1 Therapy, No. (%)	
		Investigator Review[a]	Central Review[b]
No. of patients	112	89	74
Confirmed CR	5 (5)	3 (3)	8 (11)
Confirmed PR	43 (38)	35 (39)	25 (34)
SD	32 (29)	28 (32)	27 (37)
Confirmed ORR,[c] % (95% CI)	43 (33.6 to 52.6)	43 (32.3 to 53.6)	45 (33.0 to 56.6)
DCR,[c] % (95% CI)	71 (62.1 to 79.6)	74 (63.8 to 82.9)	81 (70.3 to 89.3)
Median DoR, months (95% CI)	7.4 (5.6 to 9.6)	7.3 (4.2 to 9.6)	7.5 (5.8 to NR)



Rosenberg J et al. J Clin Oncol. 2020 Apr 1;38(10):1041-1049

Advanced Disease: Enfortumab Vedotin

EV-103: Preliminary durability results of enfortumab vedotin plus pembrolizumab for locally advanced or metastatic urothelial carcinoma

Enfortumab vedotin 1.25 mg/kg + pembrolizumab (200 mg) in 1L cisplatin-ineligible la/mUC patients (N=45)

Patient Population	Dose Escalation[1]	Dose Expansion Cohort A
Locally Advanced or Metastatic Urothelial Carcinoma	enfortumab vedotin + pembrolizumab cisplatin-ineligible (n=5)	enfortumab vedotin + pembrolizumab cisplatin-ineligible (n=40)

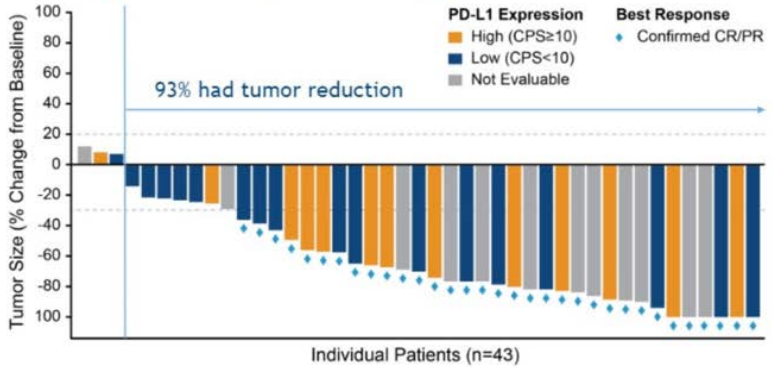
Dosing: Enfortumab vedotin on days 1 and 8 and pembrolizumab on day 1 of every 3-week cycle

Enfortumab vedotin exposure: Comparable to enfortumab vedotin monotherapy on 4-week schedule (Days 1, 8, and 15)[2]

Primary endpoints: safety and tolerability

Key secondary endpoints: dose-limiting toxicities, ORR, DOR, PFS, OS

Maximal Target Lesion Reduction by PD-L1 status and Objective Response Rate per Investigator



Confirmed ORR 95% CI	73.3% (33/45) (58.1, 85.4)
Complete response	15.6% (7/45)
Partial response	57.8% (26/45)

Best Overall Response Per RECIST v 1.1 by investigator (N=45)

- Responses observed regardless of PD-L1 expression level

Two patients did not have post-baseline response assessments before end-of-treatment: 1 withdrew consent and 1 died before any post-baseline response assessment. These patients are included in the full analysis set used to calculate ORR, but are not included in the figure above.

Horizontal lines at positive 20% and negative 30% denote thresholds for target lesions for disease progression and response, respectively.

