7th ANNUAL UC COURSE

Emerging personalized therapies for the management of urothelial carcinomas

7th MAY 2026
MADRID

The optimal management of FGFR + disease

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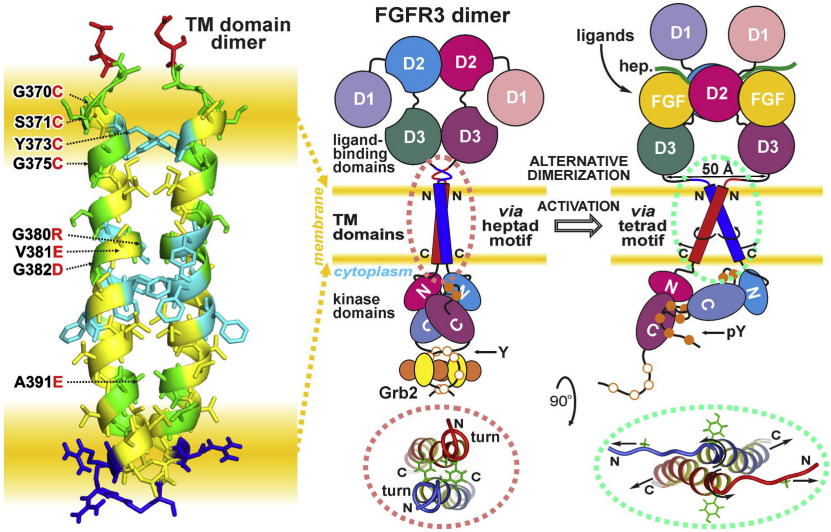
COIs

Advisory Board: Astellas , Arcus Biosciences, Astra Zeneca, BMS; EISAI, Ipsen, Janssen , MSD, Pfizer

Invited Speaker: Astellas, Adium, Astra Zeneca, Bayer, BMS, Ipsen,, Merck, MSD, Novartis, Pierre Fabre, Pfizer, Roche

- Family of 4 receptor tyrosine kinases (FGFR1–4);
- FGFR5/FGFRL1 lacks kinase domain Physiologic roles: embryogenesis, wound healing, angiogenesis, phosphate homeostasis (FGFR1 + Klotho axis)
- Oncogenic activation = mutations, amplifications, fusions/rearrangements
- Fusions force receptor dimerization → constitutive kinase → MAPK + PI3K-AKT + STAT signaling



Katoh M. *Nat Rev Clin Oncol* 2019;16:105–122 Babina IS, Turner NC. *Nat Rev Cancer* 2017;17:318–332

Targeted treatment begins with testing:

Identify FGFR+ patients today

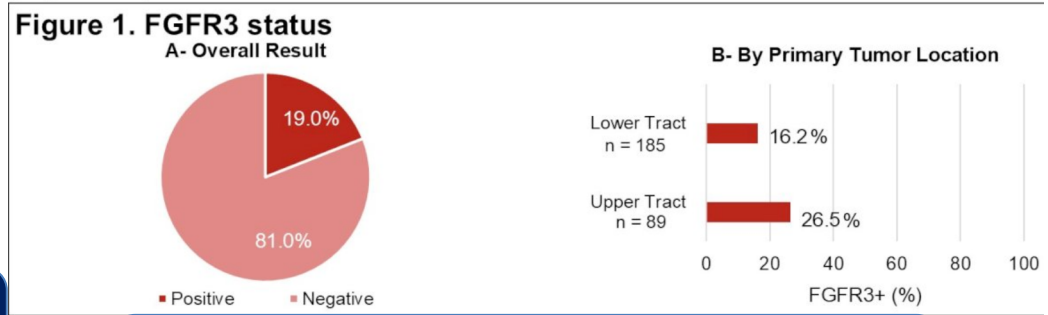
~20% testados

Table 1. Patient Demographics

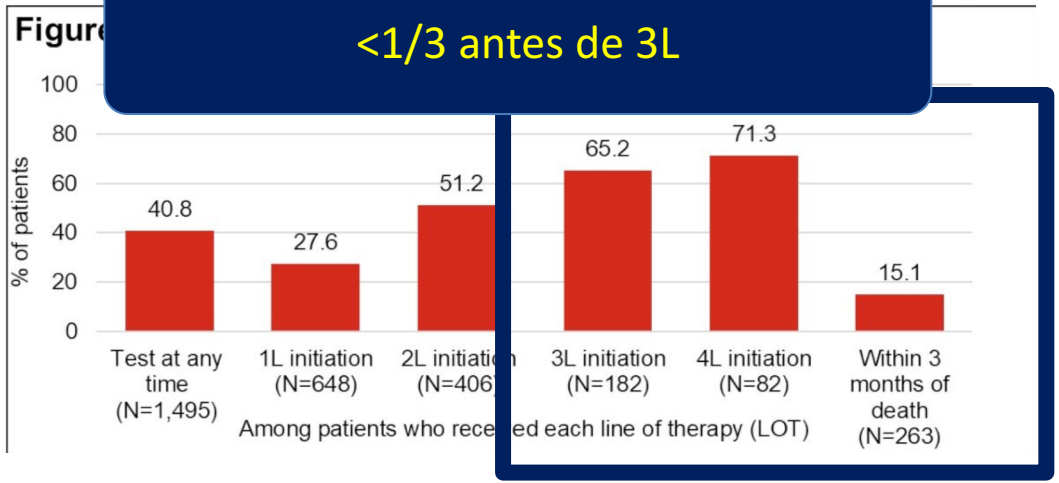
Characteristic	Overall Patients N = 3,661 (100%)	Genomic Testing Status with FGFR3: With Genomic Test N = 1,495 (40.8%)	Genomic Testing Status with FGFR3: Without Genomic Test N = 2,166 (59.2%)
(Md. Q1, Q3)	74.0 (67.0, 81.0)	73.0 (67.0, 80.0)	75.0 (68.0, 81.0)
Race, n (%) #			
White	2,514 (68.7%)	1,029 (68.8%)	1,485 (68.6%)
Black	197 (5.4%)	61 (4.1%)	136 (6.3%)
Asian	39 (1.1%)	18 (1.2%)	21 (1.0%)
Other	219 (6.0%)	89 (6.0%)	130 (6.0%)
Unknown	692 (18.9%)	298 (19.9%)	394 (18.2%)
Practice Type, n (%) #*			
2L	514 (14.0%)	282 (18.9%)	232 (10.7%)
3L	164 (4.5%)	116 (7.8%)	48 (2.2%)
4L+	115 (3.1%)	85 (5.7%)	30 (1.4%)
ECOG at advanced diagnosis, n (%) #*			
0-1	1,426 (39.0%)	689 (46.1%)	737 (34.0%)
2+	348 (9.5%)	148 (9.9%)	200 (9.2%)
Unknown	1,887 (51.5%)	658 (44.0%)	1,229 (56.7%)
Stage at initial MIBC diagnosis*			
Localized MIBC	1,183 (32.3%)	450 (30.1%)	733 (33.8%)
Locally Advanced	947 (25.9%)	298 (19.9%)	649 (30.0%)
Metastatic	1,489 (40.7%)	731 (48.9%)	758 (35.0%)
Not documented	42 (1.1%)	16 (1.1%)	26 (1.2%)
Primary Site, n (%) *			
Upper tract	721 (19.7%)	342 (22.9%)	379 (17.5%)
Lower tract	2,940 (80.3%)	1,153 (77.1%)	1,787 (82.5%)
NGS FGFR3 tested			
Yes	-	1,465 (98%)	-
No	-	30 (2.0%)	-

