

# III JORNADA TRASLACIONAL DE ONCOLOGÍA DE PRECISIÓN:

A TRAVÉS DE LAS VÍAS DE SEÑALIZACIÓN  
SEVILLA, 12 Y 13 DE FEBRERO DE 2026

# ANTI-TROP2: PAPEL EN LOS TUMORES GINECOLÓGICOS

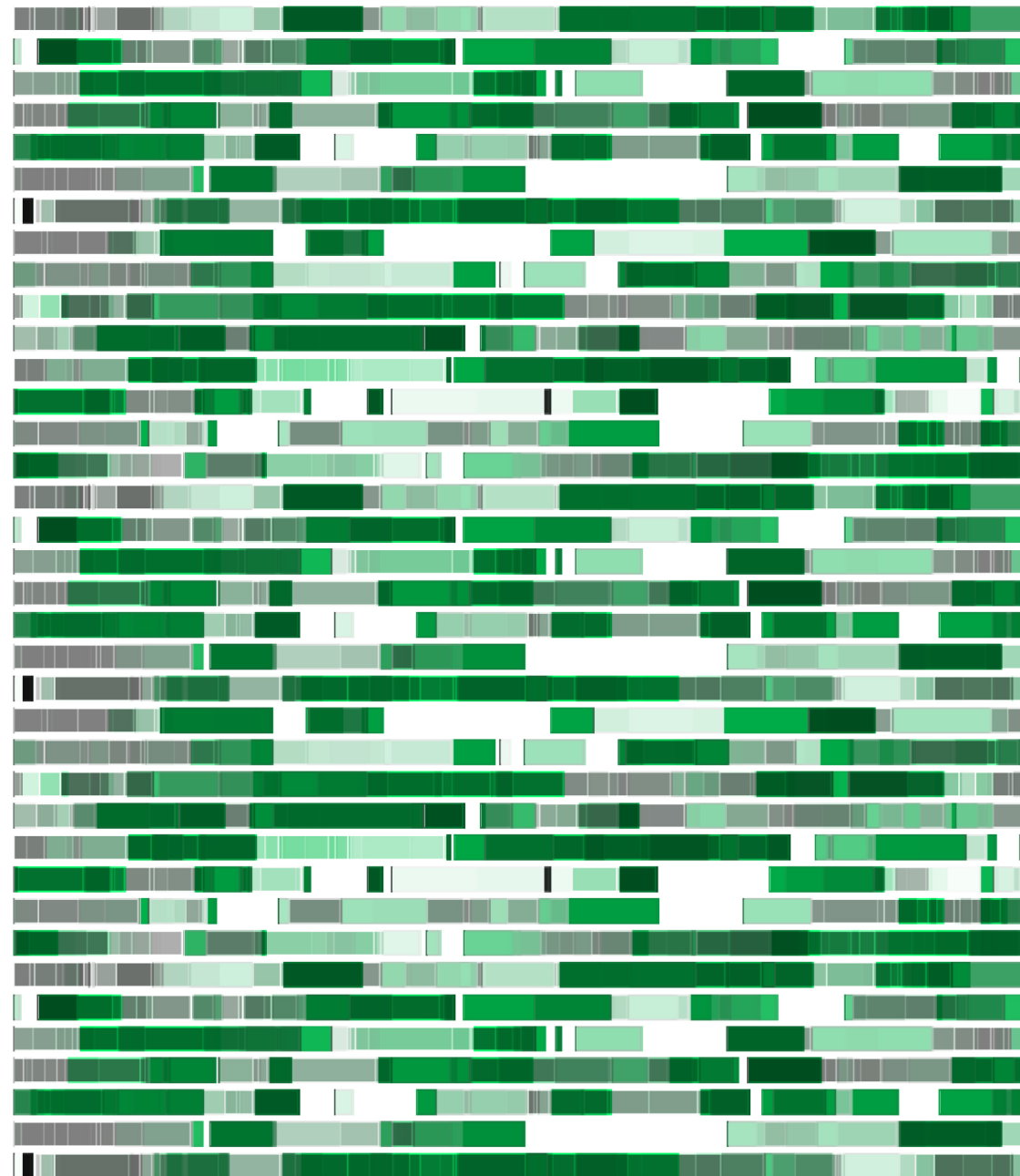
Purificación Estévez García

Unidad Tumores Ginecológicos y Genitourinarios

Oncología Médica H. Virgen del Rocío (Sevilla)

Organizador por:

**HENDERE HEALTHCARE**





## CONFLICTOS DE INTERÉS

### ✓PONENCIAS, ASISTENCIA A CONGRESOS Y GASTOS DE VIAJE:

GSK, ASTRA-ZENECA, MSD, PHARMAMAR, PHARMA&, EISAI.

### ✓ADVISORY BOARDS:

GSK, ASTRA-ZENECA, MSD, PHARMA&, EISAI, ABBIE.



## TUMORES GINECOLÓGICOS: PLATINO SIGUE SIENDO LA BASE DEL TRATAMIENTO 1ª L

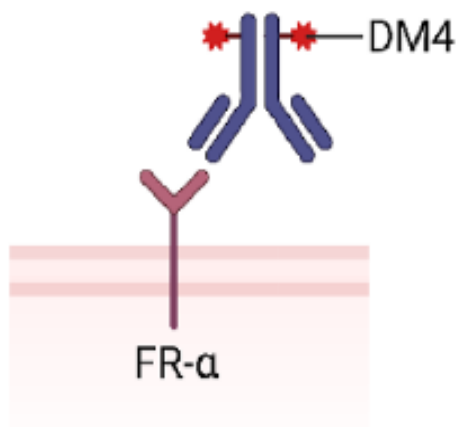
OVARIO	ENDOMETRIO	CÉRVIX
<b>Carboplatino + paclitaxel</b> +/- Bevacizumab +/- iPARP	<b>Carboplatino + paclitaxel</b> + IO (MMRd y MMRp)	<b>Carbo/Cisplatino + paclitaxel</b> +/- Bevacizumab + IO (CPS $\geq$ 1)

- ✓ A pesar de **elevada ORR**, muchas pacientes presentarán **progresión o recaída** con escasas opciones terapéuticas posteriores.
- ✓ En los últimos años, **aprobación de tratamiento en 2ª línea con beneficio en SG: Pembrolizumab + lenvatinib (CE), cemiplimab (CC)**, aunque limitados por la **introducción de IO en 1ª línea**.

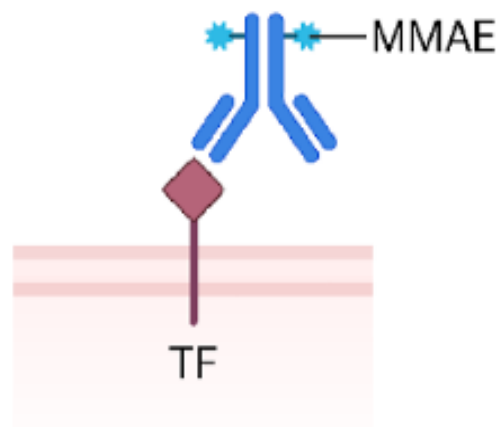


# ADCs : UNA REALIDAD EN TUMORES GINECOLÓGICOS

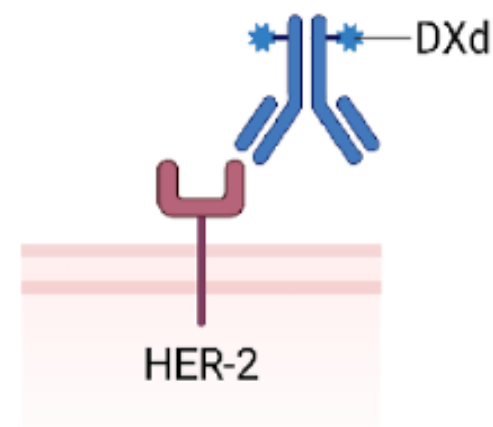
**Mirvetuximab soravtansine  
(MIRV)**



**Tisotumab vedotin  
(TV)**



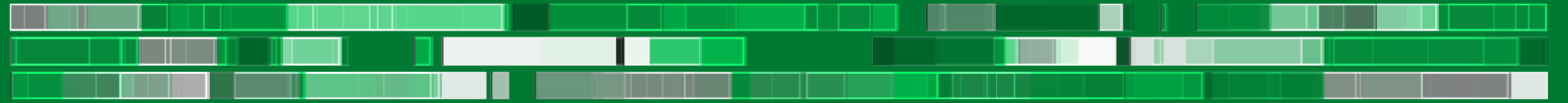
**Trastuzumab deruxetecan  
(T-DXd)**



OVARIO	CÉRVIX	TUMORES HER2 +++
<ul style="list-style-type: none"> <li>✓ FDA (marzo 24)</li> <li>✓ EMA (nov 2024)</li> </ul>	<ul style="list-style-type: none"> <li>✓ FDA (abril 24)</li> <li>✓ EMA (marzo 25)</li> </ul>	<ul style="list-style-type: none"> <li>✓ FDA (abril 24)</li> </ul>
Programa acceso expandido España	Programa acceso expandido España	Opinión positiva EMA (sept 25)

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ANTI-TROP2



## TROPHOBLAST CELL SURFACE ANTIGEN 2 (TROP2)

- ✓ **Glicoproteína transmembrana** descubierta en el **tejido placentario**.
- ✓ **Expresión en múltiples tejidos epiteliales normales**, especialmente en la mucosa oral y la piel.
- ✓ **Sobreexpresión en amplia variedad de tumores**.
- ✓ Promueve el **crecimiento, la invasión y la migración de las células tumorales** al intervenir en vías de señalización relacionadas con el calcio, expresión de ciclinas y disminución de adhesión de fibronectina.
- ✓ **Peor pronóstico**.

