
II JORNADA DE ACTUALIZACIÓN EN
**URO-ONCOLOGÍA:**
UPDATE 2025

Madrid, 25 de febrero de 2025

# Secuenciación terapéutica: 2as y 3as líneas

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# Conflictos de interés

- He proporcionado asesoramiento científico a ***IPSEN, Novartis, Bristol-Meyers-Squibb, Johnson & Johnson, Sanofi, Bayer, Merck, MSD.***

- He participado en reuniones médicas organizadas por ***Novartis, Astellas, Bristol-Meyers-Squibb, Johnson and Johnson, IPSEN, Sanofi, Pierre-Fabre , Astra-Zeneca.***

- He recibido pagos por presentaciones y asesoría de ***Bristol-Meyers-Squibb, Johnson and Johnson, Roche, IPSEN, Merck, Novartis, Pierre-Fabre.***

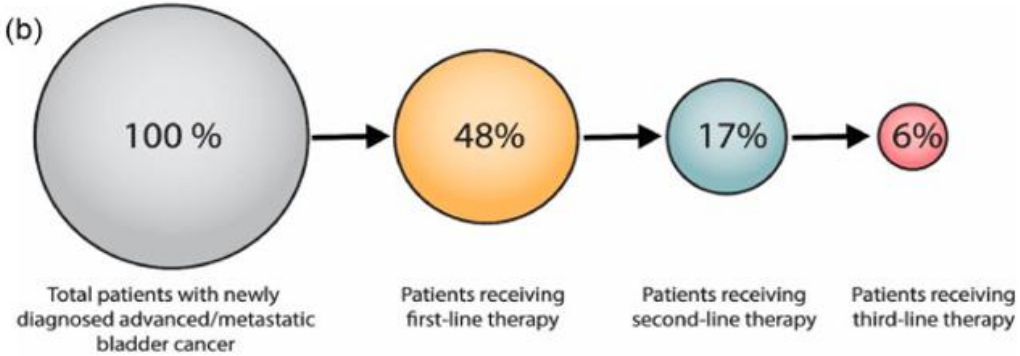
# ¿Por qué hablamos de secuencia?

| | MVAC | CisGem | HR | CisG-A (JAVELIN) | CISG/BSC (JAVELIN) | HR | CISG-N (C-901) | CIS-G (C-901) | HR | P-E (EV-302) | QT | HR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fase | III | | | III | | | III | | | III | | |
| n | 202 | 203 | | 389 | 350 | | 304 | 304 | | 243 | 232 | |
| O.1º | SG | | | SG | | | SG/SLP (BICR) | | | SG/SLP (BICR) | | |
| ORR | 38.1 | 44.5 | 0.97 | 9.7 | 1.4 | 7.46 | 57.6 | 43.1 | | 70.8 | 53.0 | p<0.01 |
| SLP | 7.4 | 7.4 | 1.05 | 5.7 + 4 | 2.0 | 0.56 | 7.9 | 7.6 | 0.72 | 14.6 | 6.5 | 0.48 |
| **SG** | **14.8** | **13.8** | **1.04** | **25.3** | **16.5** | **0.69** | **21.7** | **18.9** | **0.78** | **31.5** | **18.4** | **0.53** |

| | MCAVi | CarboG | HR | CARBG-A (JAVELIN) | CARBG/BSC (JAVELIN) | HR | P-E (EV-302) | QT | HR | P-E (EV-103,K) | NORSE |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Fase | III | | | III | | | III | | | II | II |
| n | 119 | 119 | | 147 | 122 | | 194 | 209 | | 76 | 44 |
| O.1º | SG | | | SG | | | SG/SLP(BICR) | | | ORR(BICR) | |
| ORR | 30.3 | 41.2 | p=0.08 | 9.7 | 1.4 | 7.46 | 63.9 | 34.9 | p<0.01 | 64.5 | 54.5 |
| SLP | 8.1 | 9.3 | 0.94 | 3.7+4 | 2.0 | 0.48 | 10.6 | 6.1 | 0.43 | NR | 10.97 |
| SG | 4.2 | 5.8 | 0.78 | 20.8 | 13 | 0.66 | NR | 12.7 | 0.43 | 22.3 | 12m:68% |

*Von der Maase H, et al. JCO2020; Sridhar SS, et al. ASCOGU2023; Van der Heijden M, et al. ESMO 2023, NEJM2023; Powles T, NEJM 2023*
*De Santis M, et al. JCO 2012; Sridhar SS, et al. ASCOGU2023; Powles T, ESMO 2023;O´Donnel PH, et al. JCO 2023; Van der Heijen M, et al. ASCO2024;Siefker-Radtke A, et al. ASCO2023*

# ¿Por qué hablamos de secuencia?

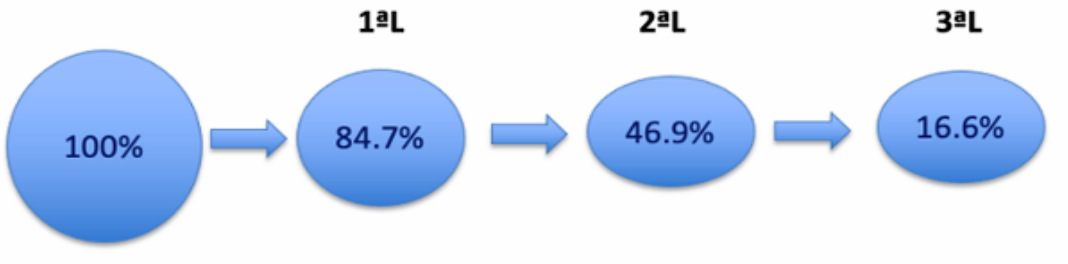



*Swami U, Grivas P, Pal S, Agarwal N. Cancer Treat and Research 2021*

# ¿Por qué hablamos de secuencia?


Análisis multivariado 3L: ECOG>/1, IMC<21Kg/m2, NRL>/3 basal pre1a línea

*Kita Y, et al. Int J of Urology 2024*




*Puente J, et al. ASCOGU2023*

# Secuencia, ¿después de qué?

## Pasado

## Presente

## Presente próximo

## Futuro

# Secuencia. Pasado

**Cisplatino-gemcitabina/Carboplatino-gemcitabina**

**PE**

| | VFN | Docetaxel | Atezolizumab IMVIGOR211 | Pembrolizumab KEYNOTE045 |
|---|---|---|---|---|
| Fase | III | II | III | III |
| ORR (%) | 8.6 | 13 | 15 (23 IC2/3) | 21.1 |
| RC (%) | 0 | 0 | | |
| SLP (m) | 3 | 4 | 2.1 | 2.1 |
| SG (m) | 6.9 | 9 | 8.6 | 10.3 |
| AES (G3-5,%) | 50 | 60 | 18 | 15 |

