

XV SIMPOSIUM BASES BIOLÓGICAS DEL CÁNCER E INNOVACIÓN TERAPÉUTICA

MÁS DE 20 AÑOS A LA VANGUARDIA DE LA FORMACIÓN
EN LA BIOLOGÍA Y TRATAMIENTO DEL CÁNCER

17, 18 Y 19 DE MAYO DE 2023

VISIÓN ACTUAL Y NUEVOS RETOS EN EL TRATAMIENTO SISTÉMICO DEL CÁNCER UROTELIAL AVANZADO

Sergio Vázquez Estévez

Servicio de Oncología Médica

Hospital Universitario Lucus Augusti. Lugo





MY DISCLOSURES

Honoraria as consultant on advisory boards: Pfizer, Astellas, Janssen, MSD, Bayer, Roche, BMS, AstraZeneca, Ipsen, Janssen, Organon and Merck.

Honoraria as speaker: Lilly, Astellas, Bayer, Roche, Ipsen, Janssen, Takeda, Merck, Organon and AstraZeneca.

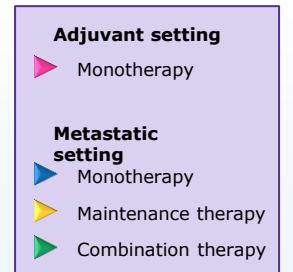
Travel grants: Pfizer, Roche, Ipsen and AstraZeneca



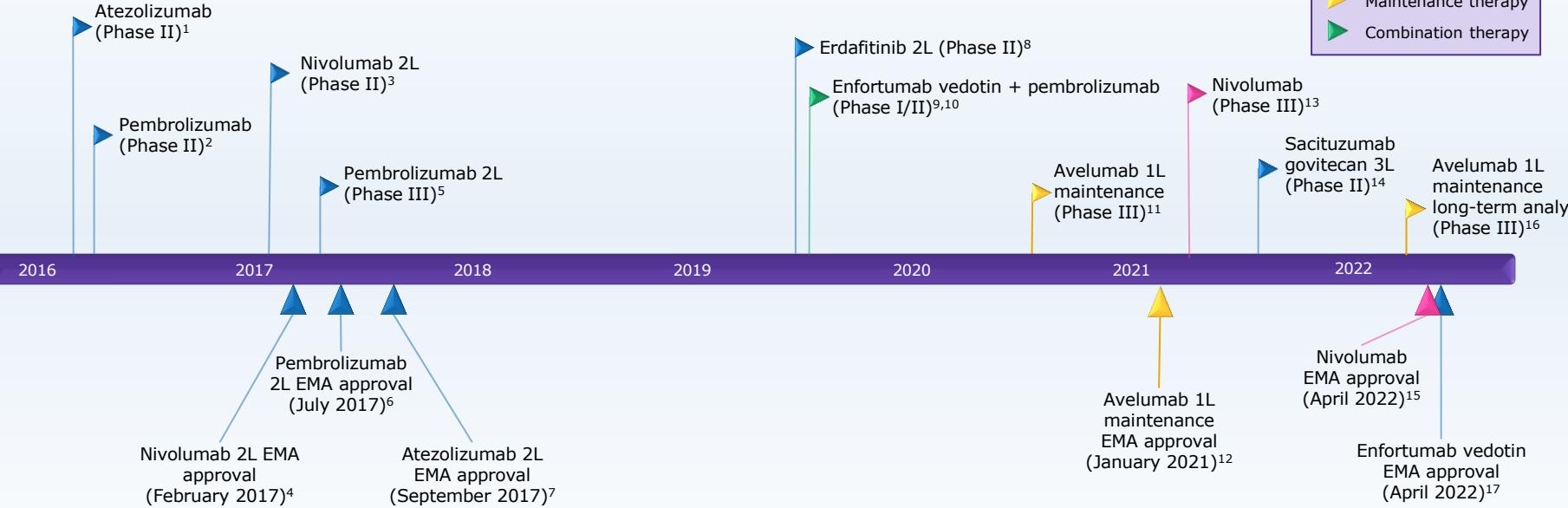
BACKGROUND

Evolution of systemic therapy for bladder cancer

Development and approval of systemic therapies for bladder cancer has been rapid (2016–present)



Data release



1L, first line; 2L, second line; 3L, third line; EMA, European Medicines Agency.

1. Rosenberg JE, et al. Lancet 2016;387:1909–1920; 2. Balar A, et al. ESMO 2016 (Abstract No. LBA32_PR – presentation); 3. Sharma P, et al. Lancet Oncol 2017;18:312–322; 4. Bristol Myers Squibb. 2017. Available at <https://news.bms.com/news/details/2017/European-Commission-Approves-Bristol-Myers-Squibbs-Odipivo-nivolumab-for-Previously-Treated-Locally-Advanced-Unresectable-or-Metastatic-Urothelial-Carcinoma-in-Adults-After-Failure-of-Prior-Platinum-Containing-Therapy/default.aspx> (last accessed August 2022); 5. Bellmunt J, et al. N Engl J Med 2017;376:1015–1026; 6. ESMO. 2017. Available at <https://www.esmo.org/oncology-news/archive/ema-adopts-a-new-indication-for-pembrolizumab2> (last accessed August 2022); 7. Roche. 2017. Available at <https://www.roche.com/media/releases/med-cor-2017-09-22c> (last accessed August 2022); 8. Loriot Y, et al. N Engl J Med 2019;381:338–341; 9. Hoimes CJ, et al. ESMO 2019 (Abstract No. 9010 – presentation); 10. NCT03288545. Available at <https://clinicaltrials.gov/ct2/show/NCT03288545> (last accessed August 2022); 11. Powles T, et al. ASCO 2020 (Abstract No. LBA1 – presentation); 12. Merck. 2021. Available at <https://www.merckgroup.com/press-releases/2021/jan/en/Bavencio-1L-UC-EU-Approval-EN.pdf> (last accessed August 2022); 13. Bajorin DF, et al. N Engl J Med 2021;384:2102–2114; 14. Tagawa ST, et al. J Clin Oncol 2021;39:2474–2485; 15. Bristol Myers Squibb. 2022. Available at <https://news.bms.com/news/corporate-financial/2022/Bristol-Myers-Squibb-Receives-European-Commission-Approval-for-Odipivo-nivolumab-as-Adjuvant-Treatment-for-Patients-with-Radically-Resected-High-Risk-Muscle-Invasive-Urothelial-Carcinoma-with-Tumor-Cell-PD-L1-Expression-1/default.aspx> (last accessed August 2022); 16. Powles T, et al. ASCO GU 2022 (Abstract No. 487 – poster); 17. Astellas. 2022. Available at <https://newsroom.astellas.us/2022-04-13-European-Commission-Approves-PADCEV-TM-enfortumab-vedotin-for-Locally-Advanced-or-Metastatic-Urothelial-Cancer> (last accessed August 2022).



Definitions: Platinum eligibility

PLATINUM-ELIGIBLE		PLATINUM-INELIGIBLE
Cisplatin-eligible	Carboplatin-eligible	
ECOG PS 0-1 AND	ECOG PS 2 OR	<i>ANY of the following:</i>
GFR > 50-60ml/min AND	GFR 30-60ml/min OR	GFR <30ml/min
Audiometric hearing loss < Grade 2 AND	not fulfilling other cisplatin-eligibility criteria	ECOG PS ≥3
Peripheral neuropathy < Grade 2 AND		ECOG PS 2 and GFR < 60ml/min
Cardiac insufficiency < NYHA class III		Comorbidities ≥ Grade 3



Define correct category for each patient

Gupta et al. ASCO GU 2019

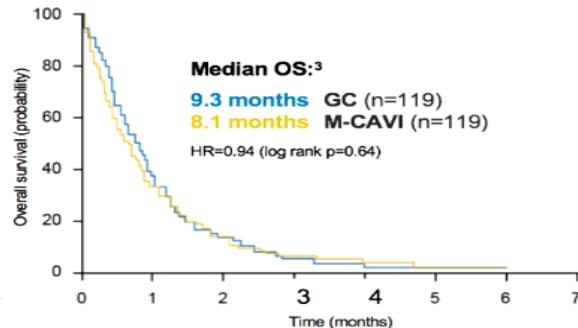
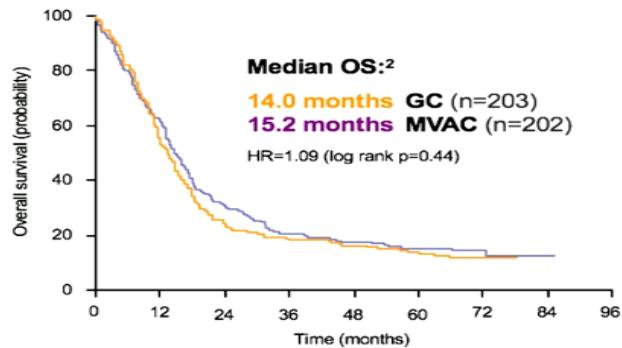
Treatment options in first-line mUC

Fit patients

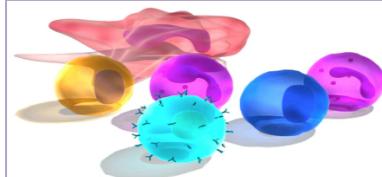
ORR 50% (12% CR)
ORR + SD: 83%
Median PFS 7.7 months
Median OS 15 months
1 y OS: 60%

Unfit patients

ORR 36% (3%)
ORR + SD: 73%
Median PFS 5.8 months
Median OS 9 months
1 y OS: 37%



Second-line immunotherapy in urothelial cancer



	IMvigor 211	KEYNOTE 045	CheckMate 275	JAVELIN bladder	NCT01693562
Fármaco	Atezolizumab	Pembrolizumab	Nivolumab	Avelumab	Durvalumab
Diseño	Fase III	Fase III	Fase II	Fase I/II	Fase I/II
Tamaño	931	542	238	249	191
Comparador	QT (VFL/taxanos)	QT (VFL/taxanos)	-	-	-
RG	23% (IC2/3)	21.1%	20%	17%	16.5%
SLP	2.3 meses	2.1 meses	2.0 meses	1.5 mes	1.5 mes
SG	11.1 meses (IC2/3)	10.3 meses	8.57 meses	-	-

Bellmunt J, et al. N Engl J Med. 2017; 376(11): 1.015.
 Powles T, et al. Lancet. 2018; 391(10122): 748.
 Sharma P, et al. Lancet Oncol. 2017; 18(3): 312.
 Powles T, et al. JAMA Oncol. 2017; 3(9): e172411.
 Patel et al. Lancet Oncol. 2018; 19: 51.

