III JORNADA TRASLACIONAL
DE ONCOLOGÍA DE PRECISIÓN:
A TRAVÉS DE LAS VÍAS DE SEÑALIZACIÓN
SEVILLA, 12 Y 13 DE FEBRERO DE 2026

ANTI-TROP2:
ESCENARIO EN CÁNCER DE MAMA TRIPLE NEGATIVO

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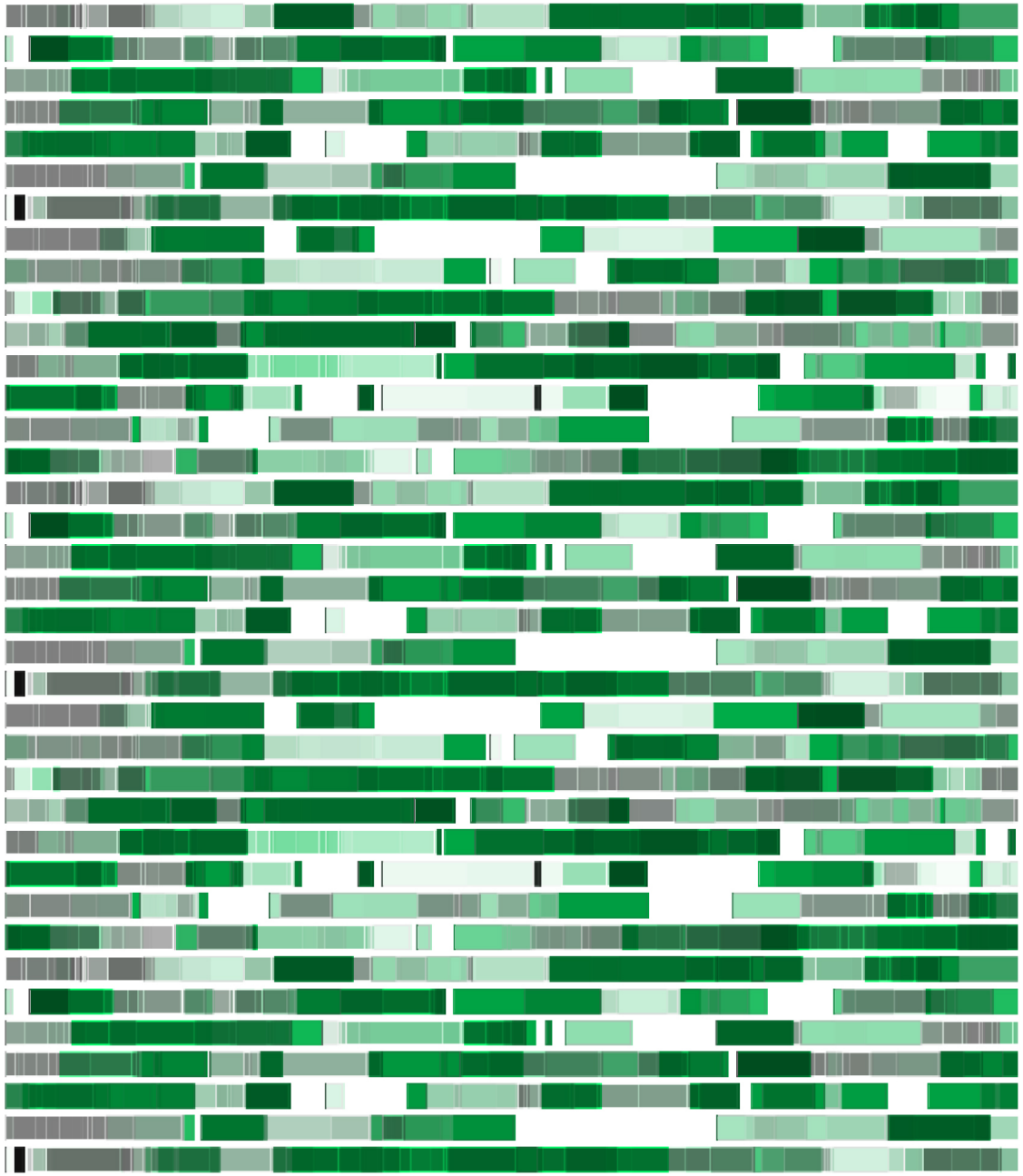
HENDERE HEALTHCARE



TROP-2 EN CÁNCER DE MAMA TRIPLE NEGATIVO

TROP-2 is highly expressed across tumor types

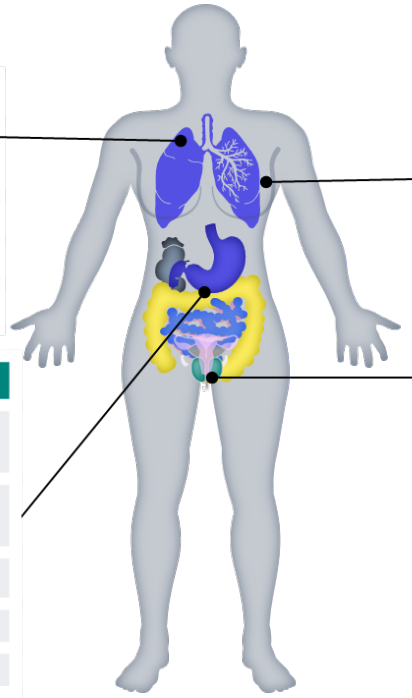
Data below indicate percentage of patients with TROP-2 overexpression, as defined by individual study[a]

Lung[1,a,b]

Cancer subtype	% patients with high expression (n/N)
Adenocarcinomas	64% (172/270)
Squamous cell carcinoma	75% (150/201)
High-grade neuroendocrine tumor	18% (21/115)

GI cancers[a,b]

Cancer subtype	% patients with high expression (n/N)
Pancreatic cancer	30% (15/50)[2] to 55% (109/197)[3]
Gastric cancer	66.3% (398/600)[4]
Gallbladder cancer	55.9% (52/93)[5]
Colon cancer	68.4 (371/542)[6]



Breast cancer[7,a,b]

Cancer subtype	% patients with high expression (n/N)
ER+	50% (11/22)
HER2+	74% (26/35)
TNBC	93% (26/28)

Gynecologic cancers[a,b]

Cancer subtype	% patients with high expression (n/N)
Epithelial ovarian cancers	47% (42/90)[8,c]
Endometrial cancers	57.6% (68/118)[9]
Cervical cancers	60.4% (64/106)[10]

[a]For full context about how overexpression was defined in each study, please check individual references. [b]This slide includes representative data for included tumor types. For more granular data, refer to slides 10, 12, and 13 for expression levels by specific histology for gynecologic, GI, and lung cancers, respectively. [c]This study reported moderate to strong TROP-2 expression scores (2+/3+).[8]

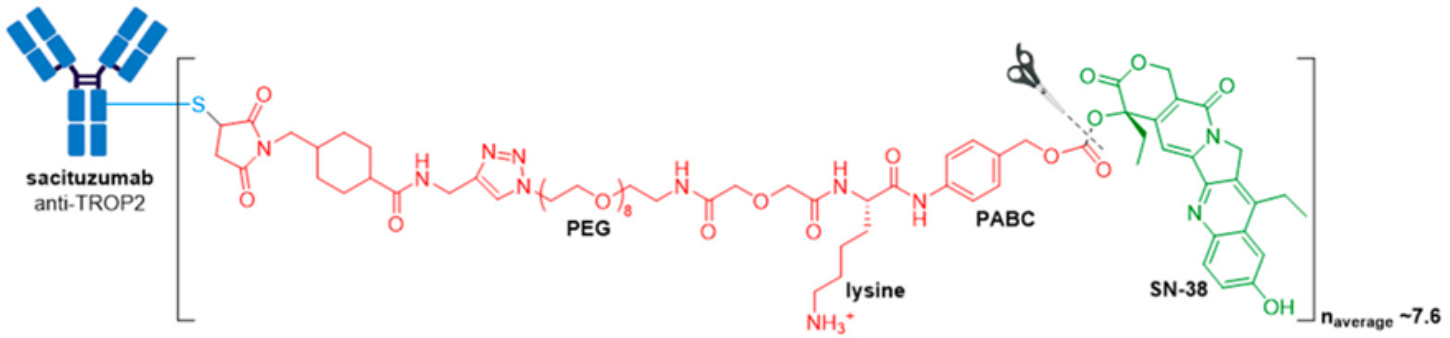
ER, estrogen receptor; GI, gastrointestinal; HER2, human epidermal growth factor receptor; TNBC, triple-negative breast cancer; TROP-2, trophoblast cell surface antigen.

1. Inamura K et al. *Oncotarget*. 2017;8(17):28725-28735. 2. Mas L et al. *Clin Res Hepatol Gastroenterol*. 2023;47(4):102108. 3. Fong D et al. *Br J Cancer*. 2008;99(8):1290-1295. 4. Zhao W et al. *Oncotarget*. 2016;7(5):6136-6145.
5. Chen MB et al. *Tumour Biol*. 2014;35(11):11565-11569 6. Fang YJ et al. *Int J Colorectal Dis*. 2009;24(8):875-884. 7. Aslan M et al. *NPJ Breast Cancer*. 2021;7(1):141. 8. Perrone E et al. *Front Oncol*. 2020;10:118.
9. Bignotti et al. *BMC Clin Pathol*. 2012;12:22. 10. Liu T et al. *PLoS One*. 2013;8(9):e75864.