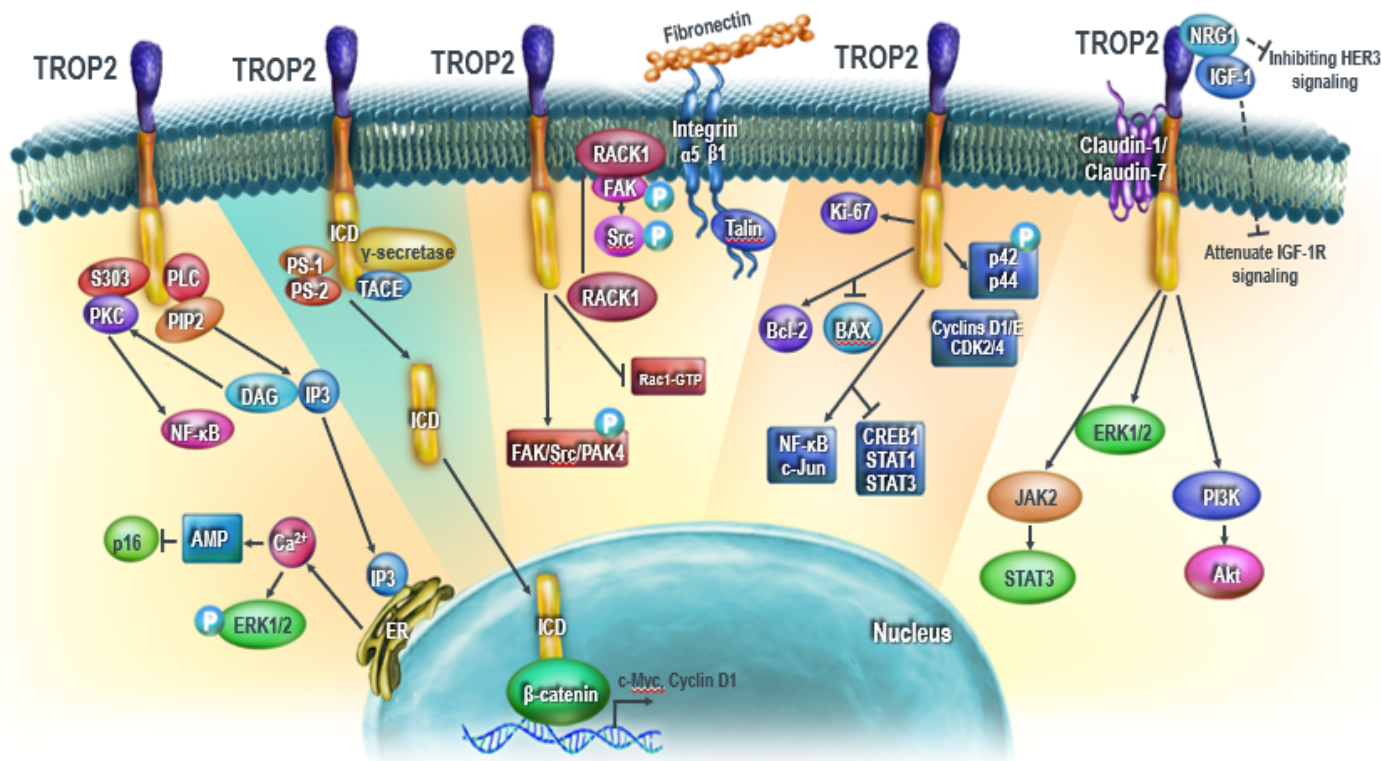
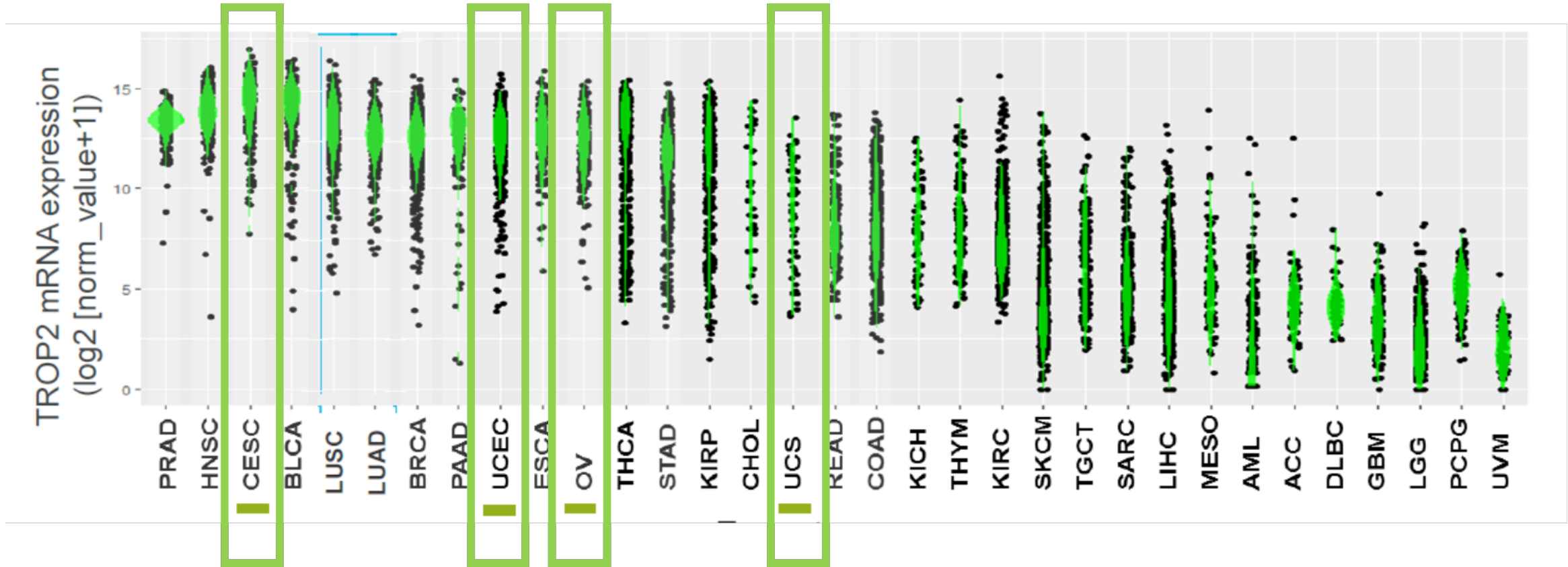


Image adapted from Liu et al. *Pharmacol Ther* 2022;239:108296.

Shvartsur, *Cancer* 2015; Lombardi, *Cancers (Basel)* 2023; Zaman, *OncoTargetTher* 2019.