Sólo 40% testados

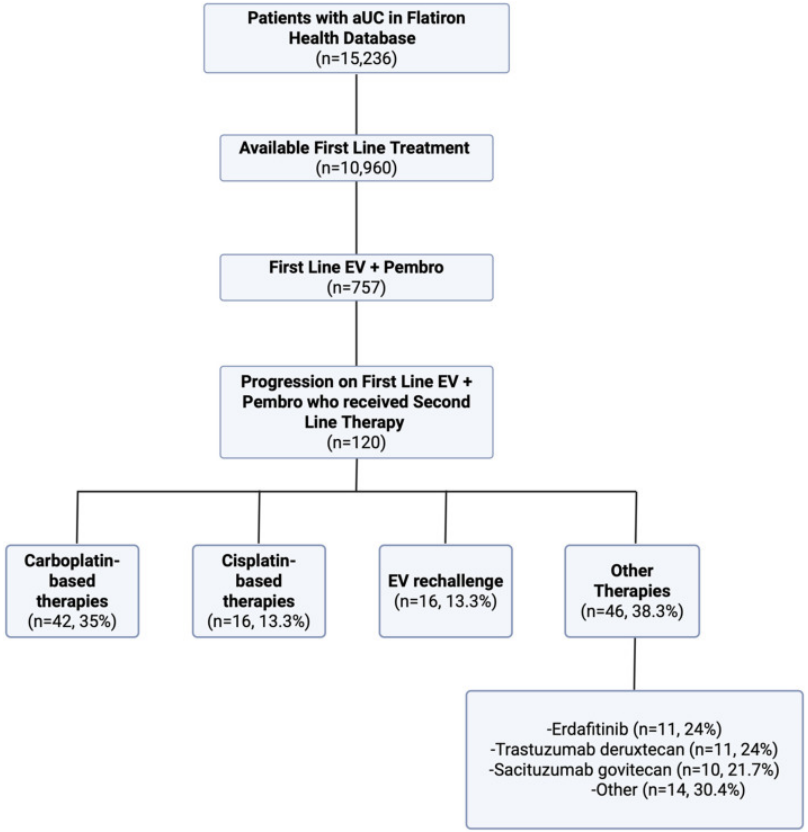
Figure 1. FGFR3 status



<1/3 antes de 3L

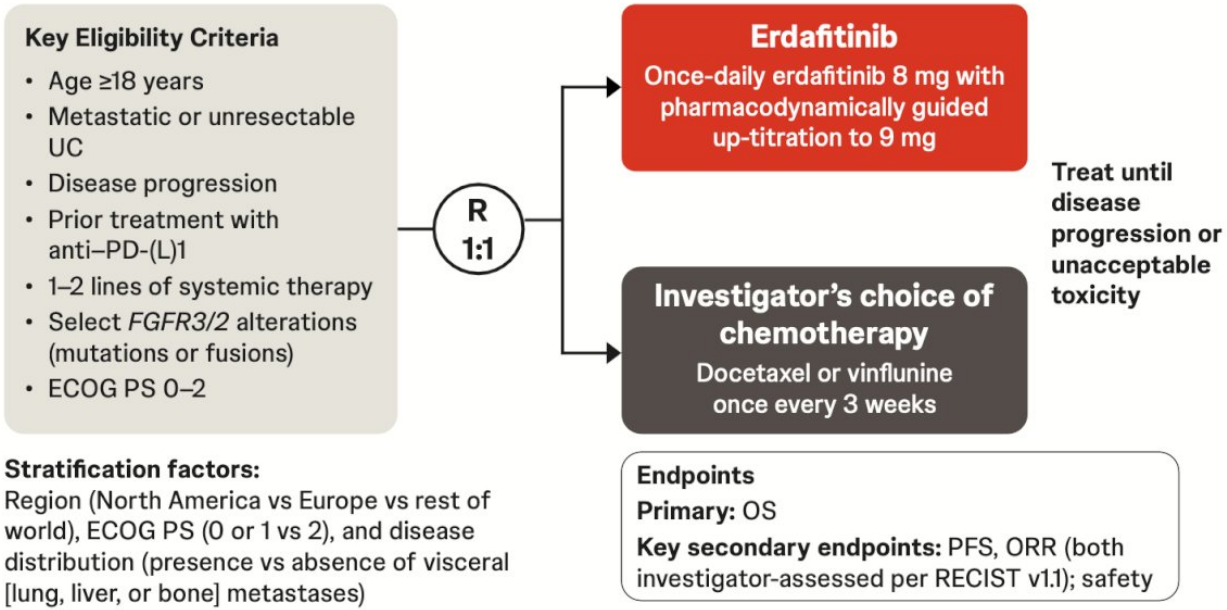


Emily Nash Smyth et al. ASCO GU 2026



Gebrael G. *et al.* (2026). *Bladder Cancer.*

Figure 1: THOR Cohort 1 study design



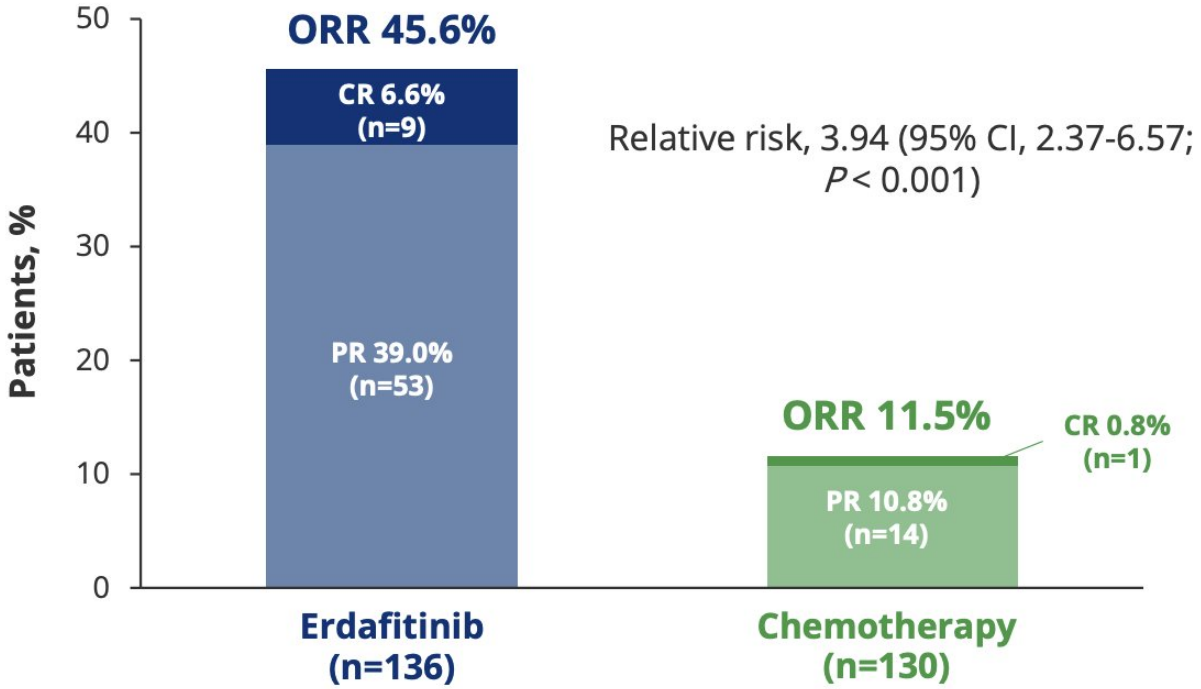
ECOG PS, Eastern Cooperative Oncology Group performance status; FGFR, fibroblast growth receptor; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; UC, urothelial carcinoma.

Loriot Y. *et al.* (2023). *N Engl J Med.*

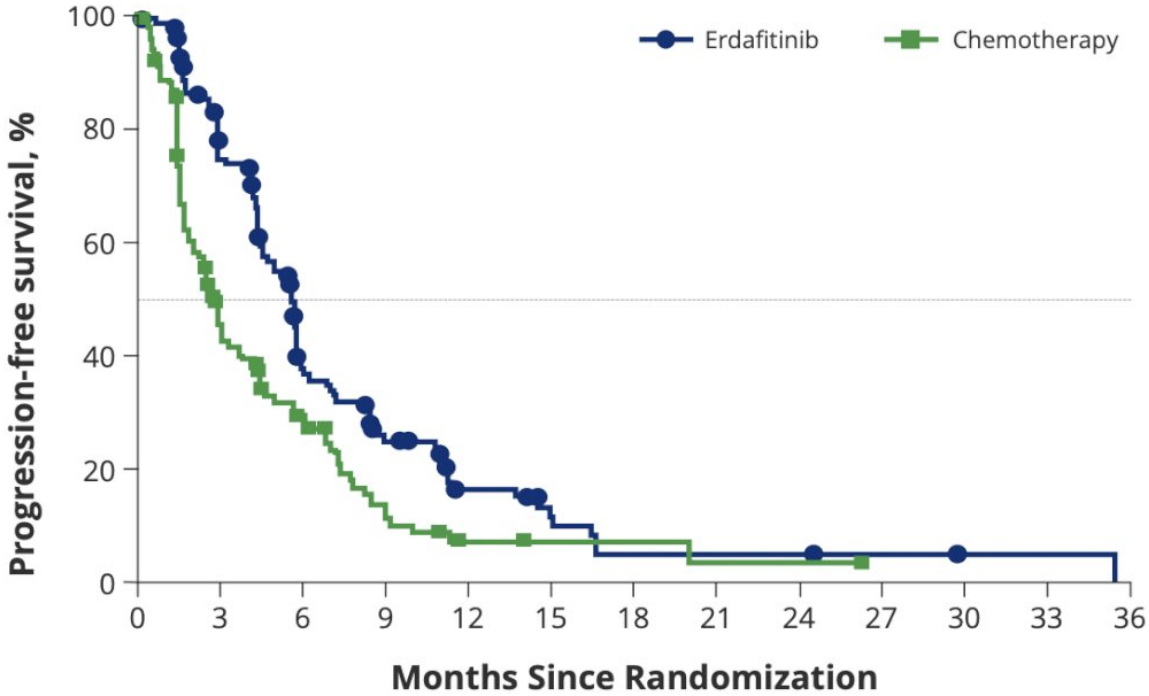
Characteristic	Erdafitinib (n=136)	Chemotherapy (n=130)
Age, median (range), years	66 (32-85)	69 (35-86)
Men, n (%)	96 (70.6)	94 (72.3)
Race, n (%)		
White	81 (59.6)	63 (48.5)
Asian	37 (27.2)	40 (30.8)
Black or African American	0	1 (0.8)
Multiple	0	1 (0.8)
Not reported	18 (13.2)	25 (19.2)
Presence of visceral metastases, n (%)	101 (74.3)	97 (74.6)
Liver	31 (22.8)	38 (29.2)

Characteristic	Erdafitinib (n=136)	Chemotherapy (n=130)
ECOG PS 0-1, n (%)	124 (91.2)	117 (90)
Primary tumor upper tract, n (%)	41 (30.1)	48 (36.9)
PD-L1 low (CPS <10), n (%)	89 (92.7)[a]	68 (86.1)[a]
FGFRalt, n (%)[b]	(n=135)	(n=129)
Mutations	108 (79.4)	107 (82.3)
Fusions	25 (18.4)	19 (14.6)
Mutations and fusions	2 (1.5)	3 (2.3)
Prior lines of systemic therapy[c]		
1 line	45 (33.1)	33 (25.4)
2 lines	90 (66.2)	97 (74.6)