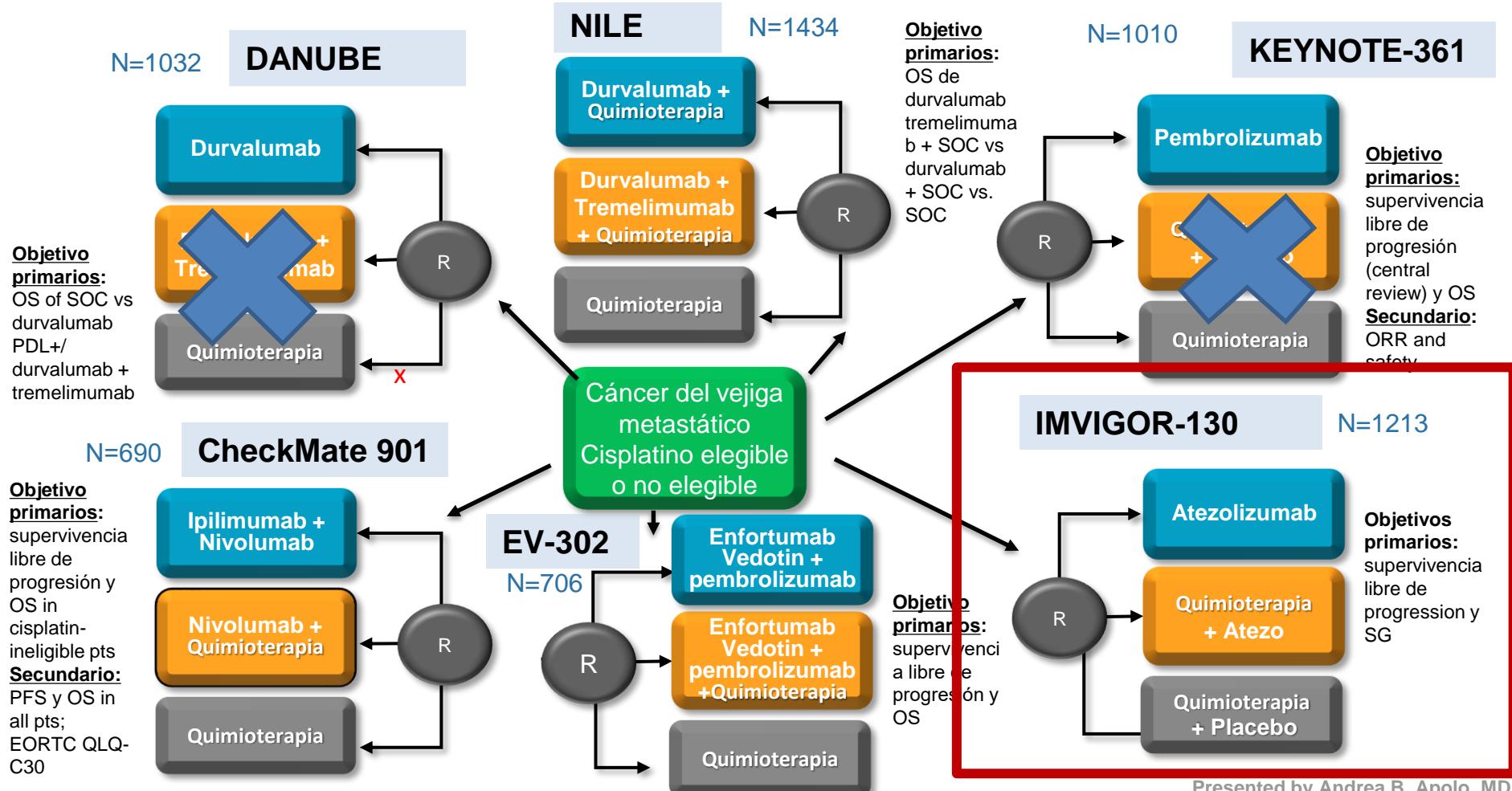


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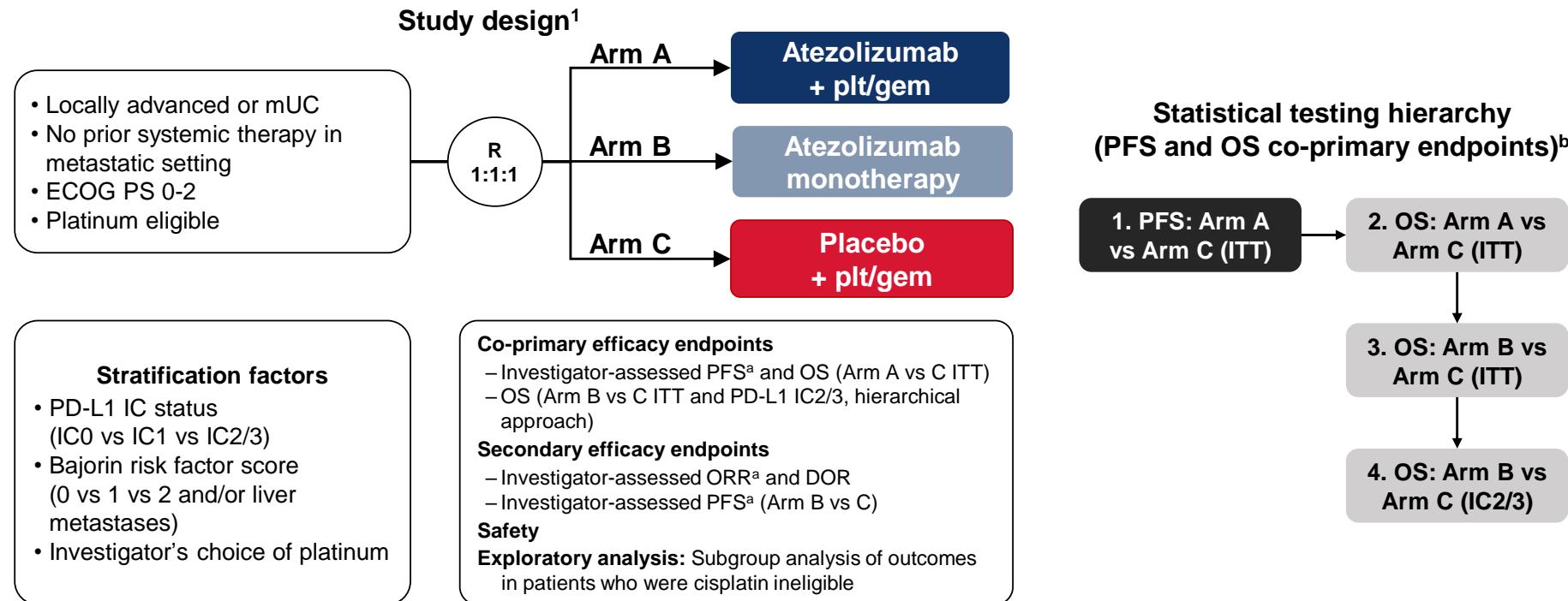


COMBOS DE QT + IO

Chemotherapy Plus Immunotherapy as First-line Treatment for Metastatic UC



IMvigor130: a global, randomized, Phase III study (NCT02807636)

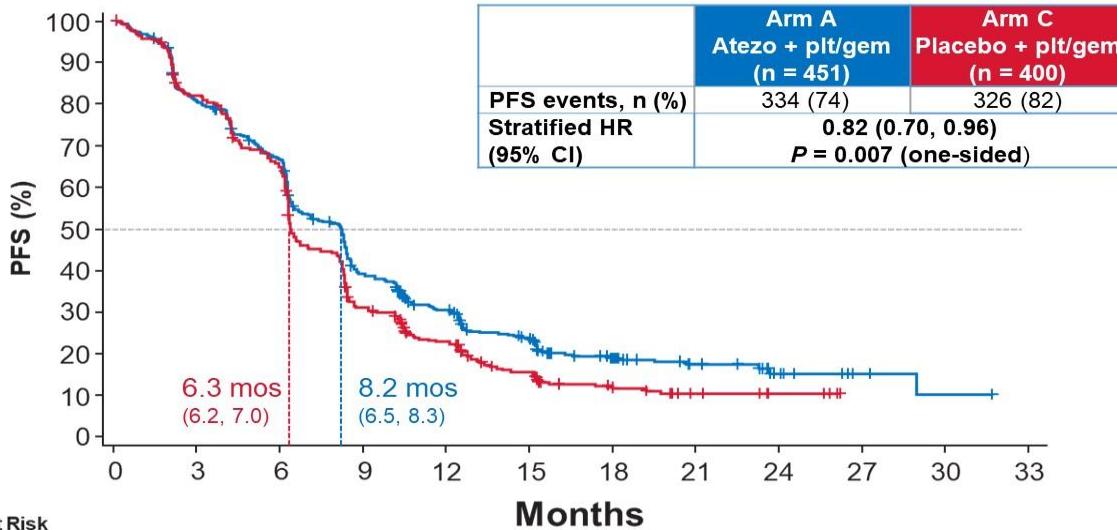


ITT, intention to treat; KPS, Karnofsky performance status.

^a Per RECIST 1.1. ^b Final OS analysis planned to occur after approximately 667 OS events in Arms A and C. 1. Galsky, et al. Lancet. 2020;395:1547-57.

IMvigor130: First PFS Analysis in the ITT Population

BARCELONA
2019 ESMO congress



- Primary analysis demonstrated a statistically significant PFS benefit
- OS interim analysis was promising but did not reach statistical significance

Grande, ESMO 2019

ASCO Genitourinary
Cancers Symposium

#GU23

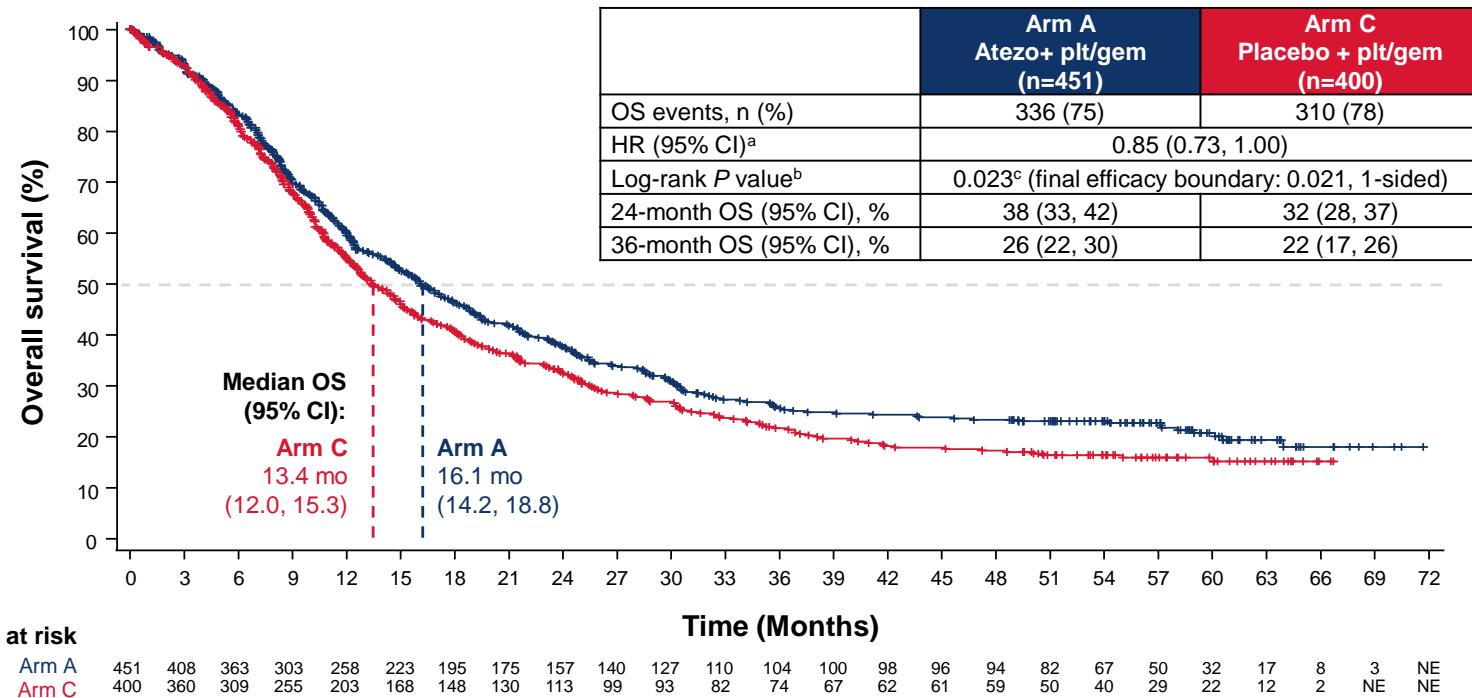
PRESENTED BY: Andrea B. Apolo, MD

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@apolo_andrea

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Final OS analysis in the ITT population



Clinical cutoff: Aug 31, 2022. Median survival follow-up: 13.4 months. NE, not estimable. ^a Stratified by PD-L1 status, Bajorin risk factors and/or liver metastases, investigator's choice of plt/gem and enrollment stage. ^b P value is 1-sided. ^c Not statistically significant (final efficacy boundary was adjusted from prior analyses).