Treatment-Related Adverse Events of Clinical Interest (AECI)

- Rates of peripheral neuropathy, rash, and hyperglycemia similar to enfortumab vedotin monotherapy
- No new safety signal with the combination

AECI: categorized by related MedDRA terms	Patients (N=45) n (%)		Time to first onset (months) median (min, max)
	Any Grade	≥Grade 3[1]	Any Grade
Peripheral neuropathy	25 (56)	2 (4)	2.3 (1, 12)
Rash	28 (62)	6 (13)	0.7 (0, 12)
Hyperglycemia[2]	5 (11)	3 (7)	0.5 (0, 3)

AECI: determined by investigator	Patients (N=45) n (%)	
	Any Grade	≥Grade 3[1]
Immune-mediated AE requiring systemic steroids	13 (29)	8 (18)[3]

[1] No Grade 5 TRAE of Clinical Interest
[2] Blood glucose assessments were non-fasting.
[3] Grade 3 events: arthralgia, dermatitis bullous, pneumonitis, lipase increased, rash erythematous, rash maculo-papular, tubulointerstitial nephritis; Grade 4: dermatitis bullous, myasthenia gravis

Rosenberg JE et al. Presented at the Genitourinary Cancers Symposium 2020 (Abstract 441)

Advanced Disease: Enfortumab Vedotin

Impact on Patient Care and Treatment Algorithm

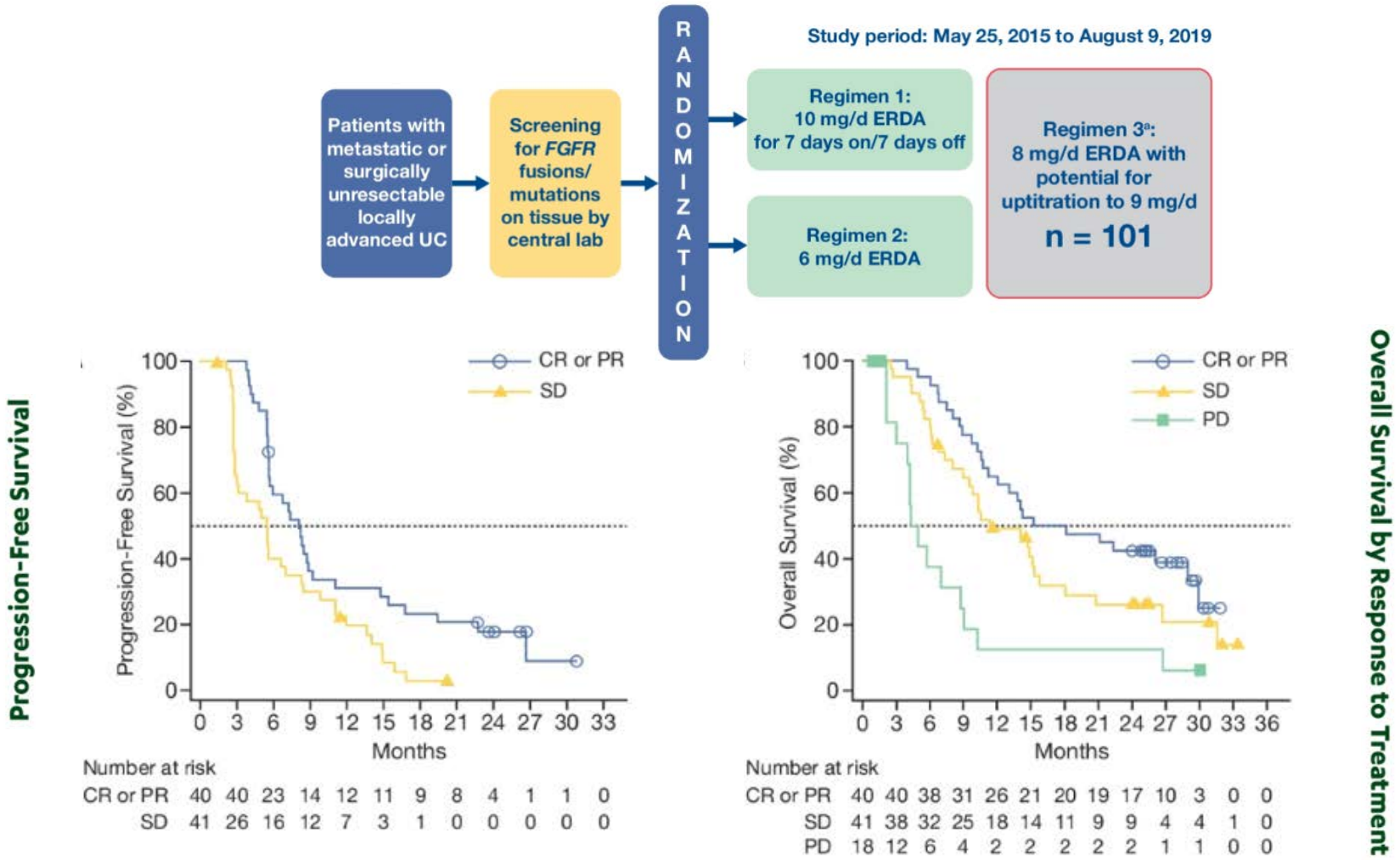
- Enfortumab vedotin has substantial activity in patients with advanced urothelial cancer, with prior platinum and prior IO
- Data for the combination of enfortumab with pembrolizumab are even more compelling, but waiting for confirmatory studies
- Do bear in mind toxicities of neuropathy and rash with enfortumab