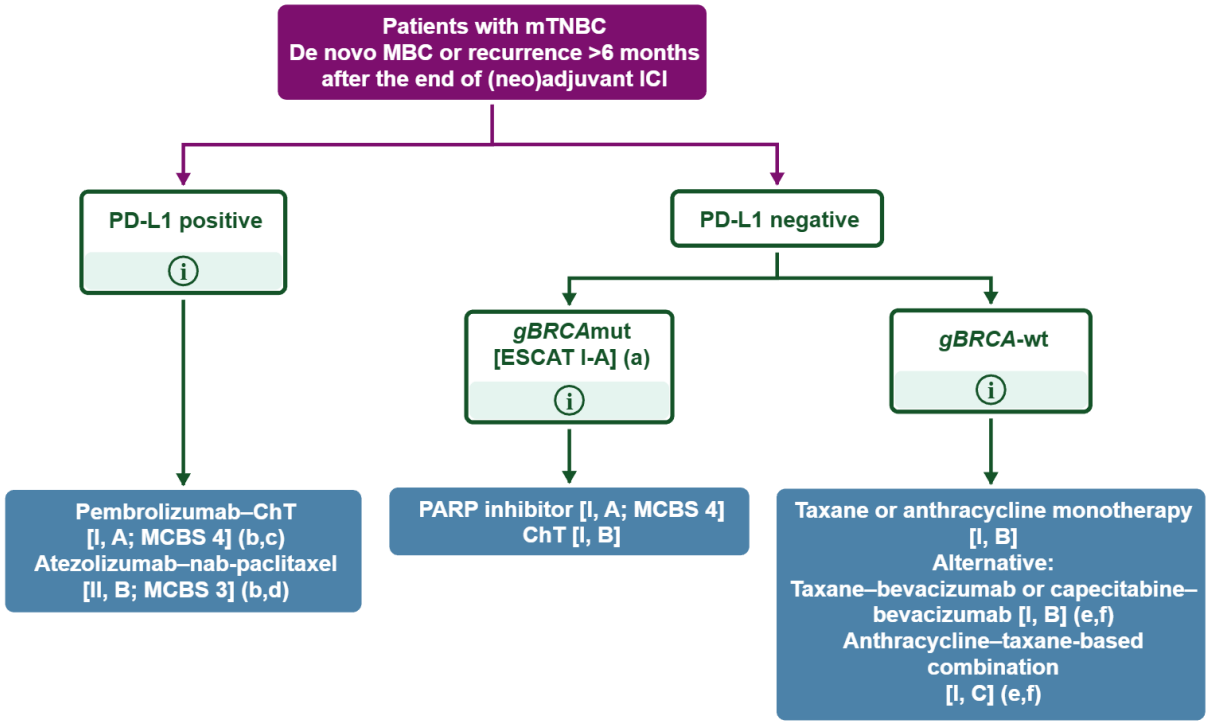
SACITUZUMAB-GOVITECÁN

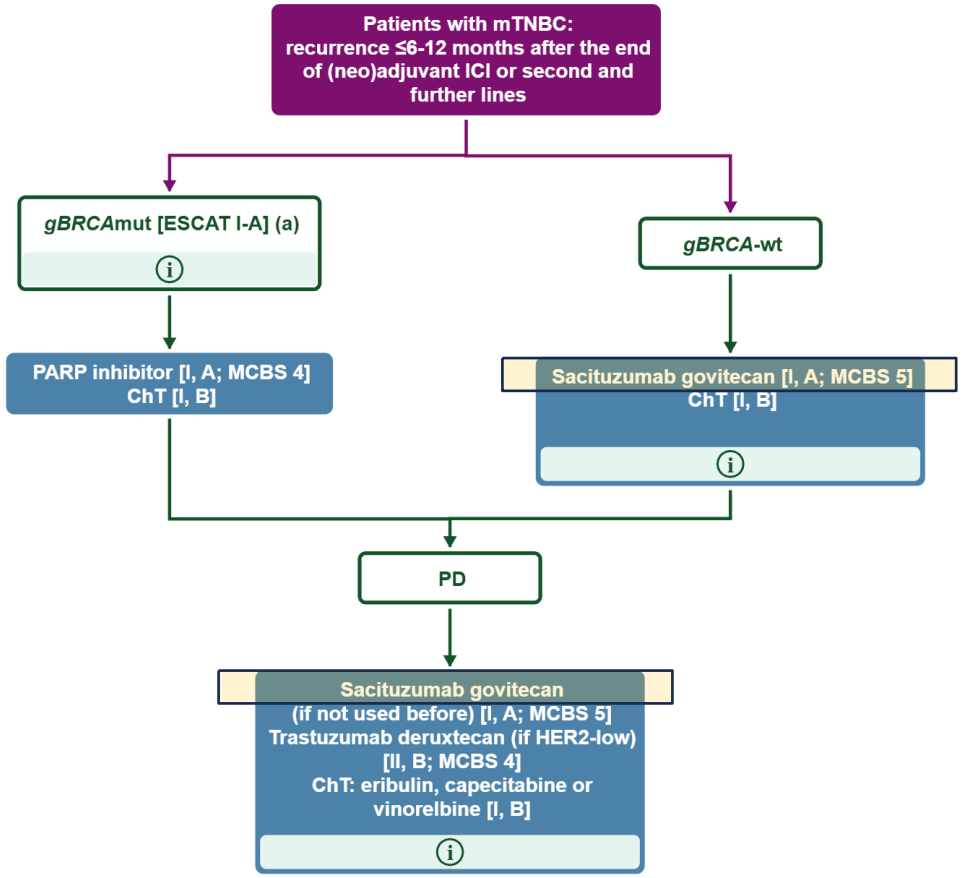
Sacituzumab govitecan linker-payload

– DAR 7.6



ESCENARIO ACTUAL





2ª LÍNEA: ASCENT

The NEW ENGLAND JOURNAL of MEDICINE

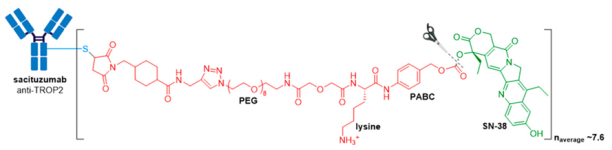
ORIGINAL ARTICLE

Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer

A. Bardia, S.A. Hurvitz, S.M. Tolaney, D. Loirat, K. Punie, M. Oliveira, A. Brufsky, S.D. Sardesai, K. Kalinsky, A.B. Zelnak, R. Weaver, T. Traina, F. Dalenc, P. Aftimos, F. Lynce, S. Diab, J. Cortés, J. O'Shaughnessy, V. Diéras, C. Ferrario, P. Schmid, L.A. Carey, L. Gianni, M.J. Piccart, S. Loibl, D.M. Goldenberg, Q. Hong, M.S. Olivo, L.M. Itri, and H.S. Rugo, for the ASCENT Clinical Trial Investigators*

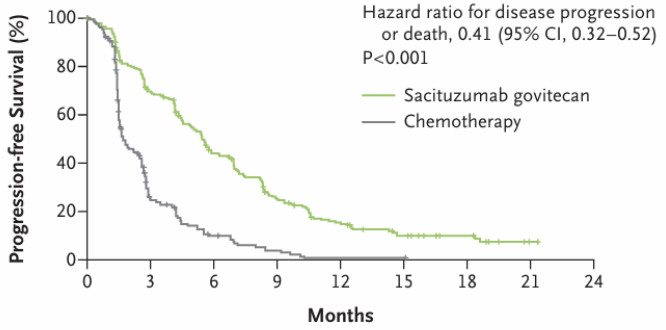
Sacituzumab govitecan linker-payload

– DAR 7.6



A Progression-free Survival among Patients without Brain Metastases

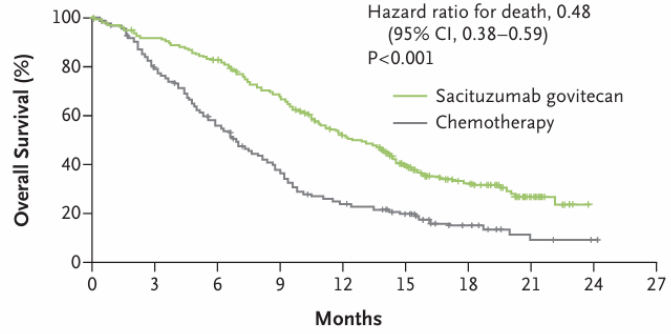
	No. of Patients	No. of Events	Median Progression-free Survival (mo (95% CI))
Sacituzumab Govitecan	235	166	5.6 (4.3–6.3)
Chemotherapy	233	150	1.7 (1.5–2.6)



No. at Risk								
Sacituzumab govitecan	235	154	91	49	28	15	9	1
Chemotherapy	233	39	14	5	1	1	0	0

B Overall Survival among Patients without Brain Metastases

	No. of Patients	No. of Events	Median Overall Survival (mo (95% CI))
Sacituzumab Govitecan	235	155	12.1 (10.7–14.0)
Chemotherapy	233	185	6.7 (5.8–7.7)



No. at Risk									
Sacituzumab govitecan	235	214	190	153	107	70	37	13	0
Chemotherapy	233	173	117	74	45	30	11	3	1

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Table 2. Summary of Treatment Efficacy, as Determined by Independent Central Review.*

Variable	Patients without Brain Metastases		Full Population†	
	Sacituzumab Govitecan (N=235)	Chemotherapy (N=233)	Sacituzumab Govitecan (N=267)	Chemotherapy (N=262)
Median progression-free survival (95% CI) — mo	5.6 (4.3–6.3)	1.7 (1.5–2.6)	4.8 (4.1–5.8)	1.7 (1.5–2.5)
Hazard ratio for disease progression or death (95% CI)	0.41 (0.32–0.52)‡		0.43 (0.35–0.54)	
Median overall survival (95% CI) — mo	12.1 (10.7–14.0)	6.7 (5.8–7.7)	11.8 (10.5–13.8)	6.9 (5.9–7.7)
Hazard ratio for death (95% CI)	0.48 (0.38–0.59)‡		0.51 (0.41–0.62)	
Objective response — no. of patients (%)§	82 (35)	11 (5)	83 (31)	11 (4)
Complete response	10 (4)	2 (1)	10 (4)	2 (1)
Partial response	72 (31)	9 (4)	73 (27)	9 (3)
Clinical benefit — no. of patients (%)¶	105 (45)	20 (9)	108 (40)	21 (8)
Stable disease — no. of patients (%)	81 (34)	62 (27)	96 (36)	71 (27)
Stable disease for ≥6 mo	23 (10)	9 (4)	25 (9)	10 (4)
Progressive disease — no. of patients (%)	54 (23)	89 (38)	65 (24)	100 (38)
Response could not be evaluated — no. of patients (%)‖	18 (8)	71 (30)	23 (9)	80 (31)
Median time to response (95% CI) — mo	1.5 (0.7–10.6)	1.5 (1.3–4.2)	1.5 (0.7–10.6)	1.5 (1.3–4.2)
Median duration of response (95% CI) — mo	6.3 (5.5–9.0)	3.6 (2.8–NE)	6.3 (5.5–9.0)	3.6 (2.8–NE)
Hazard ratio (95% CI)	0.39 (0.14–1.07)			