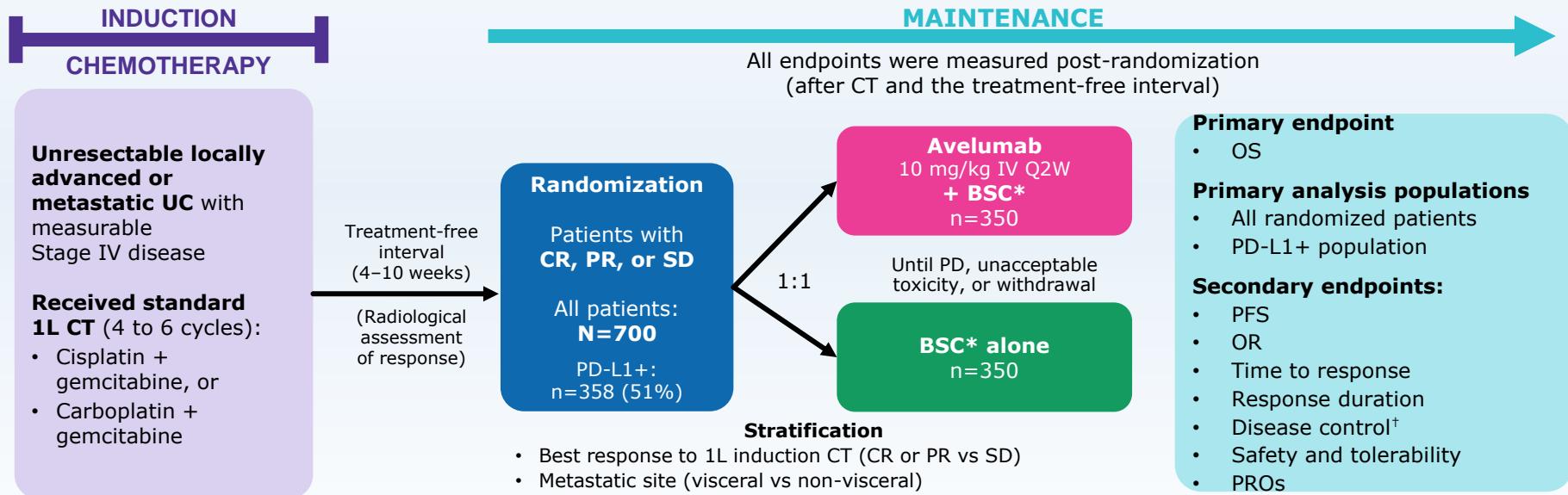


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MANTENIMIENTO

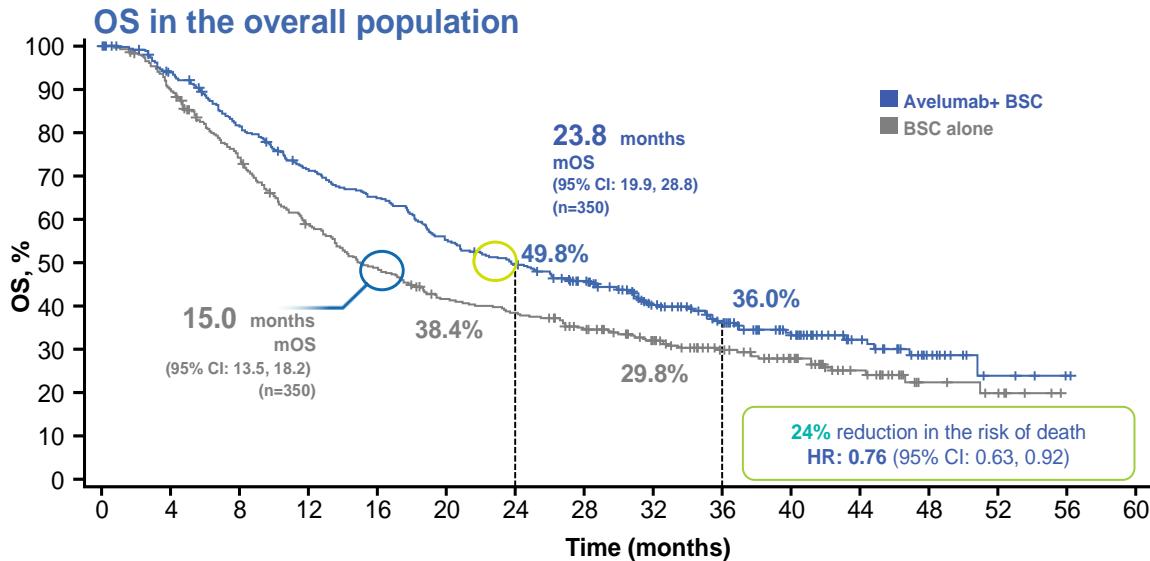
Phase III JAVELIN Bladder 100 Trial^{11,18}



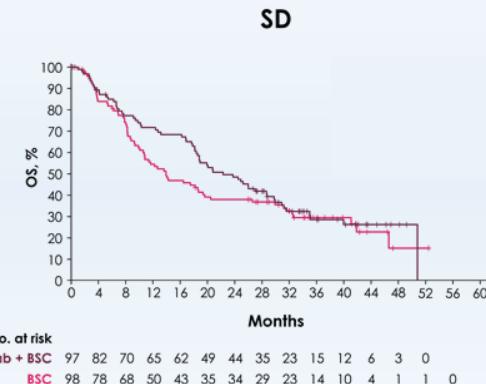
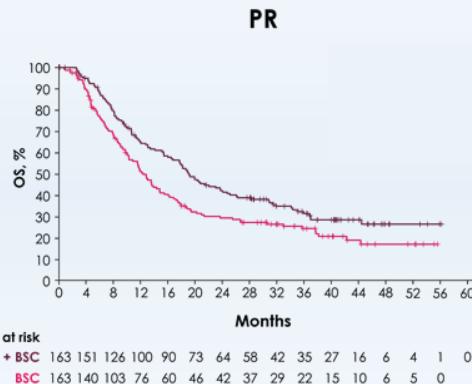
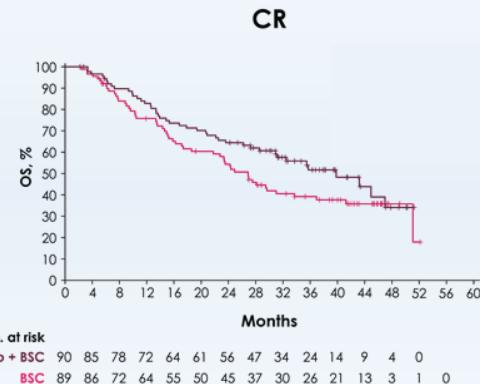
*Supportive care was administered per local practice based on patient needs and clinical judgment and included antibiotics, nutritional support, hydration, and pain management; other systemic antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable; [†]Defined as response + stable disease for ≥6 weeks.

1L, first line; BSC, best supportive care; CR, complete response; CT, chemotherapy; IO, immunotherapy; IV, intravenous; OR, objective response; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; PRO, patient-reported outcomes; Q2W, every 2 weeks; SD, stable disease; UC, urothelial carcinoma.

11. Powles T, et al. ASCO 2020 (Abstract No. LBA1 – presentation); 18. Powles T, et al. N Engl J Med 2020;383:1218–1230.



Results from the JAVELIN Bladder 100 trial demonstrated long-term OS benefit with avelumab 1L maintenance irrespective of best response to 1L CT¹⁹



Median OS, months (95% CI)	
Avelumab + BSC	39.8 (28.5–NE)
BSC alone	26.8 (18.5–33.6)
HR, 0.72 (95% CI, 0.482–1.076)	

Median OS, months (95% CI)	
Avelumab + BSC	19.2 (16.0–23.8)
BSC alone	12.8 (10.3–14.8)
HR, 0.70 (95% CI, 0.541–0.914)	

Median OS, months (95% CI)	
Avelumab + BSC	22.3 (18.2–28.8)
BSC alone	14.0 (10.6–19.6)
HR, 0.84 (95% CI, 0.596–1.188)	

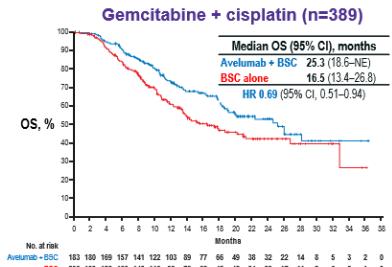
Data cut-off: June 4, 2021

1L, first line; BSC, best supportive care; CI, confidence interval; CR, complete response; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival; PR, partial response; SD, stable disease.

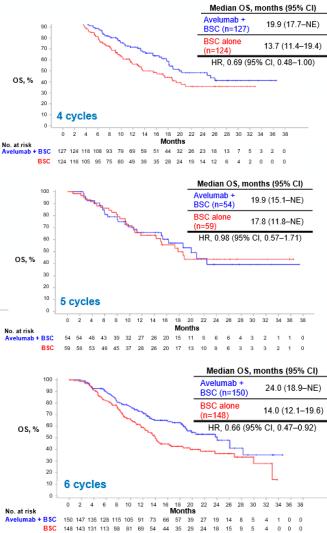
19. Pérez Valderrama B, et al. ASCO 2022 (Abstract No. 4559 – poster).

OS benefit with avelumab 1L maintenance occurred irrespective of 1L CT regimen or number of cycles of 1L platinum-based CT^{19,20}

OS by 1L CT regimen¹⁹



OS by number of 1L platinum-based CT cycles²⁰



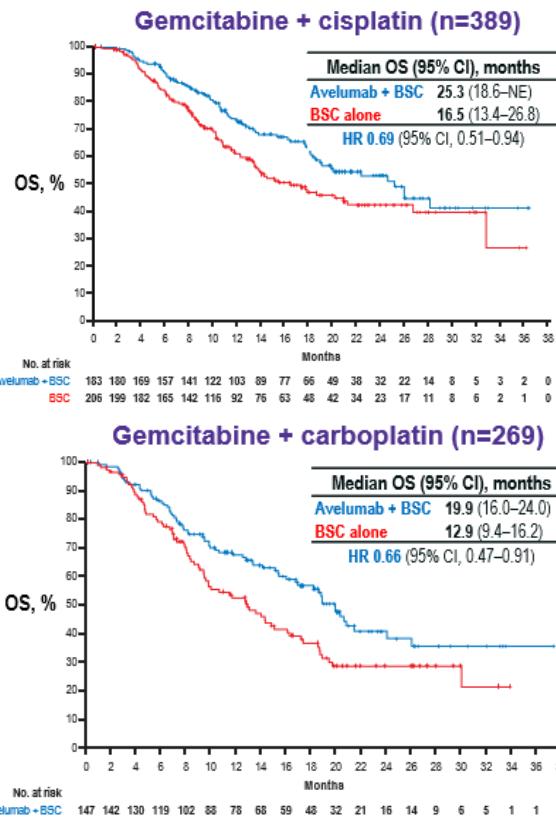
Treatment choices can
be made on an
individual patient basis

1L, first line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival.

19. Grivas P, et al. ESMO 2020 (Abstract 704MO – presentation); 20. Loriot Y, et al. ASCO GU 2021 (Abstract 438 - poster).

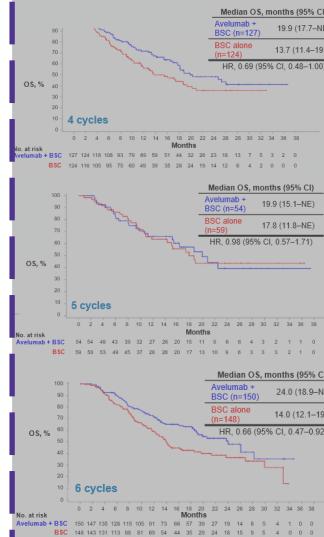
JAVELIN Bladder 100 data facilitate flexibility of 1L in real-world clinical practice (1)

OS by 1L CT regimen¹⁹



Maintenance occurred irrespective of 1L CT regimen or cycles of 1L platinum-based CT^{19,20}

OS by number of 1L platinum-based CT cycles²⁰

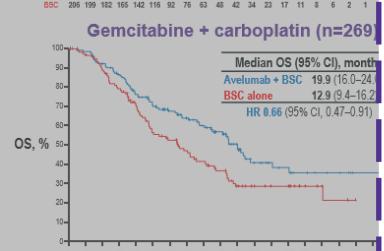
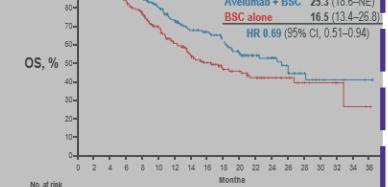
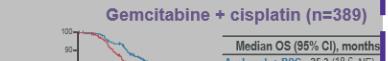


Treatment choices can be made on an individual patient basis

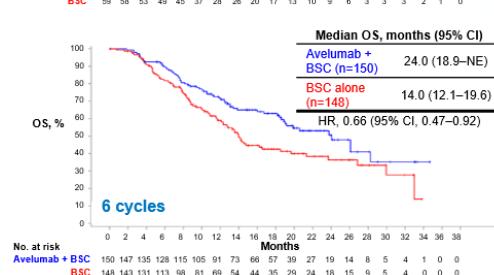
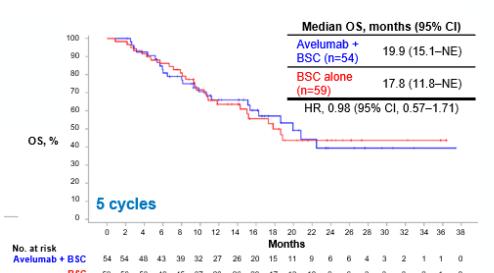
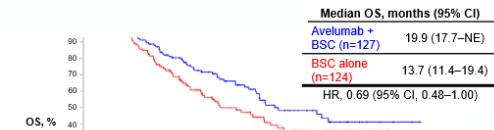
JAVELIN Bladder platinum-based

OS benefit with a
platinum-based

OS by 1L CT regime



OS by number of 1L platinum-based CT cycles²⁰



of 1L practice (1)