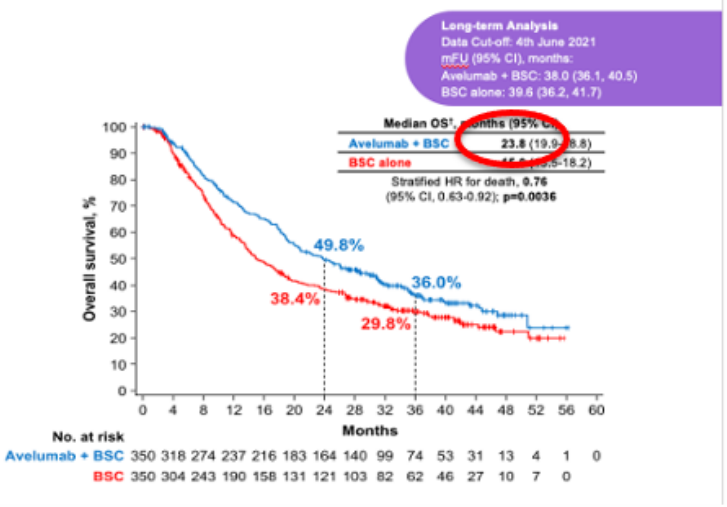
N=4

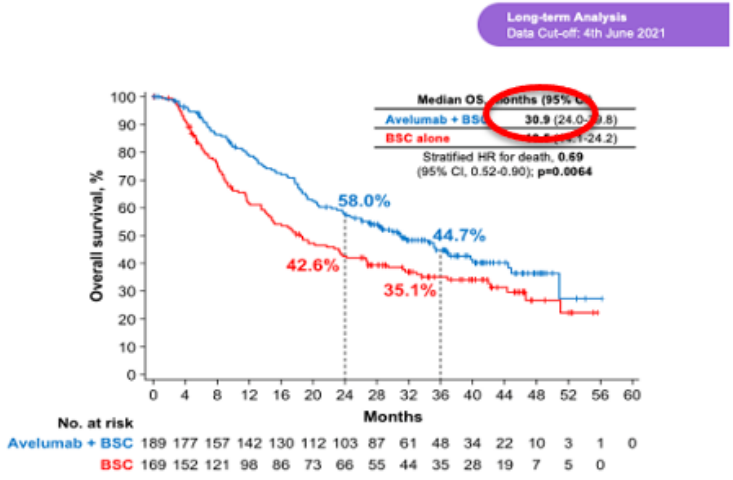
cidad

2012

*Bellmunt J, et al.Ann Oncol 2013; Albani C, et al. Exp Op Inv Drugs, 2015; Powles T, et al. Lancet 2018; Bellmunt J, et al. N Engl J Med 2017*

# Secuencia. Presente



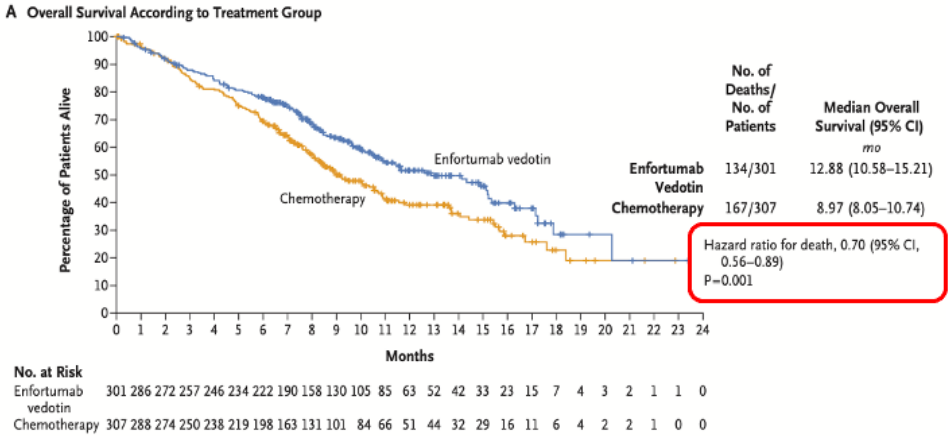




| | Avelumab+BSC | BSC alone | HR |
|---|---|---|---|
| OS desde inicio QT | **29.7** (25.2-34) | 20.5 (19.0-23.5) | 0.77 (0.60-0.90) |
| Cisplatino gemcitabina | **31** (24.9-37.1) | 23 (19.2-30.9) | 0.79 (0.61-1.02) |
| Carboplatino gemcitabina | **25.8** (22.8-33-3) | 17.6 (14.8-21-3) | 0.69 (0.51-0.92) |

*Powles T, et al. ASCO2020; N Engl J Med 2020; J Clin Oncol 2023*

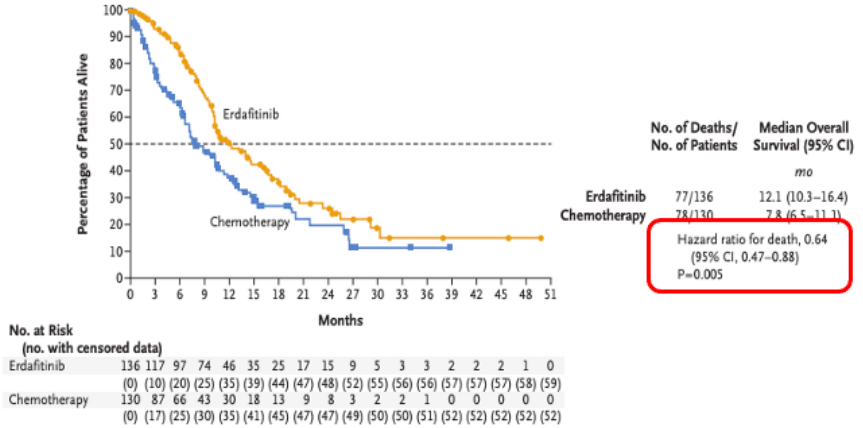
# Secuencia. Presente

- **Phase III EV301**




*Powles T, et al. NEJM 2021*

- **Phase III THOR. Cohort 1**




*Loriot Y, et al. N Engl Med 2023*

# Secuencia. Presente

## *SG ha quedado en un intento*

| | VFN | Docetaxel | EV | Erdafitinib | SG |
|---|---|---|---|---|---|
| Fase | III | II | III | III | III |
| ORR (%) | 8.6 | 13 | 40 | 45.6 | 23 |
| RC (%) | 0 | 0 | 4.9 | 6.6 | 5 |
| SLP (m) | 3 | 4 | 5.55 | 5.6 | 4.2 |
| SG (m) | 6.9 | 9 | 12.88 | 12.1 | 10.3 |
| AES (G3-5,%) | 50 | 60 | 51.4 | 45.9 | 67 |

*Bellmunt J, et al.Ann Oncol 2013; Albani C, et al. Exp Op Inv Drugs, 2015; Rosenberg JE, et al. Ann Oncol 2023; Loriot Y, et al. N Engl Med 2023; Powles T, et al. Ann Oncol 2025*

# ¿Qué datos hay de secuencia en los pivotales? JAVELIN100

Subsequent treatment consisted of treatment options available in 2021

| n, (%) | **Total of patients** (N = 700) | | **Patients discontinuing avelumab 1L maintenance, due to PD** (n = 484) | |
|---|---|---|---|---|
| | **Avelumab + BSC** (n = 350) | **BSC alone** (n = 350) | **Avelumab + BSC** (n = 209) | **BSC alone** (n = 275) |
| **Patients who discontinued avelumab 1L maintenance and received subsequent treatment** | 185 (52.9) | 252 (72.0) | **158 (75.6)** | **225 (81.8)** |
| PD-1 or PD-L1 inhibitor | 40 (11.4) | 186 (53.1) | 27 (12.9) | 166 (60.4) |
| FGFR inhibitor | 10 (2.9) | 13 (3.7) | 10 (4.8) | 11 (4.0) |
| Any other drug | 177 (50.6) | 156 (44.6)* | 151 (72.2) | 139 (50.5) |
| **Ongoing avelumab 1L maintenance treatment** | 43 (12.3) | 10 (2.9) | – | – |

**The most common other drugs received following avelumab 1L maintenance were** gemcitabine (n = 87), carboplatin (n = 66), paclitaxel (n = 60), vinflunine (n = 46),cisplatin (n = 37) and EV (n=9)