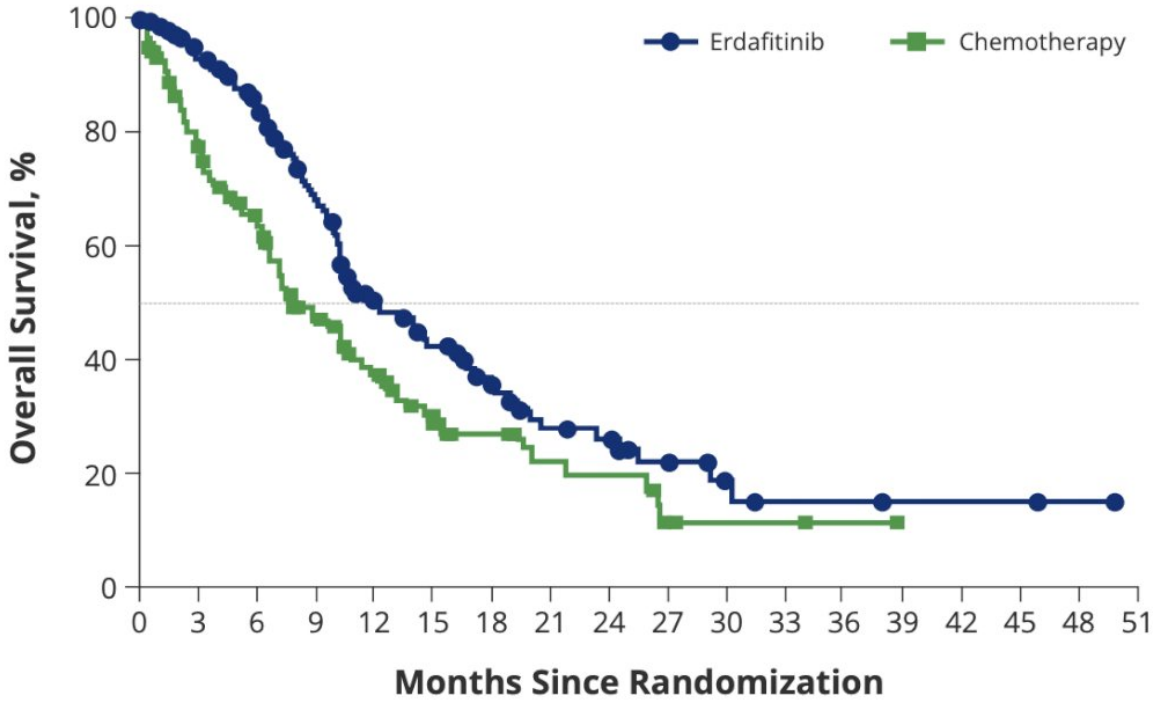
Loriot Y. *et al.* (2023). *N Engl J Med.*



Loriot Y. *et al.* (2023). *N Engl J Med.*



Loriot Y. *et al.* (2023). *N Engl J Med.*



No. at risk																	
Erdafitinib	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
Chemotherapy	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0

Loriot Y. *et al.* (2023). *N Engl J Med.*

	HR and 95% CI	Erdafitinib n/N[a]	Erdafitinib Median	Chemotherapy n/N[a]	Chemotherapy Median	HR and 95% CI
Overall		77/136	12.1	78/130	7.8	0.64 (0.47-0.88)
FGFR alteration type						
Translocation		13/25	16.4	15/19	8.0	0.49 (0.23-1.03)
Mutation		63/108	10.9	60/107	7.7	0.67 (0.47-0.95)
Baseline ECOG PS						
0-1		70/125	12.2	71/119	8.7	0.65 (0.46-0.90)
2		7/11	6.1	7/11	2.8	0.47 (0.16-1.35)
Lines of prior treatment						
1 line		27/45	14.0	21/33	7.8	0.61 (0.35-1.09)
2 lines		49/90	11.6	57/97	7.7	0.67 (0.45-0.98)
Visceral metastasis						
Presence		59/103	12.2	57/101	7.7	0.65 (0.45-0.93)
Absence		18/33	10.6	21/29	8.8	0.61 (0.32-1.14)
Primary tumor location						
Upper tract		16/41	23.3	27/48	7.2	0.34 (0.18-0.64)
Lower tract		61/95	10.5	51/82	9.6	0.82 (0.56-1.18)
Chemotherapy						
Docetaxel		77/136	12.1	40/69	10.6	0.76 (0.52-1.11)
Vinflunine		77/136	12.1	30/43	7.7	0.60 (0.39-0.92)

0.10 ← 1.00 → 10.00

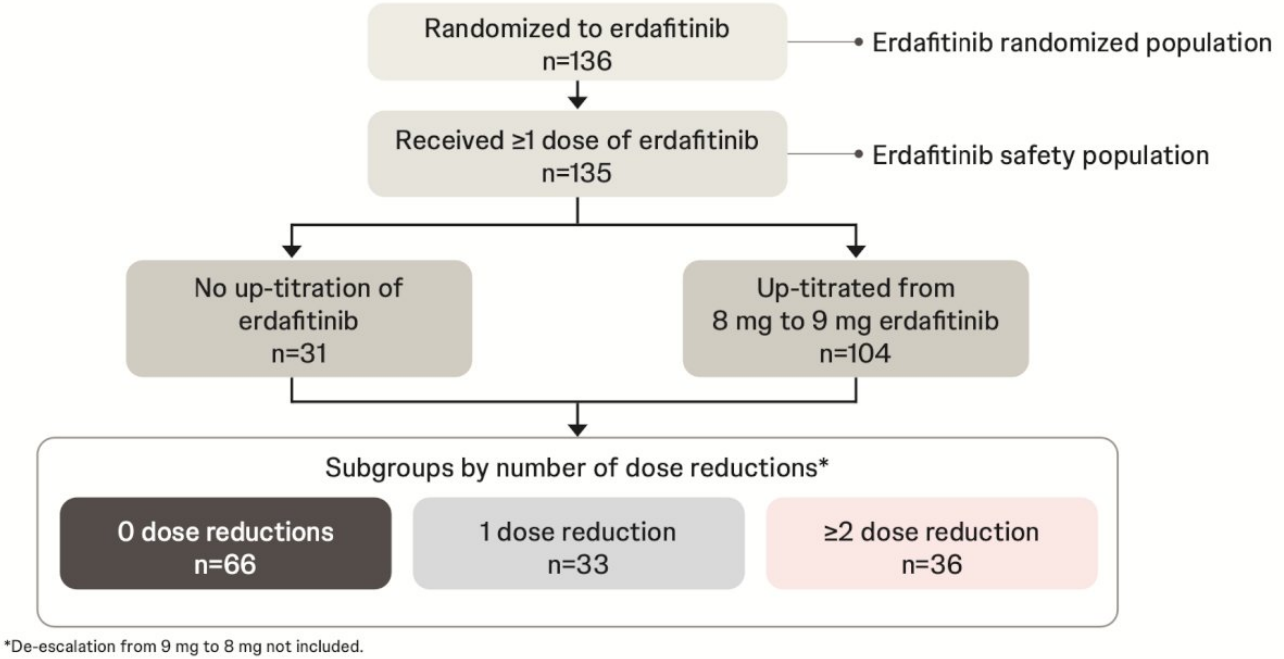
Favors erdafitinib — Favors chemotherapy