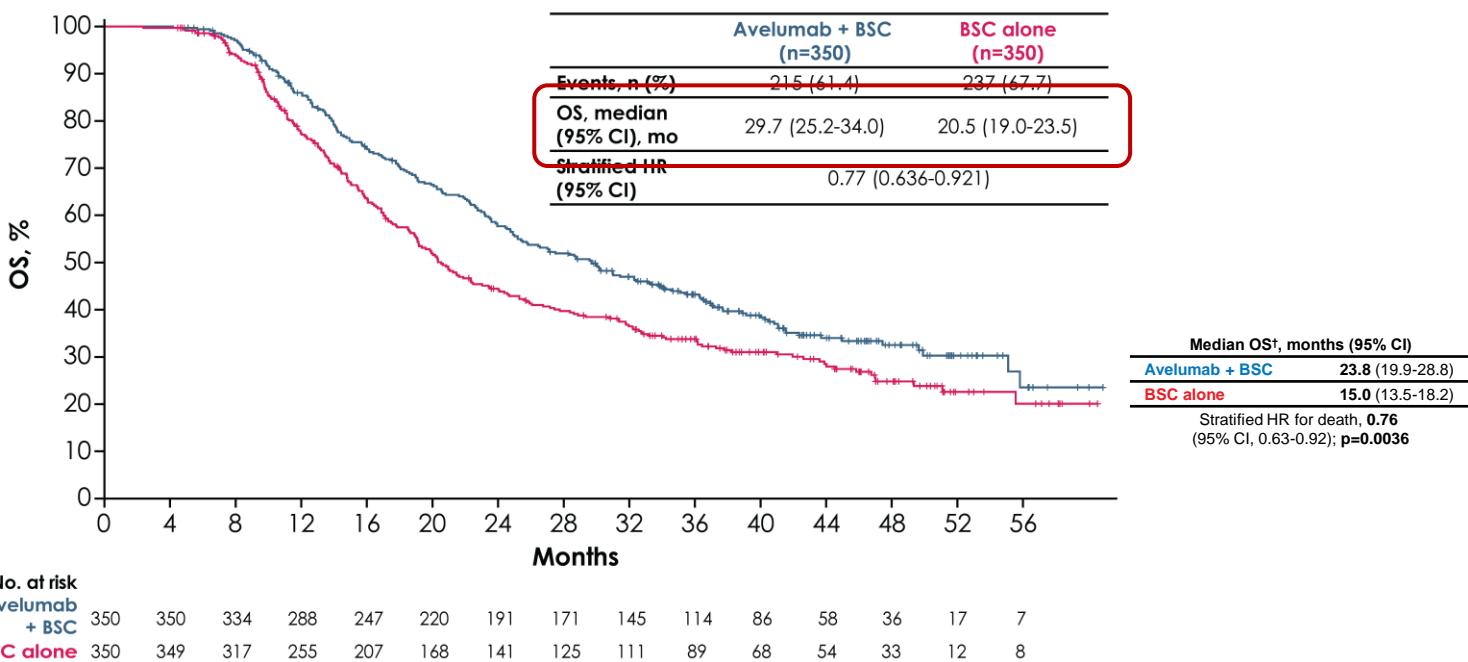
of 1L CT regimen or
0

treatment choices can
be made on an
individual patient basis

Figure 4. OS from the start of 1L chemotherapy

Median follow-up:

- Avelumab + BSC: 38.0 months (95% CI, 36.1–40.5)
- BSC alone: 39.6 months (95% CI, 36.2–41.7)

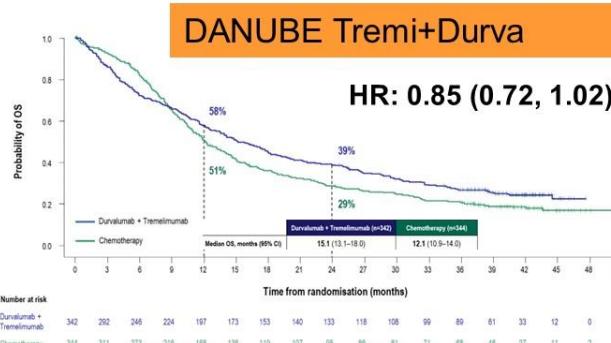
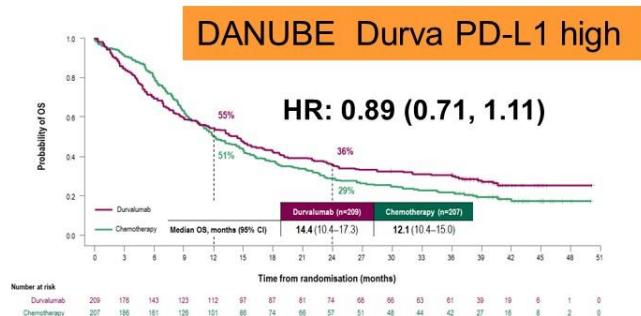
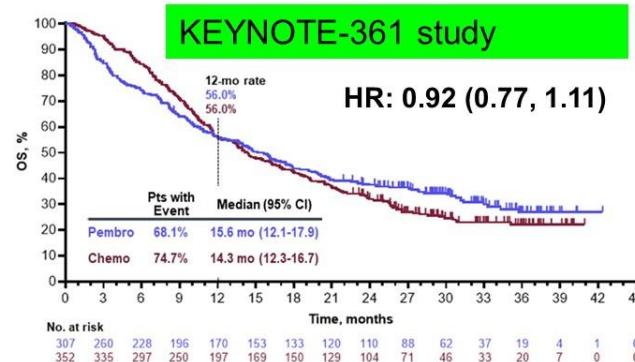
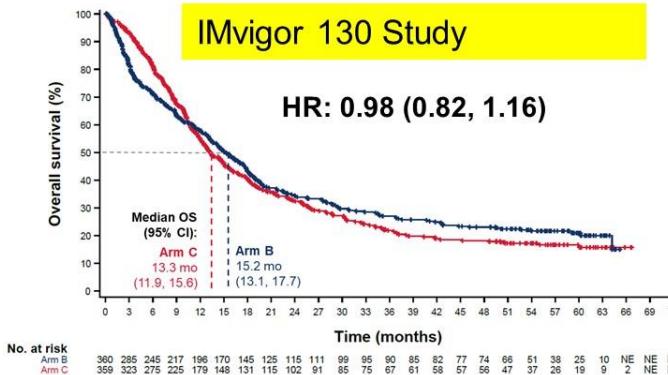


1L, first line; BSC, best supportive care; HR, hazard ratio; OS, overall survival.



POBLACIÓN CIS-INELIGIBLE

Monotherapy CPI vs Platinum-based chemo



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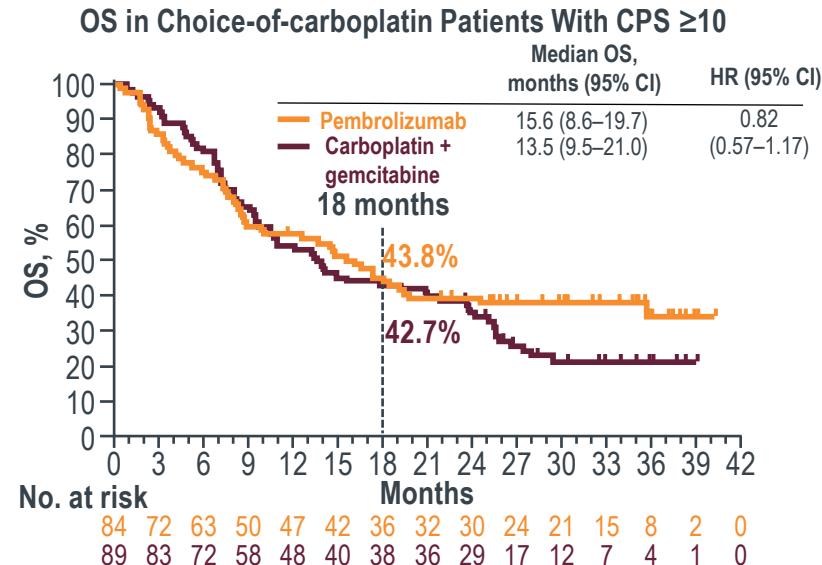
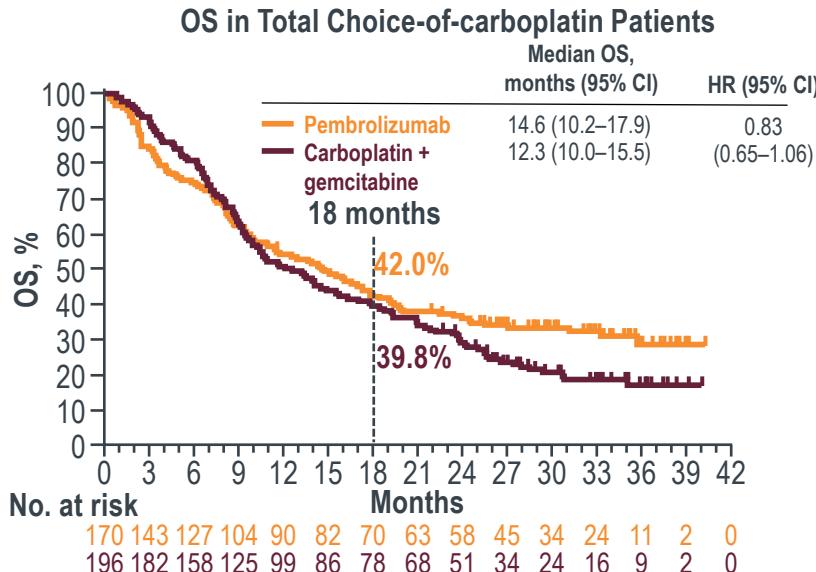
PRESENTED BY: Andrea B. Apolo, MD

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OS in choice-of-carboplatin patients

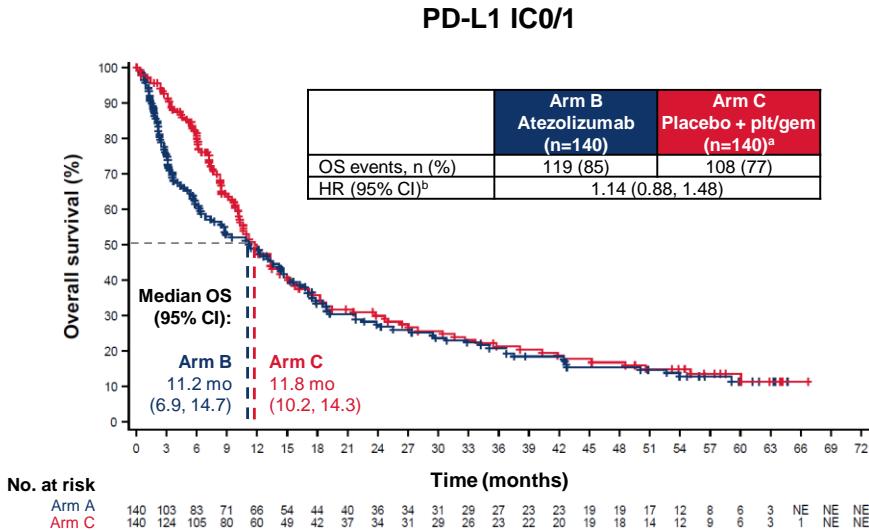
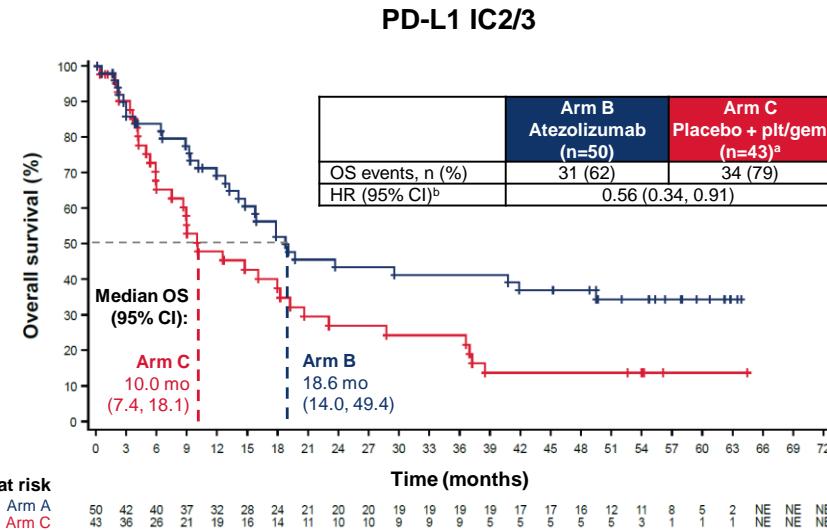


Kaplan-Meier estimates.