# Secuencia. Presente próximo estudio Checkmate-901

**Table S3. Subsequent Cancer Therapy Summary.**

| Category, n (%) | Nivolumab+ Gemcitabine–Cisplatin (N=304) | Gemcitabine–Cisplatin (N=304) |
|---|---|---|
| Patients with any subsequent therapy* | 127 (41.8) | 171 (56.3) |
| Patients who received subsequent radiotherapy | 31 (10.2) | 36 (11.8) |
| Patients who received subsequent surgery | 26 (8.6) | 22 (7.2) |
| Patients who received subsequent systemic therapy† | 108 (35.5) | 156 (51.3) |
| Anti–PD-1 | 22 (7.2) | 72 (23.7) |
| Nivolumab | 6 (2.0) | 5 (1.6) |
| Pembrolizumab | 14 (4.6) | 54 (17.8) |
| Toripalimab | 0 | 6 (2.0) |
| Anti–PD-L1 | 3 (1.0) | 52 (17.1) |
| Atezolizumab | 0 | 13 (4.3) |
| Avelumab | 3 (1.0) | 32 (10.5) |
| Durvalumab | 0 | 7 (2.3) |
| Other immunotherapy | 3 (1.0) | 2 (0.7) |
| Platinum-based chemotherapy | 25 (8.2) | 26 (8.6) |
| Carboplatin | 12 (3.9) | 7 (2.3) |
| Cisplatin | 11 (3.6) | 18 (5.9) |
| Unassigned | 91 (29.9) | 81 (26.6) |
| Antineoplastic | 2 (0.7) | 3 (1.0) |
| Cabozantinib | 2 (0.7) | 4 (1.3) |
| Disitamab vedotin | 3 (1.0) | 2 (0.7) |
| Docetaxel | 10 (3.3) | 5 (1.6) |
| Doxorubicin | 0 | 3 (1.0) |
| Enfortumab vedotin | 10 (3.3) | 9 (3.0) |
| Erdafitinib | 6 (2.0) | 4 (1.3) |
| Gemcitabine | 23 (7.6) | 18 (5.9) |
| Herbs | 4 (1.3) | 1 (0.3) |
| Investigational antineoplastic | 11 (3.6) | 11 (3.6) |
| Methotrexate | 2 (0.7) | 4 (1.3) |
| Monoclonal antibody | 4 (1.3) | 3 (1.0) |
| Paclitaxel | 16 (5.3) | 25 (8.2) |

QT platino 8.2%
Gemcitabina 7.6%
AntiPD1 7.2%
Paclitaxel 5.3%
Docetaxel 3.3%
EV 3.3%
Erdafitinib 2.0%

*Van der Heijden M, et al. ESMO 2023, N Engl Med 2023 suppl*

# Secuencia. Presente próximo EV-302

**Table S3. Summary of Subsequent Therapy**

| Parameters | Enfortumab vedotin–pembrolizumab (N=442) | Chemotherapy (N=444) |
|---|---|---|
| Number of patients (percent) | | |
| Patients who remained on treatment | 144 (32.6) | 0 |
| Patients who received subsequent anticancer therapies | 140 (31.7) | 313 (70.5) |
| First subsequent systemic therapy | 128 (29.0) | 294 (66.2) |
| Platinum-based therapy | 110 (24.9) | 17 (3.8) |
| PD-1/PD-L1 inhibitor-containing therapy | 7 (1.6) | 260 (58.6) |
| Maintenance therapy*,† | 0 | 143 (32.2) |
| Avelumab | 0 | 135 (30.4) |
| Other therapy | 7 (1.6) | 117 (26.4) |

*Included atezolizumab, avelumab, ipilimumab, M 6223, nivolumab, Nktr 255, and pembrolizumab.
†Maintenance therapy was permitted in the trial after platinum-based chemotherapy.
PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.

*Powles T, et al. NEJM 2024, supplem.*

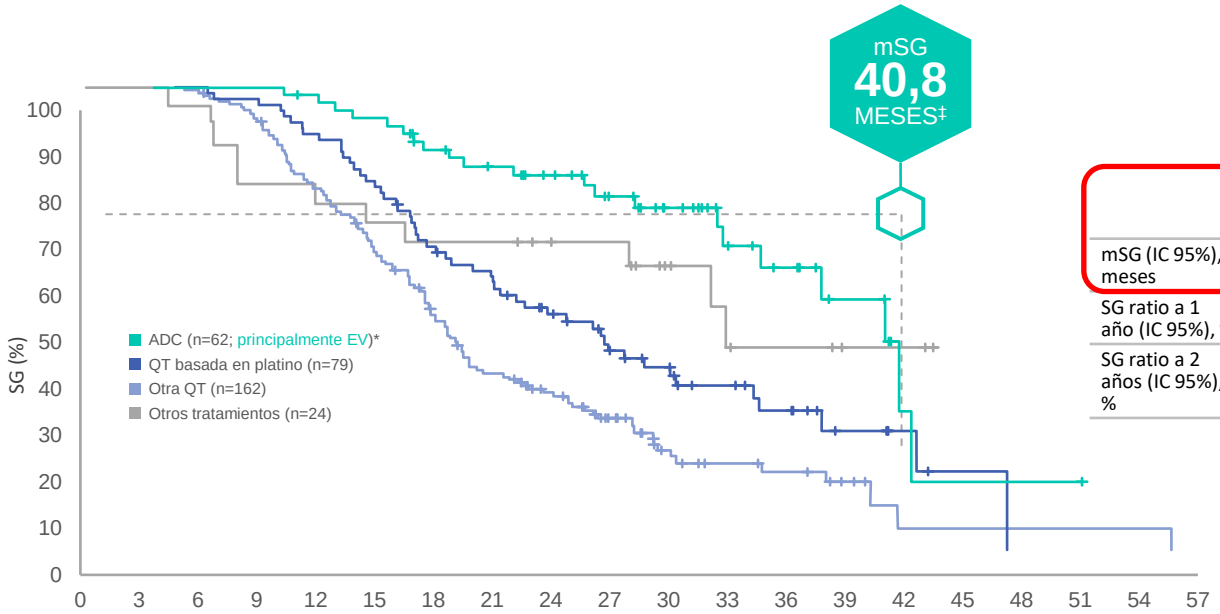
# ¿Qué datos hay de secuencia en vida real? AVENANCE


**Después de ≥2 años de seguimiento, la mayoría de los pacientes seguían recibieron tratamiento de mantenimiento de 1L con Bavencio® (21,0 %) o tratamiento de 2L (55,5 %)[1]**

*Barthélémy P, et al. Abstract 561. Presented at ASCO GU Cancers Symposium, January 25–27, 2024, San Francisco, CA, USA.*

# ¿Qué datos hay de secuencia en vida real? AVENANCE

## SG por tratamiento de 2L medida desde el inicio del QT de 1L (n=326)




| | 2L ADC (n=62) | QTBP (n=79) | Otra QT (n=162) | Otros tratamientos (n=24) |
|---|---|---|---|---|
| mSG (IC 95%), meses | 40,8 (32,6–42,1) | 24,5 (19,8–29,8) | 17,9 (16,5–19,2) | 32,6 (14,3–NE) |
| SG ratio a 1 año (IC 95%), % | 96,69 (87,42, 99,16) | 88,61 (79,25, 93,90) | 78,17 (70,94, 83,81) | 75,00 (52,62, 87,91) |
| SG ratio a 2 años (IC 95%), % | 81,08 (68,40, 89,06) | 51,03 (39,39, 61,53) | 33,48 (26,12, 40,99) | 66,67 (44,28, 81,73) |

*Barthelemy P, et al. ASCOGU 2024*

# Secuencia. Presente próximo EV-302

## *Evidencia de secuencia tras P-EV*

**Table 1 – Current evidence on treatment outcomes following enfortumab vedotin and/or ICI treatment**

| Treatment | Design | Relevant prior therapy received by the majority of patients | Pts | ORR (%) | mPFS (mo) | mOS (mo) |
|---|---|---|---|---|---|---|
| Platinum-based CTx [2] | RS | Prior ICI + prior EV (Rechallenge) | 25 | 32 | 8 | 12 |
| Platinum-based CTx [3] | RS | Prior ICI | 51 | 45 | 4.3 | 11.9 |
| Sacituzumab govitecan [4] | PCT | Prior ICI (entire cohort) | 113[a] | 28[a] | 5.4[a] | 10.9[a] |
| | | Prior ICI + prior EV (subgroup) | 10[b] | 30[b] | | |
| Sacituzumab govitecan [5] | RS | Prior ICI + prior EV | 84 | 23 | 3.5 | 6.0 |
| Sacituzumab govitecan [6] | RS | Prior ICI + prior EV | 17 | 21 | 2.4 | – |
| Erdafitinib [7] | PCT | Prior ICI | 136 | 46 | 5.7 | 12.1 |
| Erdafitinib [8] | RS | Prior ICI + prior EV | 15 | 31 | 5 | 10 |

CTx = chemotherapy; EC = enfortumab vedotin; ICI = immune checkpoint inhibitor; ORR = objective response rate; mOS = median overall survival; mPFS = median progression-free survival; Pts = patients; RS = retrospective study; PCT = prospective clinical trial.

