Immunotherapy in Kidney & Bladder Cancers

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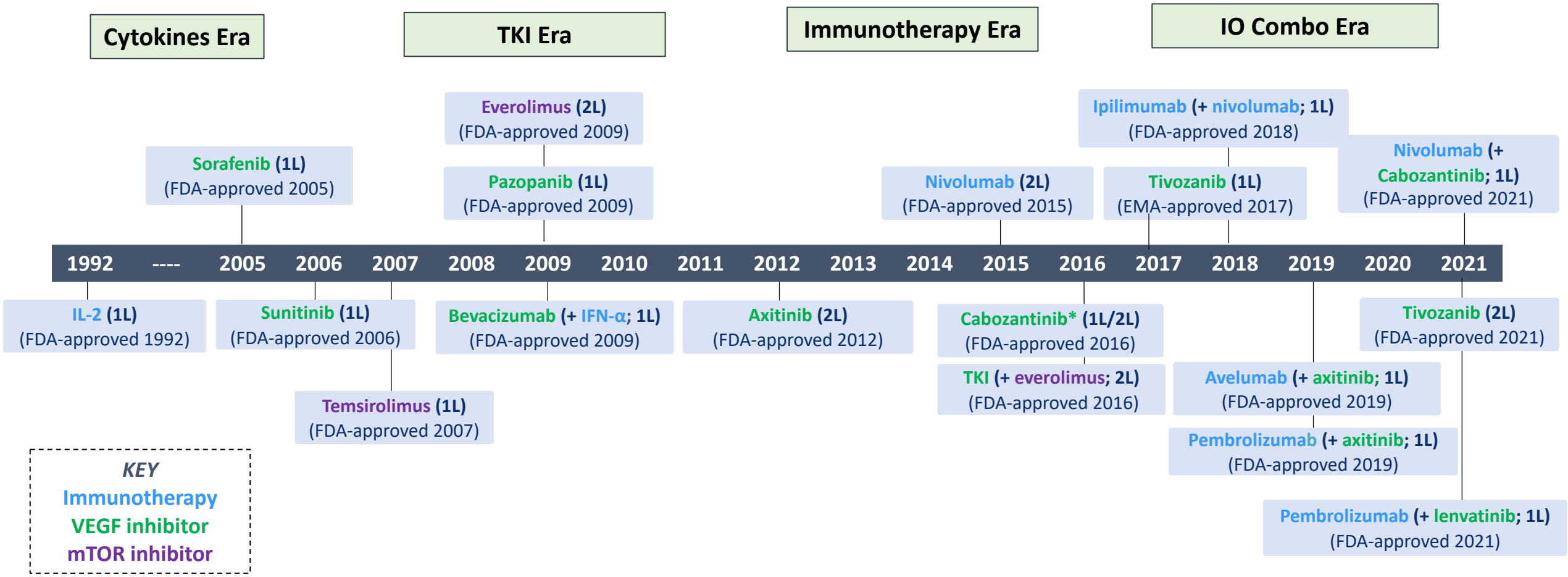
Renal Cell Cancer

Evolution of Systemic Therapy in Metastatic RCC



1L = first line; 2L= second line; IFN-α = interferon alpha; IL = interleukin; IO = immunotherapy; mTOR, mammalian target of rapamycin;TKI = tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; VEGFR-2 = VEGF receptor-2

*Cabozantinib inhibits VEGFR-2, but also c-MET and AXL.22.

Dizman N, et al. *Nature Reviews Nephrol.* 2020;16:435–451.

Food and Drug Administration. Drug Approvals and Databases. https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases.

Metastatic RCC– Frontline

NCCN Recommendations in ccRCC

FIRST-LINE THERAPY FOR CLEAR CELL HISTOLOGY			
Risk	**Preferred Regimens**	**Other Recommended Regimens**	**Useful in Certain Circumstances**
Favorable[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1)	• Axitinib + avelumab[b] • Cabozantinib (category 2B) • Ipilimumab + nivolumab[b] • Pazopanib • Sunitinib	• Active surveillance[c] • Axitinib (category 2B) • High-dose IL-2[d] (category 2B)
Poor/ intermediate[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Ipilimumab + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1) • Cabozantinib	• Axitinib + avelumab[b] • Pazopanib • Sunitinib	• Axitinib (category 2B) • High-dose IL-2[d] (category 3) • Temsirolimus[e] (category 3)

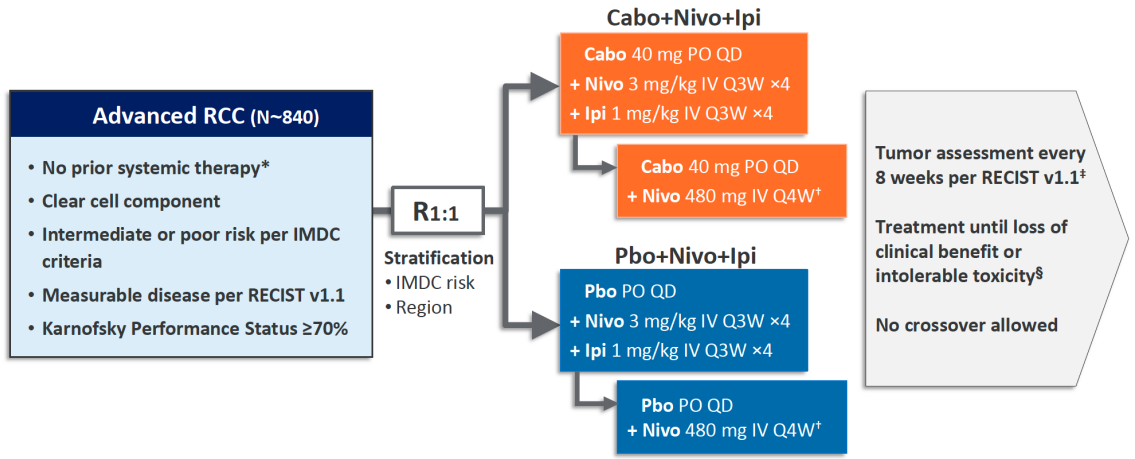
Results From Front-Line IO-Combination Trials

	CheckMate 214 (Ipi/Nivo)[1] (n=550 vs n=546)	KEYNOTE-426 (Axi/Pembro)[2] (n=432 vs n=429)	CheckMate 9ER (Cabo/Nivo)[3] (n=323 vs n=328)	CLEAR (Len/Pembro)[4] (N=355 vs n=357)
HR mOS, months	**0.72** 55.7 vs 38.4	**0.73** 45.7 vs 40.1	**0.70** 37.7 vs 34.3	**0.72** NR vs NR
Landmark OS 12 mo Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%	**90%** vs. 79% **74%** vs. 66%	**86%** vs. 76% **70%** vs 60%	**90%** vs 79% (est.) **79%** vs. 70%
HR mPFS, months	**0.86** **12.3** vs 12.3	**0.68** **15.7** vs 11.1	**0.56** **16.6** vs 8.3	**0.39** **23.9** vs 9.2
ORR, %	**39** vs 32	**60** vs 40	**56** vs 28	**71** vs 36
CR, %	**12** vs 3	**10** vs 4	**12** vs 5	**16** vs 4
Med f/u, months	**67.7**	**42.8**	**32.9**	**33.7**
Primary PD, %	**18**	**11**	**6**	**5**

1. Consistent OS benefit relative to sunitinib control arm; median survival immature for IO/TKIs
2. IO/TKIs with higher ORR (more tumor shrinkage), longer PFS and less early PD
3. Ipi/Nivo has the longest follow-up and potentially most durable benefit

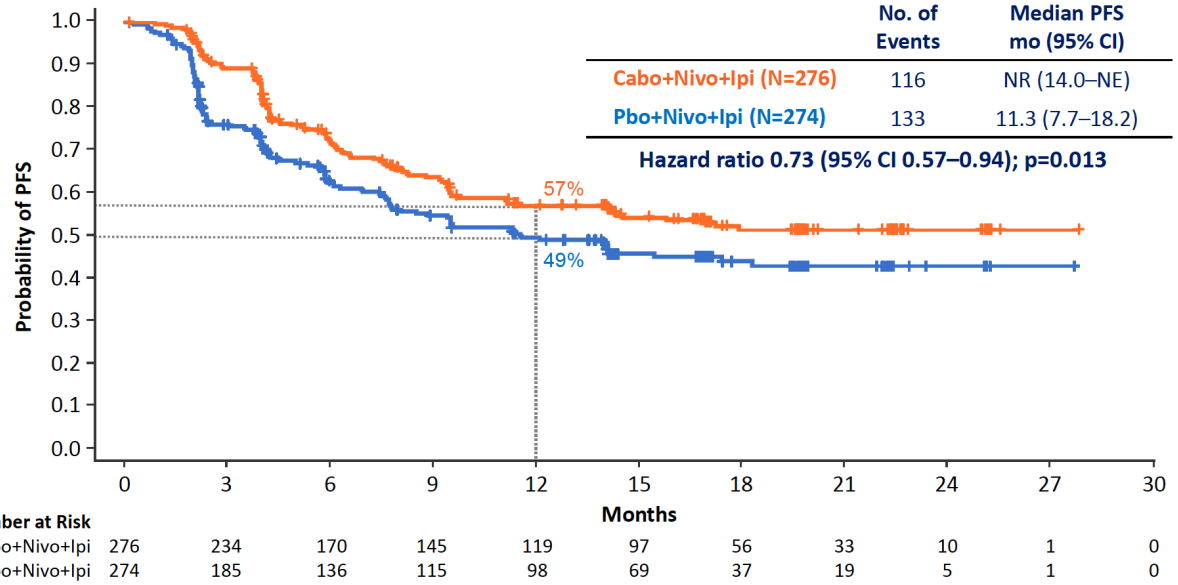
Triplet Therapy: COSMIC 313

COSMIC-313 Study Design



- First trial to use Ipi/Nivo doublet as the comparator arm
- Met primary endpoint of PFS
- Greater toxicity in Ipi/Nivo/Cabo arm
- OS data immature

Progression-Free Survival: Final Analysis (PITT Population)