Loriot Y. *et al.* (2023). *N Engl J Med.*


TRATAMIENTO INNOVADOR DEL CARCINOMA UROTELIAL METASTÁSICO: UN PASO ADELANTE, PERO...
EL ELEFANTE EN LA HABITACIÓN
TOXICIDAD DE ERDAFITINIB
$C_{25}H_{31}N_7O_2$
OJO: RETINOPATÍA SEROSA CENTRAL
EYE: CSR/RPED
UÑAS: ONICOLISIS
NAILS: ONYCHOLYSIS
FOSFATO ALTO: HIPERFOSFATEMIA
HIGH PHOSPHATE
BOCA SECA / ESTOMATITIS
DRY MOUTH / STOMATITIS
CANSANCIO
FATIGUE
CREATININA ALTA
HIGH CREATININE

Impact of Dose Reductions on the Efficacy of Erdafitinib in Patients with Advanced or Metastatic Urothelial Carcinoma (mUC): A Post-hoc Analysis of the Phase 3 THOR Study Cohort-1 Evaluating Erdafitinib versus Chemotherapy

Figure 2: Disposition of patients included in subgroup analyses by dose reductions



*De-escalation from 9 mg to 8 mg not included.

Giannatempo P. Presented at the European Society of Medical Oncology (ESMO) Annual Congress, Berlin, 2025

Impact of Dose Reductions on the Efficacy of Erdafitinib in Patients with Advanced or Metastatic Urothelial Carcinoma (mUC): A Post-hoc Analysis of the Phase 3 THOR Study Cohort-1 Evaluating Erdafitinib versus Chemotherapy

Table 1: Baseline characteristics by number of erdafitinib dose reductions

Characteristics	Number of dose reductions		
	0 (n=66)	1 (n=33)	≥2 (n=36)
Age, median (range), years	65.0 (34–84)	65.0 (32–85)	69.5 (50–81)
Age, n (%)			
<65 years	32 (48.5)	16 (48.5)	11 (30.6)
65–69 years	13 (19.7)	9 (27.3)	7 (19.4)
70–74 years	9 (13.6)	1 (3.0)	11 (30.6)
≥75 years	12 (18.2)	7 (21.2)	7 (19.4)
Female, n (%)	17 (25.8)	12 (36.4)	11 (30.6)
Race, n (%)			
Asian	13 (19.7)	11 (33.3)	13 (36.1)
White	45 (68.2)	17 (51.5)	18 (50.0)
Not reported	8 (12.1)	5 (15.2)	5 (13.9)
Primary tumor location, n (%)			
Lower tract	51 (77.3)	22 (66.7)	21 (58.3)
Upper tract	15 (22.7)	11 (33.3)	15 (41.7)
Visceral metastases, n (%)			
Present	51 (77.3)	24 (72.7)	25 (69.4)
Absent	15 (22.7)	9 (27.3)	11 (30.6)
PD-(L)1 status, n/total (%)			
CPS ≥10	5/46 (10.9)	0/22 (0)	2/27 (7.4)
CPS <10	41/46 (89.1)	22/22 (100)	25/27 (92.6)
Previous lines of systemic therapy, n (%)			
1	24 (36.4)	11 (33.3)	10 (27.8)
2	42 (63.6)	22 (66.7)	25 (69.4)
3	0	0	1 (2.8)

CPS, combined positive score; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1

Giannatempo P. Presented at the European Society of Medical Oncology (ESMO) Annual Congress, Berlin, 2025

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Table 2: OS and PFS by number of erdafitinib dose reductions

	Erdafitinib randomized population (n=136)	Erdafitinib safety population		
		Number of dose reductions		
		0 (n=66)	1 (n=33)	≥2 (n=36)
Overall Survival				
Median (95% CI), mo	12.1 (10.3, 16.4)	10.0 (8.1, 10.9)	10.3 (8.5, 16.8)	23.2 (18.2, NE)
6-mo rate (95% CI), %	85 (77, 90)	77 (63, 86)	87 (69, 95)	97 (81, 100)
12-mo rate (95% CI), %	51 (41, 60)	36 (23, 50)	43 (24, 60)	81 (63, 91)
PFS				
Median (95% CI), mo	5.6 (4.4, 5.7)	4.2 (2.8, 5.4)	5.6 (4.0, 5.9)	10.8 (5.8, 13.7)
6-mo rate (95% CI), %	37 (28, 46)	20 (10, 32)	31 (15, 49)	68 (50, 81)
12-mo rate (95% CI), %	17 (10, 25)	7 (2, 16)	10 (1, 32)	34 (18, 51)

Mo, months; OS, overall survival; PFS, progression-free survival.