[a] Entire cohort.

[b] Post-EV subgroup.

*Brown J and Koshkin V, Eur Urol 2024*

# V-302

*s P-EV*

Re: Cisplatin 2nd lin

EV_Biom...U

Hi Maria,

Thank you for reachin
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conferences. The dat
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on biomarkers of resp
attaching that here.
Please let me know if

Best,

Vadim S Koshkin
Associate Professor
University of California San Francisco

**Table 1 – Comparison of outcomes by genomic biomarker status**

| Alteration or biomarker | Objective response | | | | PFS | | Overall survival | |
|---|---|---|---|---|---|---|---|---|
| | ORR (%) | | OR (95% CI) | *p* value | HR (95% CI) | *p* value | HR (95% CI) | *p* value |
| | BM$^+$ | BM$^-$ | | | | | | |
| *TERTp* [a] (*n* = 91) | 57 | 52 | 1.23 (0.64–2.39) | 0.5 | 0.86 (0.56–1.32) | 0.5 | 0.77 (0.46–1.29) | 0.3 |
| *TP53* [a] (*n* = 87) | 58 | 50 | 1.40 (0.73–2.70) | 0.3 | 0.81 (0.53–1.26) | 0.4 | 1.27 (0.74–2.18) | 0.4 |
| *ARID1A* [a] (*n* = 29) | 57 | 54 | 1.10 (0.45–2.77) | 0.8 | 1.18 (0.68–2.04) | 0.6 | 1.15 (0.60–2.23) | 0.7 |
| *CDKN2A* [a] (*n* = 39) | 56 | 54 | 1.08 (0.50–2.36) | 0.9 | 1.73 (1.07–2.78) | **0.025** | 1.49 (0.85–2.62) | 0.2 |
| *CDKN2B* [a] (*n* = 28) | 50 | 55 | 0.81 (0.33–1.95) | 0.6 | 2.01 (1.19–3.39) | **0.009** | 1.63 (0.89–2.99) | 0.11 |
| *FGFR3* [a] (*n* = 34) | 47 | 57 | 0.68 (0.31–1.49) | 0.3 | 1.31 (0.79–2.16) | 0.3 | 1.12 (0.61–2.04) | 0.7 |
| *ERBB2* [a] (*n* = 19) | 67 | 52 | 1.82 (0.71–5.07) | 0.2 | 0.64 (0.33–1.25) | 0.2 | 0.68 (0.29–1.58) | 0.4 |
| *CCND1* [a] (*n* = 17) | 57 | 54 | 1.13 (0.37–3.59) | 0.8 | 1.23 (0.63–2.37) | 0.6 | 1.18 (0.56–2.49) | 0.7 |
| *KDM6A* [a] (*n* = 26) | 65 | 52 | 1.70 (0.69–4.49) | 0.3 | 1.12 (0.65–1.91) | 0.7 | 0.49 (0.21–1.15) | 0.10 |
| *PIK3CA* [a] (*n* = 20) | 60 | 54 | 1.30 (0.50–3.52) | 0.6 | 1.08 (0.60–1.96) | 0.8 | 1.17 (0.58–2.39) | 0.7 |
| *RB1* [a] (*n* = 20) | 41 | 56 | 0.54 (0.19–1.51) | 0.2 | 0.62 (0.30–1.30) | 0.2 | 0.92 (0.42–2.03) | 0.8 |
| *TSC1* [a] (*n* = 15) | 87 | 51 | 6.30 (1.66–41.34) | **0.018** | 0.62 (0.25–1.53) | 0.3 | 0.38 (0.09–1.55) | 0.2 |
| DDR mutation [a,b] (*n* = 20) | 42 | 54% | 0.56 (0.21–1.49) | 0.2 | 0.91 (0.48–1.72) | 0.8 | 0.91 (0.43–1.93) | 0.8 |
| TMB high [c] (*n* = 32) | 53 | 50% | 1.14 (0.50–2.90) | 0.8 | 0.66 (0.38–1.16) | 0.15 | 0.41 (0.19–0.86) | **0.017** |

BM$^+$ = biomarker-positive group; BM$^-$ = biomarker-negative group; CI = confidence interval; DDR = DNA damage repair; HR = hazard ratio; OR = odds ratio; ORR = objective response rate; PFS = progression-free survival; TMB = tumor mutational burden (TMB high defined as ≥10 mutations/Mb).

[a] 155 evaluable for OS, 135 evaluable for PFS, and 145 evaluable for ORR.

[b] DDR mutations: *BRCA1*, *BRCA2*, *ATM*, *BARD1*, *CDK12*, *CHEK2*, *PALB2*, *PPP2R2A*, *RAD51B*.

[c] 113 evaluable for OS, 98 evaluable for PFS, and 96 evaluable for ORR.

Real-
Vedo
Admi

Table 4. 2L

Carboplatin, g

Cisplatin, gem

Erdafitinib, n

Gemcitabine,

## Abstract 770: Survey-based study of treatment sequencing after first-line (1L) Enfortumab vedotin/Pembrolizumab (EVP) in the evolving landscape of locally advanced/metastatic urothelial cancer (UC)

Priyanka V. Chablani, MD,[1] Ali R. Khaki, MD,[2] Karine Tawagi, MD,[3] Petros Grivas, MD, PhD,[4] Jeannie Hoffman-Censits, MD,[5] Matt D. Galsky, MD,[6] Shilpa Gupta, MD,[7] Vadim S. Koshkin, MD,[8] Elizabeth R. Plimack, MD,[9] Jonathan E. Rosenberg, MD,[10] Peter H. O'Donnell, MD[11]

[1] University of Pittsburgh Medical Center, [2] Stanford University Medical Center, [3] University of Illinois Chicago Medical Center, [4] University of Washington & Fred Hutch Cancer Center, [5] Johns Hopkins Medical Center, [6] Mount Sinai Medical Center, [7] Cleveland Clinic Cancer Center, [8] University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, [9] Fox Chase Cancer Center, [10] Memorial Sloan Kettering Cancer Center, [11] University of Chicago Medical Center

### Background

- EVP is a preferred 1L option for patients (pts) with advanced/metastatic UC.
- We sought to understand how genitourinary (GU) medical oncologists in the US treat pts who progress on 1L EVP, and their comfort level with immune checkpoint inhibitor (ICI) rechallenge after prior ICI exposure.