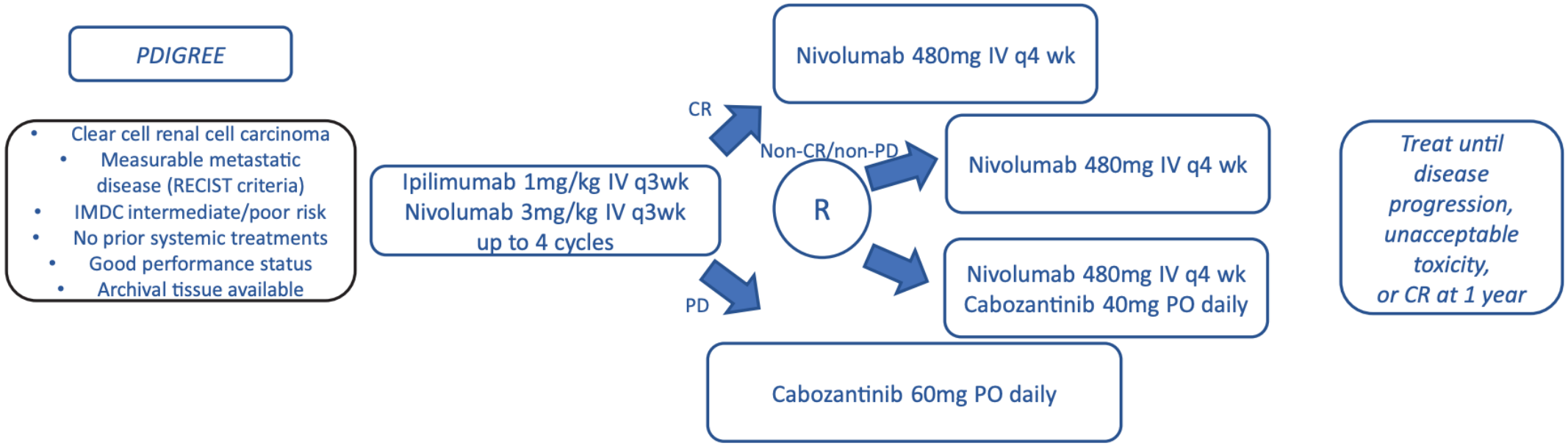


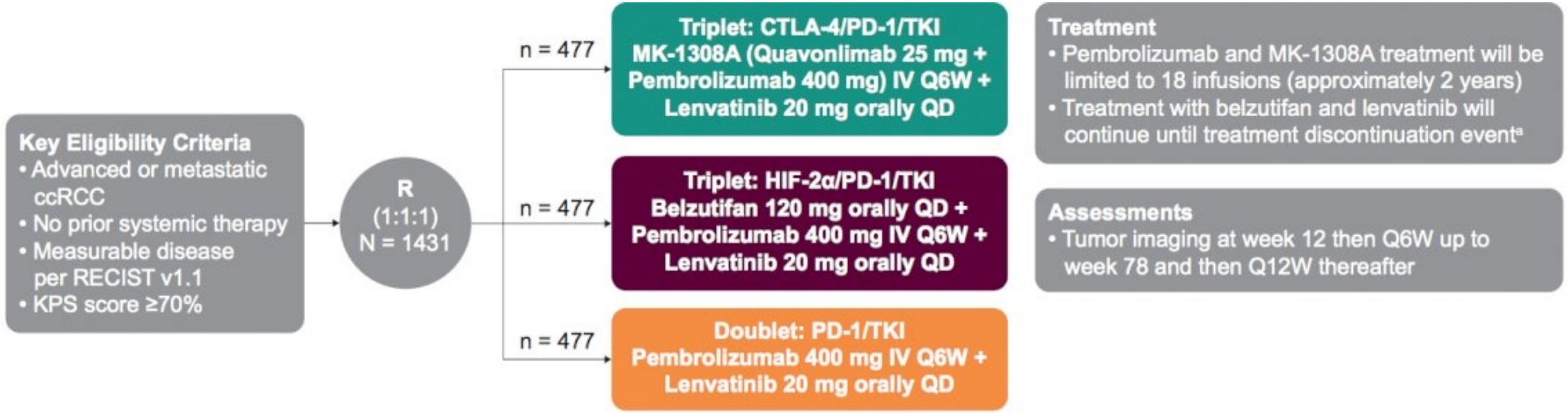
Tumor Response (PITT Population)

	Cabo+Nivo+Ipi (N=276)	Pbo+Nivo+Ipi (N=274)
Objective response rate (95% CI), %	43 (37.2–49.2)	36 (30.1–41.8)
Best overall response, n (%)		
Complete response	7 (3)	9 (3)
Partial response	112 (41)	89 (32)
Stable disease	119 (43)	100 (36)
Progressive disease	23 (8)	55 (20)
Not evaluable	15 (5)	21 (8)
Disease control rate, %	86	72
Median time to objective response (range), mo	2.4 (1.5–17.1)	2.3 (1.9–16.8)
Median duration of response (95% CI), mo	NR (20.2–NE)	NR (NE–NE)

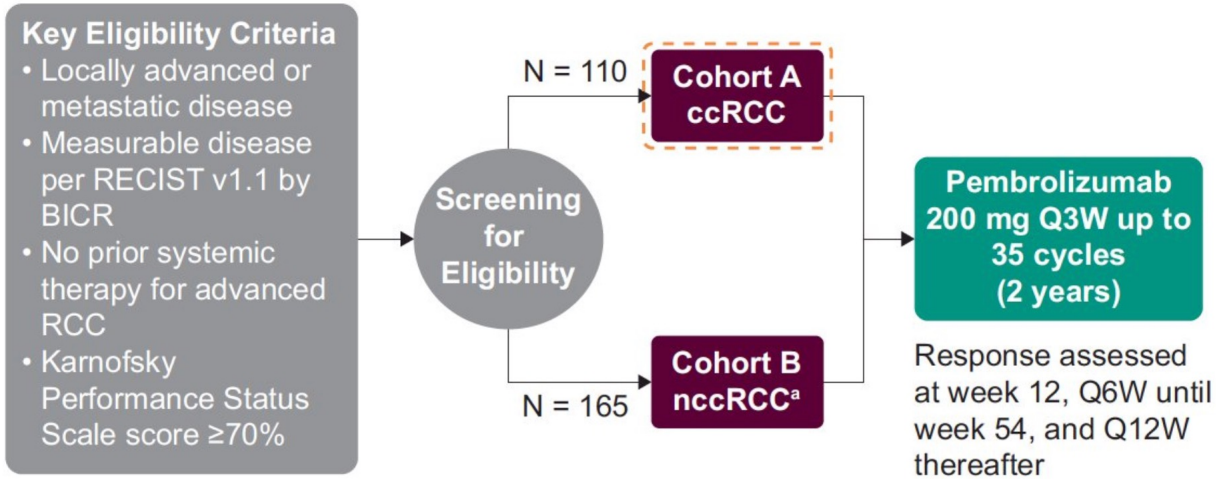
Tumor response per RECIST v1.1 by BIRC
Disease control rate = complete response + partial response + stable disease

Ongoing Studies: PDIGREE and MK3475-03A





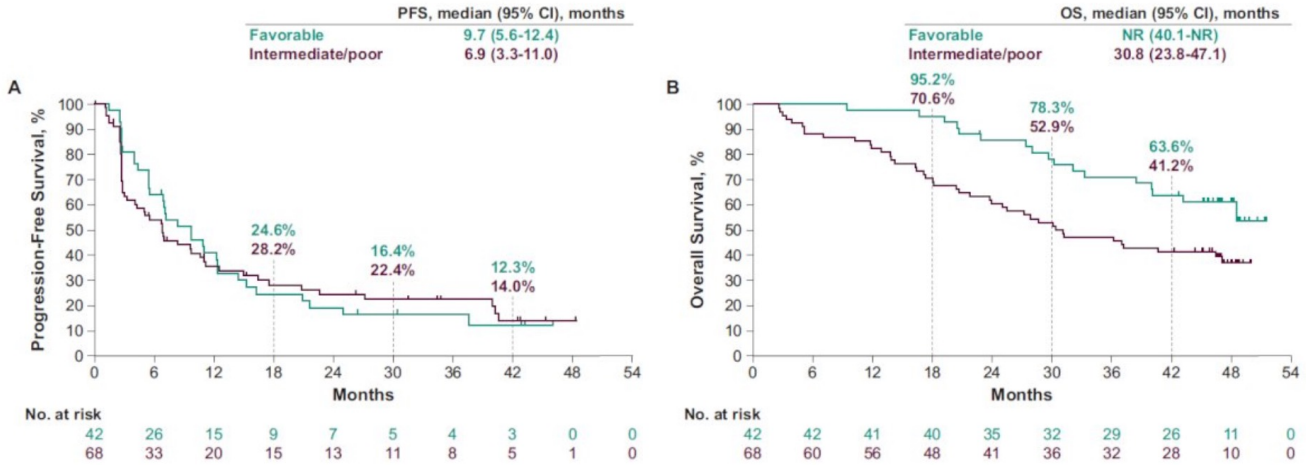
Single Agent IO Data: Keynote-427



End Points

- **Primary:** ORR (RECIST v1.1 by BICR)
- **Secondary:** OS, PFS, DOR, DCR (RECIST v1.1 by BICR), and safety

Cohort A: ORR 36 %



RCC--Second Line and Beyond

Second-Line Therapy: Preferred NCCN Recommendations

	Nivolumab vs evero[2] N = 821	Cabozantinib vs evero[3] N = 658	Lenvatinib + evero vs lenvatinib or evero[4] N = 153
Trial	Phase 3 CM-025	Phase 3 METEOR	Phase 2 Study 205
Patient population	TKI-refractory (72% 1 prior)	TKI-refractory (71% 1 prior)	TKI-refractory (100% 1 prior)
Primary end point	OS	PFS (IRC)	PFS (INV)
Risk, favorable/int/poor	35/49/16	45/42/12	24/37/39
ORR, %	25	17	43
PFS, mo	4.6	7.4 (HR 0.51; 95% CI, 0·41–0·62; P <.0001)	14.6 (HR, 0.40; 95% CI, 0.24-0.68; P = .0005 vs evero)
OS, mo	25.0 (HR, 0.73; 95% CI, 0.57-0.93; P =.002)	21.4	25.5
Dose reductions	N/A	62%	71%
AE discontinuation	8%	12%	24%
Toxicity	18% G3 1% G4 (tx-related)	71% G3/4	57% G3 14% G4

AE, adverse event; discontinuation; evero, everolimus; tx, treatment.

1. Rini et al., *Lancet*. 2011;378:1931; 2. Motzer et al., *N Engl J Med*. 2015;373:1803;
3. Choueiri et al., *Lancet Oncol.* 2016;17:917-927; 4. Motzer et al., *Lancet Oncol*. 2015;16:1473

Post-IO Treatment

Key Inclusion Criteria
- Metastatic clear cell RCC
- Measurable disease per irRECIST[1]
- Disease progression after PD-1/PD-L1 treatment:
  - ≥ 2 doses of anti-PD-1/PD-L1
  - Defined by RECIST v1.1; confirmed ≥ 4 weeks

Study Treatment

Lenvatinib[a]
20 mg/day PO
+
Pembrolizumab[b]
200 mg/3 weeks IV

Primary End Point[c]
- Objective response rate at week 24

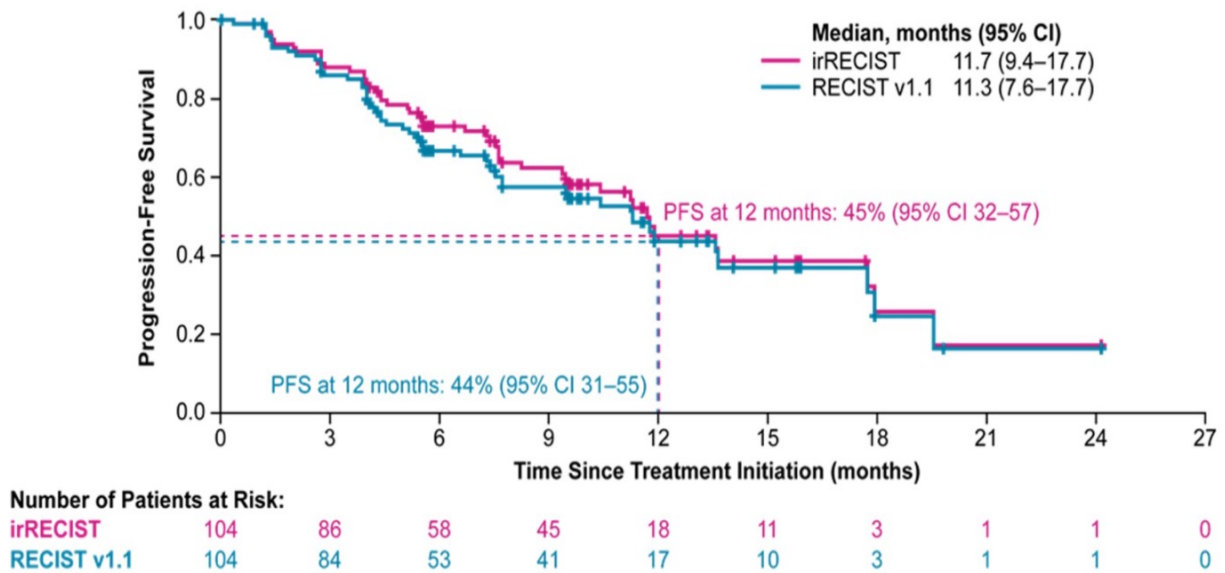
Secondary End Points
- Objective response rate[c]
- Progression-free survival[c]
- Overall survival
- Safety and tolerability

Tumor Response by Investigator Assessment

Parameter	irRECIST N = 104	RECIST v1.1[a] N = 104
ORR at week 24, % (95% CI)	51 (41–61)	–
ORR, % (95% CI)	55 (45–65)	52 (42–62)
Best objective response, %		
Partial response	55	52
Stable disease	36	38
Progressive disease	5	6
Not evaluable	5	5
Median DOR, months (95% CI)	12 (9–18)	12 (9–18)

[a] Up to 10 target lesions could be selected (up to 5 per organ).