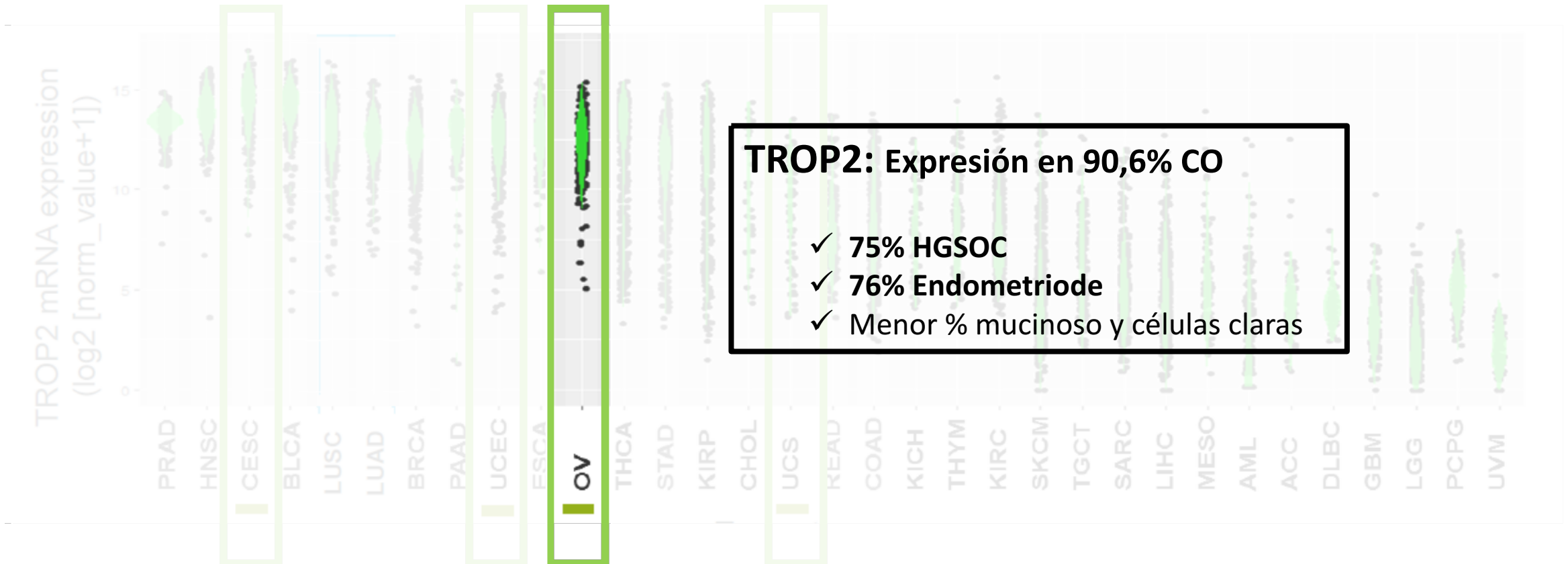
# ANTI-TROP2: DIANA TERAPÉUTICA EN TUMORES GINECOLÓGICOS







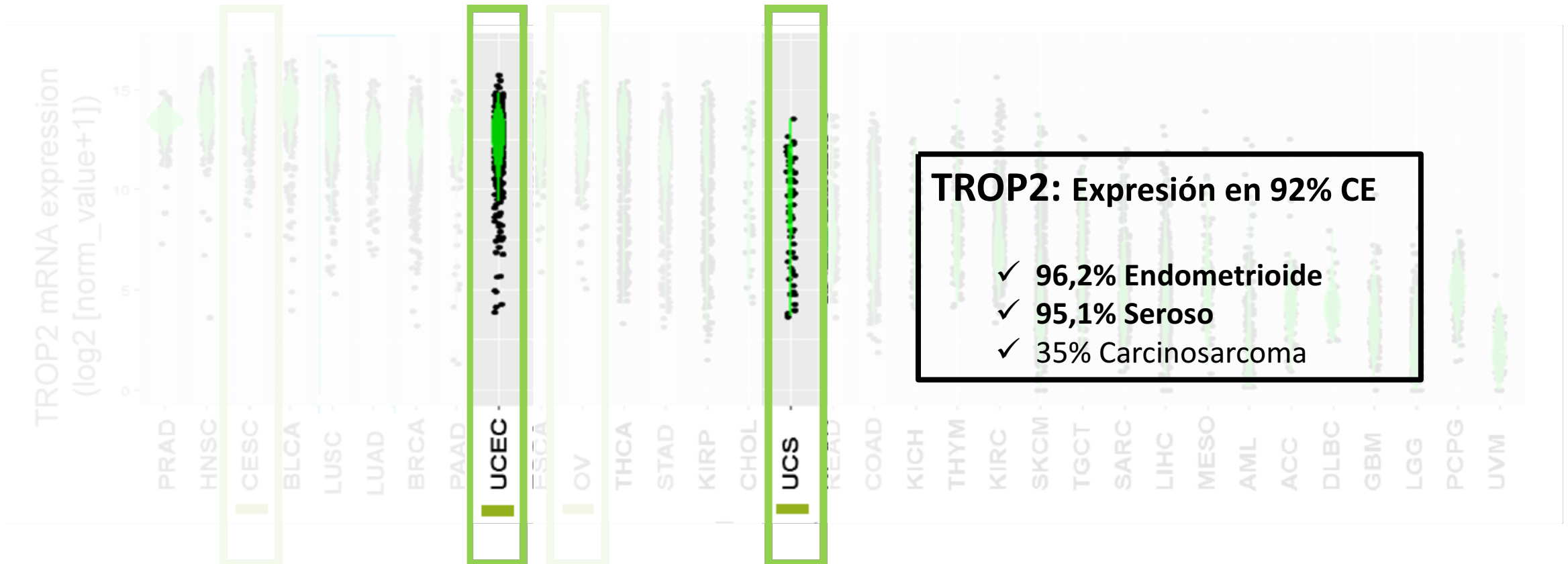
# ANTI-TROP2: DIANA TERAPÉUTICA EN CÁNCER DE OVARIO





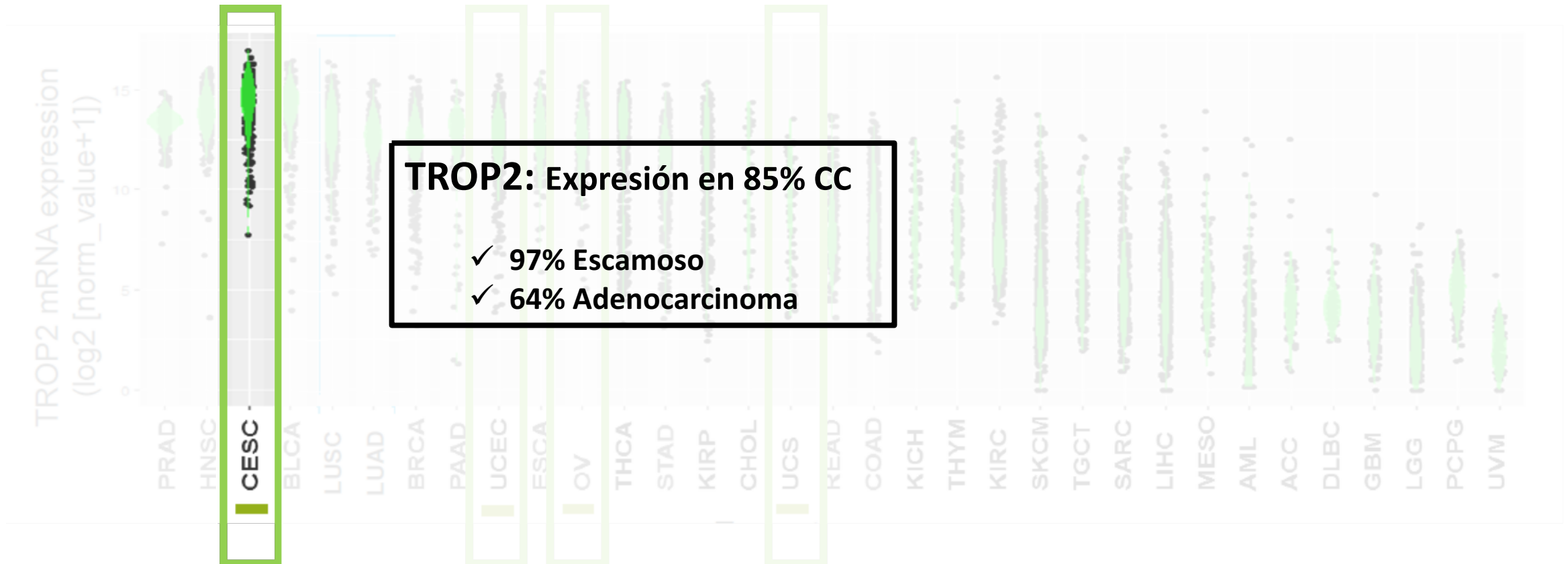


# ANTI-TROP2: DIANA TERAPÉUTICA EN CÁNCER DE ENDOMETRIO





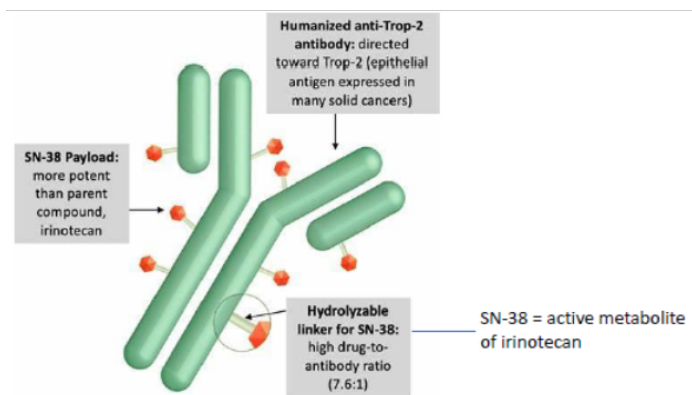
# ANTI-TROP2: DIANA TERAPÉUTICA EN CÁNCER DE CÉRVIX