Data cutoff date: April 29, 2020.

Powles T et al. Presented at ASCO-GU 2021; abstract 450.

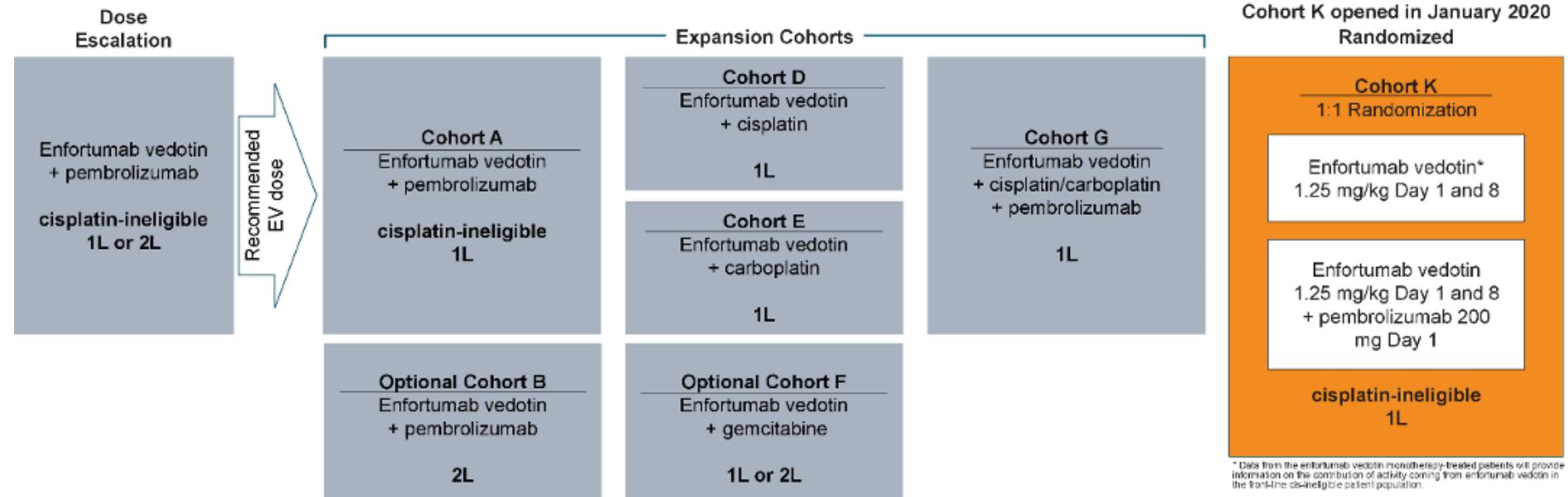
OS in the cisplatin-ineligible population by PD-L1 status



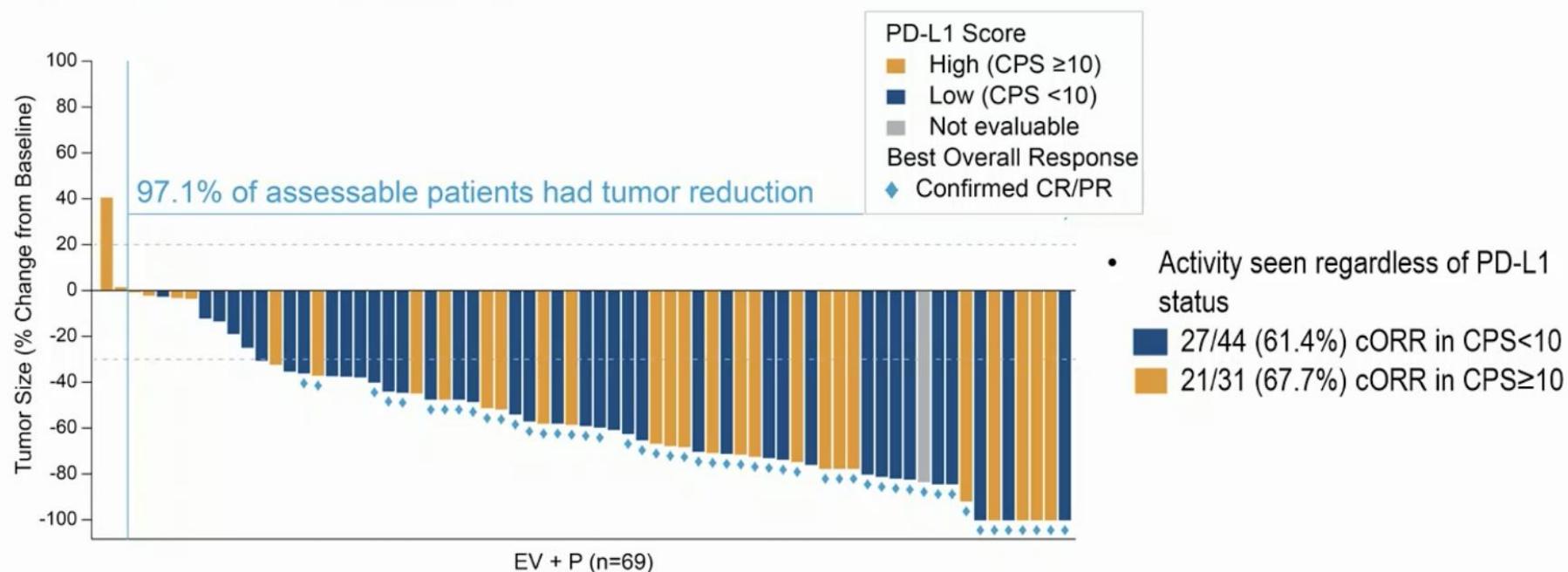
Clinical cutoff: Aug 31, 2022. Median survival follow-up: 13.4 months.

^a Comparison included only patients concurrently enrolled with Arm B. ^b Unstratified.

Study EV-103 (cohort K) EV + Pembro in untreated cis-ineligible mUC

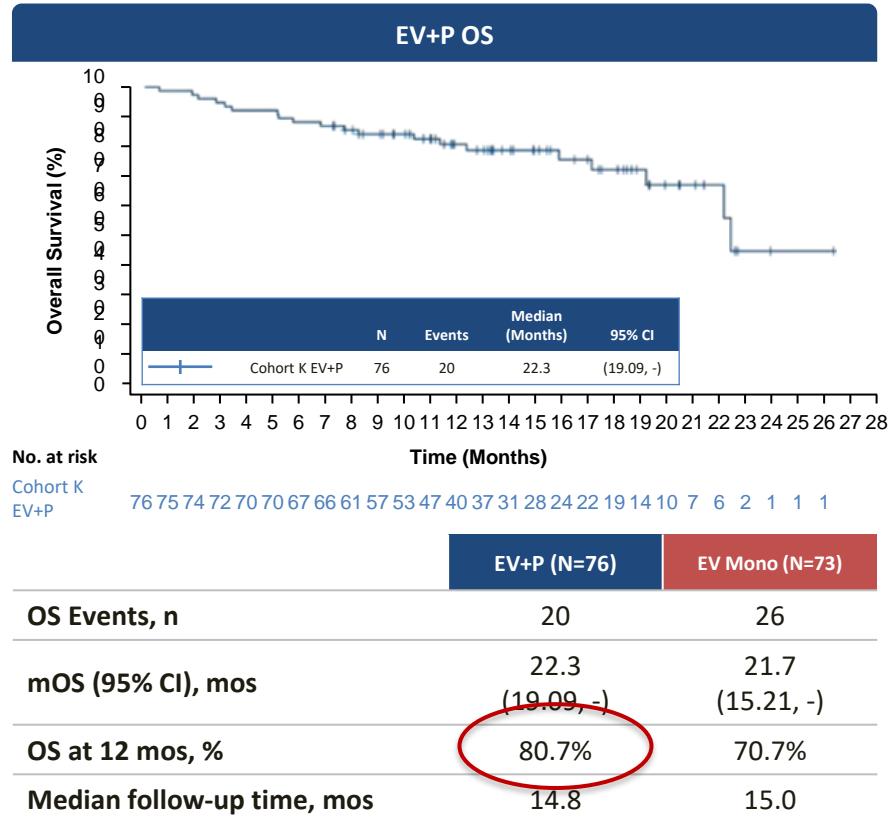
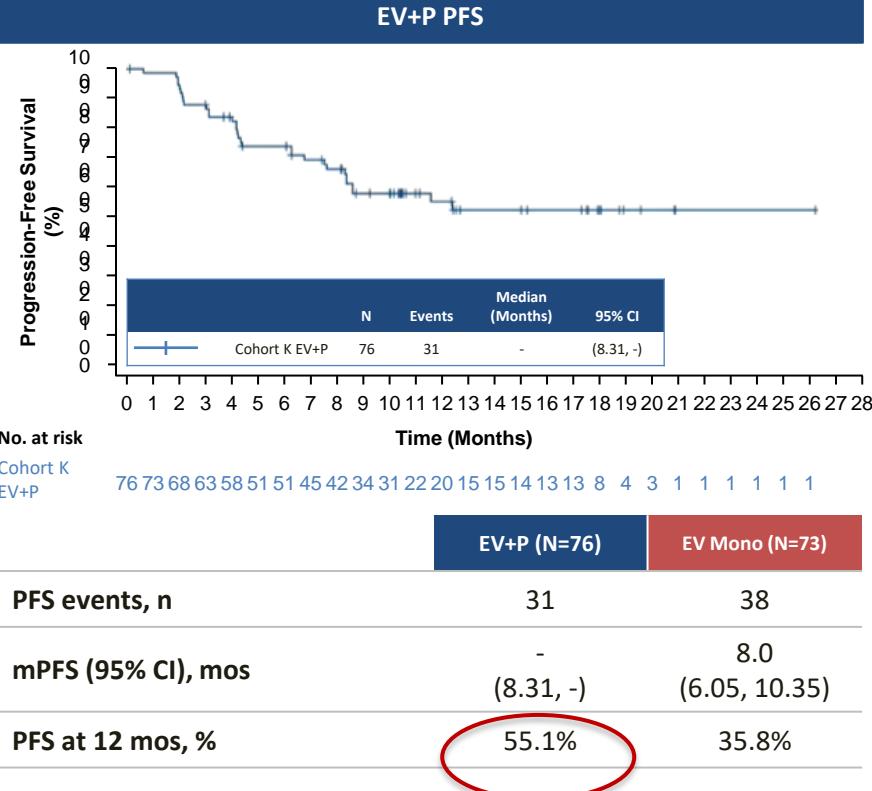


Study EV-103 (cohort K): Percent reduction from target lesion by BICR



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

Study EV-103 (cohort K): PFS & OS





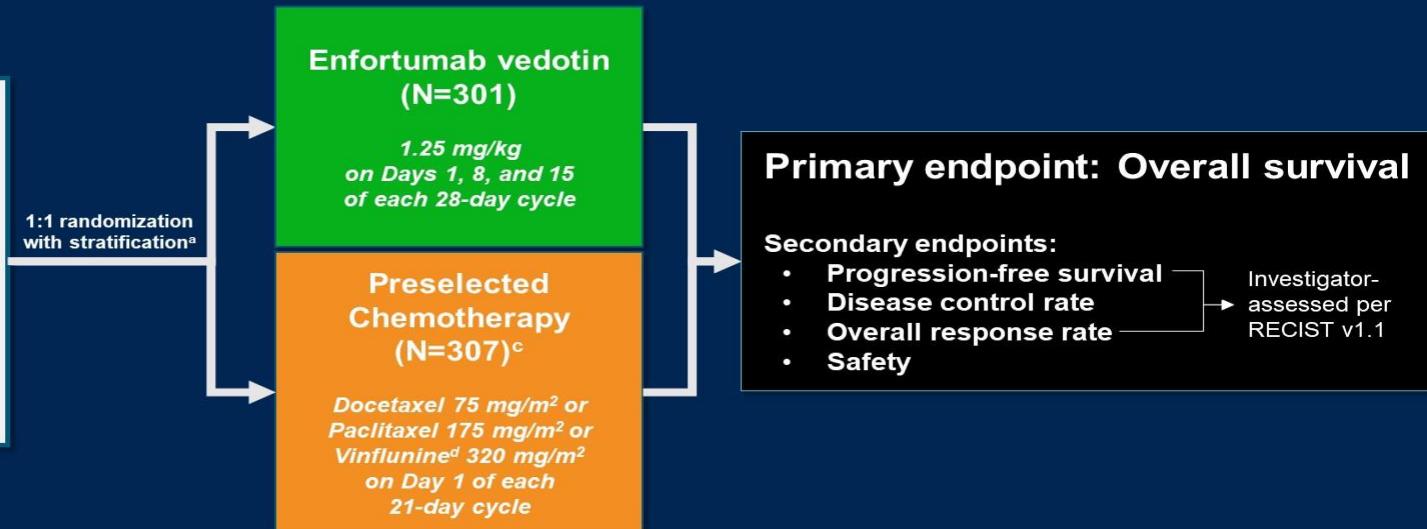
POBLACIÓN PRETRATADA: ADC



EV-301 Open-Label Phase 3 Trial Design

Key eligibility criteria:

- Histologically/cytologically confirmed UC, including with squamous differentiation or mixed cell types
- Radiographic progression or relapse during or after PD-1/L1 treatment for advanced UC
- Prior platinum-containing regimen for advanced UC^b
- ECOG PS 0 or 1



^aStratification variables were ECOG performance status (0 or 1), regions of the world (United States, western Europe, or rest of world), liver metastasis (yes or no).