Implications for Future Research

- Confirmatory Phase III studies of enfortumab versus chemotherapy will read out soon
- Upfront enfortumab with pembrolizumab being explored in confirmatory studies

Advanced Disease: Erdafitinib

Erdafitinib in locally advanced or mUC: Long-term outcomes in BLC2001



Siefker-Radtke AO et al. Presented at ASCO 2020 (Abstract 5015)

Advanced Disease: Erdafitinib

Impact on Patient Care and Treatment Algorithm

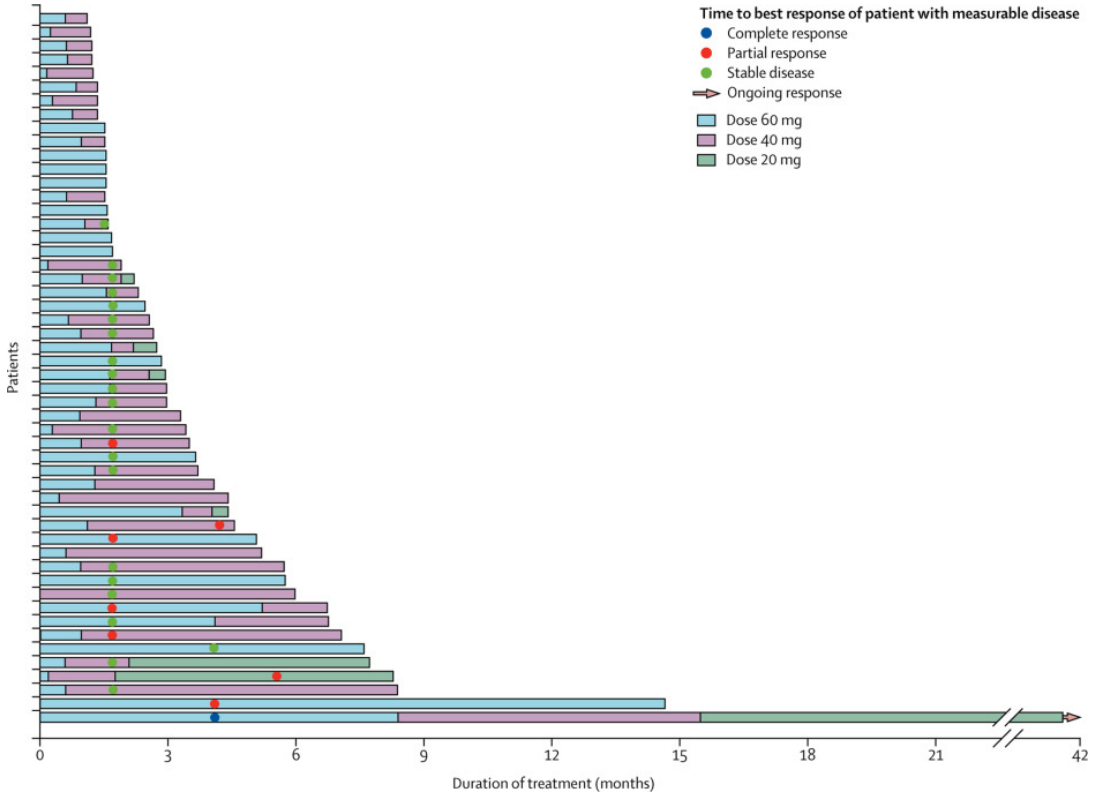
- Obtain molecular profiling in your patients early
- Erdafitinib does lead to meaningful and somewhat durable responses
- Toxicities (e.g., ocular toxicities, hyperphosphatemia) do require nuanced management