Table 3. Summary of Treatment-Related Adverse Events in the Safety Population.*

Adverse Event	Sacituzumab Govitecan (N=258)			Chemotherapy (N=224)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	252 (98)	117 (45)	48 (19)	192 (86)	71 (32)	33 (15)
Hematologic event						
Neutropenia†	163 (63)	88 (34)	44 (17)	96 (43)	45 (20)	29 (13)
Anemia‡	89 (34)	20 (8)	0	54 (24)	11 (5)	0
Leukopenia§	41 (16)	23 (9)	3 (1)	25 (11)	10 (4)	2 (1)
Thrombocytopenia¶	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
Gastrointestinal event						
Diarrhea	153 (59)	27 (10)	0	27 (12)	1 (<1)	0
Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
Vomiting	75 (29)	2 (1)	1 (<1)	23 (10)	1 (<1)	0
Constipation	44 (17)	0	0	32 (14)	0	0
Abdominal pain	29 (11)	3 (1)	0	9 (4)	1 (<1)	0
General disorders and administration-site conditions						
Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0
Asthenia	31 (12)	2 (1)	0	23 (10)	3 (1)	0
Skin and subcutaneous disorders: alopecia‖	119 (46)	0	0	35 (16)	0	0
Metabolism and nutrition disorders: decreased appetite	51 (20)	4 (2)	0	32 (14)	1 (<1)	0
Nervous system disorders**††	64 (25)	1 (<1)	0	53 (24)	5 (2)	0
Respiratory, thoracic, and mediastinal disorders††	41 (16)	5 (2)‡‡	0	17 (8)	1 (<1)	0
Musculoskeletal and connective-tissue disorders††	32 (12)	0	0	28 (12)	3 (1)	0
Infections and infestations††	30 (12)	6 (2)	1 (<1)	22 (10)	4 (2)	3 (1)

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ESCENARIO PREVISIBLE

National Comprehensive Cancer Network®

CYTOTOXIC REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[a]

HR-Negative and HER2-Negative (Triple-Negative Breast Cancer; TNBC)		
See BINV-Q 1 of 15 for Considerations for systemic therapy.		
Setting	**Subtype/Biomarker**	**Regimen**
First Line	PD-L1 CPS ≥10[i] regardless of germline *BRCA1/2* PV status[b]	• Chemotherapy (Albumin-bound Paclitaxel, Carboplatin/Gemcitabine, or Paclitaxel,)[j] + Pembrolizumab (category 1, preferred) • Sacituzumab govitecan-hziy + Pembrolizumab (preferred)
	PD-L1 CPS <10[i] and no germline *BRCA1/2* PV[b]	• Sacituzumab govitecan-hziy (category 1, preferred)[k] • Datopotamab deruxtecan-dlnk (other recommended) • Systemic chemotherapy BINV-Q 5 of 15
	PD-L1 CPS <10[i] and germline *BRCA1/2* PV[b]	• PARPi (Olaparib or Talazoparib) (category 1, preferred) • Platinum (Carboplatin or Cisplatin) (category 1, preferred)
Second Line	Germline *BRCA1/2* PV[b]	PARPi (category 1, preferred)
	Any	Sacituzumab govitecan-hziy[l] (category 1, preferred)
		Systemic chemotherapy BINV-Q 5 of 15 or targeted agents BINV-Q 7 of 15
	No germline *BRCA1/2* PV[b] and HER2 (*ERBB2*) IHC 1+ or 2+/ISH negative[d]	Fam-trastuzumab deruxtecan-nxki[m] (other recommended)
Third Line and Beyond	Biomarker positive (ie, MSI-H, *NTRK1/2/3* and *RET* gene fusions, TMB-H)	Targeted agents and emerging biomarker options BINV-Q 7 of 15 and BINV-Q 8 of 15
	Any	Systemic chemotherapy BINV-Q 5 of 15

1ª LÍNEA PD-L1 POSITIVO: ASCENT-04

The NEW ENGLAND JOURNAL of MEDICINE

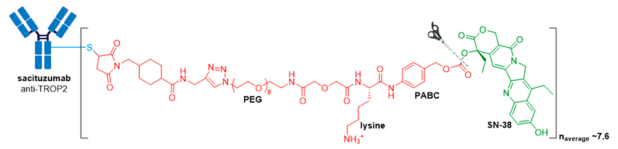
ORIGINAL ARTICLE

Sacituzumab Govitecan plus Pembrolizumab for Advanced Triple-Negative Breast Cancer

S.M. Tolaney,[1] E. de Azambuja,[2] K. Kalinsky,[3] S. Loi,[4] S.-B. Kim,[5] C. Yam,[6] B. Rapoport,[7,8] S.-A. Im,[9] B. Pistilli,[10] W. Mchayleh,[11] D.W. Cescon,[12] J. Watanabe,[13] M.A.L. Bañuelas,[14] R. Freitas-Junior,[15] J. Salvador Bofill,[16] M. Afshari,[17] D. Gary,[17] L. Wang,[17] C. Lai,[17] and P. Schmid,[18] for the ASCENT-04/KEYNOTE-D19 Clinical Trial Investigators*

Sacituzumab govitecan linker-payload

– DAR 7.6



ASCENT-04/KEYNOTE-D19 Study Design

Previously untreated, locally advanced unresectable, or metastatic TNBC[a]:

- PD-L1-positive (CPS ≥ 10 by the 22C3 assay[b])
- ≥ 6 months since treatment in curative setting (prior anti-PD-[L]1 use allowed)

N = 443

R 1:1

SG + pembro[d]
(SG 10 mg/kg IV, days 1 and 8 of 21-day cycles; pembro 200 mg, day 1 of 21-day cycles)
n = 221

Chemo* + pembro[d]
(paclitaxel 90 mg/m² OR nab-paclitaxel 100 mg/m² on days 1, 8, & 15 of 28-day cycles, OR gemcitabine 1000 mg/m² + carboplatin AUC 2 on days 1 & 8 of 21-day cycles; pembro 200 mg on day 1 of 21-day cycles)
n = 222

Eligible patients who experienced BICR-verified disease progression were offered to cross-over to receive 2L SG monotherapy

All treatment, including SG or chemo, was continued until BICR-verified disease progression or unacceptable toxicity

End points

Primary
- PFS by BICR[e]

Secondary
- OS
- ORR, DOR by BICR[e]
- Safety
- QoL

Stratification factors:
- De novo mTNBC[c] vs recurrent within 6 to 12 months from completion of treatment in curative setting vs recurrent > 12 months from completion of treatment in curative setting
- US/Canada/Western Europe vs the rest of the world
- Prior exposure to anti-PD-(L)1 (yes vs no)

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1ª LÍNEA PD-L1 POSITIVO: ASCENT-04

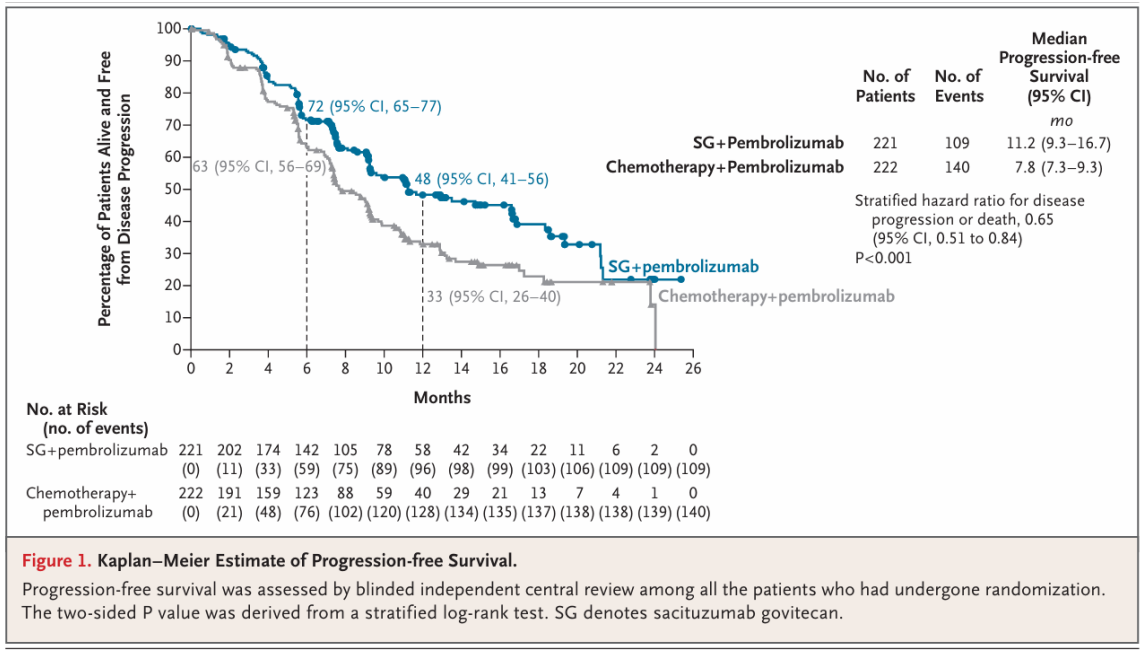
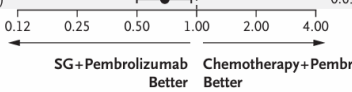


Figure 1. Kaplan–Meier Estimate of Progression-free Survival.

Progression-free survival was assessed by blinded independent central review among all the patients who had undergone randomization. The two-sided P value was derived from a stratified log-rank test. SG denotes sacituzumab govitecan.