^bIf used in the adjuvant/neoadjuvant setting, progression must be within 12 months of completion.

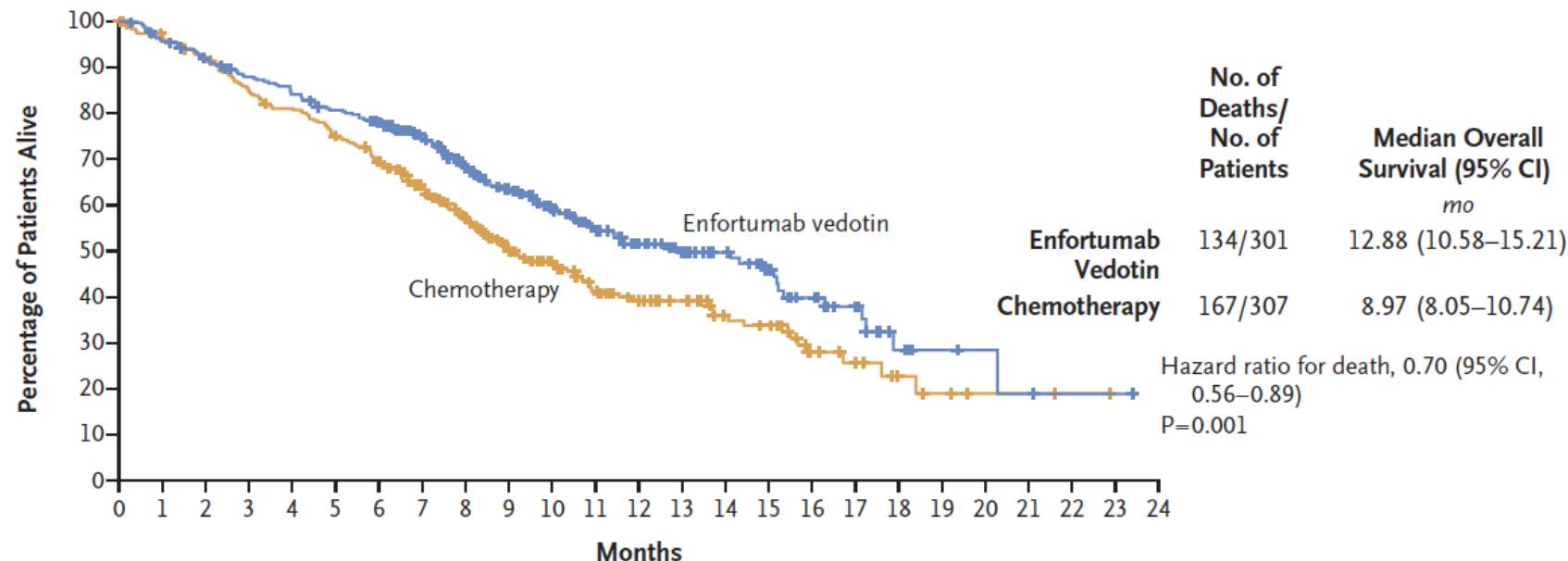
^cInvestigator selected prior to randomization.

^dIn countries where approved; overall proportion of patients receiving vinflunine capped at 35%.

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PD-1/L1, programmed cell death protein-1/programmed death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; UC, advanced urothelial carcinoma.

EV-301: Phase 3 trial of Enfortumab Vedotin vs chemotherapy in previously treated patients

A Overall Survival According to Treatment Group

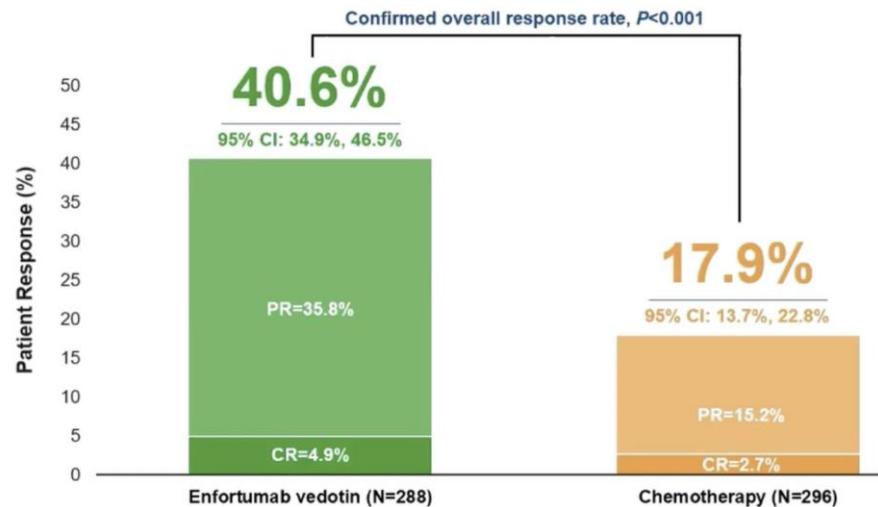
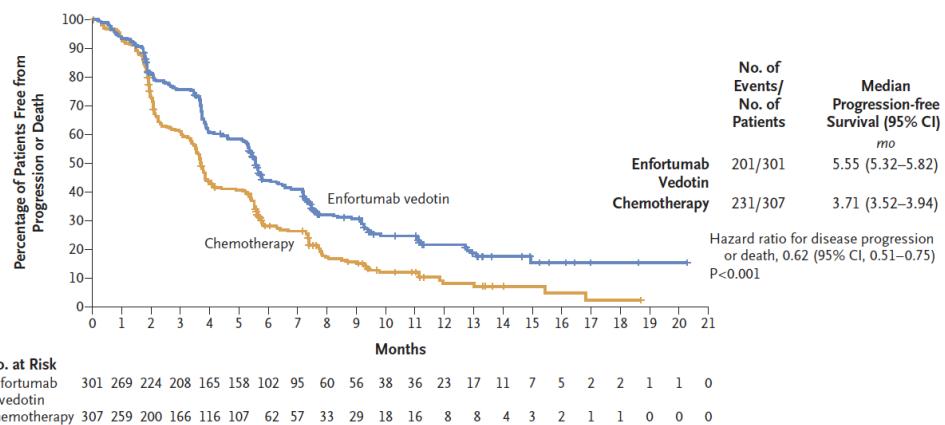


No. at Risk

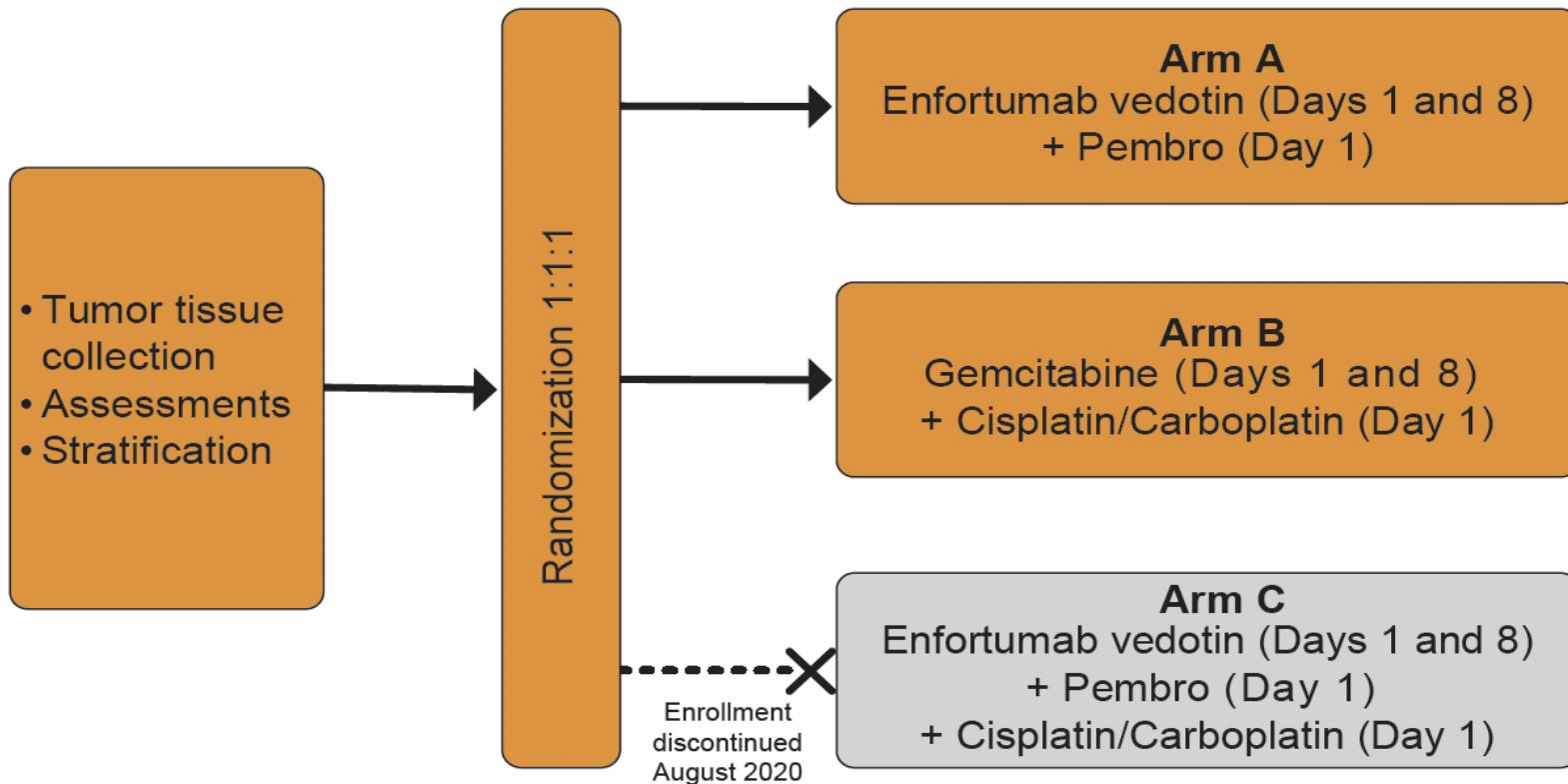
Enfortumab vedotin	301 286 272 257 246 234 222 190 158 130 105 85 63 52 42 33 23 15 7 4 3 2 1 1 0
Chemotherapy	307 288 274 250 238 219 198 163 131 101 84 66 51 44 32 29 16 11 6 4 2 2 1 0 0

EV-301: Phase 3 trial of Enfortumab Vedotin vs chemotherapy in previously treated patients

Sites of metastasis — no./total no. (%)		
Lymph node only	34/301 (11.3)	28/306 (9.2)
Visceral site	234/301 (77.7)	250/306 (81.7)
Liver	93/301 (30.9)	95/307 (30.9)
Previous systemic therapies — no. (%)		
1–2	262 (87.0)	270 (87.9)
≥3	39 (13.0)	37 (12.1)
Best response among patients who previously received checkpoint inhibitor treatment — no. (%)¶		
Response	61 (20.3)	50 (16.3)
No response	207 (68.8)	215 (70.0)



Study EV-302: phase 3 trial of EV + Pembro vs platinum-based chemo in 1st line mUC



TROPHY-U-01 cohorts

1

Cohort 1 (2L+): pts with mUC who have progressed after prior platinum-based and CPI-based therapies



SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle

2

Cohort 2 (2L+): pts with mUC ineligible for platinum-based therapy and who have progressed after prior CPI-based therapies



SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle

3

Cohort 3 (2L): CPI-naïve pts with mUC who have progressed after prior platinum-based therapies



SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle + pembrolizumab 200mg IV on Day 1 of 21-day cycle

Continue treatment until progressive disease, unacceptable toxicity or loss of clinical benefit

TROPHY-U-01: cohort 1 (2L+: after chemo & IO)