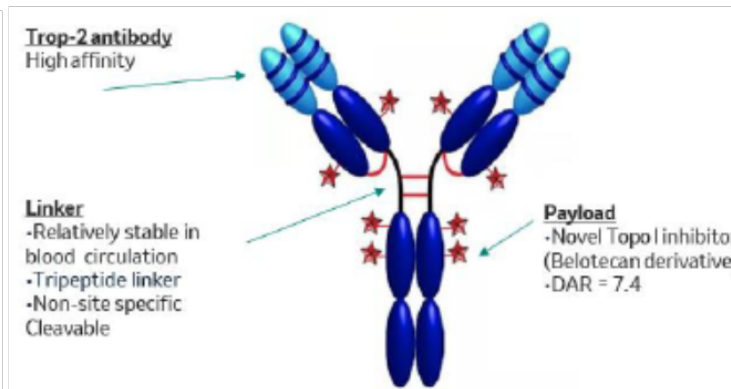


# ANTI-TROP2 EN CÁNCER GINECOLÓGICO

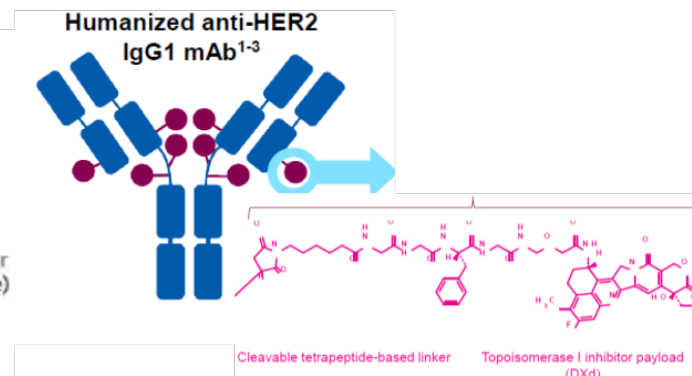
## Sacituzumab Govitecan



## Sacituzumab Tirumotecan



## Datopotamab Deruxtecan



Payload	SN-38 (Irinotecan metabolite)	KL610023 (belotecan derived)	Deruxtecan
Mec. action	Topoisomerase-I inhibitor	Topoisomerase-I inhibitor	Topoisomerase-I inhibitor
Linker	Dipeptide (cleavable) pH-sensitive hydrolysable linker	Dipeptide (cleavable) sulfonyl pyrimidine CL2A-carbonate linker	Tetrapeptide (cleavable) based linker
DAR	7,5	7,4	4

III JORNADA TRASLACIONAL  
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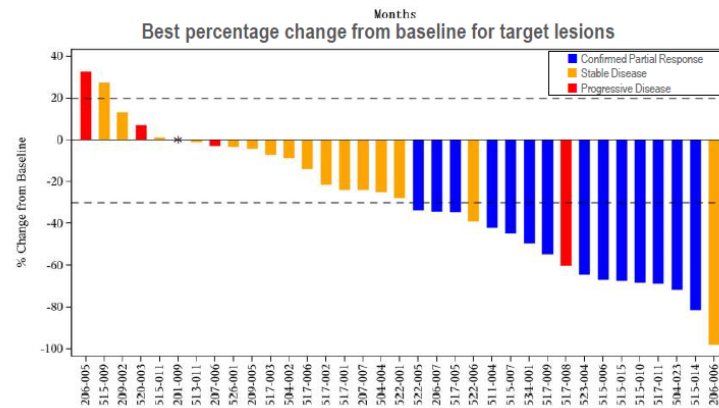
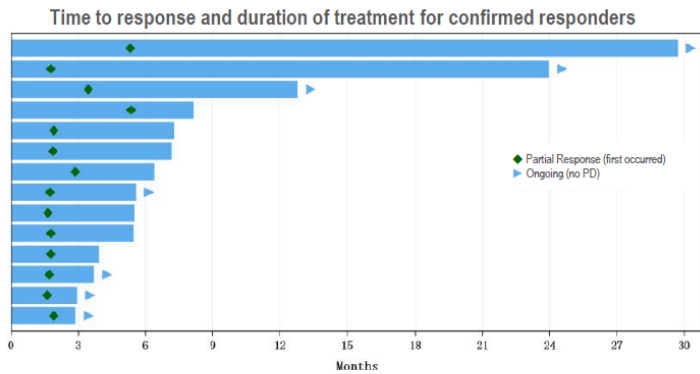
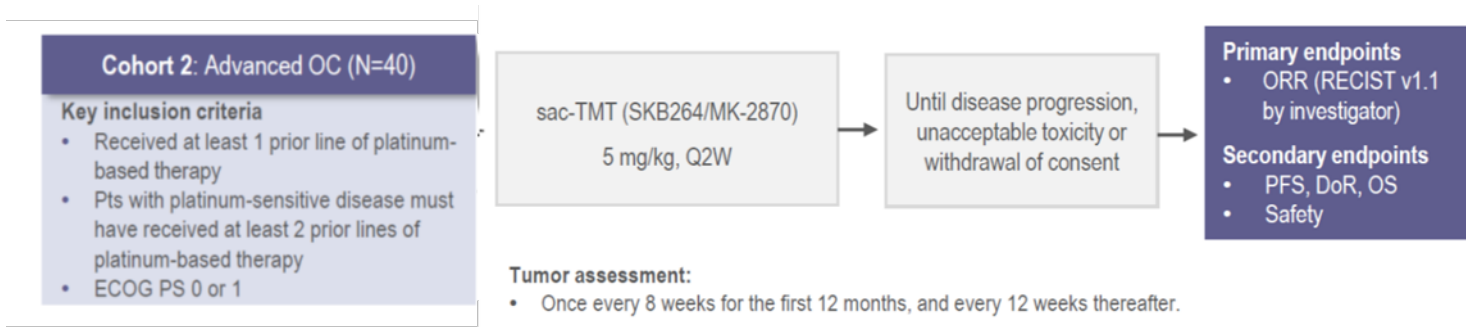
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# ANTI-TROP2: CÁNCER DE OVARIO



# SAC-TMT EN CO: FASE II KL264-I-01



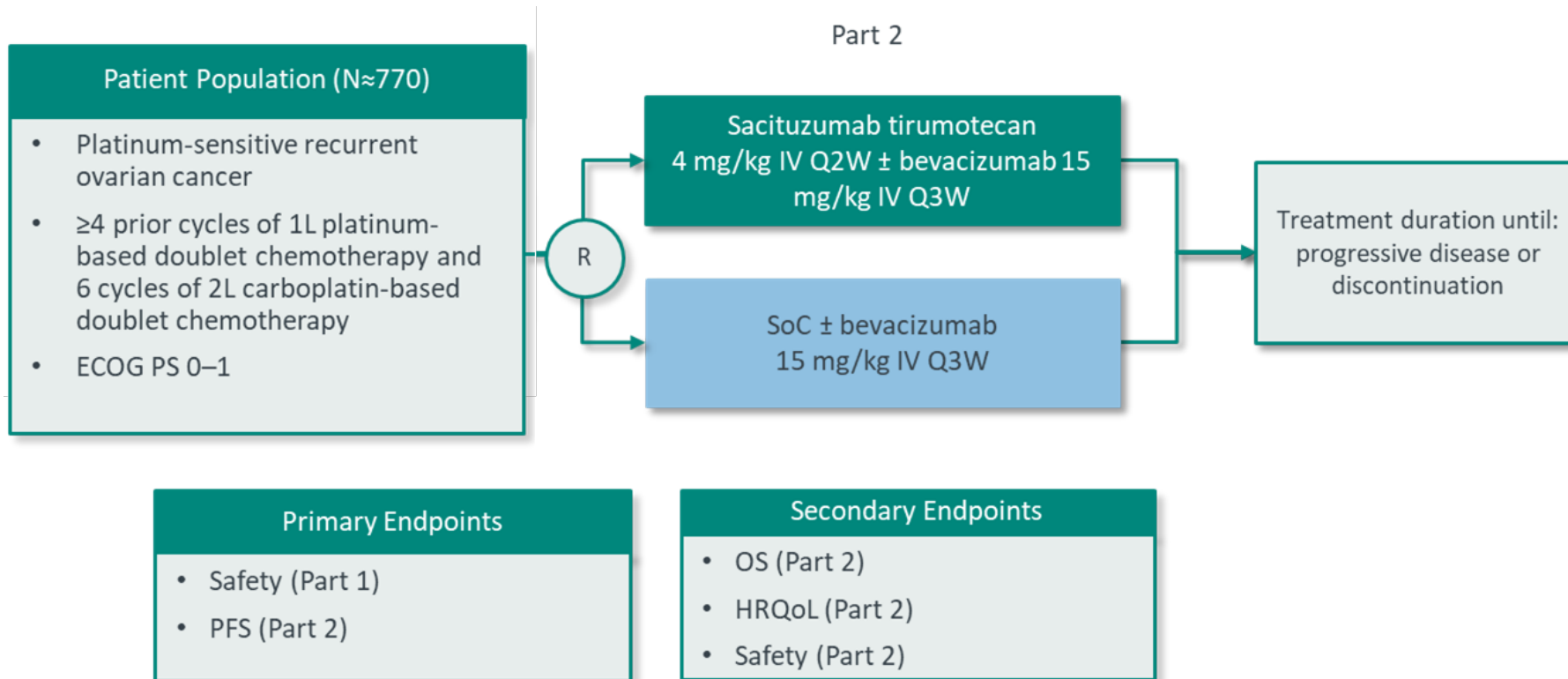
	OC (N = 40) <sup>a</sup>
<b>ORR, % (n/N)</b>	<b>40.0 (16/40)</b>
Confirmed ORR	35.0 (14/40)
<b>Subgroups</b>	
TROP2 H-score > 200	61.5 (8/13)
Platinum resistant	37.1 (13/35)
<b>DCR, % (n/N)</b>	<b>75.0 (30/40)</b>
PR	40.0 (16/40)
SD	35.0 (14/40)
<b>DoR</b>	
Median (range), months	5.3 (2.1, 24.4+)
<b>PFS</b>	
Median (95% CI), months	6.0 (3.9, 7.3)

a. Responses assessed per RECIST v1.1 by investigator.