Subgroup	No. of Patients: SG+ Pembrolizumab	No. of Patients: Chemotherapy+ Pembrolizumab	Median Progression-free Survival (95% CI) mo: SG+ Pembrolizumab	Median Progression-free Survival (95% CI) mo: Chemotherapy+ Pembrolizumab	Unstratified Hazard Ratio for Disease Progression or Death (95% CI)
Intention-to-treat population	221	222	11.2 (9.3–16.7)	7.8 (7.3–9.3)	0.66 (0.51–0.85)
Age					
<65 yr	163	165	11.3 (9.3–16.8)	7.5 (7.0–9.2)	0.61 (0.45–0.82)
≥65 yr	58	57	11.1 (7.5–NR)	9.3 (7.3–13.2)	0.85 (0.52–1.39)
ECOG performance-status score					
0	156	154	12.9 (9.3–16.8)	8.7 (7.3–9.9)	0.65 (0.48–0.88)
≥1	65	67	9.2 (7.5–18.3)	7.5 (5.6–9.3)	0.66 (0.43–1.03)
Geographic region					
Canada, the United States, or western Europe	85	85	11.7 (7.5–19.4)	7.4 (5.7–9.9)	0.65 (0.43–0.98)
Rest of the world	136	137	11.2 (9.3–16.7)	8.4 (7.4–9.3)	0.66 (0.48–0.91)
Disease status					
Metastatic at initial diagnosis	75	75	8.1 (7.3–18.6)	7.7 (6.1–11.9)	0.89 (0.59–1.34)
Recurrent, 6–12 mo after completion of curative-intent treatment	40	40	9.9 (5.7–16.8)	7.2 (4.4–9.1)	0.62 (0.36–1.08)
Recurrent, >12 mo after completion of curative-intent treatment	106	107	16.6 (11.0–NR)	8.7 (7.3–10.8)	0.52 (0.35–0.76)
Previous anti–PD-1 or anti–PD-L1 therapy					
Yes	9	11	7.5 (0.9–NR)	6.6 (2.1–NR)	1.08 (0.31–3.75)
No	212	211	11.7 (9.3–16.8)	7.8 (7.4–9.3)	0.65 (0.50–0.84)
Chemotherapy selected before randomization					
Taxane	116	114	11.1 (8.6–16.7)	9.2 (7.2–12.9)	0.82 (0.58–1.17)
Gemcitabine–carboplatin	105	108	11.3 (9.2–21.2)	7.4 (6.9–9.0)	0.52 (0.36–0.75)
Race					
White	139	118	11.1 (9.2–21.2)	7.7 (6.9–10.8)	0.66 (0.47–0.93)
Asian	43	63	16.7 (7.5–NR)	8.7 (7.2–9.9)	0.57 (0.33–0.99)
Other	35	28	11.3 (7.4–16.6)	6.0 (3.8–7.5)	0.38 (0.20–0.69)
History of liver metastasis					
Yes	55	57	7.3 (5.5–9.3)	5.6 (5.4–8.5)	0.84 (0.53–1.32)
No	166	165	16.6 (11.1–21.2)	9.0 (7.4–9.9)	0.59 (0.44–0.80)
History of brain metastasis					
Yes	8	6	5.7 (0.5–NR)	3.7 (1.3–NR)	0.64 (0.19–2.14)
No	213	216	11.7 (9.3–16.8)	8.4 (7.4–9.3)	0.65 (0.50–0.84)
Menopausal status					
Premenopausal	81	77	9.3 (7.4–19.4)	7.4 (5.6–9.3)	0.62 (0.41–0.94)
Postmenopausal	140	145	12.9 (9.3–18.3)	8.4 (7.4–10.8)	0.69 (0.50–0.94)



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1ª LÍNEA PD-L1 POSITIVO: ASCENT-04

Figure 1. Exposure-Adjusted Incidence Rates

TEAEs	SG + Pembro (n = 221) n (%)	SG + Pembro (n = 221) EAIR (95% CI)	Chemo + Pembro (n = 220) n (%)	Chemo + Pembro (n = 220) EAIR (95% CI)	EAIR Difference (95% CI)
Grade ≥ 3	158 (71)	2.19 (1.86, 2.56)	154 (70)	2.13 (1.81, 2.49)	0.06 (−0.43, 0.55)
Serious	84 (38)	0.59 (0.47, 0.73)	68 (31)	0.52 (0.41, 0.66)	0.06 (−0.12, 0.25)
Led to any dose interruption	171 (77)	2.75 (2.35, 3.19)	162 (74)	2.59 (2.21, 3.02)	0.16 (−0.43, 0.75)
Led to SG/chemo dose reduction	78 (35)	0.62 (0.49, 0.78)	96 (44)	0.94 (0.76, 1.14)	−0.31 (−0.56, −0.08)
Led to any treatment discontinuation	26 (12)	0.15 (0.10, 0.21)	68 (31)	0.53 (0.41, 0.67)	−0.38 (−0.53, −0.25)
Treatment-related, grade ≥ 3	149 (67)	1.95 (1.65, 2.29)	141 (64)	1.76 (1.48, 2.07)	0.20 (−0.24, 0.64)
Treatment-related, serious	61 (28)	0.41 (0.31, 0.52)	42 (19)	0.29 (0.21, 0.40)	0.11 (−0.03, 0.25)
Neutropenia[a]	143 (65)	2.13 (1.79, 2.51)	132 (60)	1.77 (1.48, 2.10)	0.36 (−0.11, 0.84)
Anemia[b]	81 (37)	0.62 (0.49, 0.77)	112 (51)	1.21 (0.99, 1.45)	−0.59 (−0.86, −0.33)
Thrombocytopenia[c]	10 (5)	0.06 (0.03, 0.10)	63 (29)	0.49 (0.38, 0.63)	−0.44 (−0.58, −0.31)
Diarrhea	155 (70)	2.05 (1.74, 2.40)	63 (29)	0.53 (0.41, 0.68)	1.52 (1.18, 1.89)
Colitis[d]	13 (6)	0.07 (0.04, 0.13)	3 (1)	0.02 (0.00, 0.06)	0.05 (0.00, 0.11)
Nausea	150 (68)	1.94 (1.64, 2.28)	83 (38)	0.78 (0.62, 0.97)	1.16 (0.81, 1.53)
Pneumonitis[e]	6 (3)	0.03 (0.01, 0.07)	17 (8)	0.11 (0.06, 0.18)	−0.08 (−0.15, −0.02)
Fatigue[f]	129 (58)	1.51 (1.26, 1.79)	123 (56)	1.55 (1.29, 1.85)	−0.04 (−0.43, 0.35)
Peripheral neuropathy	15 (7)	0.09 (0.05, 0.14)	46 (21)	0.35 (0.26, 0.47)	−0.26 (−0.39, −0.15)

Table 1. Pembrolizumab TEAEs of Special Interest[a]

AEOSI Category, n (%)	SG + Pembro (n = 221)		Chemo + Pembro (n = 220)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Hypothyroidism	16 (7)	1 (< 1)	35 (16)	0
Colitis	13 (6)	4 (2)	3 (1)	1 (< 1)
Infusion reactions	11 (5)	3 (1)	19 (9)	5 (2)
Hyperthyroidism	8 (4)	0	14 (6)	0
Pneumonitis	6 (3)	4 (2)	17 (8)	3 (1)

Kalinsky et al. SABCS 2025

1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: ASCENT-03

Objective

- To evaluate the efficacy and safety of sacituzumab govitecan compared with chemotherapy in previously untreated patients with advanced inoperable/metastatic TNBC who are unable to receive PD-(L)1i

Key inclusion criteria

- Previously untreated, locally advanced inoperable or mTNBC*
- Not candidates for PD-(L)1i:
  - PD-L1-† tumors (CPS <10)
  - PD-L1+† tumors (CPS ≥10) and previously treated with a PD-(L)1i in a curative setting
  - Ineligible for PD-(L)1i due to comorbidity
- ≥6 months since treatment in curative setting
- Previously treated, stable CNS metastases were allowed

(N=558)

R 1:1

Sacituzumab govitecan
10 mg/kg IV D1 & 8 of 21-day cycles
(n=279)

Stratification factors
- United States/Canada/Western Europe vs rest of world
- De novo mTNBC (<35%) vs recurrent within 6–12 mo of treatment vs recurrent after >12 mo from treatment in a curative setting

Chemotherapy
Paclitaxel 90 mg/m^2 OR nab-paclitaxel 100 mg/m^2 D1, 8, and 15 of 28-day cycles OR gemcitabine 1000 mg/m^2 + carboplatin AUC2 D1 & 8 of 21-day cycles
(n=279)

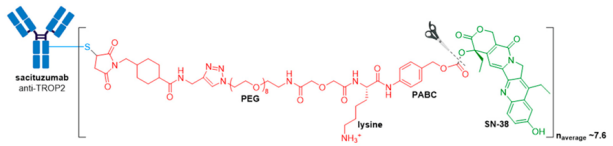
Treatment continued until BICR-verified progression or unacceptable toxicity

Primary endpoint
- PFS (BICR)‡

Secondary endpoints
- OS, ORR, DoR, TTR (BICR), QoL, safety

*TNBC status was centrally confirmed and determined according to standard ASCO-CAP criteria.
†PD-L1 CPS was centrally confirmed and defined using PD-L1 IHC 22C3 assay (Dako, Agilent Technologies). ‡Per-RECIST v1.1.
Cortés JC, et al. Ann Oncol 2025;36(suppl):Abstract LBA20.

Sacituzumab govitecan linker-payload
– DAR 7.6



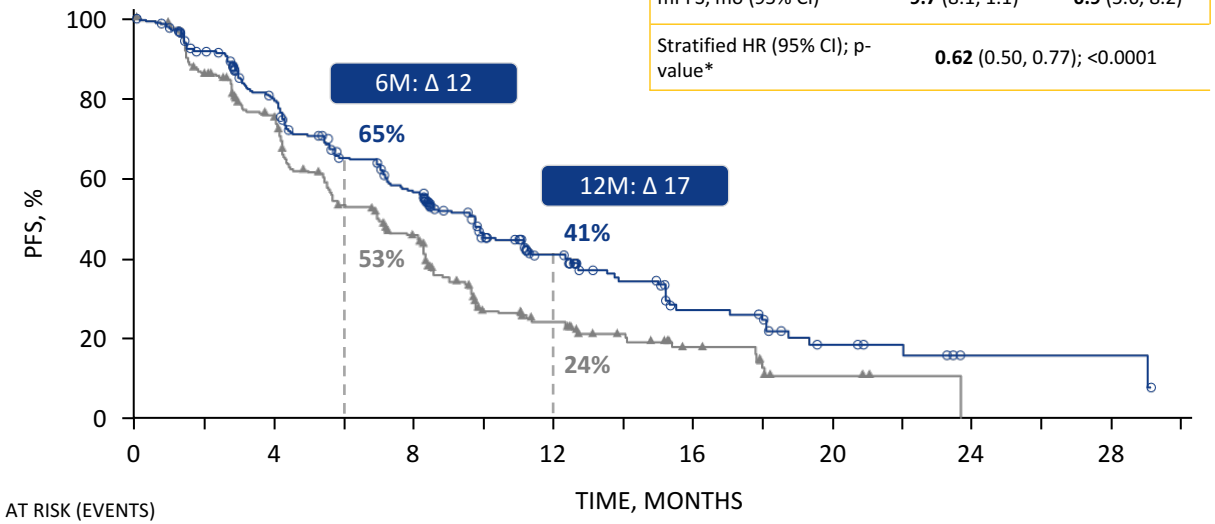
CROSSOVER PERMITIDO!!