PFS Kaplan–Meier Curves by irRECIST[a] and RECIST v1.1[a,b]



Lee at al, ASCO 2021

Ongoing Studies of Post-IO Treatment: CONTACT-03 and TINIVO-2

- Histologically confirmed advanced, metastatic ccRCC or nccRCC
- Radiographic progression during or following ICI treatment

R
1:1

N ≈ 500

Atezolizumab *IV*
1200 mg q3w
+
Cabozantinib *po*
60 mg qd

Cabozantinib *po*
60 mg qd

No crossover allowed

Treatment until loss of clinical benefit or unacceptable toxicity

Survival follow-up

N=326

Histologically/cytologically confirmed recurrent or mRCC

ECOG PS 0-1

1 or 2 prior lines of therapy, including an immmunotherapy

Stratified by IMDC risk score and prior lines of therapy

Randomization 1:1

4-week treatment cycles
(2+ cycles required for assessment)

Combination therapy (n=163)
Tivozanib 0.89[a] mg PO QD for 21 days on/7 days off
Nivolumab 480 mg IV Q4W

Monotherapy (n=163)
Tivozanib 1.34 mg PO QD for 21 days on/7 days off

Non-Clear Cell RCC

KEYNOTE-B61: Pembrolizumab + Lenvatinib in nccRCC

Study Design of KEYNOTE-B61 (NCT04704219)

Key Eligibility Criteria

- Histologically confirmed diagnosis of nccRCC (per investigator)
- Locally advanced/metastatic disease
- No prior systemic therapy
- Measurable disease per RECIST v1.1
- Tumor tissue sample available
- KPS ≥70%

N ≈ 152 (planned)

Pembrolizumab 400 mg IV Q6W for ≤18 cycles[a] (~2 years) + Lenvatinib 20 mg PO QD

Tumor Assessments

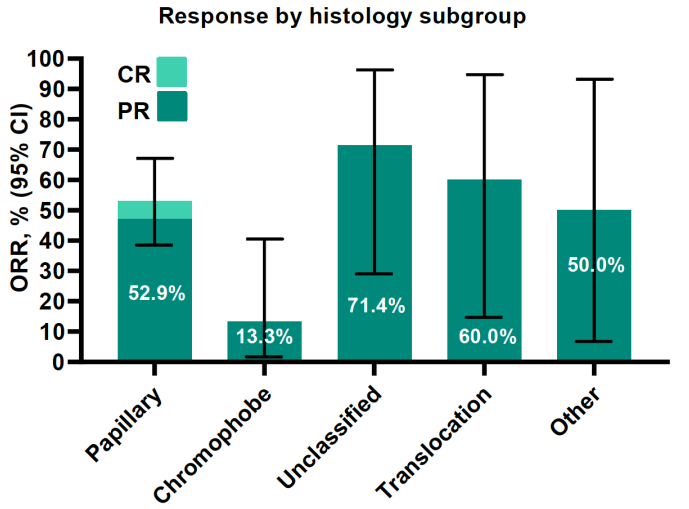
- 12 weeks from allocation then Q6W for 54 weeks then Q12W thereafter

End Points

- Primary: ORR per RECIST v1.1 by BICR
- Secondary: CBR, DCR, DOR, and PFS per RECIST v1.1 by BICR; OS, safety and tolerability

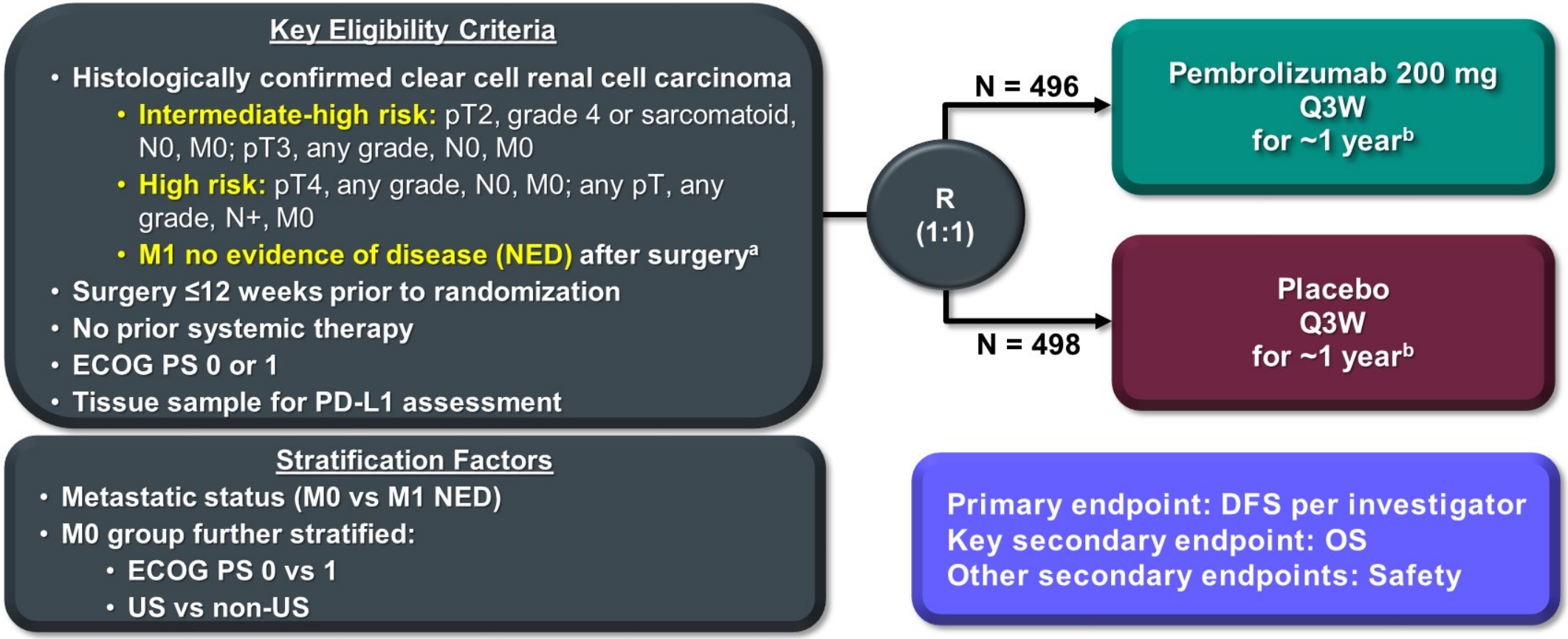
Best Confirmed Objective Response: Efficacy Population[a]

	Efficacy Population n = 82
ORR (CR + PR), % (95% CI)	47.6 (36.4-58.9)
DCR (CR + PR + SD), % (95% CI)	79.3 (68.9-87.4)
Best response, n (%)	
CR	3 (3.7)
PR	36 (43.9)
SD	26 (31.7)
PD	9 (11.0)
NE[b]	1 (1.2)
NA[c]	7 (8.5)



RCC– Adjuvant Therapy

KEYNOTE-564 (NCT03142334) Study Design

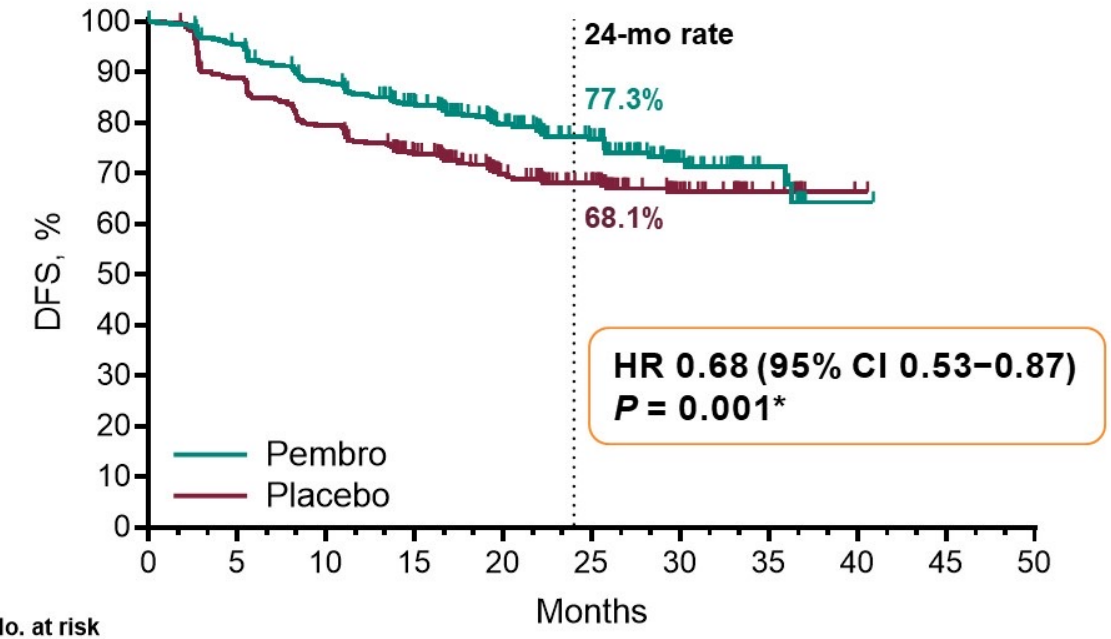


- Median (range) time from randomization to cutoff: 30.1 (20.8−47.5) months

Q3W, every 3 weeks.
[a]M1 NED: no evidence of disease after primary tumor + soft tissue metastases completely resected ≤1 year from nephrectomy; [b]≤17 cycles of treatment were equivalent to ~1 year.
Data cutoff date: June 14, 2021.