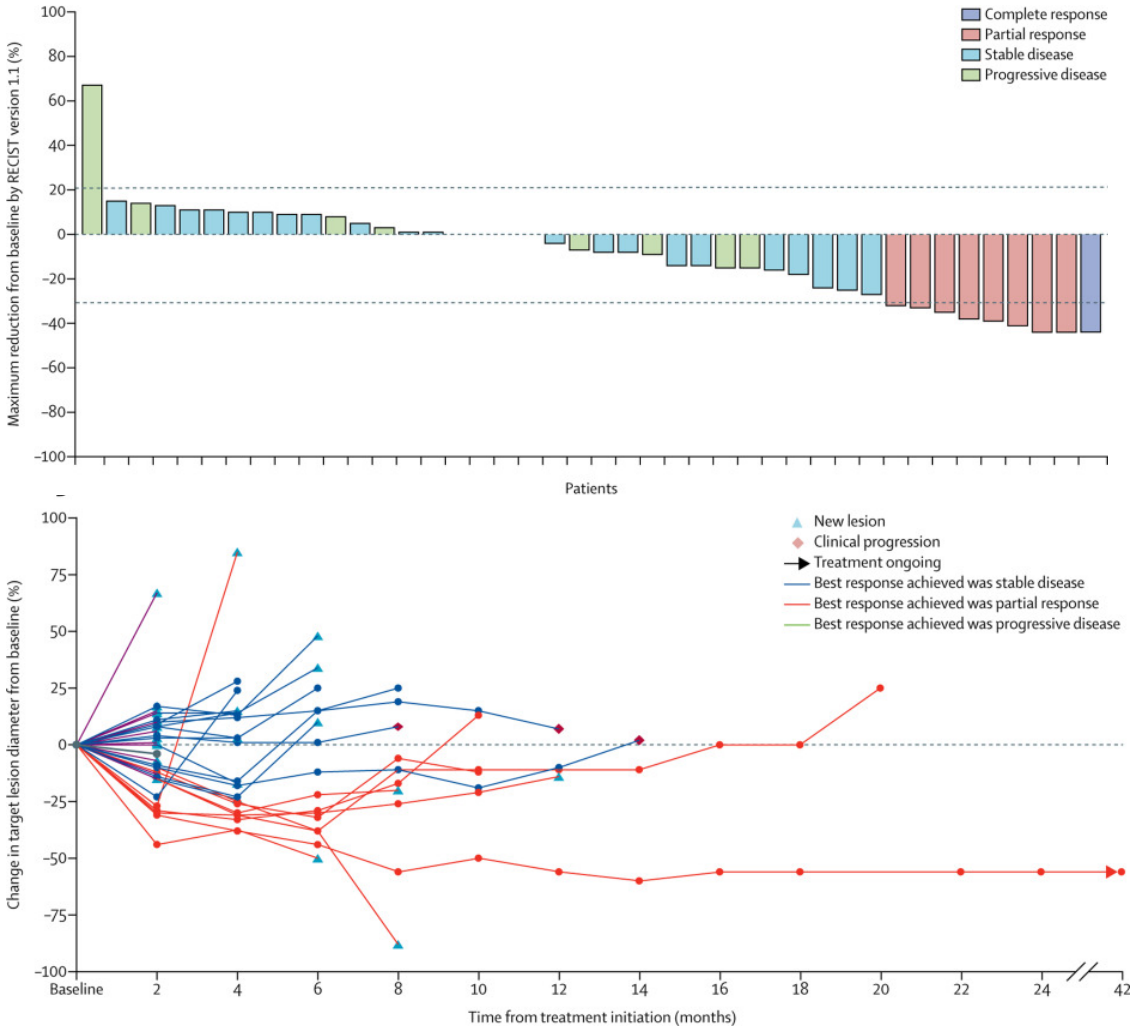
Implications for Future Research

- Adjuvant infigratinib (a distinct FGFR3 inhibitor) is being explored currently
- Combinations of erdafitinib and IO under investigation

Advanced Disease: Platinum-Refractory mUBC

Cabozantinib in patients with platinum-refractory metastatic urothelial carcinoma: an open-label, single-centre, phase 2 trial