Cortés et al. NEJM 2025

1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: ASCENT-03

PFS (BICR)

	SG (n=279)	Chemo (n=279)
mPFS, mo (95% CI)	**9.7** (8.1, 1.1)	**6.9** (5.6, 8.2)
Stratified HR (95% CI); p-value*	**0.62** (0.50, 0.77); <0.0001	

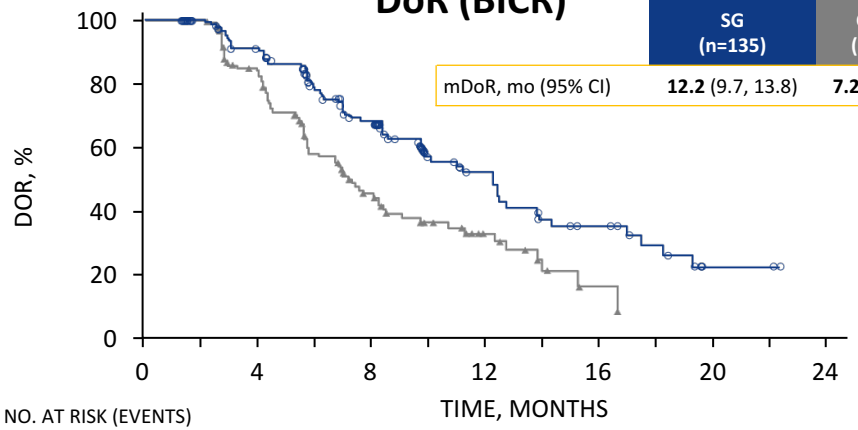


NO. AT RISK (EVENTS)

SG	279 (0)	238 (22)	199 (53)	153 (88)	128 (108)	84 (131)	60 (138)	38 (146)	23 (153)	20 (154)	10 (159)	7 (159)	2 (160)	2 (160)	2 (160)	0 (162)
Chemo	279 (0)	226 (37)	186 (65)	126 (118)	100 (135)	44 (172)	35 (176)	21 (180)	12 (183)	7 (186)	3 (187)	1 (187)	2 (188)			

DoR (BICR)

	SG (n=135)	Chemo (n= 127)
mDoR, mo (95% CI)	**12.2** (9.7, 13.8)	**7.2** (5.7, 8.4)



NO. AT RISK (EVENTS)

SG	135 (0)	128 (0)	113 (12)	86 (27)	66 (37)	36 (46)	28 (49)	18 (57)	15 (58)	9 (60)	3 (62)	3 (62)	0 (62)
Chemo	127 (0)	125 (0)	94 (21)	59 (48)	38 (60)	22 (67)	13 (69)	6 (73)	2 (74)	0 (75)			

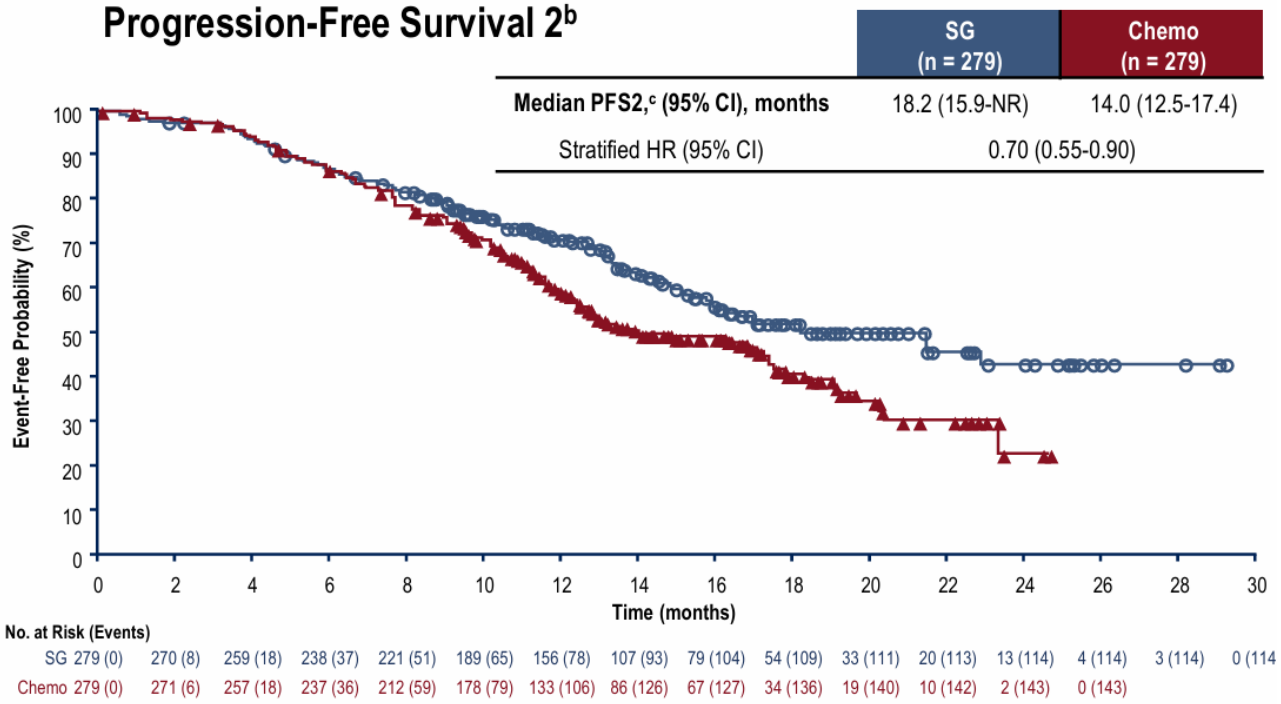
Tumor response	SG (n=279)	Chemo (n=279)
ORR, % (95% CI)	48 (42, 54)	46 (40, 52)
Odds ratio (95% CI)	1.1 (0.8, 1.6)	
BOR, n (%)		
CR	20 (7)	15 (5)
PR	115 (41)	112 (40)
SD	113 (41)	101 (36)
PD	14 (5)	36 (13)
NE	17 (6)	15 (5)

Cortés et al. NEJM 2025

1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: ASCENT-03

- **Overall survival not yet mature[a]**
- Study continues to first formal OS analysis
- Of 179 patients who initiated subsequent treatment after chemo, 147 (82%) received SG

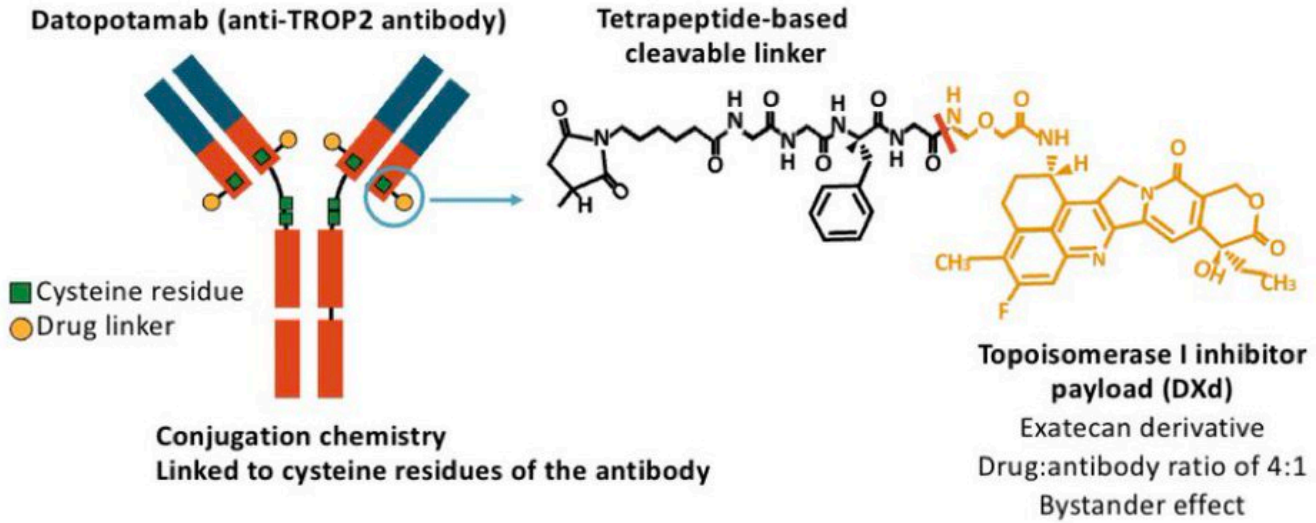
Overall survival	SG (n = 279)	Chemo (n = 279)
Number of events, %	103 (37)	103 (37)
Median (95% CI) , months	21.5 (17.7-NR)	20.2 (18.2-NR)
Stratified HR (95% CI)	0.98 (0.75-1.30)	
OS rate (95% CI), %		
12-month	75 (70-80)	73 (67-78)
24-month	46 (36-56)	42 (29-54)



At the time of primary analysis, overall survival was immature and PFS2 was longer with SG vs chemo by investigator assessment

Cortés et al. ESMO 2025

DATOPOTAMAB-DERUXTECÁN



1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: TROPION-BREAST02

Objective

- To determine the efficacy and safety of 1L Dato-DXd vs chemotherapy in patients with locally recurrent inoperable or metastatic TNBC for whom immunotherapy is not an option

Key inclusion criteria

- Histologically/cytologically documented locally recurrent inoperable/metastatic TNBC
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy is not an option
- No minimum DFI
- ECOG PS 0–1

(N=644)

R 1:1

Dato-DXd
6mg/kg IV, Day 1 q3w
(n=323)

Stratification
- Geographic region
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])‡
- DFI history (de novo vs prior DFI 0–12 mo vs prior DFI >12 mo)§

Investigators choice of chemotherapy (ICC)*
Paclitaxel, nab-paclitaxel, capecitabine, eribulin mesylate/eribulin, carboplatin
(n=321)

Treatment continued until PD or unacceptable toxicity (or another discontinuation criterion)

Dual primary endpoints
- OS and PFS (BICR per RECIST v1.1)

Secondary endpoints
- PFS (INV), ORR, DOR, safety

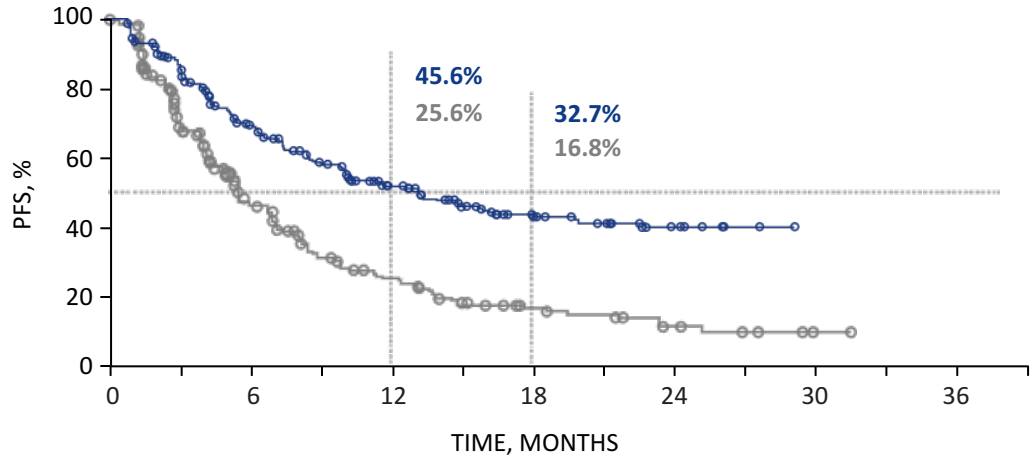
CROSSOVER NO PERMITIDO!!