Primary Endpoint: DFS, ITT Population

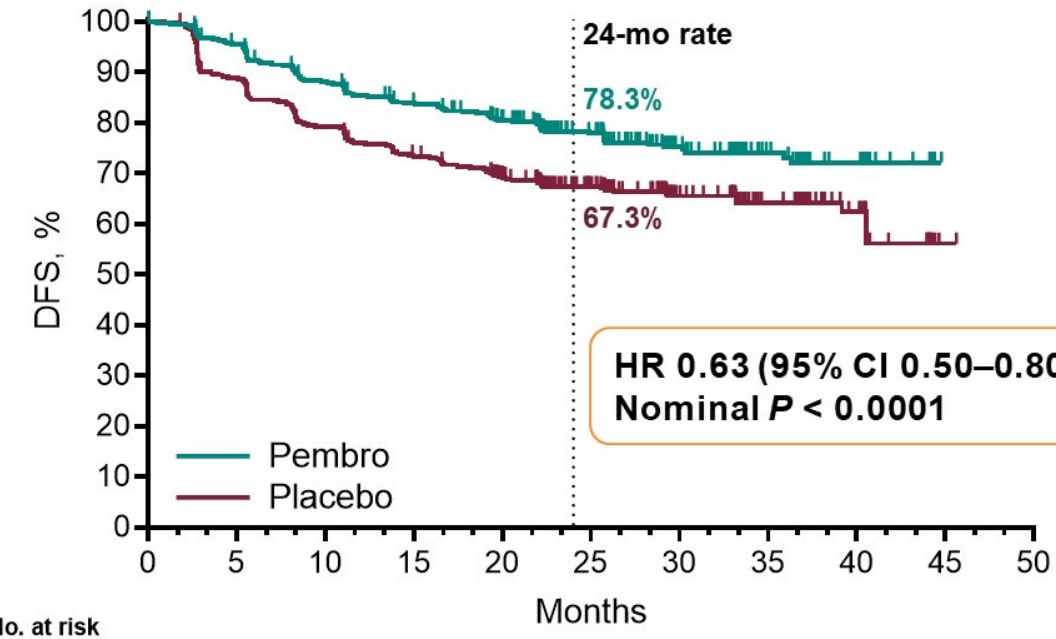
Primary Analysis: 24.1 mo Follow-Up



No. at risk											
Pembro	496	457	414	371	233	151	61	21	1	0	0
Placebo	498	436	389	341	209	145	56	19	1	0	0

	Pts w/ Event	Median, mo (95% CI)
Pembro	109	NR (NR–NR)
Placebo	151	NR (NR–NR)

Updated Analysis: 30.1 mo Follow-Up



No. at risk											
Pembro	496	458	416	389	361	255	135	77	37	0	0
Placebo	498	437	389	356	325	230	125	74	33	1	0

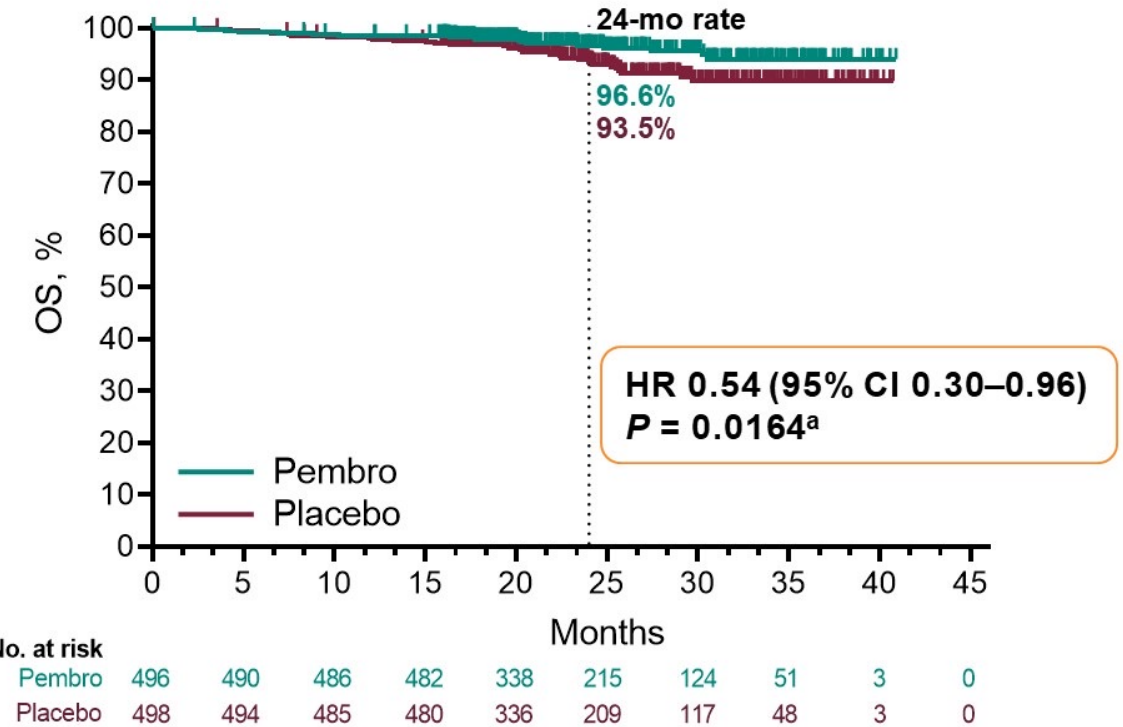
	Pts w/ Event	Median, mo (95% CI)
Pembro	114	NR (NR–NR)
Placebo	169	NR (40.5–NR)

* denotes statistical significance.

ITT population included all randomized participants. DFS, disease-free survival; NR, not reached. Primary analysis data cutoff date: December 14, 2020. Updated analysis data cutoff date: June 14, 2021.

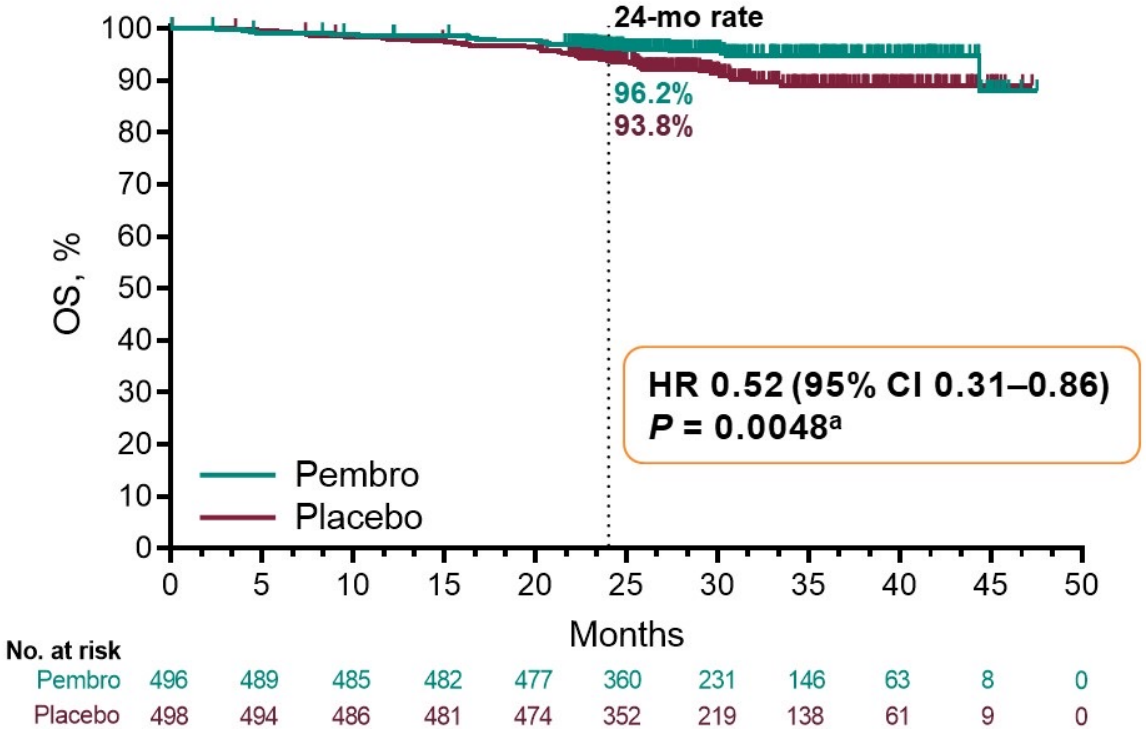
Key Secondary Endpoint: OS, ITT Population

Primary Analysis: 24.1 mo Follow-Up



	Pts w/ Event	Median, mo (95% CI)
Pembro	18	NR (NR–NR)
Placebo	33	NR (NR–NR)

Updated Analysis: 30.1 mo Follow-Up



	Pts w/ Event	Median, mo (95% CI)
Pembro	23	NR (NR–NR)
Placebo	43	NR (NR–NR)

[a]Did not cross prespecified p-value boundary for statistical significance.
ITT population included all randomized participants. NR, not reached. Primary analysis data cutoff date: December 14, 2020. Updated analysis data cutoff date: June 14, 2021.

Choueiri et al. ASCO GU 2022

Adjuvant IO Trials in RCC

Trial	Number of Patients	Inclusion Criteria	Treatment	Primary Endpoint	Results
Keynote-564[1]	994	pT2G4, pT3aG3-4, pT3b-T4Gx, pTxN1, pTxNxM1 (resected to NED within 1 year); clear cell	Pembrolizumab vs placebo	DFS	**Met Primary Endpoint**
IMmotion010[2]	778	pT2G4, pT3aG3-4, pT3b-T4Gx, pTxN1, pTxNxM1 (resected to NED*); clear cell	Atezolizumab vs placebo	DFS	Negative Study
CheckMate-914[3]	1600	pT2aG3-4N0, pT2b-T4GxN0, pTxGxN1; clear cell	Nivolumab + ipilimumab vs. nivolumab + placebo vs placebo (6 months)	DFS	Negative Study
PROSPER RCC[4]	766	T2Nx, TxN1, TxNxM1 (resected to NED); any RCC histology	Nivolumab vs observation	EFS	Negative Study
RAMPART[5]	1750	Leibovich score 3-11; any RCC histology	Durvalumab + tremelimumab vs durvalumab vs observation	DFS, OS	Expected 7/2024

*Metachronous pulmonary, lymph node, or soft tissue recurrence >12 months from nephrectomy.

DFS, disease-free survival; EFS, event-free survival; NED, no evidence of disease; RCC, renal cell carcinoma; OS, overall survival.