### Methods

- We convened a bladder cancer working group comprised of 11 expert la/m UC GU oncologists
- Working group created an 11-question survey addressing key questions regarding treatment sequencing, including treatment after 1L EVP
- We e-mailed the survey to 227 US GU oncologists from May - Aug 2024, specifically GU oncologists within Bladder Cancer Advocacy Network and those with a focus on GU in academic & community practices
- **Received 78/227 responses (34%),** majority from academic practices
- **72% reported seeing > 25 pts with la/m UC per year;** 21% seeing 11-25 pts/year
- 30% in practice 0-5 yr post-fellowship, 17% in practice > 20 yr, median in practice 6-10 yr

### Main Takeaways

- **71/227 oncologists (31%)** completed the survey question regarding 2L treatment:
- ***"If a patient has progression on first-line Enfortumab vedotin/Pembrolizumab, how likely are you to give each of the following options as second-line treatment?"***
  - Choices depicted in Results table on the right
  - 5 options given based on likelihood to use treatment
- After progression on EV/Pembro, most oncologists favored **platinum-based chemotherapy (PBC)** ***without concurrent ICI***, **PBC** ***without ICI switch maintenance***, or **erdafitinib** (***in FGFR3-altered tumors***) as **2L therapies**
- For **2L clinical trials**, more oncologists favored ***non-ICI containing*** **regimens**
- Additional data, including the impact of residual toxicity from 1L EVP on 2L treatment selection and treatment of pts with HER-2 IHC3+ tumors, are needed to better understand treatment sequencing in real world practice until clinical trial data are generated. Patient-focused surveys regarding priorities can help.
- Limitations: selection bias (mostly academic GU oncologists), small sample size

**Contact: chablanipv2@upmc.edu**

### Results

| 2L Treatment after EVP | Somewhat or very *likely* to use, % (n) | Somewhat or very *unlikely* to use, % (n) |
|---|---|---|
| Gemcitabine + Cisplatin + Nivolumab | 11 (8) | 80 (57) |
| PBC with switch maintenance ICI | 31 (22) | 62 (44) |
| PBC without switch maintenance ICI | 77 (55) | 13 (9) |
| Erdafitinib for *FGFR3*-altered patients | 87 (62) | 7 (5) |
| ICI-combination trial | 54 (38) | 35 (25) |
| Non-ICI trial | 80 (57) | 8 (6) |
| Continue EVP for progression in 1-2 sites after using local therapy (e.g. radiation) | 83 (59) | 8 (6) |
| Sacituzumab* | 56 (40) | 30 (21) |

*Sacituzumab before and after TROPICS-04 negative trial press release on 5/30/24 shifted from 63% (24/38) to 48% (16/33) somewhat/very likely to use (and 21% [8/38] to 39% [13/33] somewhat/very unlikely to use). Sacituzumab was available at time of survey, but has since lost its FDA label.

# Second-Line Platinum-Based Chemotherapy (PBT) in Patients with Metastatic Urothelial Carcinoma (mUC) Treated withFirst-Line Pembrolizumab plus Enfortumab Vedotin (P/EV): A Single-Center, Retrospective Study

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## Background

- Although the efficacy of PBT as first-line therapy for mUC has been known for more than 30 years, the recent integration of P/EV as a preferred first-line option prevented the use of evidence-based regimen. Since the available second-line regimens depend on what was given as first-line, we evaluate the efficacy and tolerability of second-line PBT in mUC patients treated with first-line P/EV.

## Methods

- We retrospectively reviewed the medical records of 37 patients with mUC who were treated with first-line P/EV, mostly in clinical trials, between Jan 2022 and Jan 2024 at Samsung Medical Center (Seoul, Korea). Patients with mUC whose disease progressed during or after first-line treatment with P/EV received PBT involving gemcitabine plus either cisplatin or carboplatin (determined on the basis of cisplatin-eligibility). Primary endpoints included safety and response rates.

## Results:

- Among a total of 37 first-line P/EV patients, 10 received second-line PBT: gemcitabine plus cisplatin (n=8) and plus carboplatin (n=2).
- The median age was 68 years (range, 48 to 82 years) and the median interval from the last dose of P/EV was 50 days (range, 15 to 89 days).
- A total of 33 PBT cycles were given (median, 2; range 1 to 6).
- One patient achieved a complete response and 3 had a stable disease.
- Although peripheral neuropathy and gastrointestinal toxicities were the most frequently encountered adverse events, safety profile was generally manageable.

## Conclusion:

- Second-line PBT for mUC patients treated with first-line P/EV does not appear highly active but the observation of responders merits further studies in those with medically-fit, platinum-eligible patients..

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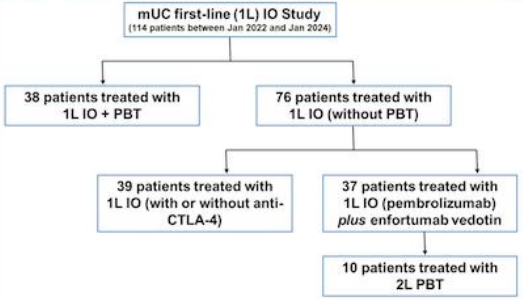
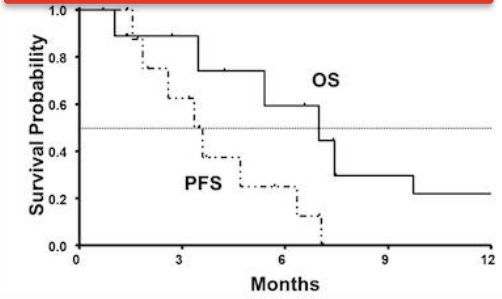
## Results/Graphs/Data




- Progression-free survival (PFS): median 3.5 months (95% CI, 2.8 to 4.2)
- Overall survival (OS): median 7.4 months (95% CI, 5.3 to 9.5)



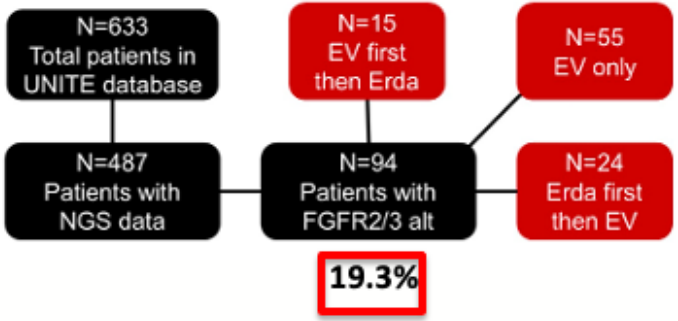
**Cisplatino-gemcitabina/Carboplatino-gemcitabina**

↓ **PE**

| | VFN | Docetaxel | Atezolizumab IMVIGOR211 | Pembrolizumab KEYNOTE045 | CisplaGem |
|---|---|---|---|---|---|
| Fase | III | II | III | III | RWD |
| ORR (%) | 8.6 | 13 | 15 (23 IC2/3) | 21.1 | |
| RC (%) | 0 | 0 | | | |
| SLP (m) | 3 | 4 | 2.1 | 2.1 | 3.5 |
| SG (m) | 6.9 | 9 | 8.6 | 10.3 | 7.4 |
| AES (G3-5,%) | 50 | 60 | 18 | 15 | |

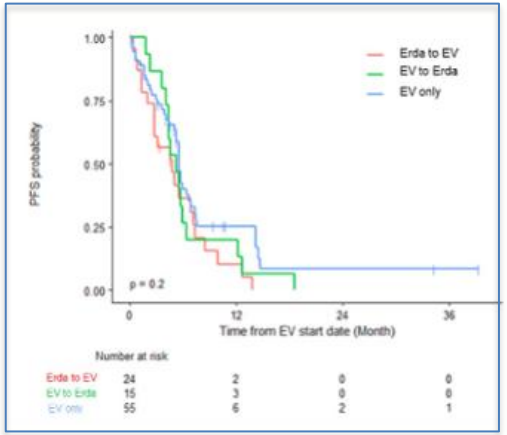
*Bellmunt J, et al.Ann Oncol 2013; Albani C, et al. Exp Op Inv Drugs, 2015; Powles T, et al. Lancet 2018; Bellmunt J, et al. N Engl J Med 2017*