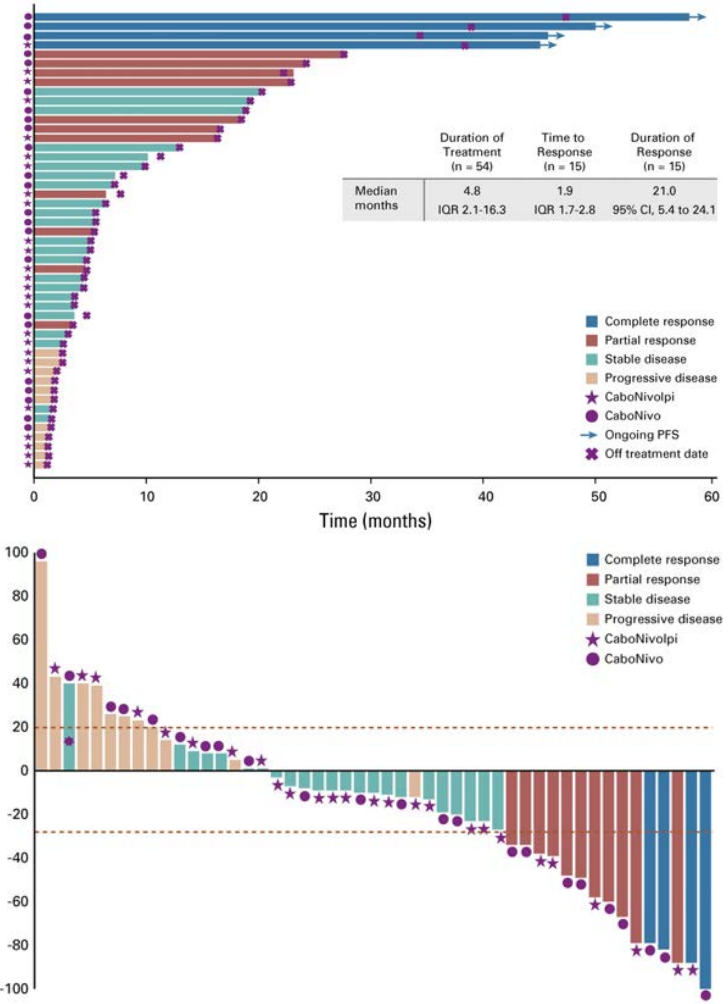




Apolo AB et al. Lancet Oncol. 2020 Aug;21(8):1099-1109; Kikuchi E, Hayakawa N. Lancet Oncol. 2020 Aug;21(8):1005-1006

Advanced Disease: Platinum-Refractory mUBC

Phase I Study of Cabozantinib and Nivolumab Alone or With Ipilimumab for Advanced or Metastatic Urothelial Carcinoma and Other Genitourinary Tumors