1

Cohort 1 (2L+): pts with mUC who have progressed after prior platinum-based and CPI-based therapies

SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle

Characteristics	N=113
Age, median (range), years	66 (33-90)
≥75, n (%)	26 (23)
Male, n (%)	88 (78)
ECOG PS, n (%)	
0	32 (28)
1	81 (72)
Type of disease, n (%)	
Metastatic urothelial cancer	108 (96)
Locally advanced unresectable	4 (3.5)
Missing	1 (0.09)
Visceral metastatic sites, n (%) ^a	75 (66)
Lung	49 (43)
Liver	38 (34)
Other	15 (13)

Characteristics	N=113
Setting of prior systemic therapy, n (%)	
Adjuvant	22 (19.5)
Metastatic	108 (95.6)
Neoadjuvant	36 (31.9)
Prior CPIs, n %	112 (99) ^b
Prior platinum anticancer therapy, n (%)	113 (100)
Cisplatin	89 (79)
Carboplatin	24 (21)
Prior enfortumab vedotin, n (%)	10 (8.8)
Prior erdafitinib, n (%)	2 (1.8)
Prior anticancer regimens, median, n (range)	3.0 (1-8)
Lines of prior metastatic regimens, n (%)	
1	22 (20)
2	30 (27)
≥3	56 (50)

Characteristics	N=113
Bellmunt risk factors ^c , n (%)	
0	18 (16)
1	54 (48)
2	32 (28)
3	9 (8)
UGT1A1 status, n (%)	
Wild-type *1/*1	45 (39.8)
Heterozygous *1/*28	47 (41.6)
Homozygous *28/*28	13 (11.5)
Missing	8 (7.1)

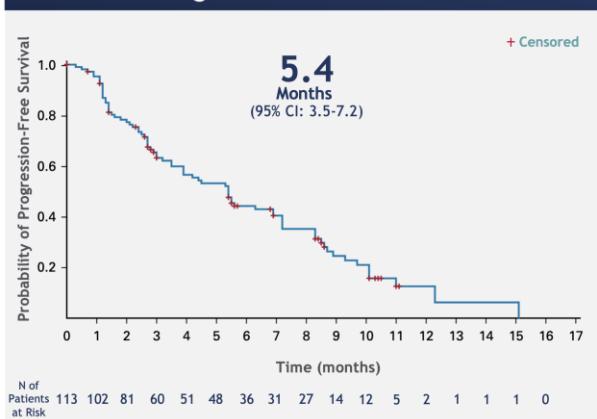
TROPHY-U-01: cohort 1 (2L+: after chemo & IO)

1

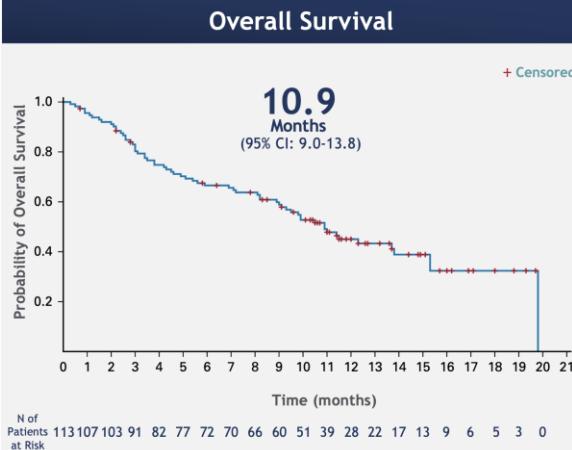
Cohort 1 (2L+): pts with mUC who have progressed after prior platinum-based and CPI-based therapies

SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle

Progression-Free Survival



Overall Survival



ORR by BICR¹

Endpoint

Cohort 1 (N=113)

ORR,^a n (%) [95% CI]

31 (27) [19-37]

CR, n (%)

6 (5)

PR, n (%)

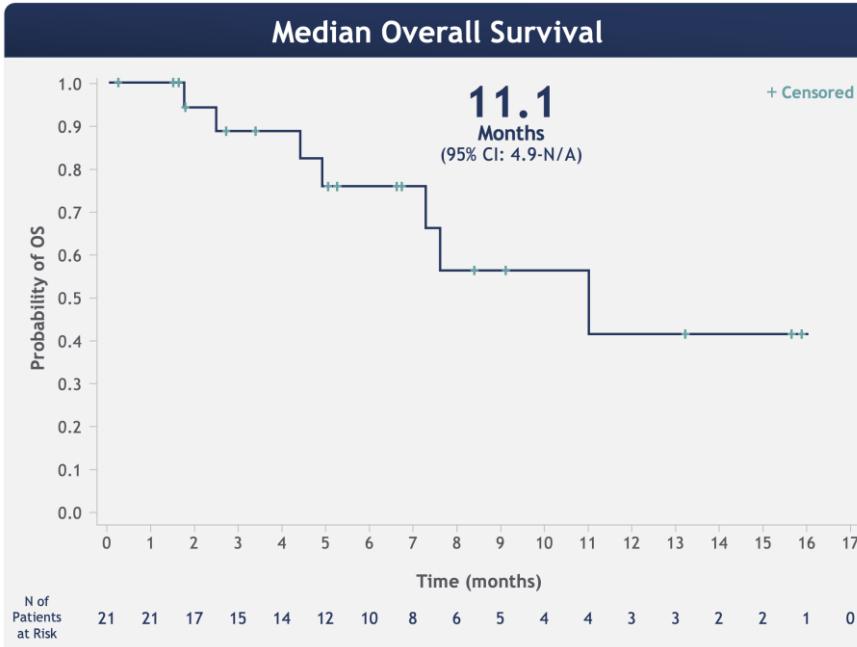
25 (22)

TROPHY-U-01: cohort 2 (2L: after IO)

2

Cohort 2 (2L+): pts with mUC ineligible for platinum-based therapy and who have progressed after prior CPI-based therapies

SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle



Endpoint	(N=21)
Median (range) follow-up, ^a mo	6.8 (1.6-18.9)
Patients continuing treatment, n (%)	9 (43)
ORR, n (%) (95% CI)	6 (29) (12-54)
CBR, n (%) [95% CI]	7 (33) [15-59]
Median DOR (95% CI), mo	NR (4.3-NR)
Median PFS, mo (95% CI)	5.5 (1.7-7.3)
Median OS, mo (95% CI)	11.1 (4.9-N/A)

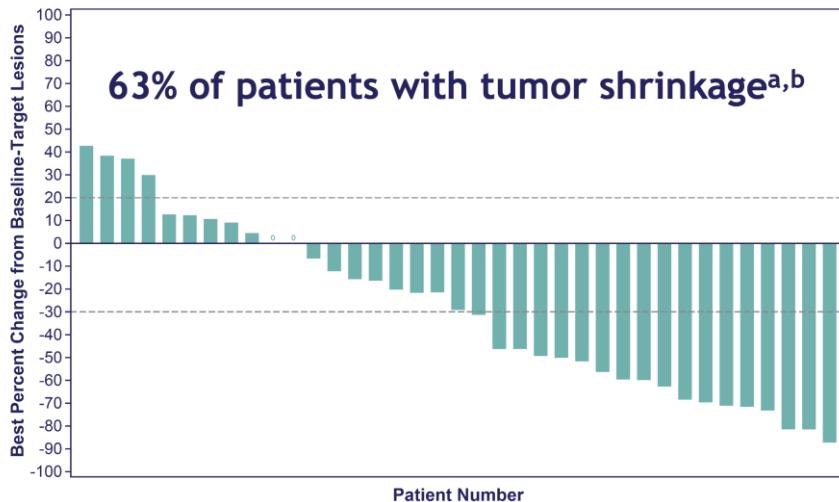
TROPHY-U-01: cohort 3 (2L: after chemo)

3

Cohort 3 (2L): CPI-naïve pts with mUC who have progressed after prior platinum-based therapies

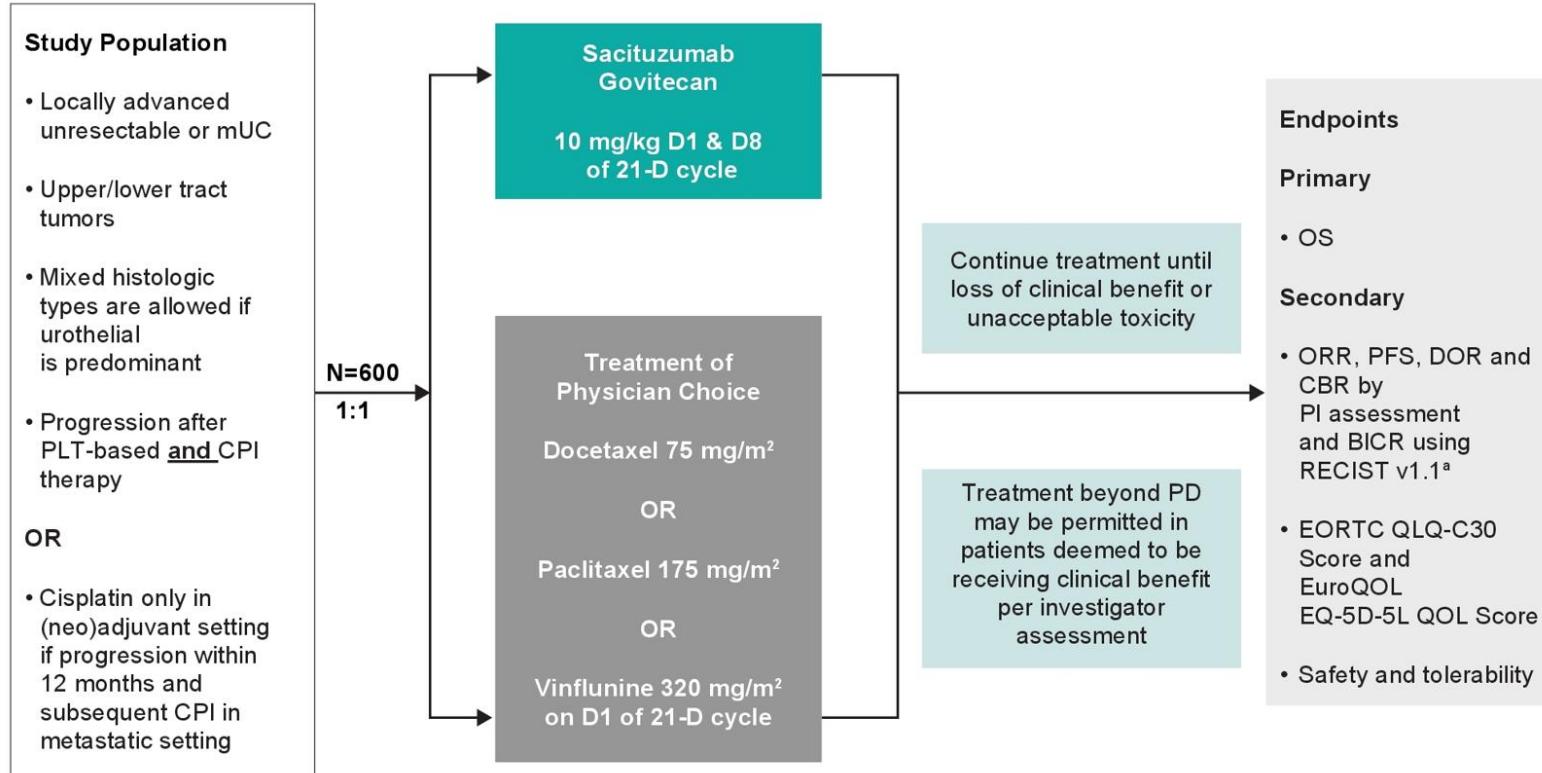
SG 10 mg/kg IV on Days 1 and 8 of 21-day cycle + pembrolizumab 200mg IV on Day 1 of 21-day cycle

- Median follow-up: 5.8 months (data cutoff date: 2021-09-24)
- Median time to response: 2 months (1.3-2.8; n=14)
- Median DOR not yet reached: N/A (2.80-N/A)
- Median PFS (95% CI), 5.5 months (1.7-NR); median OS, not reached



	Cohort 3 ^a (N=41)
Objective response rate (CR + PR), n (%) [95%CI]	14 (34) [20.1-50.6]
Objective response rate (CR + PR), evaluable patients, n (%)	14 (38)
Best overall response, n (%)	
CR	1 (2)
PR	13 (32)
SD	11 (27)
SD \geq 6 months	4 (10)
PD	12 (29)
Not assessed	4 (10)
Clinical Benefit Rate (CR + PR + SD), n (%) [95%CI]	25 (61) [44.5-75.8]

TROPiCS 04



Other antibody-drug conjugates are under development

Name	Target	Antibody/peptide	Payload	Linker
Trastuzumab emtansine	HER2	Trastuzumab	DM1	Lysine-SMCC
Trastuzumab deruxtecan		Trastuzumab	DXd	Cleavable
SYD985		Trastuzumab	Seco-duocarmycin	Cleavable
MRG002		Humanized anti-HER2	MMAE	Cleavable
Disitamab vedotin		Disitamab	MMAE	Cleavable
Sacituzumab govitecan	TROP2	Sacituzumab	Cleavable	SN-38
Datopotamab deruxtecan		Datopotamab	Cleavable	Deruxtecan
Indatuximab ravtansine	CD138	Indatuximab	DM4	Disulphide bond
BT5528	EphA2/CD137	Bicyclic peptide	MMAE	Protease cleavable peptide linker
BT8009	Nectin-4	Bicyclic peptide	MMAE	Valine-citrulline cleavable linker
BT7480 (first-in-class TICA)	Nectin-4/CD137	CD137 bicycle peptide linked to Nectin-4 binding bicycle	-	Branched trimeric polyethylene glycol linker

DXD, deruxtecan; EphA2, erythropoietin-producing hepatocellular A2; MMAE, monomethyl auristatin E.