# SAC-TMT EN CO RECAÍDA PLATINO-S: FASE III TROFUSE-022

Sac-TMT Maintenance Treatment ± Bevacizumab versus Standard of Care in Patients with Platinum-Sensitive Recurrent Ovarian Cancer





## SAC-TMT EN CO MANTENIMIENTO 1ª L HRD NEGATIVO: FASE III TROFUSE-021

A phase III, randomized, open-label, multicenter study to evaluate the efficacy and safety of **sacituzumab tirumotecan in combination with or without bevacizumab compared with standard of care as first-line maintenance** treatment for patients with newly diagnosed advanced HRD-Negative Ovarian Cancer following platinum-based chemotherapy.





# DATO-DXD EN CO: FASE II TROPION-PANTUMORO3

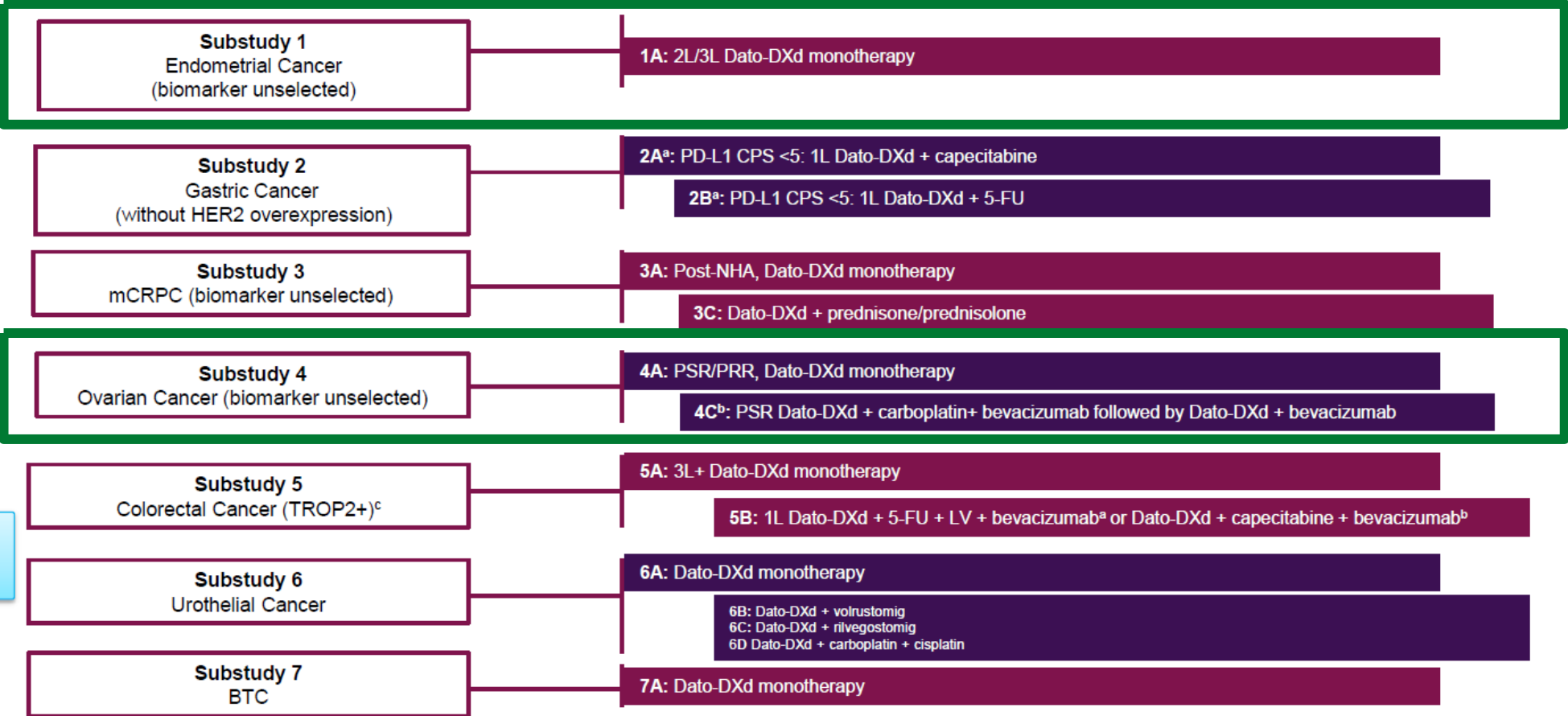
A Phase 2, Multicenter, Open-Label, Modular Study Evaluating the Efficacy and Safety of Dato-DXd as Monotherapy and in Combination With Anticancer Agents in Advanced/Metastatic Solid Tumors

## Study Design

**Patients with advanced/metastatic solid tumors (N≈531)**

- Previously treated with 0–2 lines of chemotherapy
- ECOG PS 0 or 1

Locations: North America, Europe, Asia  
ClinicalTrials.gov Identifier: NCT05489211





# DATO-DXD EN CO: FASE II TROPION-PANTUMORO3

## Ovarian cancer (TROP2 expression unselected)

- High-grade serous or endometrioid ovarian, fallopian tube, or primary peritoneal carcinoma
- ECOG PS 0 or 1
- Progressed on  $\geq 1$  line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease; platinum-sensitive and resistant disease allowed\*

N=35

Dato-DXd†  
6 mg/kg IV Q3W

### Endpoints

#### Primary

- ORR by investigator per RECIST v1.1
- Safety & tolerability

#### Secondary

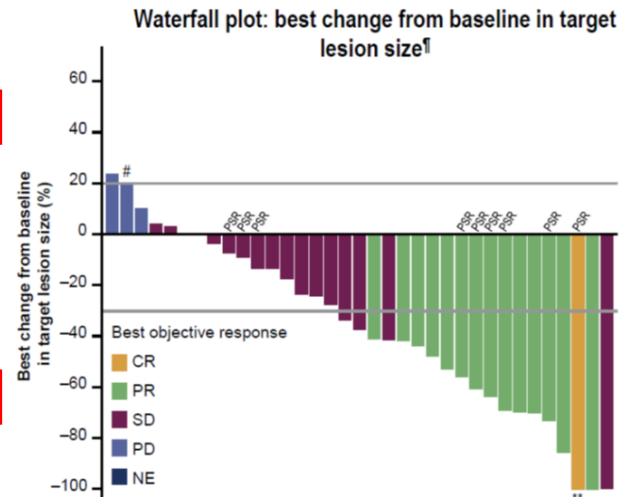
- PFS, DoR, DCR by investigator
- PK and immunogenicity

#### Exploratory

- OS
- Biomarker analyses

- As of June 14, 2024, median duration of follow-up\* was 14.5 months (range 10.4–15.4) in the ovarian cohort

	Ovarian		
	Total (N=35)	Platinum-sensitive (n=9)	Platinum-resistant (n=26)
<b>Confirmed ORR, % (95% CI)</b>	42.9 (26.3–60.6)	66.7 (29.9–92.5)	34.6 (17.2–55.7)
<b>Best overall response, n (%)</b>			
CR	1 (2.9)	1 (11.1)	0 (0.0)
PR	14 (40.0)	5 (55.6)	9 (34.6)
SD†	17 (48.6)	3 (33.3)	14 (53.8)
PD‡	3 (8.6)	0 (0.0)	3 (11.5)
NE§	0 (0.0)	0 (0.0)	0 (0.0)
<b>Median time to response, months (range)</b>	1.4 (1.2–8.2)	–	–
<b>Median DoR, months (95% CI)</b>	5.7 (2.9–NC)	8.5 (2.7–NC)	5.6 (2.9–NC)
<b>DCR at 12 weeks,¶ % (80% CI)</b>	85.7 (75.1–92.9)	100 (77.4–100.0)	80.8 (67.2–90.3)
<b>Median PFS, months (95% CI)</b>	5.6 (4.1–7.0)	–	–