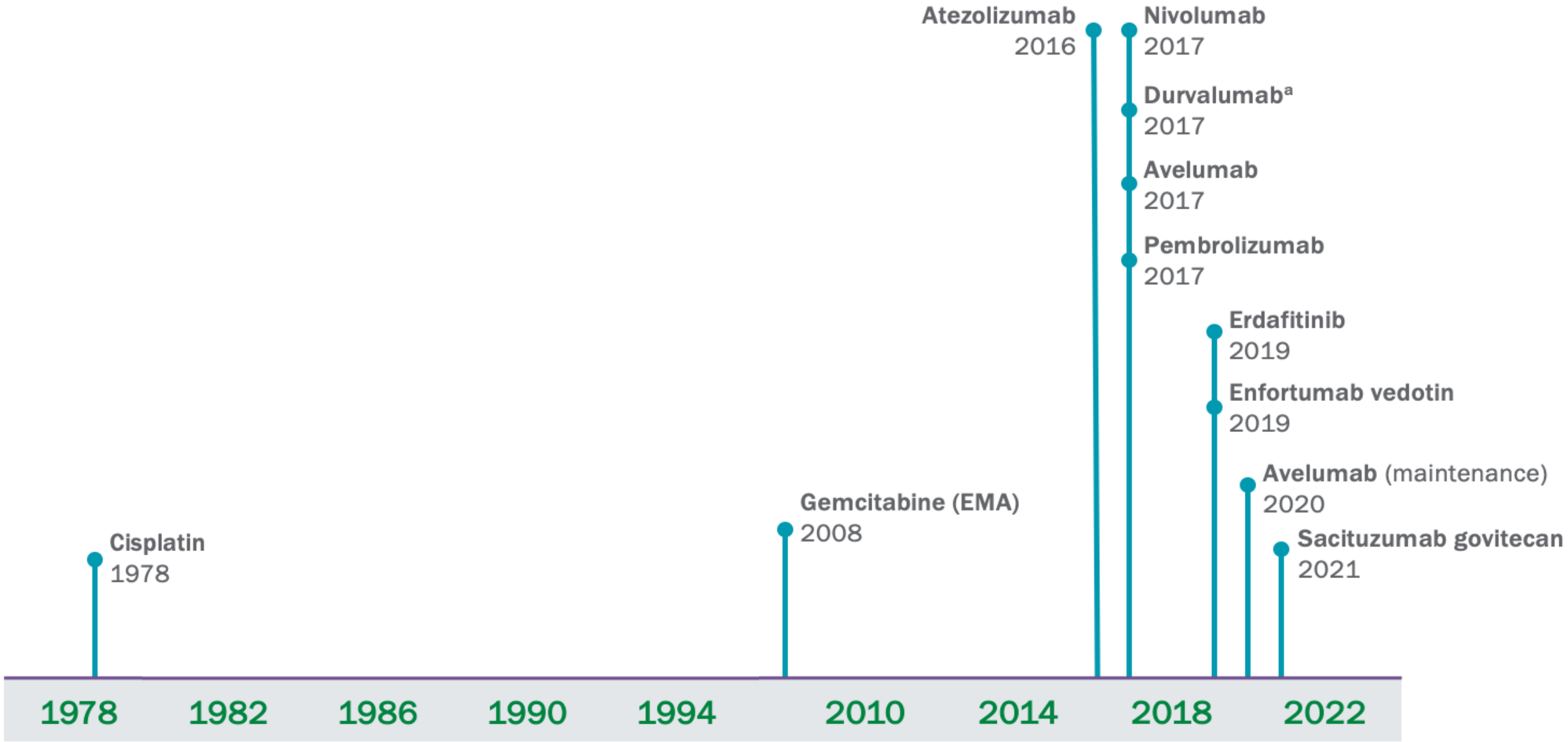
1. Choueiri TK et al. *N Engl J Med*. 2021;385:683-694. 2. NCT03024996. 3. NCT03138512. 4. NCT03055013. 5. NCT03288532.

RCC Summary

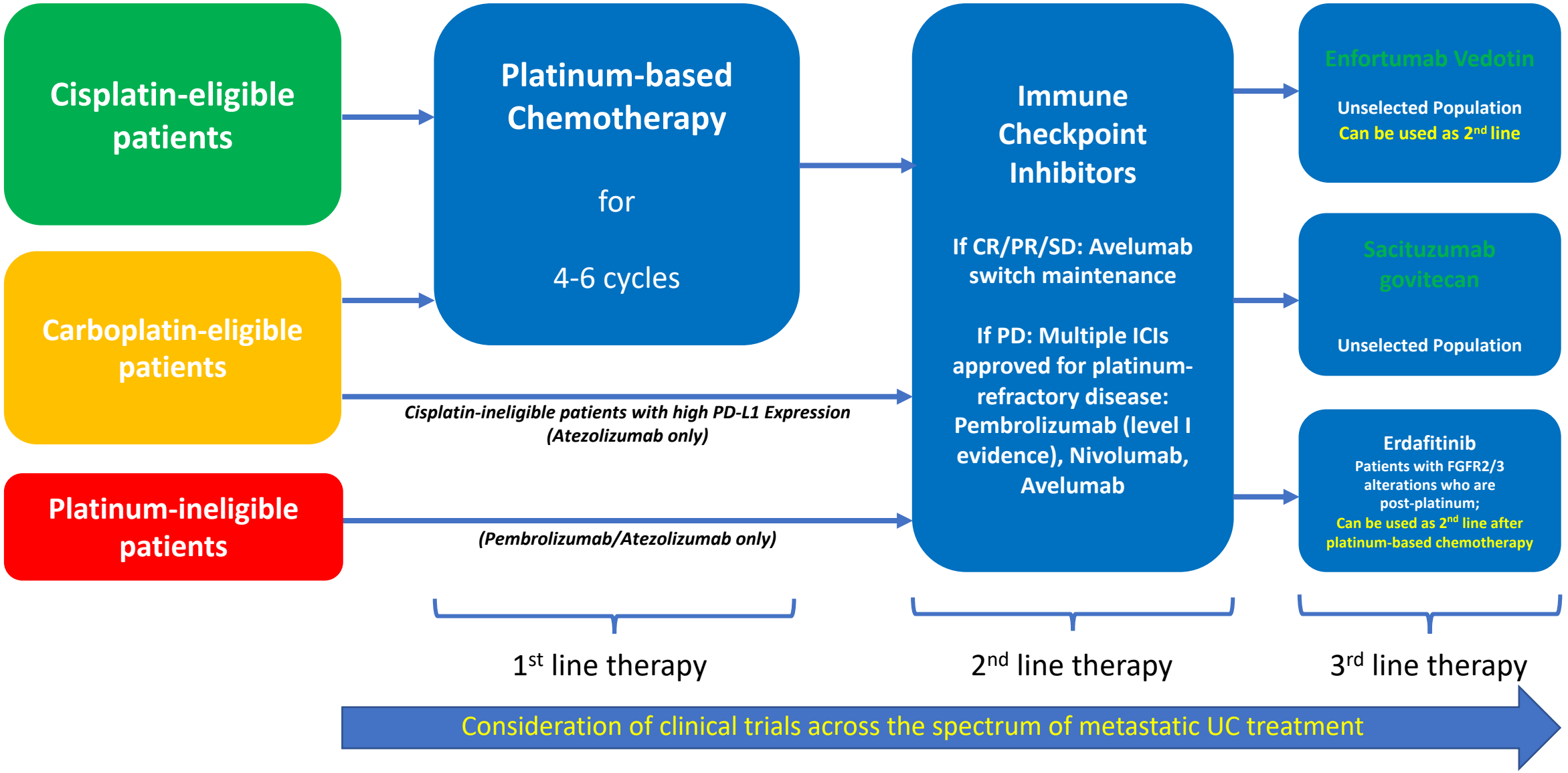
- Pembrolizumab is the only immune checkpoint inhibitor approved as adjuvant treatment for RCC
  - Approval for pembrolizumab based on DFS endpoint with OS still pending
  - Several other negative adjuvant IO studies (atezolizumab, nivolumab, ipi/nivo)
- IO/TKI combinations remain the gold standard for treatment-naïve patients with metastatic RCC
- TKIs remain the current SOC for most patients in the treament-refractory space, however nivolumab is also an option
- Rechallenge with IO/TKI combinations emerging as potential option in the IO-refractory space
- nccRCC (papillary, unclassified, translocation, etc) might benefit from IO-TKI combinations

Urothelial Carcinoma

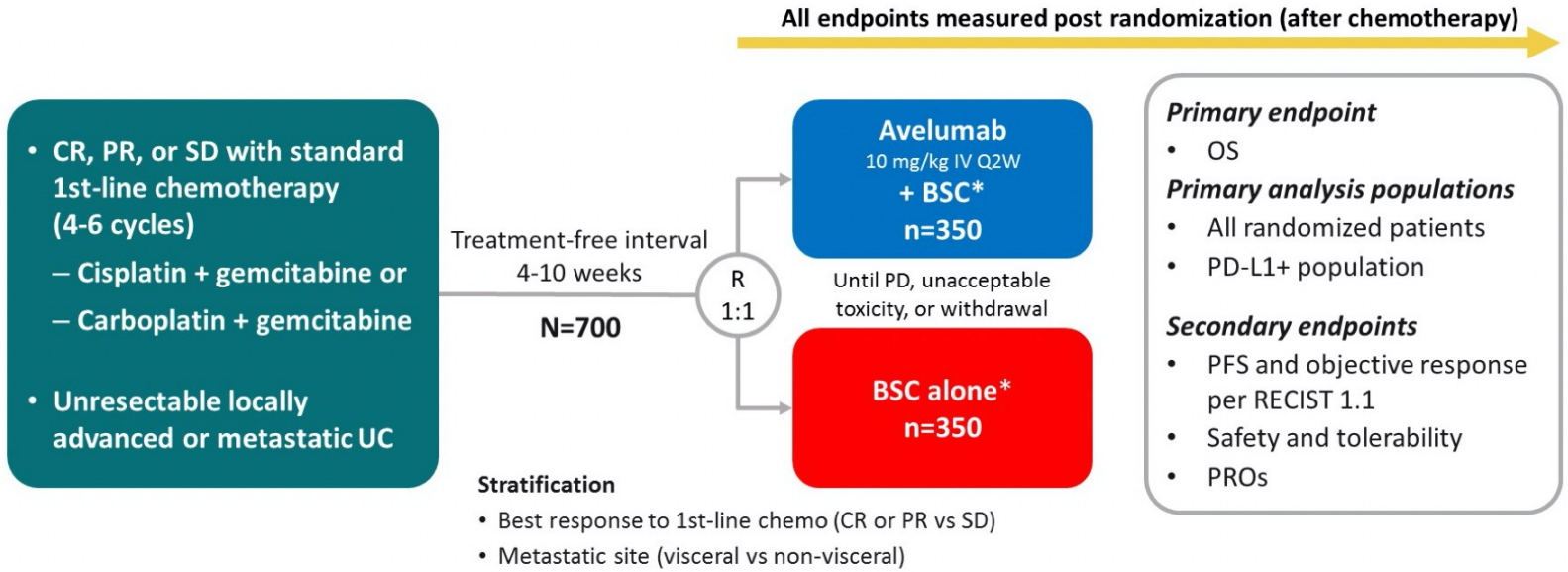
Drug Approvals in Metastatic Urothelial Carcinoma