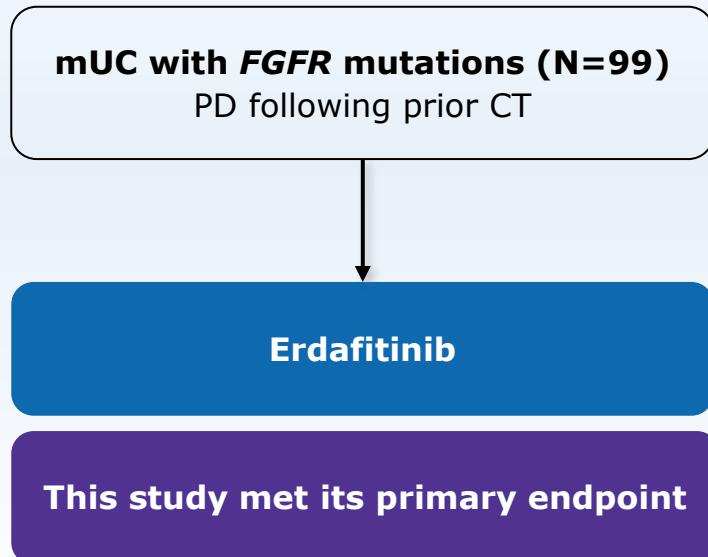
46. Schönfeld K, et al. J Hematol Oncol 2017;10:13; 47. Bicycle Press Release. October 2021; Available at <https://investors.bicycletherapeutics.com/node/8161/pdf> (last accessed August 2022); 48. Papadopoulos K, et al. ASCO 2022 (Abstract no. TPS2689 – poster); 49. Ungaro A, et al. Cells 2022;11:803; 50. Meric-Bernstam F, et al. ASCO 2021 (Abstract 9058 – presentation); 51. Yu J, et al. Front Mol Biosci 2022;9:847835.



POBLACIÓN PRETRATADA: ANTI-FGFR

Erdafitinib for 2L/3L patients with mUC and FGFR mutations

BLC2001 (selected 2L/3L regimen, Phase II)⁸



	Initial analysis ⁸	24-month follow-up analysis ⁵²
ORR, % (primary endpoint):	40	40
mOS, months (secondary endpoint):	13.8	11.3
mPFS, months (secondary endpoint):	5.5	5.5
Grade ≥3 TRAEs, % (secondary endpoint):	46	52

2L, second line; 3L, third line; CT, chemotherapy; FGFR, fibroblast growth factor receptor; mOS, median overall survival; mPFS, median progression-free survival; mUC, metastatic urothelial carcinoma; ORR, objective response rate; PD, progressive disease; TRAE, treatment-related adverse event.
8. Loriot Y, et al. N Engl J Med 2019;381:338–348; 52. Siefker-Radtke AO, et al. Lancet Oncol 2022;23:248–258.

Erdafitinib in mUC: THOR trial

FDA

INDICATIONS AND USAGE

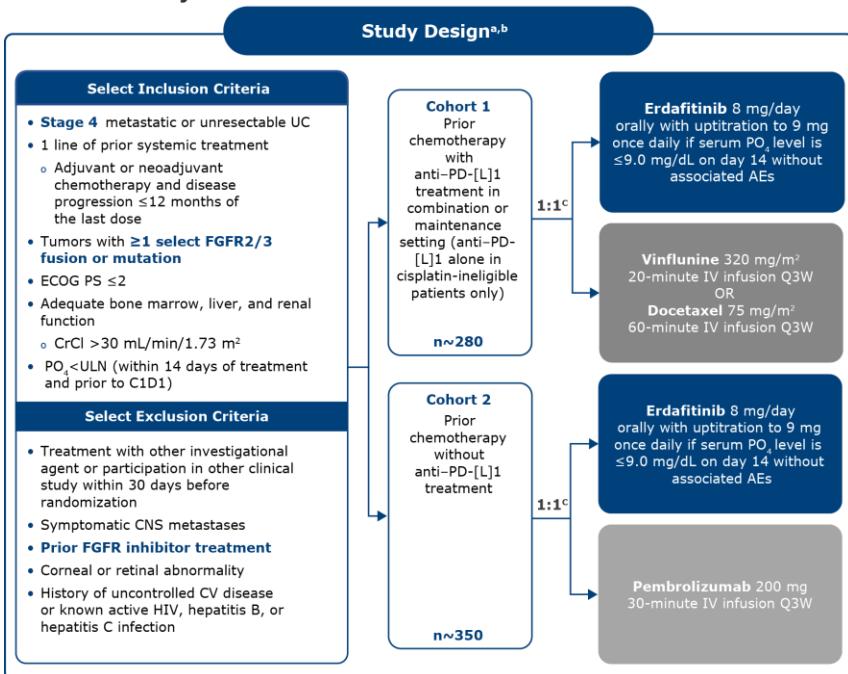
BALVERSA is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has

- susceptible FGFR3 or FGFR2 genetic alterations and
- progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for BALVERSA. (1, 2.1)

The therascreen FGFR RGQ RT-PCR Kit is a real-time, reverse transcription PCR test for the qualitative detection of two point mutations in exon 7 [p.R248C (c.742C>T), p.S249C (c.746C>G)], two point mutations in exon 10 [p.G370C (c.1108G>T) and p.Y373C (c.1118A>G)] and two fusions (FGFR3:TACC3v1 and FGFR3:TACC3v3) in the fibroblast growth factor receptor 3 (FGFR3) gene in RNA samples derived from formalin-fixed paraffin-embedded (FFPE) urothelial tumor tissue. The test is indicated for use as an aid in identifying patients with cases of urothelial cancer (UC) which harbor these alterations and are therefore eligible for treatment with BALVERSA™ (erdafitinib).

THOR Study





OTRAS ESTRATEGIAS

New combinations and strategies in 1st line mUC

Chemo + IO

IMvigor-130 (CT+atezo)
Keynote-361
(CT+pembro)
NILE (CT+durva)
CheckMate-901 (CT+nivo)

IO + IO

Danube (Durva+Treme)
CheckMate-901 (Nivo+Ipi)

ADC + IO

EV-302 (EV + pembro)
TROPHY-U-01 Cohort 3
(SG+ pembro)
DV-001 (Disitamab
Vedotinib+pembro)

FGFR + IO

NORSE (Erda+cetrelimab)
FORT-2 (Roga+atezo)
FIGHT-205
(Pemi+pembro)

PARP + IO

BAYOU (Durva+Olaparib)

TKI + IO

LEAP-011
(Lenva+pembro)
COSMIC-021
(Cabo+atezo)

Novel combo maintenance

MAINCAV (avelumab + cabozantinib)
PRESERVE-3 (Trilaciclib+avelumab)
MEET-URO-12 (niraparib)
ATLANTIS (rucaparib or cabo)
JAVELIN-BLADDER-MEDLEY (avelumab +
Sacizutumab/M6223(TIGIT)/NKTR-255(IL-
15))

New targets are under investigation for the treatment of bladder cancer

Cancer cell

- HER2
- HER3
- Trop2
- Nectin4
- SDC1

Immune cell

- TIGIT
- LAG-3

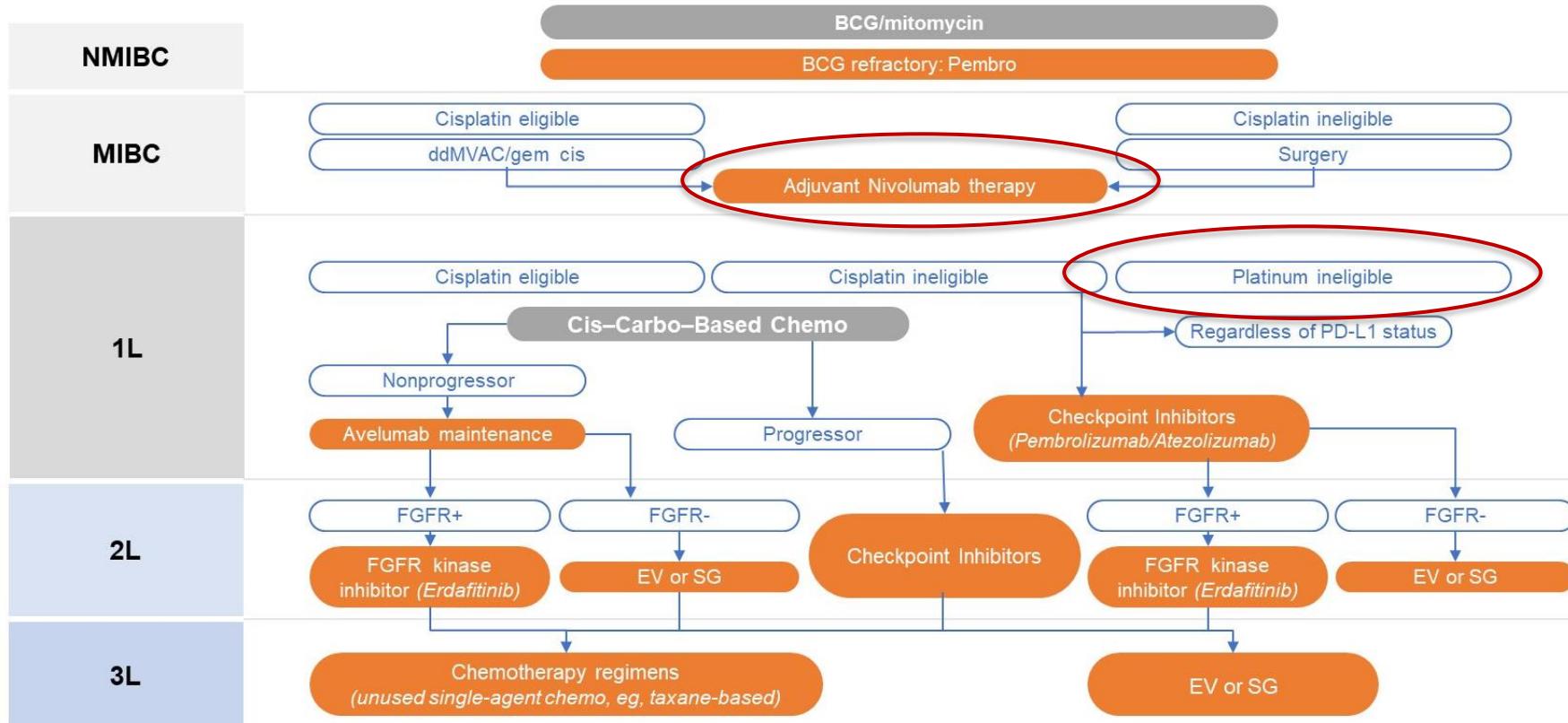
HER, human epidermal growth factor receptor; LAG-3, lymphocyte-activation gene 3; SDC, syndecan 1; TIGIT, T cell immunoreceptor with Ig and ITIM domains; Trop 2, trophoblast cell surface antigen 2.

53. Nelson BE, et al. *Front Oncol* 2021;11:705294; 54. Yang Z, et al. *Am J Physiol Cell Physiol* 2022;323:C29–45; 55. Wu K, et al. *Front Pharmacol* 2022;12:801493; 56. NCT04112498. Available at <https://clinicaltrials.gov/ct2/show/NCT04112498> (last accessed August 2022).



CONCLUSIONES

Therapeutic journey of an ideal patient





XV SIMPOSIUM
BASES BIOLÓGICAS DEL CÁNCER
E INNOVACIÓN TERAPÉUTICA



GRACIAS