- ✓ CO platino-resistente 74,3%
- ✓ CO platino-sensible 25,7%
- ✓  $\geq 2$  líneas 68%
- ✓ Beva previo 71%
- ✓ iPARP previo 18%

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# ANTI-TROP2: CÁNCER DE ENDOMETRIO

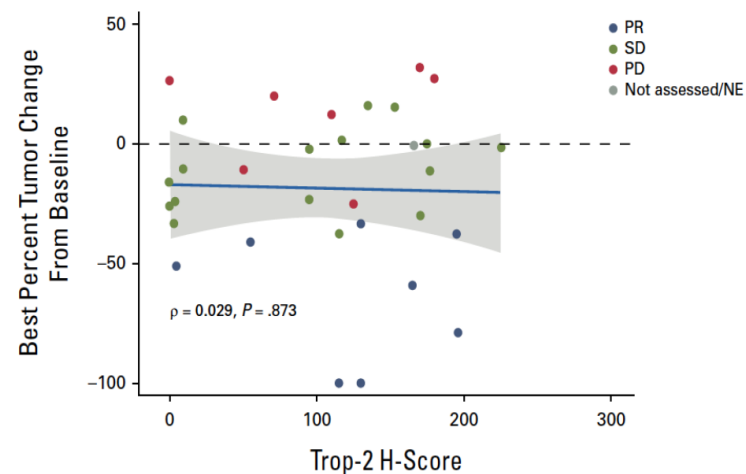


# SG EN CE: FASE II BASKET TROPICS-03

**TABLE 1. Baseline Demographics and Clinical Characteristics**

Characteristic	SG (N = 41)
Age at study entry, years, median (range)	68 (44-83)
Race, No. (%)	
White	21 (51)
Black or African-American	1 (2)
Asian	8 (20)
Other	5 (12)
Not reported	6 (15)
ECOG performance status, No. (%)	
0	18 (44)
1	23 (56)
Microsatellite instability high, No. (%)	
Yes <sup>a</sup>	8 (20)
No	32 (78)
Not available	1 (2)
Histologic/cytologic diagnosis, No. (%)	
Serous	17 (42)
Endometrioid	20 (49)
Others	4 (10)
No. of previous anticancer regimen, No. (%)	
1	3 (7)
2	13 (32)
3	16 (39)
>3	9 (22)
Previous anticancer regimens, median (range)	3 (1-6)
Previous anticancer therapy type, No. (%)	
Chemotherapy	41 (100)
Hormonal therapy	5 (12)
Immunotherapy	35 (85)
Targeted agents	26 (63)
Other	1 (2)
Chemotherapy + IO, <sup>b</sup> No. (%)	35 (85)
Trop-2 expression	
Median H-score (range)	115 (0-245)

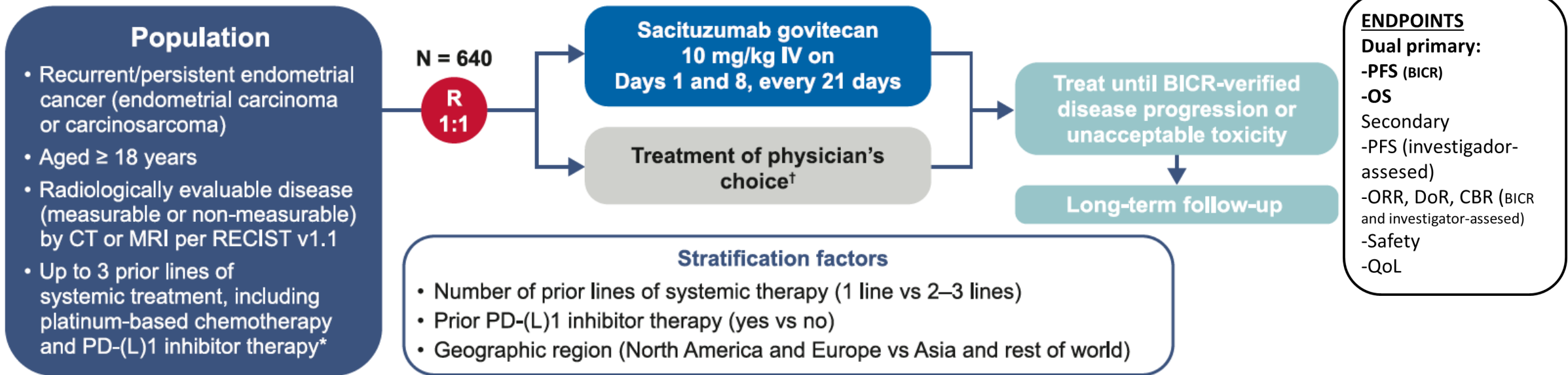
Variable	All Patients (N = 41)
ORR (confirmed CR + PR), No. (%)	9 (22)
95% CI	11 to 38
Best overall response, No. (%)	
Confirmed CR	0
Confirmed PR	9 (22)
SD	18 (44)
PD	8 (20)
NE	2 (5)
Not assessed <sup>a</sup>	4 (10)
Clinical benefit rate (confirmed CR + PR + SD ≥6 months), No. (%)	13 (32)
95% CI	18-48
Time to response, months <sup>b,c</sup>	
Median (range)	2.8 (1.4-5.8)
DOR, months <sup>b,d</sup>	
Median (95% CI)	8.8 (2.8 to NE)





# SG EN CE: FASE III ASCENT-GYN-01

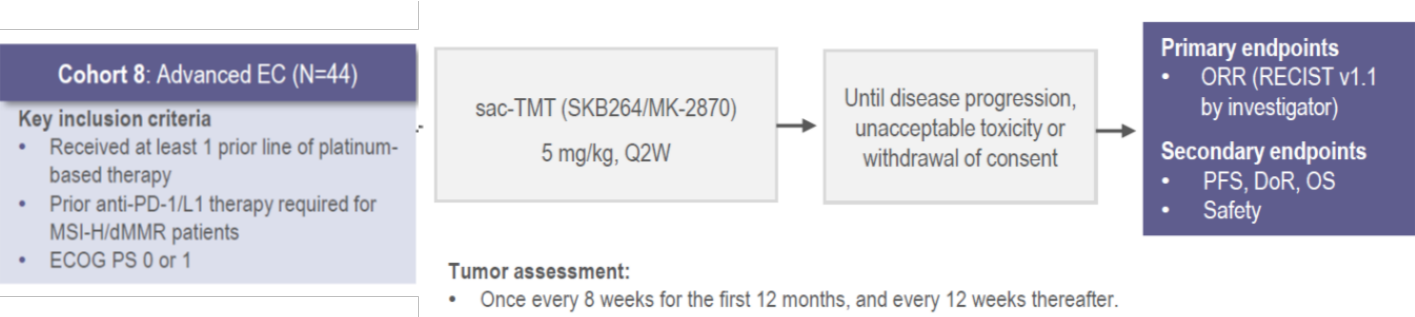
A randomized, phase III study of sacituzumab govitecan versus treatment of the physician's choice in patients with endometrial cancer after platinum-based chemotherapy and immunotherapy: the ASCENT-GYN-01 study (GOG-3104/ENGOT-en26/APGOT-EN2)



<sup>†</sup>Doxorubicin 60 mg/m<sup>2</sup> IV on Day 1 every 21 days or paclitaxel 80 mg/m<sup>2</sup> IV on Days 1, 8, and 15, every 28 days.