Giannatempo P. Presented at the European Society of Medical Oncology (ESMO) Annual Congress, Berlin, 2025

Impact of Dose Reductions on the Efficacy of Erdafitinib in Patients with Advanced or Metastatic Urothelial Carcinoma (mUC): A Post-hoc Analysis of the Phase 3 THOR Study Cohort-1 Evaluating Erdafitinib versus Chemotherapy

Table 4: TEAEs leading to dose reduction of erdafitinib with incidence ≥10%

n (%)	Number of dose reductions	
	1 (n=33[a])	≥2 (n=36)
Stomatitis	7 (21.2)	12 (33.3)
Palmar-plantar erythrodysesthesia	2 (6.1)	10 (27.8)
Onycholysis	5 (15.2)	7 (19.4)
Onychomadesis	4 (12.1)	5 (13.9)
Diarrhea	3 (9.1)	5 (13.9)
Dry mouth	2 (6.1)	4 (11.1)
Hyperphosphatemia	2 (6.1)	4 (11.1)

AE, adverse event; TEAE, treatment-emergent adverse event. [a]One of these 33 participants is not included in this analysis as they did not meet the criterion for dose reduction based on the exposure data. However, the AE data indicate that the participant had a dose reduction due to an AE.

Giannatempo P. Presented at the European Society of Medical Oncology (ESMO) Annual Congress, Berlin, 2025

Impact of Dose Reductions on the Efficacy of Erdafitinib in Patients with Advanced or Metastatic Urothelial Carcinoma (mUC): A Post-hoc Analysis of the Phase 3 THOR Study Cohort-1 Evaluating Erdafitinib versus Chemotherapy

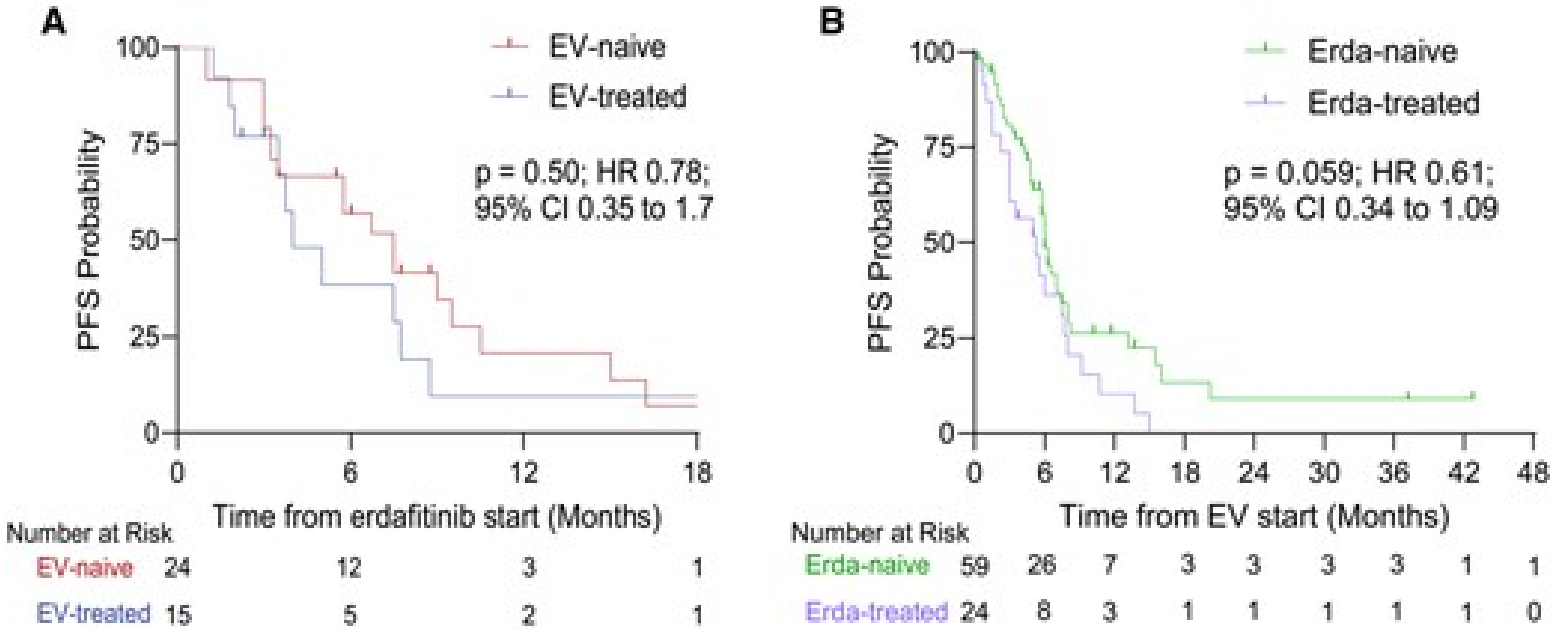
Table 3: Objective responses by number of erdafitinib dose reductions (unconfirmed)

n (%)	Erdafitinib randomized population (n=136)	Erdafitinib safety population		
		Number of dose reductions		
		0 (n=66)	1 (n=33)	≥2 (n=36)
ORR	62 (45.6)	22 (33.3)	17 (51.5)	23 (63.9)
Best overall response				
Complete response	9 (6.6)	0	4 (12.1)	5 (13.9)
Partial response	53 (39.0)	22 (33.3)	13 (39.4)	18 (50.0)
Stable disease	50 (36.8)	24 (36.4)	14 (42.4)	12 (33.3)
Progressive disease	14 (10.3)	11 (16.7)	2 (6.1)	1 (2.8)
Not evaluable	10 (7.4)	9 (13.6)	0	0
Disease control rate[a]	112 (82.4)	46 (69.7)	31 (93.9)	35 (97.2)

ORR, objective response rate; [a]Complete response + partial response + stable disease.

Giannatempo P. Presented at the European Society of Medical Oncology (ESMO) Annual Congress, Berlin, 2025

Erda antes o después de EV

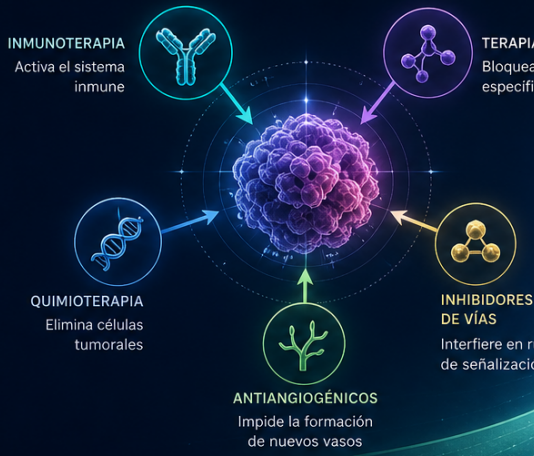


Talukder, R., et al. (2023).