Dent et al. ESMO 2025

1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: TROPION-BREAST02

Progression-free survival (BICR)

	Dato-DXd (n=323)	ICC (n=321)
Events, n (%)	199 (62)	209 (65)
mPFS, mo (95% CI)	**10.8** (8.6, 13.0)	**5.6** (5.0, 7.0)
HR (95% CI); p-value	**0.57** (0.47, 0.69); <0.0001	

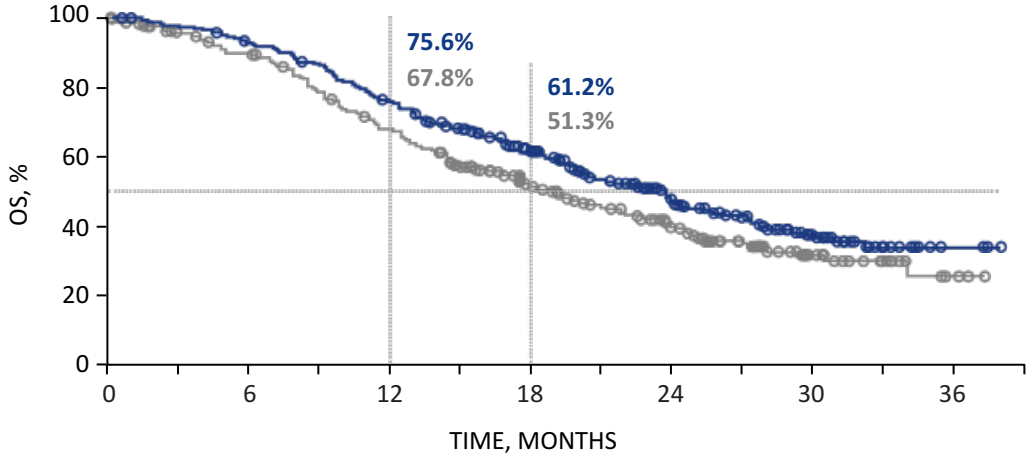


NO. AT RISK

Dato-DXd	323	265	191	150	116	84	56	41	24	20	10	5	1	0
ICC	321	191	107	64	46	29	19	16	8	6	1	0	0	0

Overall survival

	Dato-DXd (n=323)	ICC (n=321)
Events, n (%)	168 (52)	181 (56)
mOS, mo (95% CI)	**23.7** (19.8, 25.6)	**18.7** (16.0, 21.8)
HR (95% CI); p-value	**0.79** (0.64, 0.98); 0.0291	



NO. AT RISK

Dato-DXd	323	311	291	272	235	201	157	122	86	64	37	14	3	0
ICC	321	290	268	231	199	158	122	93	70	48	27	12	4	0

Dent et al. ESMO 2025

1ª LÍNEA PD-L1 NEGATIVO/INELEGIBLE: TROPION-BREAST02

TRAEs, n (%)	Dato-DXd (n=319)	ICC (n=309)
Any grade	296 (93)	257 (83)
Grade ≥3	105 (33)	89 (29)
Serious	29 (9)	26 (8)
Led to dose interruption	76 (24)	60 (19)
Led to dose reduction	85 (27)	56 (18)
Led to discontinuation	14 (4)	23 (7)

Treatment-related AESI category, n (%) Preferred term	Dato-DXd (n=319)			ICC (n=309)		
	Grade 1	Grade 2	Grade ≥3	Grade 1	Grade 2	Grade 3
Oral mucositis/stomatitis	78 (24)	87 (27)	27 (8)	22 (7)	8 (3)	0
Stomatitis	72 (23)	83 (26)	27 (8)	19 (6)	8 (3)	0
Ocular surface events*	76 (24)	50 (16)	23 (7)	9 (3)	5 (2)	1 (<1)
Dry eye	51 (16)	21 (7)	4 (1)	6 (2)	3 (1)	0
Keratitis	21 (7)	14 (4)	7 (2)	1 (<1)	0	0
Conjunctivitis	7 (2)	13 (4)	1 (<1)	0	0	0
Adjudicated drug-related ILD/pneumonitis	1 (<1)	7 (2)	1 (<1)†	1 (<1)	1 (<1)	0

Conclusions

In patients with locally recurrent inoperable/metastatic TNBC, Dato-DXd significantly improved PFS and OS vs ICC and had a manageable safety profile with similar rates of serious treatment-related adverse events observed in both treatment arms

Dent et al. ESMO 2025

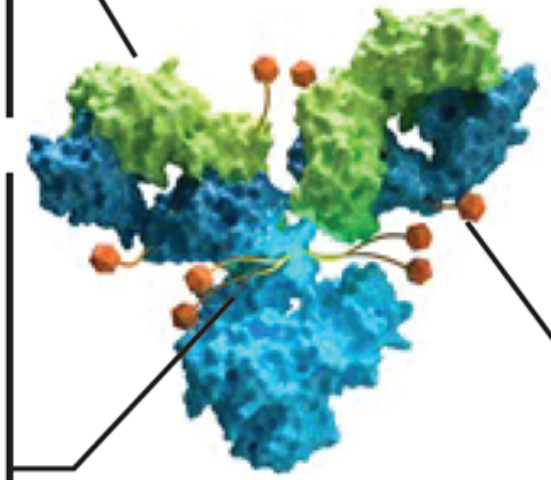
¿QUÉ VIENE?

SACITUZUMAB-TIMUROTECÁN (SAC-TMT)

Design of sac-TMT

Antibody
- hRS7, a recombinant humanized anti-TROP2 antibody with high affinity

Linker
- **Kthiol conjugation:** irreversible coupling to improve stability of ADC
- **Payload release:** intracellular cleavage and extracellular hydrolysis in TME
- **Balanced stability:** balance between efficacy and safety to expand therapeutic window



Payload
- **Novel topo I inhibitor** (belotecan derivative), highly active
- Average **DAR: 7.4** (range: 7–8)
- **Bystander effect**
- Methylsulfonyl derivatization enhances linker stability and toxin permeability

SAC-TMT

▲ Recruiting
■ Active, not recruiting
● Not yet recruiting

Trial with Spanish sites

Precision Molecular Targeting

Tissue Targeting

Phase 1/2[1]

NCT04152499 ▲ MK-2870-001
Phase 2 cohort 1: sacituzumab tirumotecan in advanced TNBC
Phase 2 cohort 6: sacituzumab tirumotecan in HR+/HER2– advanced BC
Estimated Study Completion: July 2026*

Phase 2[1]

NCT05347134 ▲ OptiTROP-Breast05
Sacituzumab tirumotecan +/- KL-A167 in recurrent or metastatic HER2– BC
Estimated Study Completion: April 2031*

Phase 3[1]

NCT06312176 ▲ TroFuse-010
Sacituzumab tirumotecan or sacituzumab tirumotecan + pembrolizumab or treatment of physician's choice (paclitaxel or nab-paclitaxel or capecitabine or liposomal doxorubicin) in advanced HR+, HER2– BC
Estimated Study Completion: April 2031*

NCT06841354 ▲ TroFuse-011
Sacituzumab tirumotecan or sacituzumab tirumotecan + pembrolizumab or treatment of physician's choice (paclitaxel,nabpaclitaxel or gemcitabine + carboplatin) in TNBC with PD-L1 CPS <10
Estimated Study Completion: May 2030*

NCT06393374 ▲ TroFuse-012
Sacituzumab tirumotecan + pembrolizumab or treatment of physician's choice (pembrolizumab or pembrolizumab + capecitabine) in TNBC
Estimated Study Completion: December 2037*

NCT06966700 ▲ TroFuse-032
Sacituzumab tirumotecan + pembrolizumab, followed by carboplatin/paclitaxel + pembrolizumab vs chemotherapy + pembrolizumab in eTNBC & ERlow-/HER2-
Estimated Study Completion: February 2035*

NCT05347134 ■ OptiTROP-Breast01
Sacituzumab tirumotecan or treatment of physician's choice (eribulin, capecitabine, gemcitabine, or vinorelbine) in TNBC
Estimated Study Completion: March 2025*

SAC-TMT

OptiTROP-Breast01: Randomized, Controlled, Open-Label Phase III Study (NCT05347134)

Patients with locally recurrent or metastatic TNBC
- Relapsed or refractory to 2 or more prior chemotherapy regimens for unresectable, locally advanced or metastatic disease
  - For prior therapy, 1 could be in the (neo)adjuvant setting, provided progression occurred during treatment or within 12 months after treatment discontinuation
- Received taxane(s) in any setting

R 1:1

Sac-TMT, 5 mg/kg IV, every 2 weeks

Physician's choice of chemotherapy: eribulin, capecitabine, gemcitabine, or vinorelbine

Treatment until disease progression, unacceptable toxicity or any other reason for discontinuation

Endpoints[a]

Primary
- PFS by BICR

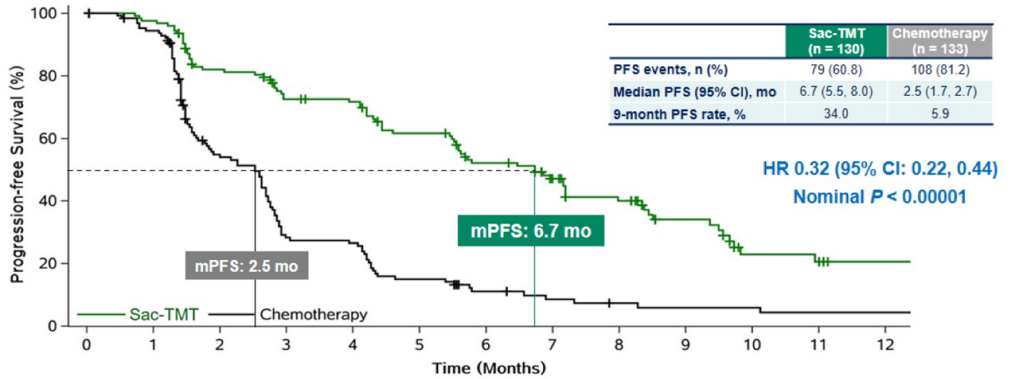
Secondary
- OS
- PFS by investigator assessment
- ORR, DOR
- Safety

Stratification factors
- Line of prior therapy (2–3 vs >3)
- Presence of liver metastases (yes vs no)

Tumor assessment
- Every 6 weeks for the first year and every 12 weeks afterward.