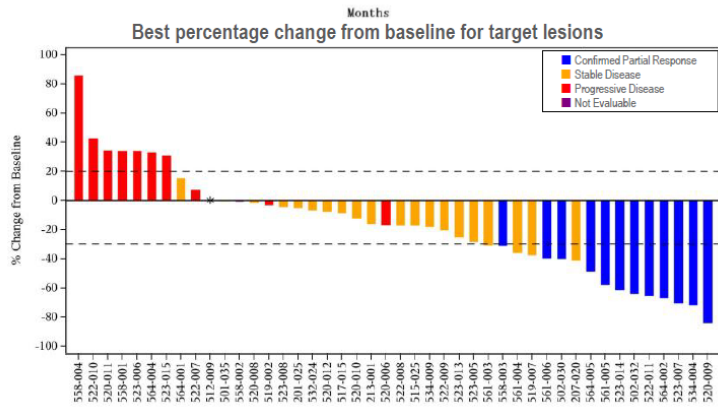
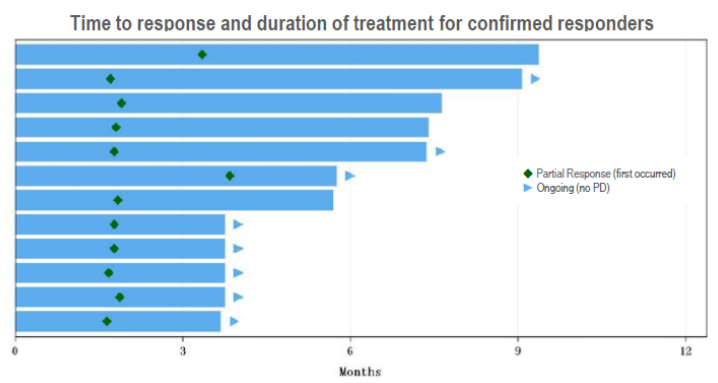


# SAC-TMT EN CE: FASE II KL264-I-01



	EC (N = 44) <sup>a</sup>
<b>ORR, % (n/N)</b>	<b>34.1 (15/44)<sup>b</sup></b>
Confirmed ORR	27.3 (12/44)
<b>Subgroups</b>	
TROP2 H-score >200	41.7 (5/12)
Prior IO	37.5 (6/16)
<b>DCR, % (n/N)</b>	<b>75.0 (33/44)</b>
PR	34.1 (15/44)
SD	40.9 (18/44)
<b>DoR</b>	
Median (range), months	5.7 (3.8, 7.4+)
<b>PFS</b>	
Median (95% CI), months	5.7 (3.7, 9.4)

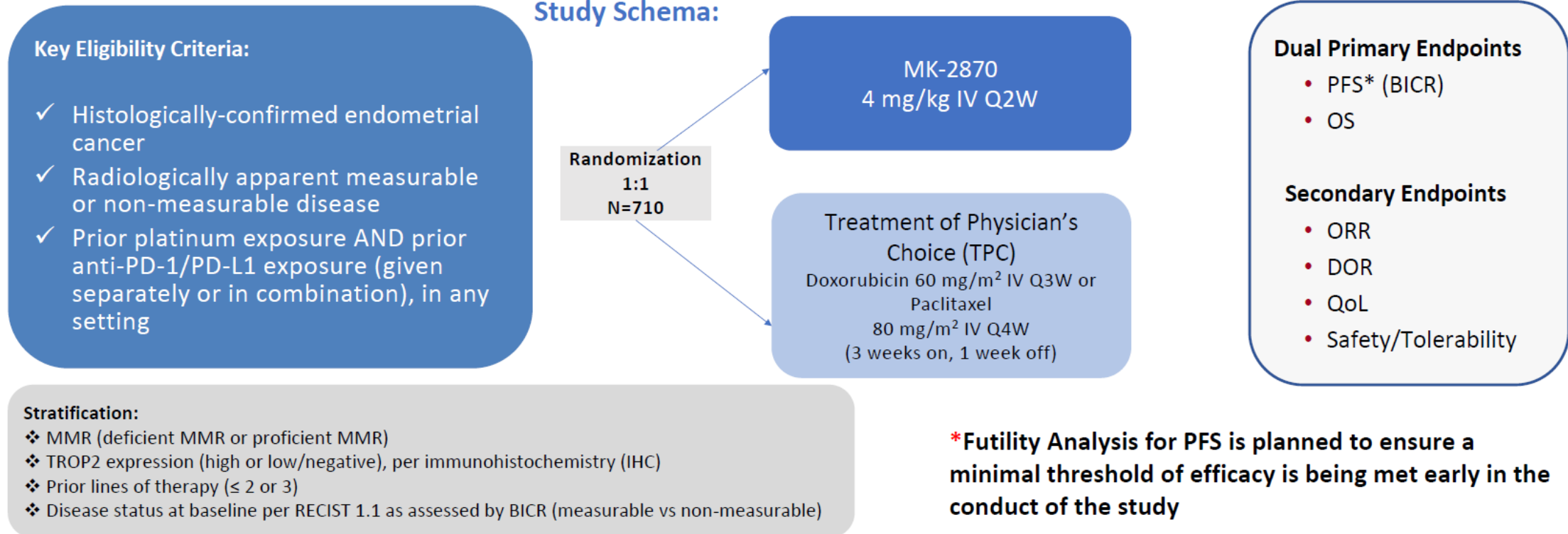
a. Responses assessed per RECIST v1.1 by investigator.  
b. Two patients with unconfirmed response were still receiving treatment at the data cutoff date.







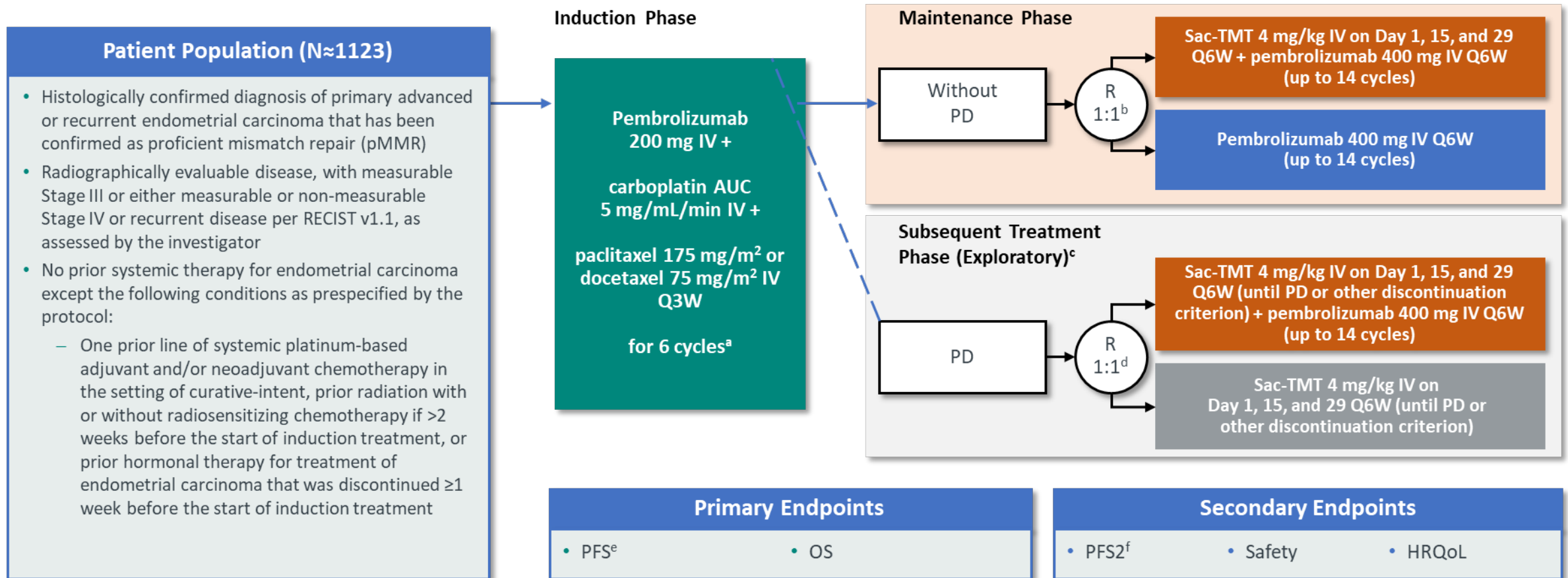
# SAC-TMT EN CE: FASE III TROFUSE-005/MK-2870-005/ENGOT-EN23







# SAC-TMT EN CE MMRP 1ª LÍNEA: FASE III TROFUSE-033/MK-2870-033



<sup>a</sup>Patients may receive an additional 2 cycles of pembrolizumab after consultation with the sponsor. <sup>b</sup>Stratified by response to pembrolizumab/carboplatin/paclitaxel (CR or PR vs SD or non-CR/non-PD), TROP2 expression (very low vs low vs medium + high), molecular subgroup (p53abn vs p53wt), cycles of pembrolizumab administered in induction (6 vs 7 or 8 cycles), and geographic region (North America, Europe, Israel, Japan, Australia, New Zealand, South Korea, and Singapore vs rest of world). <sup>c</sup>Participants whose cancer does progress will have the possibility to enter the subsequent treatment phase. <sup>d</sup>Stratified by TROP2 expression (very low vs low vs medium + high). <sup>e</sup>By BICR per RECIST v1.1. <sup>f</sup>By investigator.