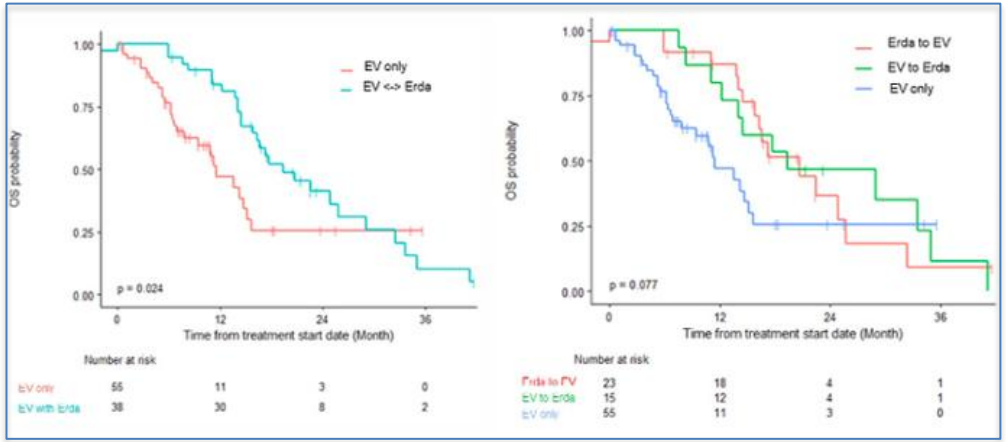
# Secuencia ADC-antiFGFR




The study endpoints were:

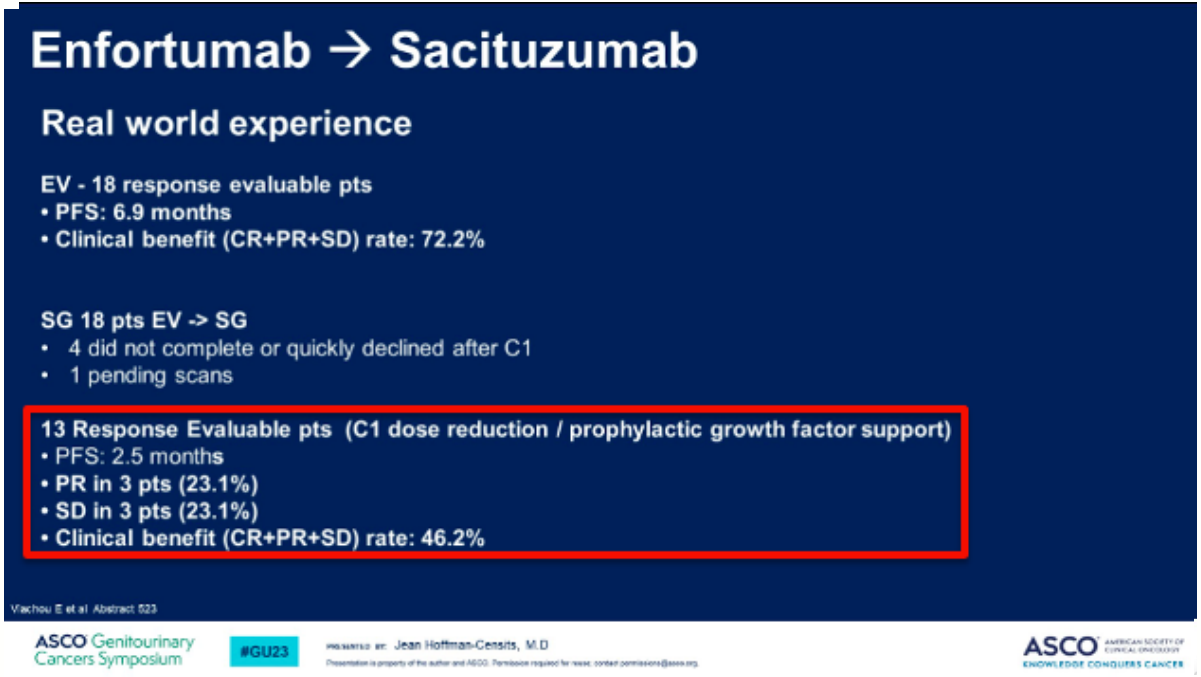
- Overall survival (OS) recorded from erdafitinib or enfortumab vedotin start (whichever administered first)
- Progression-free survival (PFS), measured from EV administration




*Jiang C, et al. ASCOGU2024*

# ¿Tiene sentido la secuencia de ADC tras ADC?



# ¿Tiene sentido la secuencia de ADC tras ADC?

## Baseline Characteristics — FORAGER-1

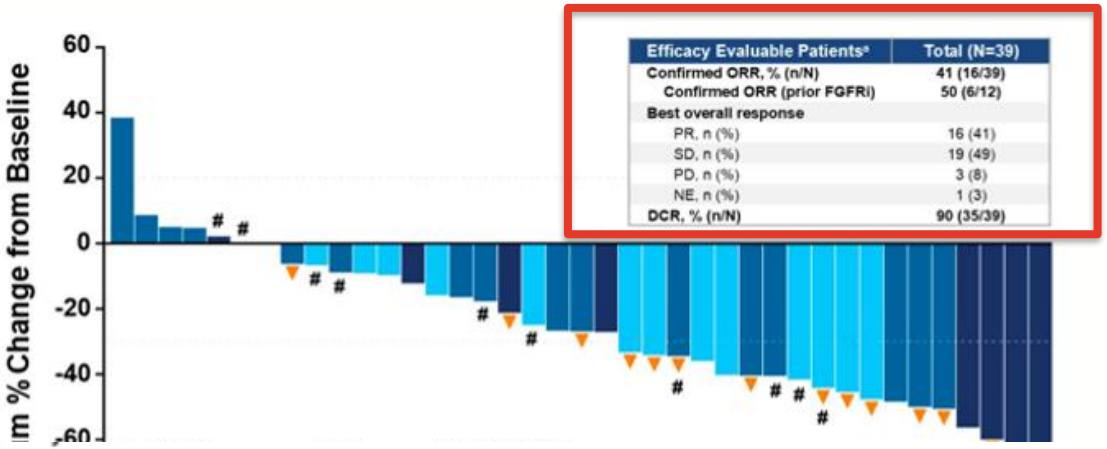


| Total Population (N=107) | |
|---|---|
| Median age, years (range) | 65 (26-93) |
| Sex, n (%) | |
| Female / Male | 37 (35) / 70 (65) |
| Race, n (%) | |
| White / Asian | 63 (59) / 38 (36) |
| Black or African American / Not reported | 3 (3) / 3 (3) |
| ECOG PS, n (%) | |
| 0 / 1 / 2[a] | 31 (29) / 75 (70) / 1 (1) |
| Tumor type, n (%)[b] | |
| Urothelial cancer | 69 (65) |
| Biliary tract cancer | 6 (6) |
| Head and neck cancer | 5 (5) |
| Lung cancer | 5 (5) |
| Esophageal cancer | 4 (4) |
| Other[c] | 17 (16) |
| Median prior regimens in advanced / metastatic setting (range) | 3 (1-7) |
| Prior FGFR3 inhibitor therapy, n (%) | 23 (21) |
| *FGFR3* alterations[d], n (%) | |
| Mutations | 60 (56) |
| Fusions | 36 (34) |
| Ligand amplifications | 11 (10) |
| FGFR3 amplifications | 7 (7) |

| Target population, mUC with mutation/fusion 200 mg, 300 mg and 400 mg BID (n=39) | |
|---|---|
| Primary tumor location, n (%) | |
| Upper tract / Lower tract | 17 (44) / 22 (56) |
| Liver metastases, n (%) | |
| Yes | 8 (21) |
| Bellmunt Score[e], % | |
| 0 / 1 / 2 / 3 | 18 / 46 / 33 / 3 |
| CrCl/eGFR, n (%) | |
| ≥60 ml/min | 22 (56) |
| Median prior regimens in advanced / metastatic setting (range) | 3 (1-6) |
| Prior Therapy, n (%) | |
| FGFR inhibitor (progressed/intolerant as reason withdrawn) | 11 (28) / 1 (3) |
| Erdafitinib | 10 (26) |
| AZD4547 | 2 (5) |
| PD-1/L1 inhibitor | 34 (87) |
| Platinum chemotherapy | 31 (79) |
| Enfortumab vedotin + Pembrolizumab | 9 (23) |
| Enfortumab vedotin monotherapy | 18 (46) |
| [illegible] alterations[d], n (%) | |
| Mutations | 32 (82) |
| Fusions | 7 (18) |

Data cutoff date of 02 Dec 2024. [a]1 patient had ECOG PS=1 at screening, but ECOG PS=2 at C1D1. [b]1 patient missing tumor type information, % calculated out of n=106 patients. [c]Other tumors include colon cancer (n=3), appendix cancer, bladder cancer, breast cancer, metastatic penile cancer, ovarian cancer, pancreatic neuroendocrine tumor, rectosigmoid junction cancer, rectal cancer, small intestinal cancer, thymic squamous cell carcinoma, unknown primary, anal squamous cell carcinoma, cervical cancer, and pancreatic cancer (n=1 each). [d]Patients may have more than one type of qualifying molecular alteration. [e]Bellmunt factors: liver metastases, hemoglobin <10 g/dL, ECOG PS >0.