Progression-Free Survival by BICR (Final Analysis)

Sac-TMT significantly improved PFS over chemotherapy with a 68% lower risk of disease progression or death.



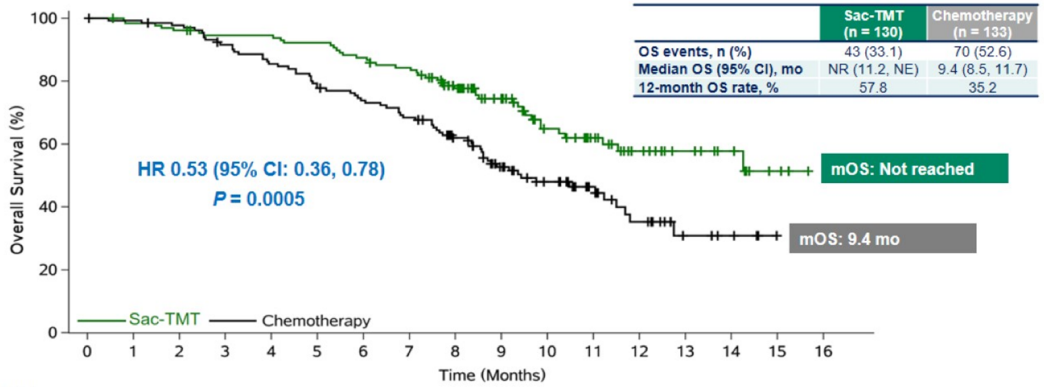
	Sac-TMT (n = 130)	Chemotherapy (n = 133)
PFS events, n (%)	79 (60.8)	108 (81.2)
Median PFS (95% CI), mo	6.7 (5.5, 8.0)	2.5 (1.7, 2.7)
9-month PFS rate, %	34.0	5.9

No. at Risk													
Sac-TMT	130	122	97	83	80	67	54	42	33	20	10	9	6
Chemotherapy	133	119	62	32	30	17	10	7	5	4	4	3	3

- PFS by investigator assessment (secondary endpoint): Median 6.5 *vs* 2.6 mo; HR 0.32 (95% CI: 0.24, 0.44)

Overall Survival (Interim Analysis)

Sac-TMT significantly improved OS over chemotherapy with a 47% lower risk of death.



	Sac-TMT (n = 130)	Chemotherapy (n = 133)
OS events, n (%)	43 (33.1)	70 (52.6)
Median OS (95% CI), mo	NR (11.2, NE)	9.4 (8.5, 11.7)
12-month OS rate, %	57.8	35.2

No. at Risk																
Sac-TMT	130	127	124	120	120	117	111	106	85	66	44	33	22	15	11	4	0
Chemotherapy	133	131	128	119	111	101	95	88	71	50	37	24	15	6	4	0	

- Efficacy boundary (corresponding to actual OS events of 113): 0.0042. The study crossed OS efficacy boundary.

Xu et al. ASCO 2024

SAC-TMT

2025 ASCO ANNUAL MEETING

Sacituzumab Tirumotecan (Sac-TMT) as First-line Treatment for Unresectable Locally Advanced/Metastatic Triple-negative Breast Cancer (a/m TNBC): Initial Results From the Phase II OptiTROP-Breast05 Study

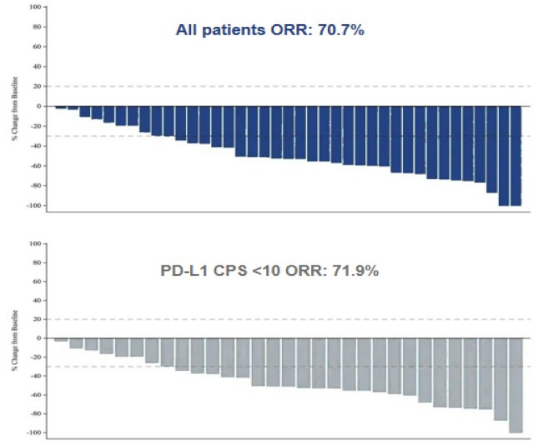
Yongmei Yin[1], Quchang Ouyang[2], Min Yan[3], Jian Zhang[4], Lihua Song[5], Wei Li[6], Yuanting Gu[7], Xiaoyu Liu[8], Jingfen Wang[9], Xiaojia Wang[10], Xi Yan[11], Jin Yang[12], Weipeng Zhao[13], Yuee Teng[14], Tingjing Yao[15], Zhengkui Sun[16], Xiaoping Jin[17], Yina Diao[17], Gesha Liu[17], Junyou Ge[17]

[1] Jiangsu Province Hospital, Nanjing, China; [2] Hunan Cancer Hospital, Changsha, China; [3] Henan Cancer Hospital, Zhengzhou, China; [4] Fudan University Cancer Hospital, Shanghai, China; [5] Shandong Cancer Hospital and Institute, Jinan, China; [6] The First Hospital of Jilin University, Changchun, China; [7] The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [8] Chongqing Cancer Hospital, Chongqing, China; [9] Linyi Cancer Hospital, Linyi, China; [10] Zhejiang Cancer Hospital, Hangzhou, China; [11] West China Hospital of Sichuan University, Chengdu, China; [12] The First Affiliated Hospital of Xi 'an Jiaotong University, Xi 'an, China; [13] Tianjin Cancer Hospital, Tianjin, China; [14] The First Hospital of China Medical University, Shenyang, China; [15] The First Affiliated Hospital of Bengbu Medical University, Bengbu, China; [16] Jiangxi Cancer Hospital, Nanchang, China;[17] Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China

Antitumor Responses

Antitumor Responses were observed regardless of PD-L1 expression.

	All patients (N = 41)	PD-L1 CPS <10[c] (N = 32)
ORR[a], n (%) (95% CI)	29 (**70.7**) (54.5, 83.9)	23 (**71.9**) (53.3, 86.3)
CR[b], n (%)	2 (4.9)	1 (3.1)
PR, n (%)	27 (65.9)	22 (68.8)
Confirmed PR, n (%)	24 (58.5)	19 (59.4)
SD, n (%)	9 (22.0)	7 (21.9)
DCR, n (%) (95% CI)	38 (**92.7**) (80.1, 98.5)	30 (**93.8**) (79.2, 99.2)

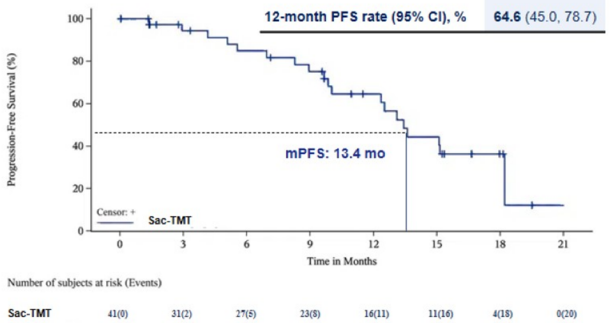


Data cutoff: Nov 18, 2024. **Median follow-up was 18.6 months.**
[a] Including confirmed PR/CR or response pending confirmation.
[b] All CRs were confirmed by investigators.
[c] PD-L1 expression was assessed at a central lab with PD-L1 IHC 22C3 pharmDx.
CR: complete response; PR: partial response; SD: stable disease.

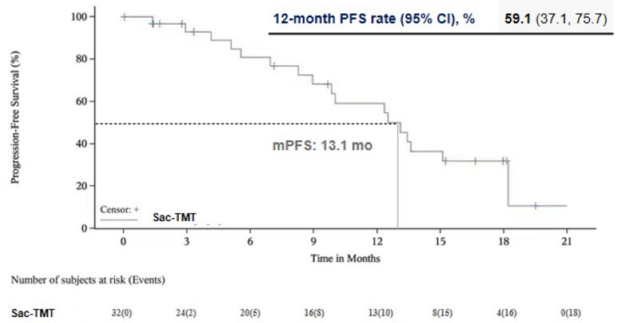
Progression-Free Survival

PFS benefits were observed regardless of PD-L1 expression.