# DATO-DXD EN CE: FASE II TROPION-PANTUMORO3

## Endometrial cancer (TROP2 expression unselected)

- Advanced/metastatic endometrial carcinoma
- All histologies (except sarcoma)
- ECOG PS 0 or 1
- Progressed on  $\geq 1$  line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease

Dato-DXd<sup>†</sup>  
6 mg/kg IV Q3W

N=40

### Endpoints

#### Primary

- ORR by investigator per RECIST v1.1
- Safety & tolerability

#### Secondary

- PFS, DoR, DCR by investigator
- PK and immunogenicity

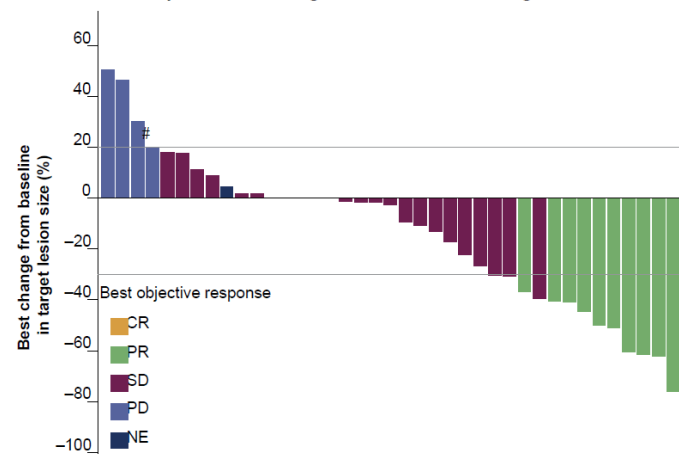
#### Exploratory

- OS
- Biomarker analyses

- As of June 14, 2024, median duration of follow-up\* was 13.6 months (range 2.1–19.6) in the endometrial cohort

	Endometrial (N=40)
Confirmed ORR, % (95% CI)	27.5 (14.6–43.9)
Best overall response, n (%)	
CR	1 (2.5)
PR	10 (25.0)
SD <sup>†</sup>	23 (57.5)
PD <sup>‡</sup>	5 (12.5)
NE <sup>§</sup>	1 (2.5)
Median time to response, months (range)	2.8 (1.4–4.2)
Median DoR, months (95% CI)	16.4 (7.1–NC)
DCR at 12 weeks, <sup>  </sup> % (80% CI)	57.5 (46.1–68.3)
Median PFS, months (95% CI)	6.3 (2.8–NC)

Waterfall plot: best change from baseline in target lesion size<sup>††</sup>



- ✓ 47%  $\geq 2$  líneas previas
- ✓ 22,5% IO previa

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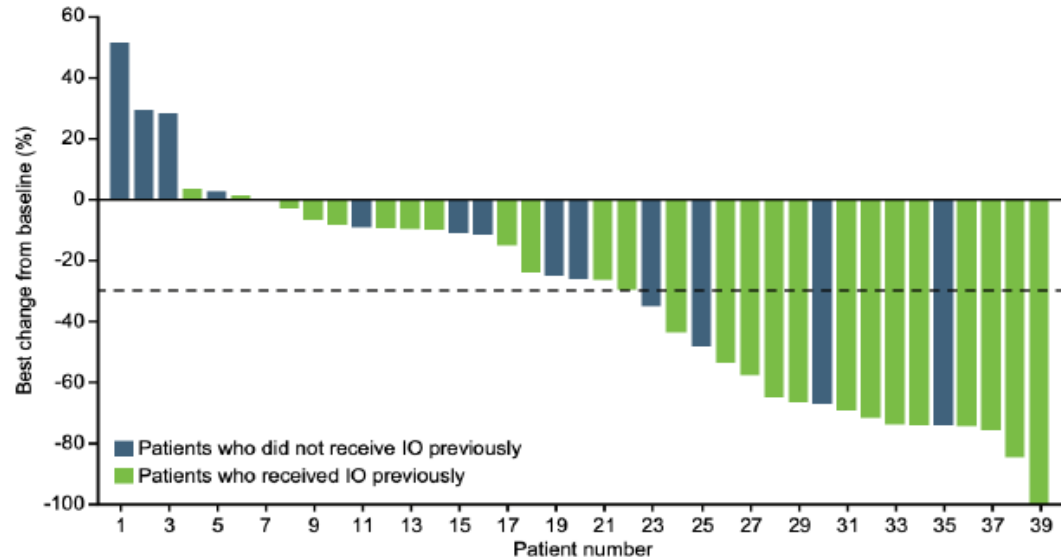
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# ANTI-TROP2: CÁNCER DE CÉRVIX



## SAC-TMT EN CC: FASE II EVER-132-003



- ✓ Fase II basket. Población CHINA
- ✓ 40 pac CC
- ✓ 68% IO previo: NO diferencias en ORR comparado con IO-naive (48%)

**Table 2**  
Summary of responses.

	FAS (n = 40)	Post-IO population (n = 27)
ORR (confirmed CR + PR), n (%)	17 (43)	13 (48)
95 % CI	27-59	29-68
Best overall response, n (%)		
Confirmed CR	1 (3)	1 (4)
Confirmed PR	16 (40)	12 (44)
SD	17 (43)	13 (48)
SD ≥6 months	5 (13)	3 (11)
Progressive disease	5 (13)	0
Not evaluable <sup>a</sup>	1 (3)	1 (4)
DCR (confirmed CR + PR, + SD), n (%)	34 (85)	26 (96)
95 % CI	70-94	81 to >99
CBR (confirmed CR + PR, + SD ≥6 months), n (%)	22 (55)	16 (59)
95 % CI	39-71	39-78
Median DOR (95 % CI), months	9.2 (4.6-11.7)	9.5 (7.0-11.7)

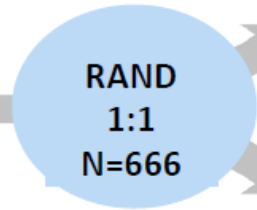
# SAC-TMT EN CC: FASE III TROFUSE-020/GOG-3101/ENGOT-CX20

## Key Eligibility Criteria:

### Recurrent or metastatic cervical cancer that:

- ✓ Has progressed on or after 1 prior line of systemic platinum doublet treatment (with or without bevacizumab)  
AND
- ✓ Has received anti-PD-1/anti-PD-L1 therapy as part of prior cervical cancer regimens

Note: May have also received and progressed on or after 2<sup>nd</sup> line treatment with tisetumab vedotin (TV)



Arm 1: MK-2870 4 mg/kg by IV q2w

Treatment of Physician's Choice (TPC)  
(*pemetrexed, topotecan, vinorelbine, gemcitabine, or irinotecan, Tisetumab Vedotin*)

PD by BICR

PD by BICR

## Primary Endpoint

- OS

## Secondary Endpoints

- PFS (BICR)
- ORR (BICR)
- DOR (BICR)
- QoL
- Safety/Tolerability

## Stratification: 3 Factors

- ❖ Prior use of bevacizumab (yes vs. no)
- ❖ TROP2 expression (low vs. high)
- ❖ Selection of ICC (TV vs. other)

# SAC-TMT EN CC EN PRIMERA LÍNEA: FASE III TROFUSE-036/ENGOT-CX22

A phase III, randomized, open-label, multicenter study to evaluate the efficacy and safety of **sacituzumab tirumotecan + pembrolizumab with or without bevacizumab compared with standard of care as first-line maintenance** treatment for patients with persistent, recurrent or newly diagnosed metastatic cervical cancer

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DE FEBRERO DE 2026



# TOXICIDAD





## TOXICIDAD ANTI-TROP2 EN TUMORES GINECOLÓGICOS

	Sacituzumab Govitecan	Sacituzumab Tirumotecan	Datopotamab Deruxtecan
GASTROINTESTINAL	<b>Diarrea 56% (14% ≥G3)</b> Náuseas / Vómitos	Náuseas 16%	Náuseas 60% G1-2 Diarrea
HEMATOLÓGICA	<b>Anemia</b> <b>Neutropenia 25% ≥G3</b>	<b>Anemia 39% (14% ≥G3)</b> <b>Neutropenia 29% (14% ≥G3)</b>	<Anemia y neutropenia
ESTOMATITIS	Poco frecuente	13-15%	<b>50-60% (3-5% G3)</b>
ALOPECIA	45%	45%	50%
OTRAS	<b>Astenia</b>	<b>ILD 3%</b>	Tox <b>Ocular 40% G1</b> (ojo seco, visión borrosa) <b>ILD 2%</b>

III JORNADA TRASLACIONAL  
DE ONCOLOGÍA DE PRECISIÓN:

A TRAVÉS DE LAS VÍAS  
DE SEÑALIZACIÓN  
SEVILLA, 12 Y 13  
DE FEBRERO DE 2026



# CONCLUSIONES Y FUTURO



## CONCLUSIONES Y RETOS

1. Los ADC constituyen ya una realidad terapéutica en tumores ginecológicos, con beneficio en supervivencia global.
2. TROP-2 se consolida como una diana relevante, con datos muy prometedores (fase II), aunque aún queda por establecer su posicionamiento terapéutico, y la identificación de biomarcadores predictivos.
3. Retos:
  1. Adecuada selección de pacientes.
  2. Secuenciación terapéutica de los distintos fármacos disponibles
  3. Manejo experto de la toxicidad específica para optimizar el beneficio.



MUCHAS  
GRACIAS

PARA MIKEL CON ❤️.

72KILOS