	No. of Patients (%)							
	Cabozantinib and Nivolumab (n = 24)				Cabozantinib, Nivolumab, and Ipilimumab (n = 30)			
	Cabozantinib 40 mg (n = 12)		Cabozantinib 60 mg (n = 12)		Cabozantinib 40 mg (n = 24)		Cabozantinib 60 mg (n = 6)	
Adverse Event	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Clinical events								
Fatigue	10 (83)	1 (8)	10 (83)	3 (25)	18 (75)	2 (8)	5 (83)	1 (17)
Diarrhea	8 (67)	0	10 (83)	1 (8)	14 (58)	2 (8)	4 (67)	0
Anorexia	7 (58)	0	9 (75)	0	10 (42)	0	5 (83)	1 (17)
Skin toxicity	9 (75)	0	5 (42)	0	16 (67)	0	3 (50)	0
Dysphonia	5 (42)	0	6 (50)	0	4 (17)	0	1 (17)	0
Nausea	4 (33)	0	7 (58)	1 (8)	10 (42)	0	5 (83)	1 (17)
Myalgia	5 (42)	0	5 (42)	0	4 (17)	0	0	0
Mucositis	2 (17)	0	8 (67)	0	9 (38)	1 (4)	2 (33)	0
Dry skin	3 (25)	0	3 (25)	0	7 (29)	0	2 (33)	0
Dry mouth	3 (25)	0	6 (50)	0	6 (25)	0	3 (50)	0
Dysgeusia	4 (33)	0	5 (42)	0	8 (33)	0	4 (67)	0
Weight loss	2 (17)	0	6 (50)	0	10 (42)	0	3 (50)	0
Vomiting	3 (25)	0	6 (50)	2 (17)	7 (29)	0	2 (33)	0
Palmar-plantar erythrodysesthesia	3 (25)	0	5 (42)	0	5 (21)	0	1 (17)	0
Abdominal pain	4 (33)	0	4 (33)	1 (8)	3 (13)	0	1 (17)	0
Sore throat	1 (8)	0	5 (42)	0	1 (3)	0	1 (17)	0
Hypertension	4 (33)	3 (25)	4 (33)	2 (17)	5 (21)	2 (8)	1 (17)	1 (17)
Headache	2 (17)	0	4 (33)	0	2 (8)	1 (4)	1 (17)	0
Cough	3 (25)	0	2 (17)	0	5 (21)	0	3 (50)	0
Blurred vision	2 (17)	0	2 (17)	0	4 (17)	0	0	0
Arthralgia	1 (8)	0	3 (25)	0	5 (21)	0	1 (17)	0
Edema limb	3 (25)	0	1 (8)	0	2 (8)	0	1 (17)	0
Constipation	2 (17)	0	2 (17)	0	4 (17)	0	0	0
Dehydration	1 (8)	0	2 (17)	2 (17)	3 (13)	0	1 (17)	0
Infection	1 (8)	0	1 (8)	1 (8)	3 (13)	0	1 (17)	0
Thromboembolic event	1 (8)	1 (8)	0	0	2 (8)	2 (8)	1 (17)	1 (17)
Fever	1 (8)	0	1 (8)	0	4 (17)	0	1 (17)	1 (17)

Apolo AB et al. J Clin Oncol. 2020 Nov 1;38(31):3672-3684

Advanced Disease: Platinum-Refractory mUBC

Impact on Patient Care and Treatment Algorithm

- Cabozantinib monotherapy has some activity in metastatic urothelial cancer
- Activity complemented by immunotherapy – is there synergy or an additive effect? Translational data support the former.

Implications for Future Research

- Cabozantinib with atezolizumab appears to hold promise with data similar to cabozantinib with nivolumab
- Will cabozantinib be developed further in urothelial cancer? Patients doing better – but still a great need for novel therapies!