¿HACIA DÓNDE VAMOS?

COMBINACIONES

Sinergia terapéutica para mejores resultados



El cáncer es complejo.
La combinación de estrategias potencia la eficacia y supera resistencias.

MEJORES FÁRMACOS

Fármacos de nueva generación más precisos y efectivos

Nuevas moléculas, nuevos mecanismos.
Fármacos más inteligentes para lograr mejores resultados con menos toxicidad.

PACIENTE EN EL CENTRO
Tratamiento personalizado
Medicina de precisión

CONCEPTO CLAVE

Combinaciones complementarias y mejores fármacos:
dos caminos convergentes hacia un mismo objetivo: mejorar la vida de nuestros pacientes.

ETCTN 10483: Phase Ib Trial of Erdafitinib (E) Combined With Enfortumab Vedotin (EV) Following Prior Therapy For Metastatic Urothelial Carcinoma (mUC) With FGFR 3/2 Alterations

Rohit K Jain[1], Yuanquan Yang[2], Laura Graham[3], Faustine Ong[4], Zhengming Chen[1], Bishoy Faltas[1], Di (Maria) Jiang[5], Risa Wong[6], Sumati Gupta[7], Anishka D'souza[8], Waddah Arafat[9], Jazlyn Heiligh[4] , Timothy W. Synold[10], Scott Tagawa[1], Lorraine Pelosof[11], Jingsong Zhang[4], Guru Sonpavde[12]

ETCTN Experimental Therapeutics Clinical Trials Network *Team Driven. Cancer Therapy Focused.*

1:Weill Cornell Medical College, New York, NY 2: Ohio State University Cancer Center ,Columbus, OH 3: University of Colorado Cancer Center, Aurora, CO 4:Moffitt Cancer Center, Tampa, FL 5: Princess Margaret Cancer Center, Toronto, ON 6: UPMC, Pittsburgh PA 7: Huntsman Cancer Institute, Salt Lake City, UT 8:USC, Los Angeles, CA 9: UT Southwestern Cancer Center, Dallas, TX 10:City of Hope Cancer Center, Duarte, CA 11:National Cancer Institute, Bethesda, MD 12: Advent Health Cancer Institute , Orlando, F

METHODS/SCHEMA

- Locally advanced unresectable or mUC
- Upper/lower tract tumors
- Mixed histology types are allowed if urothelial is predominant
- Progression after platinum-based and anti PD-1/PD-L1therapy
- Positive FGFR 3/2 activating alterations
- Measurable disease
- ECOG 0-2

Dose escalation cohort
- Erdafitinib 8 mg Q day for 28 days plus EV at starting dose of 1 mg/kg D1,8,15 every 28 days
- 3 +3 design
- 6-18 patients

Dose expansion cohort
- Erdafitinib 8 mg Q day for 28 days plus EV at RP2D on D1,8,15 every 28 days
- 12 patients

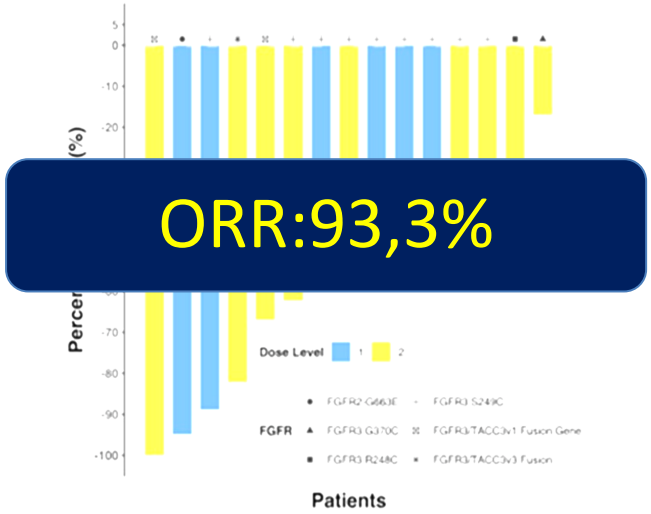
End of treatment

- ctDNA (Guardant 360 at baseline)
- Baseline FFPE tumor Tissue for PD-L1, Nectin 4 expression
- C1D15, C1D17,C2D1 plasma levels of erdafitinib and free MMAE for PK studies

- Imaging q8 weeks until progressive disease
- ctDNA (Guardant 360 at progression of disease)

- Primary endpoints: Safety, MTD and RP2D
- Secondary endpoints: Safety, ORR, DOR, PFS and OS

MTD: Maximum tolerable dose; RP2D: Recommended Phase 2 Dose; DOR: Duration of Response; DLT: Dose-Limiting Toxicity