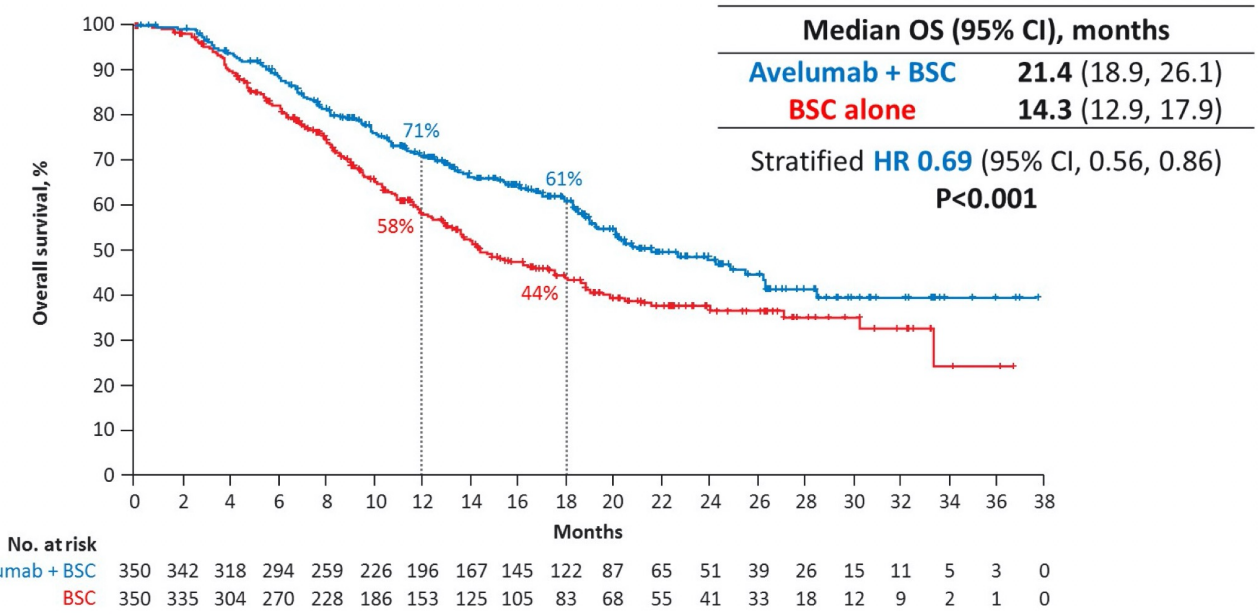


Metastatic Urothelial Carcinoma: Current Treatment Landscape



Switch-Maintenance ICI Therapy in mUC: Javelin Bladder 100 Study





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 et al, NEJM 2020

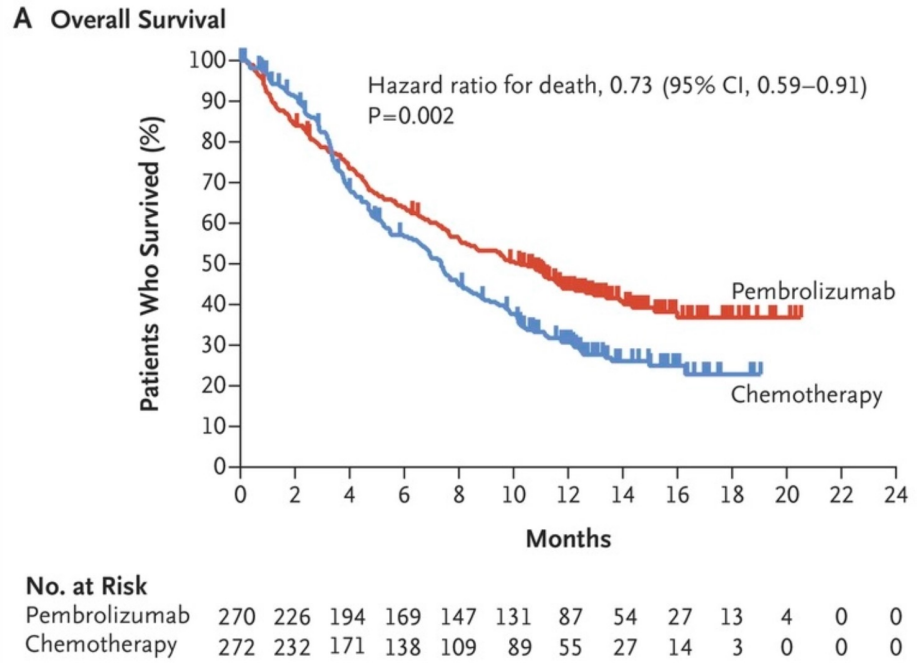
ICIs in Platinum-Refractory Setting

	Atezolizumab[1]	Pembrolizumab[2]	Nivolumab[3]	Durvalumab[4]	Avelumab[5]
Most Advanced Trial Phase	Phase III Randomized Trial (vs chemotherapy)	Phase III Randomized Trial (vs chemotherapy)	Phase II Single Arm	Phase I/II	Phase Ib
Number of Patients	931	542	265	191	161 (>6 months follow-up)
Dosing	1200mg IV every 3 weeks	200mg IV every 3 weeks	3mg/kg IV every 2 weeks	10 mg/kg IV every 2 weeks	10 mg/kg IV every 2 weeks
ORR	13.4%	21.1%	19.6%	17.8%	17.4%
ORR Among High PD-L1 Expressors	23% (among IC2/3)	21.6% (among CPS≥10%)	28.4% (among PD-L1 ≥5%)	27.6% (among PD-L1 ≥25%)	25.4% (among PD-L1 ≥5%)
Median PFS	2.1 months	2.1 months	2.0 months	1.5 months	1.5 months
Median OS	8.6 months	10.3 months	8.7 months	18.2 months	7.4 months
Grade 3/4 TRAEs	20%	15%	18%	6.8%	8.0%

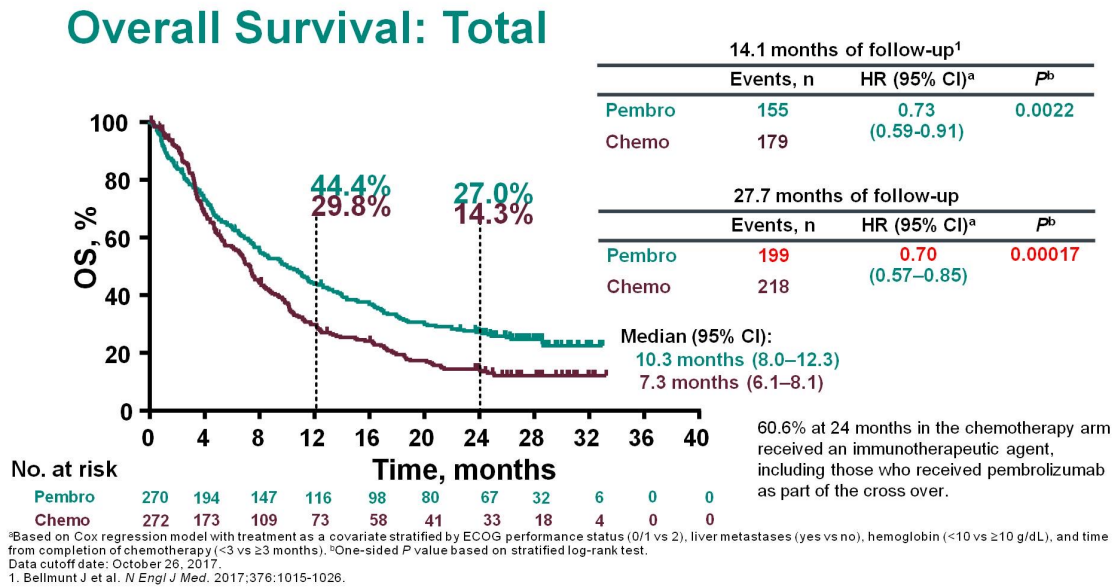
1. Powles et al 2018 2. Bellmunt et al 2017 3. Sharma et al 2017 4. Powles et al 2017 5. Patel et al 2018

Pembrolizumab for Platinum-Refractory Bladder Cancer (Keynote 045)

Randomized trial in platinum-refractory mUC patients comparing pembrolizumab vs chemotherapy (paclitaxel, docetaxel, vinflunine)



Bellmunt et al NEJM 2017



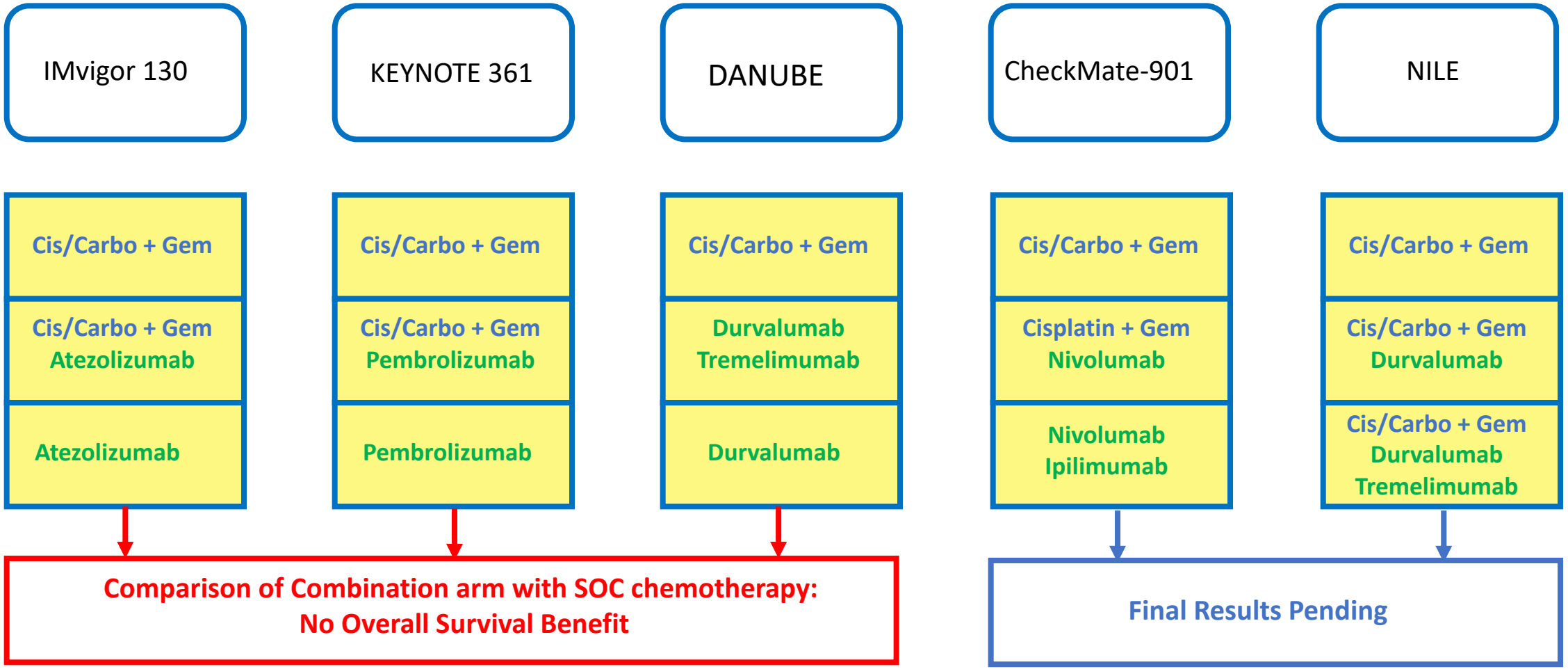
Bellmunt et al GU ASCCO 2018

ICI in Front-Line Setting (Cisplatin-ineligible)