# ¿Tiene sentido la secuencia de ADC tras ADC?

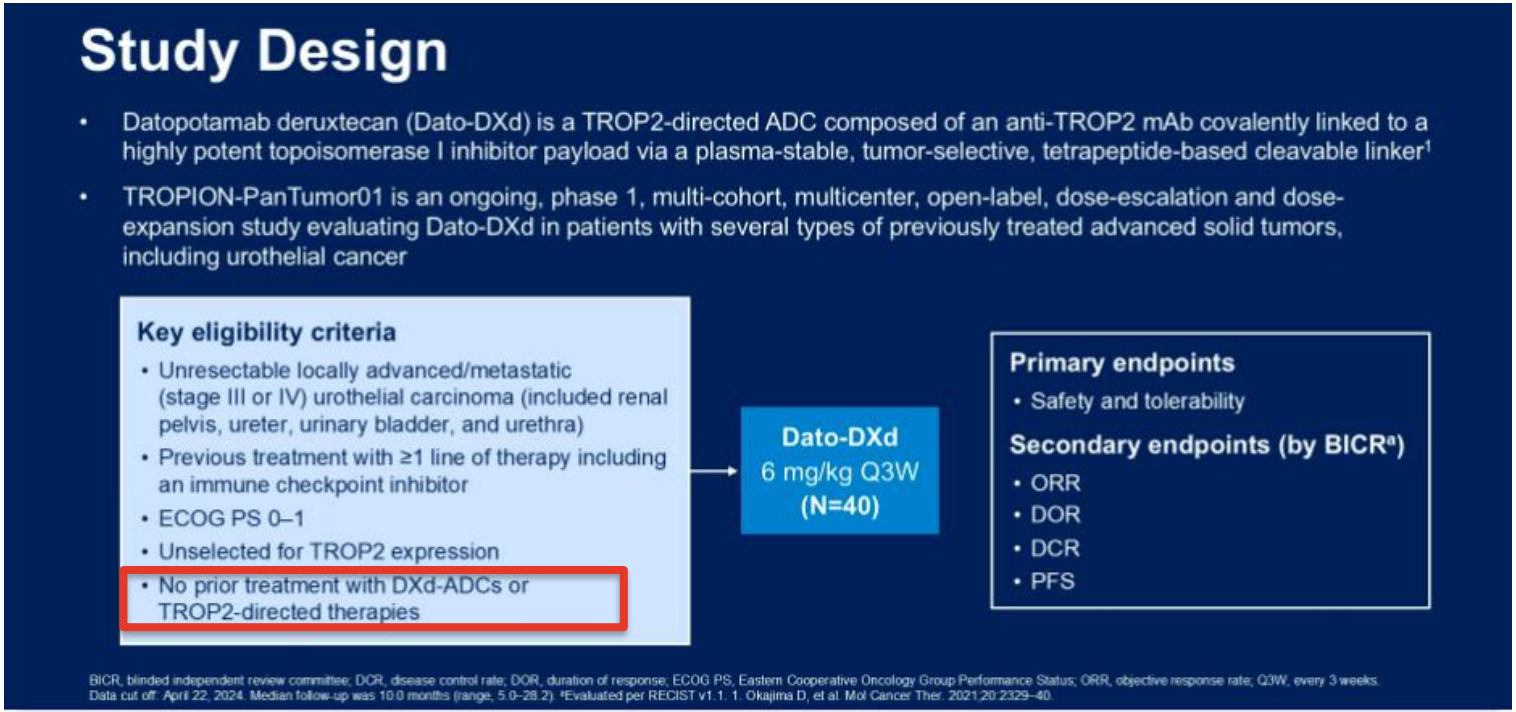



| Efficacy Evaluable Patients[a] | Total (N=39) |
|---|---|
| Confirmed ORR, % (n/N) | 41 (16/39) |
| Confirmed ORR (prior FGFRi) | 50 (6/12) |
| Best overall response | |
| PR, n (%) | 16 (41) |
| SD, n (%) | 19 (49) |
| PD, n (%) | 3 (8) |
| NE, n (%) | 1 (3) |
| DCR, % (n/N) | 90 (35/39) |

- Randomized dose finding is currently enrolling patients to 200 mg, 300 mg, and 400 mg BID to select an optimal dose for further development
- Select expansion cohorts, including enfortumab vedotin + pembrolizumab + LY3866288 (LOXO-435) in 1L *FGFR3*-altered mUC patients will open in Q1 2025

*Iyer G, ASCOGU2025*

# ¿Tiene sentido la secuencia de ADC tras ADC?



# ¿Tiene sentido la secuencia de ADC tras ADC?

## Demographics and Baseline Characteristics

| Characteristic, n (%) | Dato-DXd (N=40) |
|---|---|
| Age, years, median (range) | 66.5 (44–83) |
| Sex, male | 31 (78) |
| ECOG PS | |
| 0 | 19 (48) |
| 1 | 21 (53) |
| Stage | |
| III | 2 (5) |
| IV | 33 (83) |
| History of brain metastases[a] | 2 (5) |
| Time from diagnosis to study treatment, months, median (range) | 24 (3–342) |

| Characteristic, n (%) | Dato-DXd (N=40) |
|---|---|
| Number of prior lines of therapy (locally advanced/metastatic) | |
| 1 | 5 (13) |
| 2 | 11 (28) |
| ≥3 | 24 (60) |
| Median (range) | 3 (1–7) |
| Prior systemic treatment (any setting) | |
| Immunotherapy | 40 (100) |
| Platinum-based chemotherapy | 36 (90) |
| Taxane chemotherapy | 7 (18) |
| Enfortumab vedotin[b] | 33 (83) |

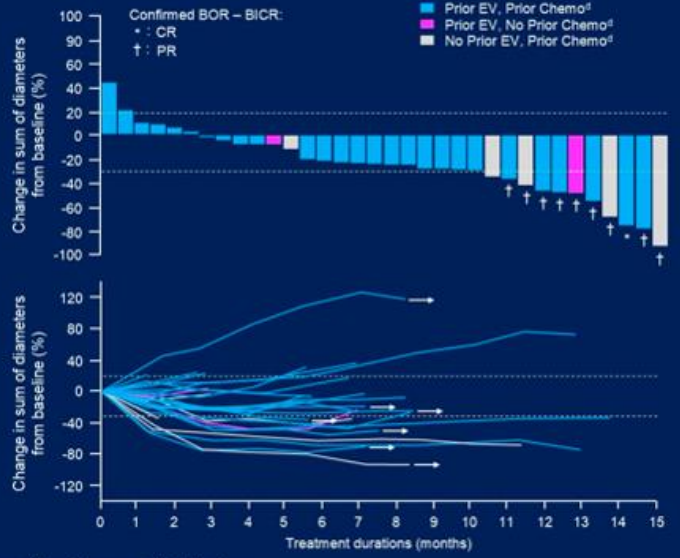
Data cut off: April 22, 2024. [a]Patients with clinically inactive brain metastases and patients with treated brain metastases who are no longer symptomatic, require no treatment with steroids, and have recovered from radiotherapy, may be included in the study. [b]All patients received enfortumab vedotin in the locally advanced/metastatic setting except one patient that received it in the adjuvant setting (other clinical trial).