Jain R.K. *et al.* (s.f.). *ETCTN 10483 (Phase Ib Trial). ASCO GU 2026*

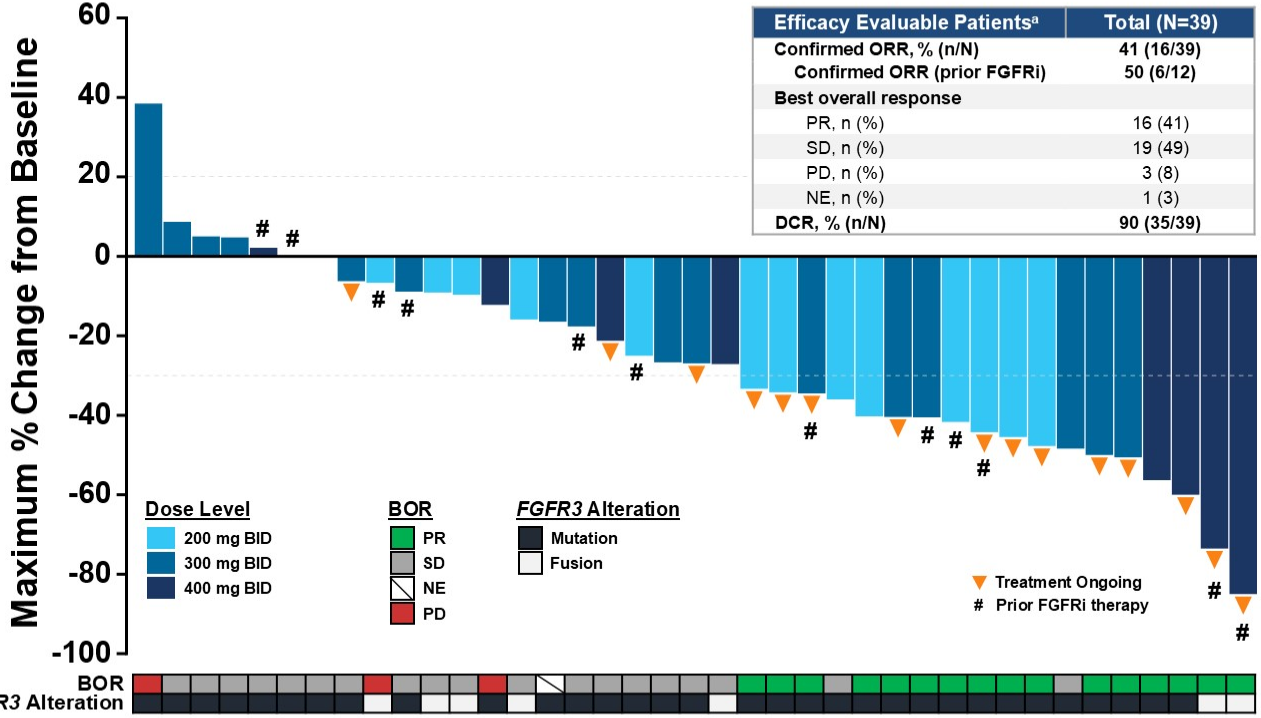
ASCO® Genitourinary Cancers Symposium

A first-in-human phase 1 study of LY3866288 (LOXO-435), a potent, highly isoform-selective FGFR3 inhibitor (FGFR3i) in advanced solid tumors with FGFR3 alterations: Initial results from FORAGER-1

Gopa Iyer[1], Hiromichi Ebi[2], Natalie Cook[3], Xin Gao[4], Shigehisa Kitano[5], Nobuaki Matsubara[6], Melissa A. Reimers[7], Arlene O. Siefker-Radtke[8], Miso Kim[9], Matthew D. Galsky[10], Debbie GJ. Robbrecht[11], Jun Guo[12], Bernhard J. Eigl[13], Clare Schaverien[14], Brent D. Butts[14], Eunice Yuen[14], Sylwia Szymczak[14], Xiang Zhao[14], Ryan C. Widau[14], Alexandra Drakaki[15]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Division of Molecular Therapeutics, Aichi Cancer Center Research Institute, Nagoya, Japan; [3]The Christie NHS Foundation Trust and Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; [4]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [5]Department of Advanced Medical Development, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [6]National Cancer Center Hospital East, Chiba, Japan; [7]Department of Internal Medicine, Washington University in St Louis, St. Louis, MO, USA; [8]Department of Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [9]Seoul National University Hospital, Seoul, Republic of Korea; [10]Division of Hematology and Medical Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [11]Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [12]Peking University Cancer Hospital & Institute, Beijing, China; [13]British Columbia Cancer Agency, Vancouver, Canada[14]; Eli Lilly and Company, Indianapolis, IN, USA; [15]Division of Hematology/Oncology, Department of Medicine, UCLA David Geffen School of Medicine, Los Angeles, CA, USA

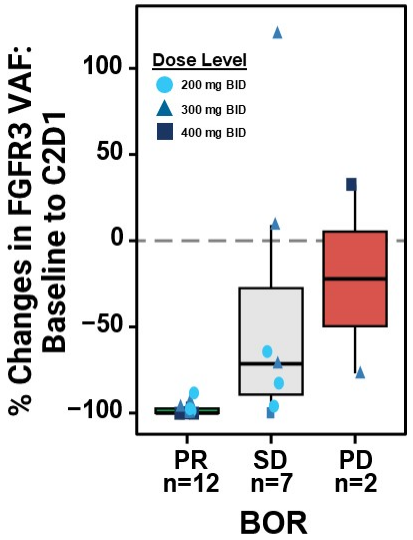
Radiographic Response and *FGFR3* Variant Allele Frequency in *FGFR3*-Altered Efficacy Evaluable mUC Patients Receiving ≥200 mg BID (n=39)



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)

- Responses were also observed in non mUC patients: intrahepatic cholangiocarcinoma and ovarian (Brenner) cancer (n=1 each).

FGFR3 Variant Allele Frequency[b]



- Decreases in FGFR3 Variant Allele Frequency (VAF) at C2D1 correlate with BOR
- 21/39 patients had detectable FGFR3 VAF at baseline

Data cutoff date of 02 Dec 2024. [a]Efficacy evaluable patients are those with measurable disease who had at least 1 post-baseline response assessment or had discontinued treatment before the first post-baseline response assessment. [b]Changes in ctDNA were assessed using Guardant 360 from patients' plasma samples.

A randomised phase III Study of Enfortumab vedotin with pembrolizumab +/-Vepugratinib 1st line in FGFR3 altered advanced urothelial cancer (FORAGER-2) NCT07218380

- 1st line metastatic UC
- FGFR3 DNA+ve
- Fit for EVP
- PS 0-2

Safety run in

R

Enfortumab vedotin with pembrolizumab + Vepugratinib

Enfortumab vedotin with pembrolizumab

Initial safety run-in enrolling Phase I data suggest tolerable and safe (n=6)

FGFR 3 screening from plasma with expected positivity of 25%

PFS is primary endpoint

Global randomized phase III needs 450 patients. EVP can start prior to randomisation to allow FGFR3 results.

El FGFR+ que no se testa, no se trata y en 2026 eso ya no tiene excusa

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- Menos del 40% de los pacientes se testan
- Menos de 1 de cada 3 antes de la tercera línea.

Con erdafitinib **demostrando OS** paciente sin test es un paciente al que le estamos robando opciones

La toxicidad no es el enemigo → es la señal de que el fármaco está funcionando

La toxicidad no es el enemigo → es la señal de que el fármaco está funcionando

- Los datos de dosis-reducción del THOR son contraintuitivos pero contundentes: los pacientes con ≥2 reducciones de dosis tienen una OS

- Tratar la toxicidad no es fracasar, es la estrategia.

Erdafitinib es el presente, pero el futuro se llama combinación y ya tiene un ORR del 93%

La mejor terapia dirigida que existe… es un oncólogo que no se rinde