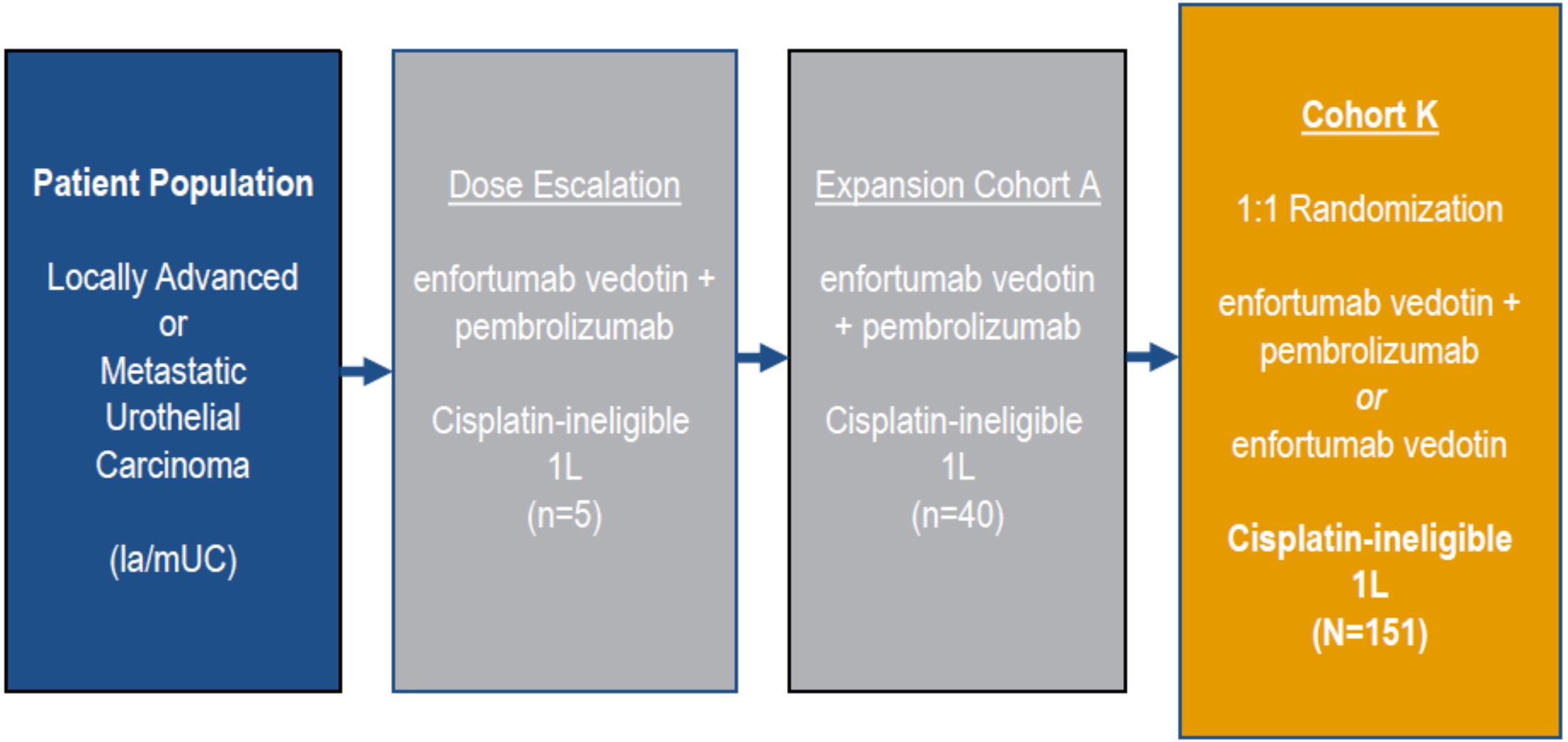
	Atezolizumab[1]	Pembrolizumab[2]
Trial Phase	Phase II Single Arm	Phase II Single Arm
Number of Patients	119	370
Dosing	1200mg IV every 3 weeks	200mg IV every 3 weeks
ORR	23% (9% CRs)	28.6% (9% CRs)
ORR Among High PD-L1 Expressors	28% (among IC2/3)	47.3% (among CPS≥10%)
Median PFS	2.7 months	2 months
Median OS	15.9 months	11.3 months
Grade 3/4 TRAEs	16%	18%

1. Balar et al 2017 2. Balar et al 2017

Frontline ICI Clinical Trials in mUC

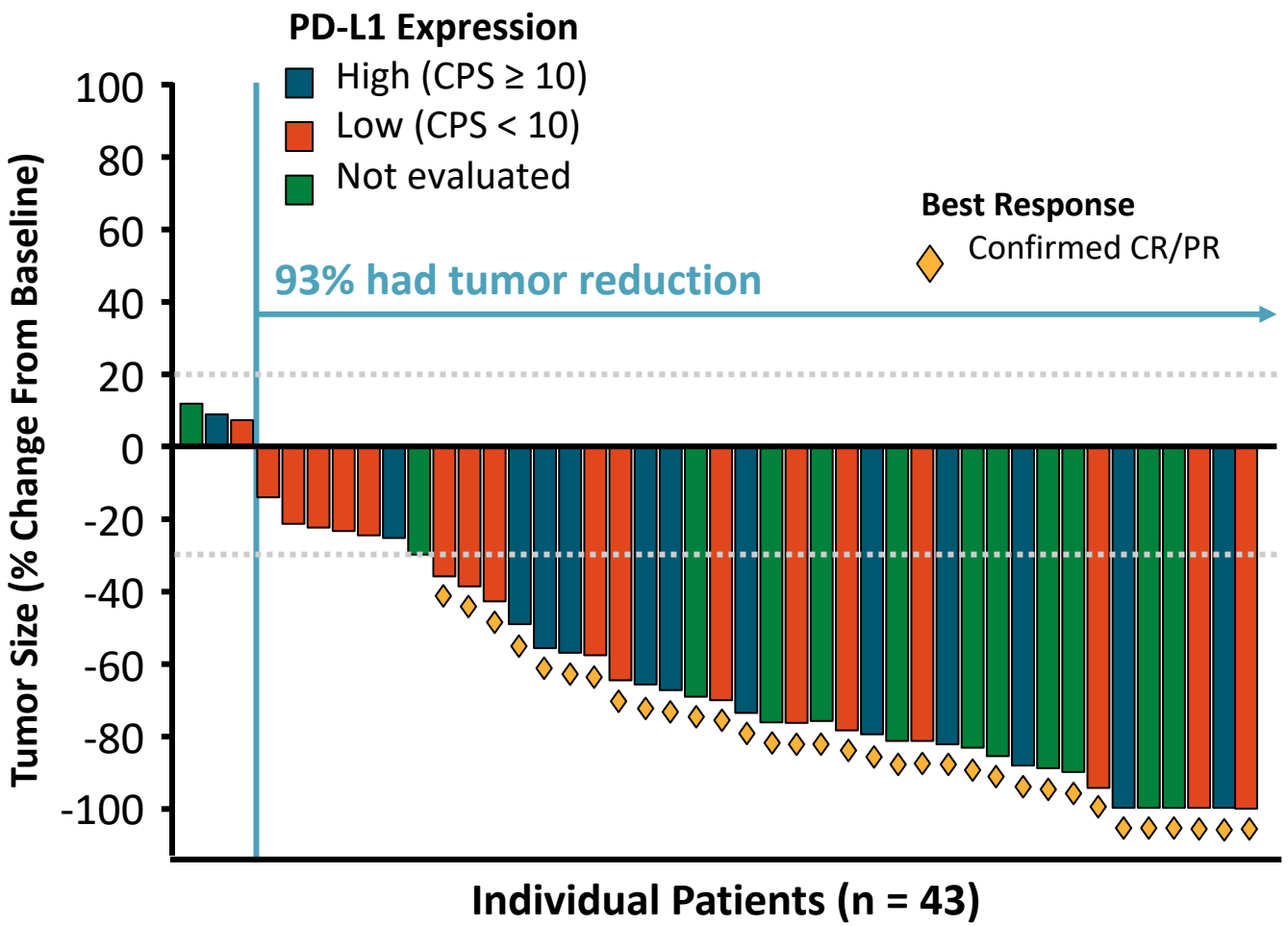


EV-103: Multicohort Study in mUC



EV-103 Cohort A: EV + Pembrolizumab

Best Overall Response	All Patients (N = 45)
Confirmed ORR, n (%) [95% CI] CR, n (%) PR, n (%)	**33 (73.3) [58.1–85.4]** 7 (15.6) 26 (57.8)
SD, n (%)	9 (20.0)
PD, n (%)	1 (2.2)
ORR in pts with liver mets, n/N (%)	8/14 (57.1)
Clinical Outcomes (Median Follow-Up 24.9 months)	**All Patients (N = 45)**
Median PFS, months, (95% CI)	**12.3 (8.0, –)**
Median OS, months, (95% CI)	**26.1 (15.7, –)**
Median DOR, months, (95% CI)	**25.6 (8.3, –)**



1. Presented by TW Friedlander at ASCO 2021 Annual Meeting June 4-8, 2021. Abstract 4528.

2. Rosenberg. ASCO 2020. Abstr 5044. Rosenberg. ASCO GU 2020. Abstr 441.

EV-103 Cohort K: Randomized cohort EV + Pembrolizumab vs EV

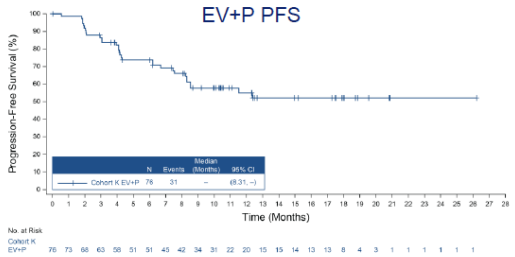
Overall Response Rate by BICR

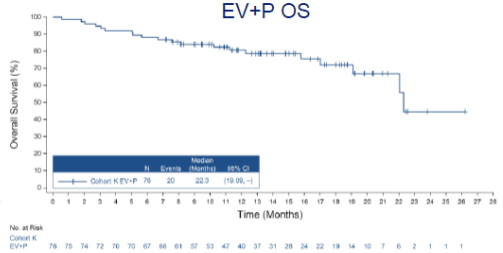
EV+P: 64.5% confirmed ORR with rapid responses

	EV+P (N=76)	EV Mono (N=73)
Confirmed ORR, n (%) (95% CI)	49 (64.5) (52.7, 75.1)	33 (45.2) (33.5, 57.3)
Best overall response, n (%)		
Complete Response	8 (10.5)	3 (4.1)
Partial Response	41 (53.9)	30 (41.1)
Stable Disease	17 (22.4)	25 (34.2)
Progressive Disease	6 (7.9)	7 (9.6)
Not Evaluable	3 (3.9)	5 (6.8)
No Assessment	1 (1.3)	3 (4.1)
Median time to objective response (range), mos	2.07 (1.1, 6.6)	2.07 (1.9, 15.4)
Median number of treatment cycles (range)	11.0 (1, 29)	8.0 (1, 33)

Progression-Free Survival per BICR and Overall Survival

Secondary Endpoints: PFS and OS for EV+P; data expected to evolve with follow-up





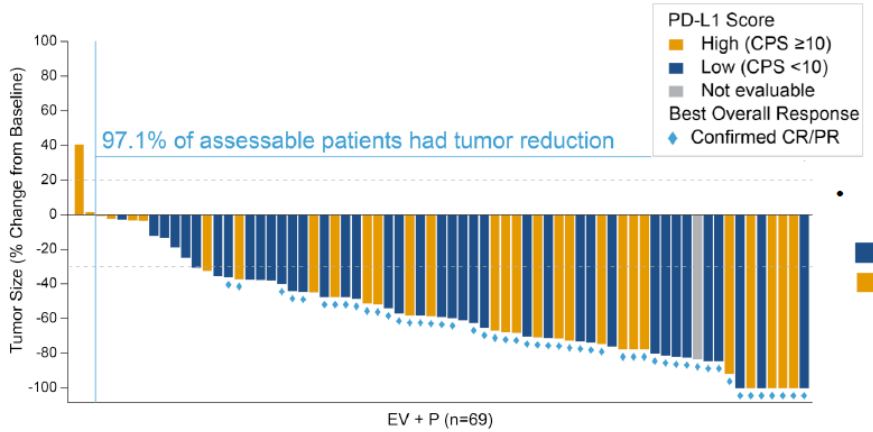
	EV+P (N=76)	EV Mono (N=73)
PFS events, n	31	38
mPFS (95% CI), mos	- (8.31, -)	8.0 (6.05, 10.35)
PFS at 12 mos, %	55.1%	35.8%