# ¿Tiene sentido la secuencia de ADC tras ADC?

## Response and Change in Tumor Burden

| Response by BICR[a] | Dato-DXd (N=40) |
|---|---|
| **ORR[b], n (%)** [95% CI] | **10 (25.0)** [12.7–41.2] |
| **DCR[c], n (%)** [95% CI] | **31 (77.5)** [61.5–89.2] |
| **BOR, n (%)** | |
| CR | 1 (2.5) |
| PR | 9 (22.5) |
| SD | 20 (50.0) |
| Non-CR/non-PD | 1 (2.5) |
| PD | 5 (12.5) |
| NE | 4 (10.0) |
| **DOR, median** (95% CI), **months** | NE (2.6–NE) |
| **6-month DOR rate, % (95% CI)** | 76.2 (33.2–93.5) |

ORR by investigator was 30.0% (n=12); all were PR




BOR, best overall response; CI, confidence interval; CR, complete response; NE, non-evaluable; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Evaluated by BICR per RECIST v1.1. [b]Responses with confirmation of CR/PR. [c]CR + PR + SD + non-CR/non-PD. [d]All patients received prior immunotherapy.

- These findings support the ongoing evaluation of Dato-DXd in patients with urothelial cancer in the phase 2 TROPION-PanTumor03 (NCT05489211) trial[1]

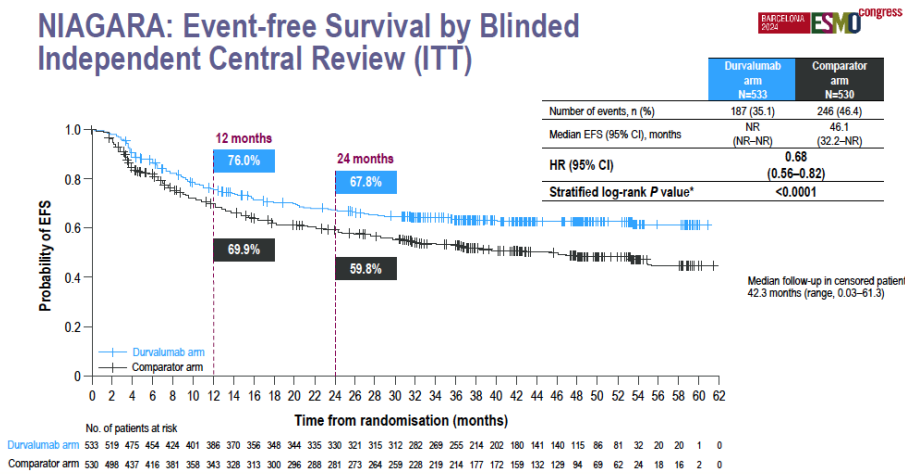
# Secuencia. Futuro. “En el horno”

| | VFN | DCT | EV | Erdafitinib | SG | Disitamab RC48/C005 | Disitamab + toripalimab | Trastuderuxtecan + nivolumab | FORAGER1 | Dato-DXD |
|---|---|---|---|---|---|---|---|---|---|---|
| Fase | III | II | III | III | III | II | Ib/II | Ib/II | I | I |
| ORR (%) | 8.6 | 13 | 40 | 45.6 | 23 | 50.5 | 73.2(2+/3+) | 36(2+/3+) | 50 | 25/30 |
| RC (%) | 0 | 0 | 4.9 | 6.6 | 5 | 1.9 | 9.8 | 13.3 | - | 2.5 |
| SLP (m) | 3 | 4 | 5.55 | 5.6 | 4.2 | 5.9 | 9.2 | 6.9 | - | 6.9 |
| SG (m) | 6.9 | 9 | 12.8 | 12.1 | 10.3 | 14.2 | 63.2%24m | 11 | - | - |
| AES (G3-5%) | 50 | 60 | 51.4 | 45.9 | 67 | 54.2 | 36.5 | 70 | 45 | 55 |

*Bellmunt J, et al.Ann Oncol 2013; Albani C, et al. Exp Op Inv Drugs,2015;Rosenberg JE, et al. Ann Oncol 2023; Loriot Y, et al. N Engl Med 2023;Powles T,Ann Oncol 2025; Sheng X, et al.J Clin Oncol 2023;Galsky M, et al. ASCO2023;Iyer G, et al. ASCOGU2025; Meric-Bemstam F, et al. ASCOGU2025*

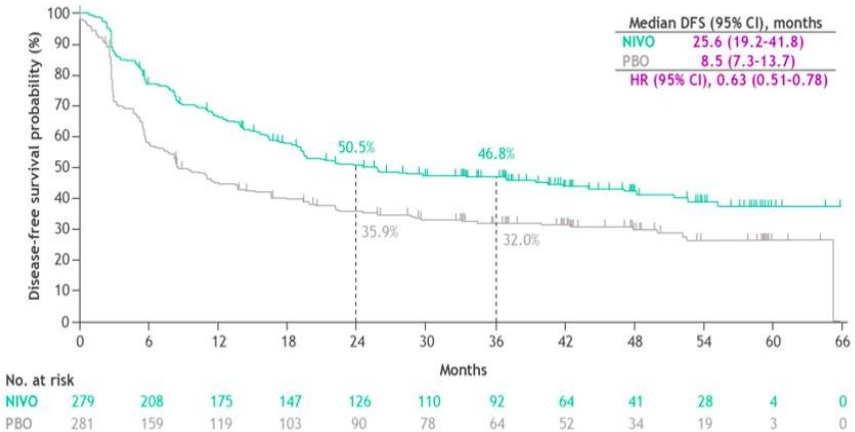
# Secuencia. ¿Y si tenemos en cuenta la adyuvancia? SLM/SLR

- **Estudio NIAGARA**




*Powles T, et al. ASCOGU2025*

- **Estudio Checkmate-274**




*Milowsky M, et al. ASCOGU 2025*

# Secuencia. IO tras IO

n=220

| Demographics and Baseline Characteristics | |
|---|---|
| **Median age, years** | 69 |
| **Primary tumor location, n (%)** | |
| Lower tract | 28 (65%) |
| Upper tract | 15 (35%) |
| **Histology, n (%)** | |
| Pure Urothelial | 27 (63%) |
| Variant Histology | 12 (28%) |
| Pure Variant | 4 (9%) |
| **Liver metastases, n (%)** | 9 (21%) |
| **ECOG PS, n (%)** | |
| 0/1 | 29 (67%) |
| ≥ 2 | 11 (26 %) |
| Unknown | 3 (7 %) |
| **Prior ICI , n (%)** | |
| Perioperative | **4 (9%)** |
| *Nivolumab* | 3 |
| *Pembrolizumab* | 1 |
| Metastatic | **39 (91%)** |
| *Pembrolizumab* | 19 |
| *Avelumab Maintenance* | 8 |
| *Nivolumab* | 6 |
| *Pembrolizumab maintenance* | 2 |
| *Atezolizumab* | 1 |
| *Ipilimumab/Nivolumab* | 1 |
| *Durvalumab/Tremelimumab* | 1 |
| *Nivolumab/NKTR214* | 1 |

ASCO GU 2025: Outcomes of Enfortumab Vedotin and Pembrolizumab for Patients Previously Treated with Immune Checkpoint Inhibitors in the UNITE Study.

| Treatment and Survival Outcomes (n=43) | |
|---|---|
| Median Follow Up | 14 months |
| Median Overall Survival | 15.4 mos (95% CI: 8.7 – NR) |
| Median Progression-Free Survival | 6.9 mos (95% CI: 3.91 – 12.2) |
| Observed Response Rate | 48% (95% CI: 31 - 66) [16/33] |
| Disease Control Rate (CR/PR/SD) | 79% (95% CI: 65 - 93) [26/33] |

*Jindal T, et al. UNITE study. ASCOGU 2025*

# Conclusiones