	All patients (N = 41)
PFS events, n (%)	20 (48.8)
Median PFS, months (95% CI)	**13.4** (9.9, 18.2)
12-month PFS rate (95% CI), %	**64.6** (45.0, 78.7)



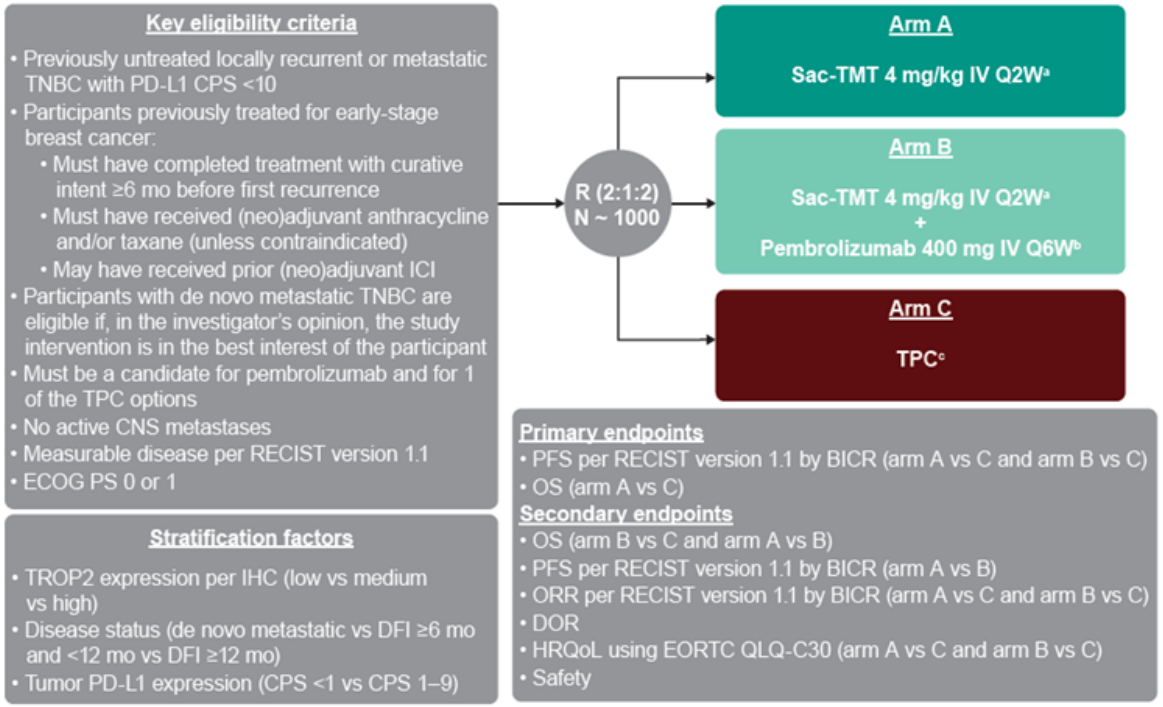
	PD-L1 CPS <10 (N = 32)
PFS events, n (%)	18 (56.3)
Median PFS, months (95% CI)	**13.1** (8.9, 18.2)
12-month PFS rate (95% CI), %	**59.1** (37.1, 75.7)



Yin et al. ASCO 2025

SAC-TMT

Study Design of TroFuse-011

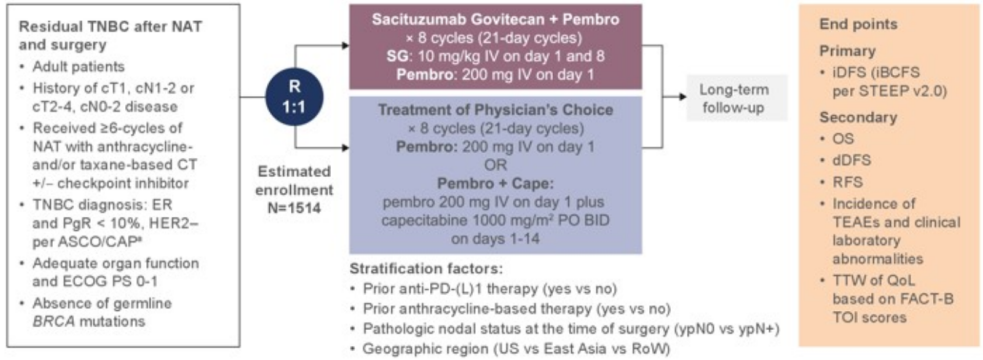


Rugo et al. ESMO 2025

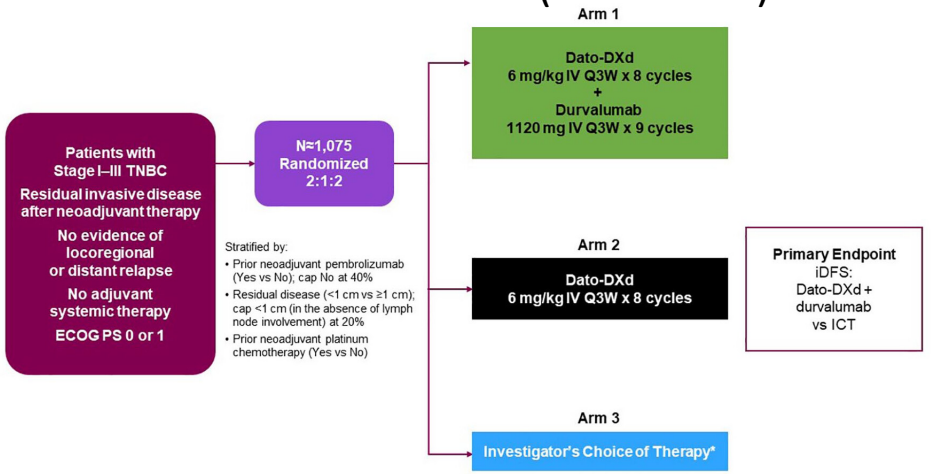
¿Y EN ENFERMEDAD PRECOZ?

ENSAYOS EN ENFERMEDAD RESIDUAL POST-NEO

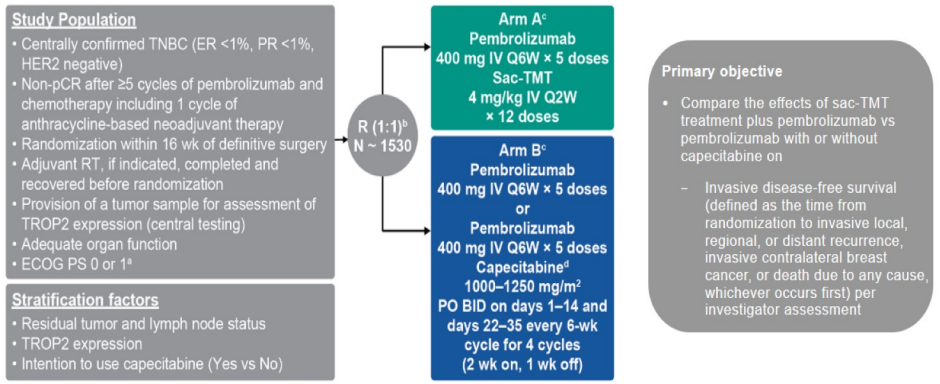
ASCENT-05 (SG)



TROPION-03 (DATO-DXD)

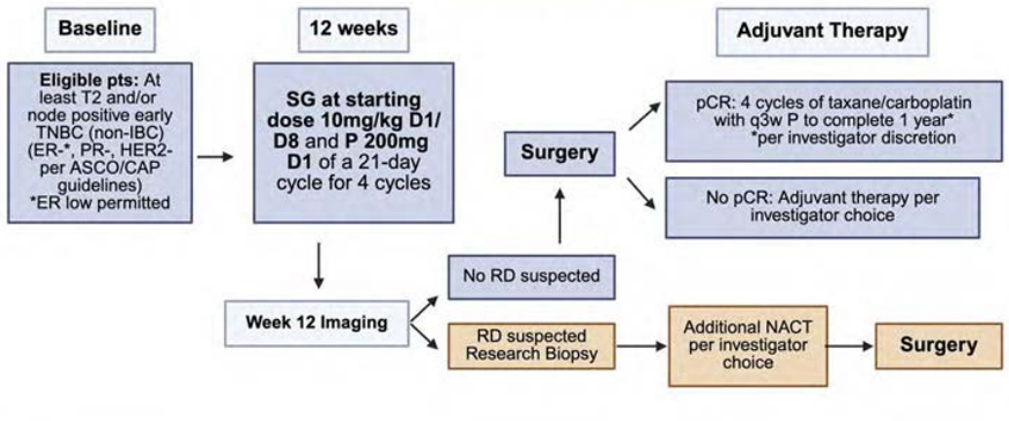


Study Design of TroFuse-012 (NCT06393374)

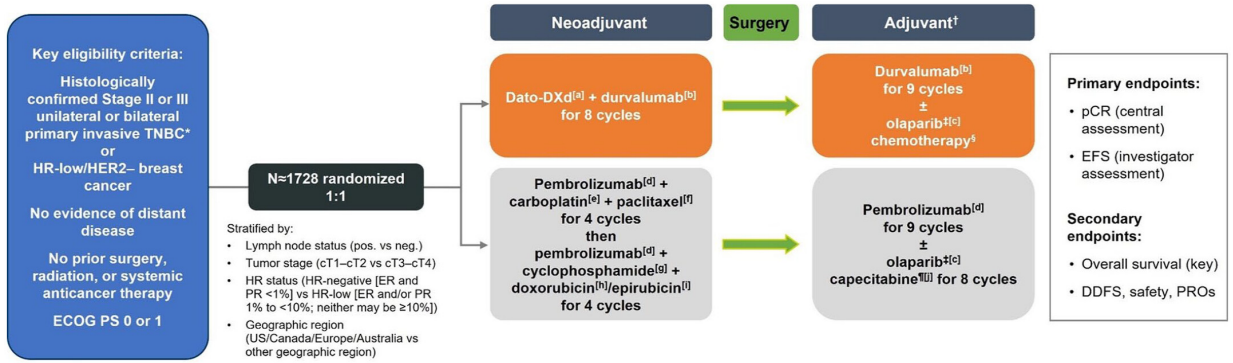


ENSAYOS EN NEOADYUVANCIA

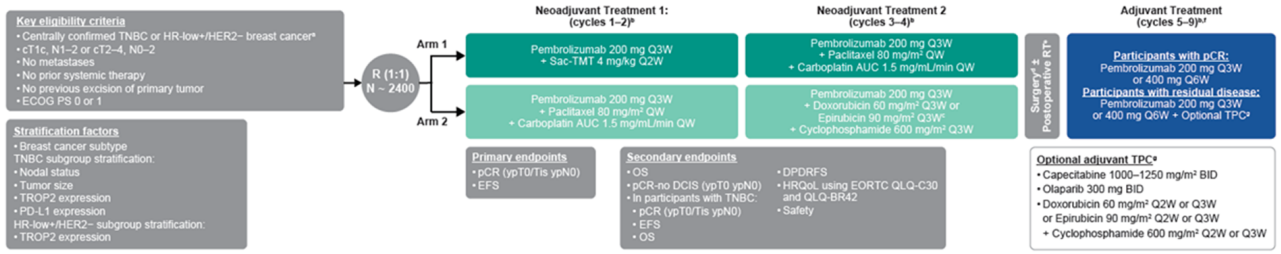
NEOSTAR (SG)



TROPION-BREAST04 (DATO-DXD)



Study Design of TroFuse-032



GRACIAS!

II JORNADA TRASLACIONAL DE ONCOLOGÍA DE PRECISIÓN: A TRAVÉS DE LAS VÍAS DE SEÑALIZACIÓN

SEVILLA, 6 Y 7 DE FEBRERO DE 2025