	EV+P (N=76)	EV Mono (N=73)
OS Events, n	20	26
mOS (95% CI), mos	22.3 (19.09, -)	21.7 (15.21, -)
OS at 12 mos, %	80.7%	70.7%
Median follow-up time, mos	14.8	15.0

PARIS 2022 ESMO congress

Jonathan E. Rosenberg, MD

EV+P: Maximum Percent Reduction from Baseline of Target Lesion by BICR



- Activity seen regardless of PD-L1 status
  - 27/44 (61.4%) cORR in CPS<10
  - 21/31 (67.7%) cORR in CPS≥10

BICR: Blinded Independent Central Review; CPS: Combined Positive Score; CR: Complete Response; PD-L1: Programmed Death-Ligand 1 PR: Partial Response

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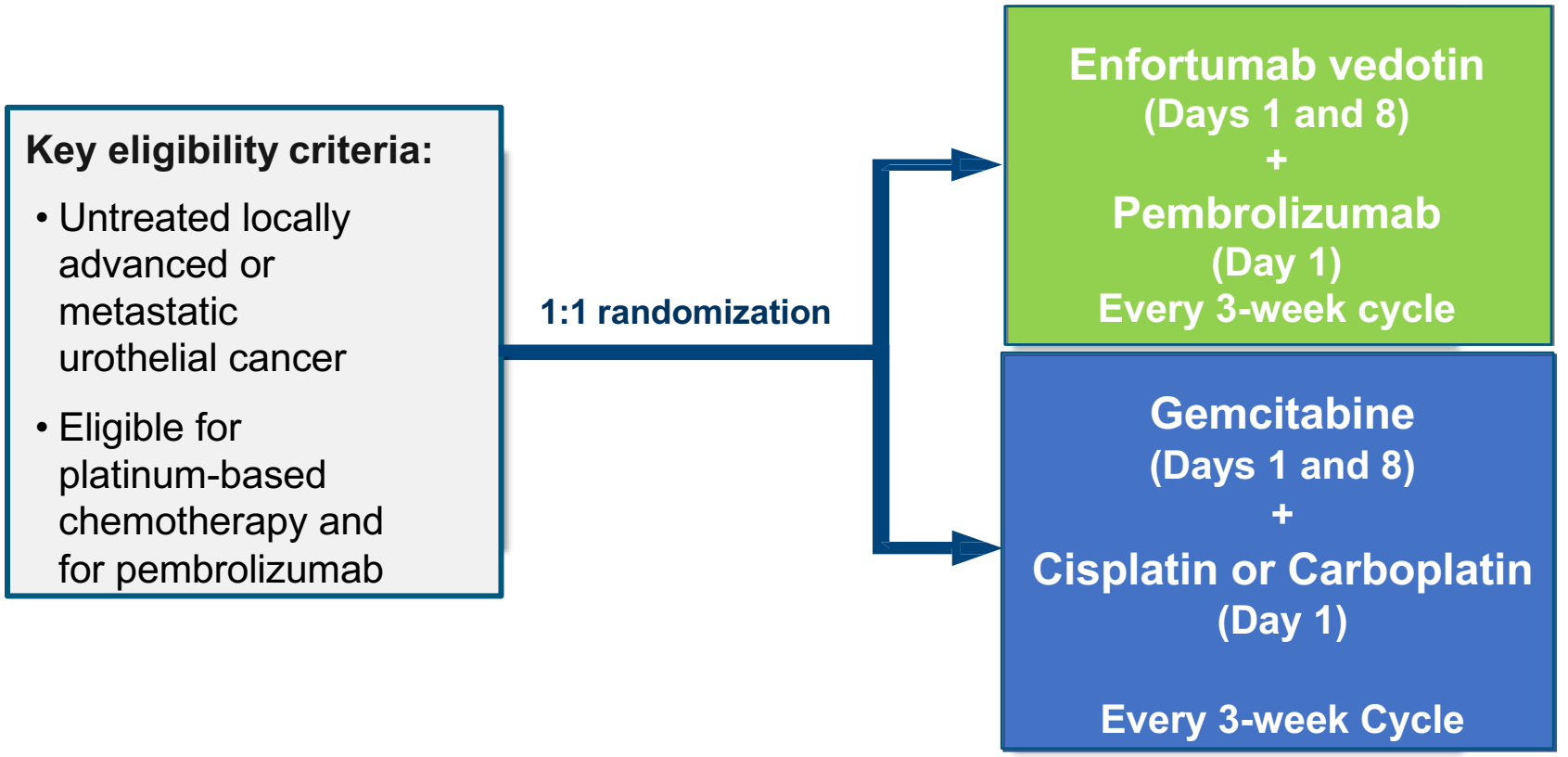
EV-302: Randomized Phase 3 Study of Enfortumab Vedotin in Combination With Pembrolizumab Versus Chemotherapy



Primary Objectives
- PFS per RECIST by central review
- OS

Secondary Objectives
- PFS per RECIST by investigator
- ORR
- DOR
- DCR
- QOL
- Safety and tolerability

Perioperative Treatment for MIBC

Neoadjuvant Therapy: Selected Trials of ICIs for MIBC

Trial	ABACUS	PURE-01	NABUCCO	GU14-188 (Cis-ineligible cohort)	GU14-188 (Cis-eligible cohort)	BLASST-1
Treatment	Atezolizumab	Pembrolizumab	Ipilimumab/ Nivolumab	Pembrolizumab + Gemcitabine	Pembrolizumab + Gemcitabine/ Cisplatin	Nivolumab + Gemcitabine / Cisplatin
Patient Population	Cisplatin-ineligible	Cisplatin-ineligible	Cisplatin-ineligible	Cisplatin-ineligible	Cisplatin-eligible	Cisplatin-eligible
Patients (N)	88	114	24	37	43	41
pCR (pT0N0)	31%	37%	46%	45%	44%	40%
Downstaging (≤pT1N0)	39%	55%	58%	52%	61%	66%

- pCR and rates of downstaging comparable to SOC cisplatin-based chemotherapy
- Randomized phase III trials including ICI/chemo combinations are ongoing in this space
- Targeted agents increasingly used in this space as well

Adjuvant Therapy for High Risk MIBC

- MIBC with high-risk features at cystectomy
  (ypT2-T4a / ypN+ with prior NAC OR pT3-T4a / pN+ not treated with NAC)
  - IMvigor 010: Adjuvant Atezolizumab vs observation — Negative Trial
  - CheckMate 274: Adjuvant Nivolumab vs placebo — ★ FDA Approved ★
  - AMBASSADOR: Adjuvant Pembrolizumab vs observation — Finished Accrual

*One year of adjuvant treatment for all trials

CheckMate 274: DFS Benefit for Adjuvant Nivolumab

Study design

- CheckMate 274 is a phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab versus placebo in patients with high-risk MIUC

N = 709

Key inclusion criteria

- Patients with ypT2-ypT4a or ypN+ MIUC who had neoadjuvant cisplatin chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior neoadjuvant cisplatin chemotherapy and not eligible/refuse adjuvant cisplatin chemotherapy
- Radical surgery within the past 120 days
- Disease-free status within 4 weeks of dosing

Stratification factors
- PD-L1 status (<1% vs ≥ 1%)[a]
- Prior neoadjuvant cisplatin-based chemotherapy
- Nodal status

R 1:1

- NIVO IV 240 mg Q2W
- PBO IV Q2W

Treat for up to 1 year of adjuvant therapy

Minimum follow-up, 5.9 months
Median follow-up in ITT population, 20.9 months (NIVO) and 19.5 months (PBO)

Primary endpoints: DFS in ITT population and DFS in all randomized patients with tumor PD-L1 ≥ 1%
Secondary endpoints: NUTRFS, DSS, and OS[b]
Exploratory endpoints included: DMFS, safety, HRQoL

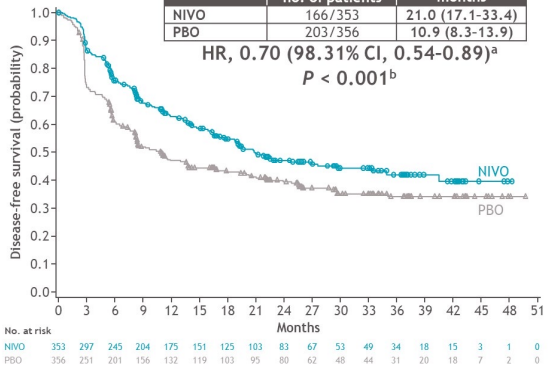
[a]Defined by the percent of positive tumor cell membrane staining in a minimum of 100 evaluable tumor cells using the PD-L1 IHC 28-8 PharmDx immunohistochemistry assay.
[b]OS data were not mature at the time of the first planned interim analysis. OS and DSS data are not presented.
DFS, disease-free survival; DMFS, distant metastasis-free survival; DSS, disease-specific survival; HRQoL, health-related quality of life; IHC, immunohistochemistry; ITT, intent-to-treat; NUTRFS, non-urothelial tract recurrence-free survival; OS, overall survival; PD-L1, programmed death ligand 1; Q2W, every 2 weeks; R, randomized.

Disease-free survival

ITT

	No. of events/ no. of patients	Median (95% CI), months
NIVO	166/353	21.0 (17.1-33.4)
PBO	203/356	10.9 (8.3-13.9)

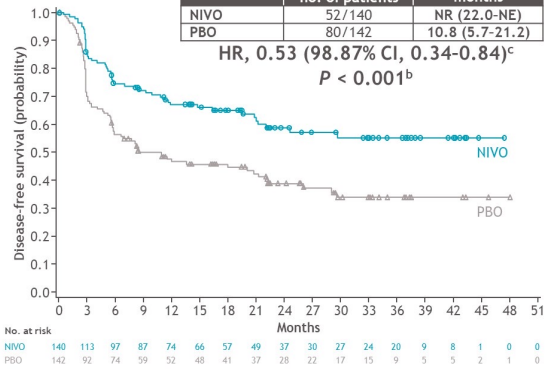
HR, 0.70 (98.31% CI, 0.54-0.89)[a]
P < 0.001[b]



PD-L1 ≥ 1%

	No. of events/ no. of patients	Median (95% CI), months
NIVO	52/140	NR (22.0-NE)
PBO	80/142	10.8 (5.7-21.2)

HR, 0.53 (98.87% CI, 0.34-0.84)[c]
P < 0.001[b]



Minimum follow-up, 5.9 months.
DFS was defined as the time between the date of randomization and the date of first recurrence (local urothelial tract, local non-urothelial tract or distant) or death.
[a]HR, 0.695 (98.31% CI, 0.541-0.894). [b]Based on a 2-sided stratified logrank test. [c]HR, 0.535 (98.87% CI, 0.340-0.842).
CI, confidence interval; NE, not estimable; NR, not reached.

Urothelial Cancer Summary

- Immune checkpoint inhibitors play a significant role in the treatment of localized and advanced UC
  - Most UC patients without contraindications will likely receive an ICI
- Adjuvant nivolumab now approved for high-risk MIBC patients
  - Neoadjuvant trials of IO and IO combinations are ongoing
- Avelumab switch maintenance is SOC for patients who derive clinical benefit from frontline platinum-based chemotherapy
- Very promising activity of ADC-IO combinations
  - Enfortumab vedotin and pembrolizumab combination may become the new SOC for the treatment of cisplatin-ineligible patients in the frontline setting

Thank you!

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