foro debate oncología

Zaragoza 26-29 septiembre 2023

Sacituzumab Govitecan

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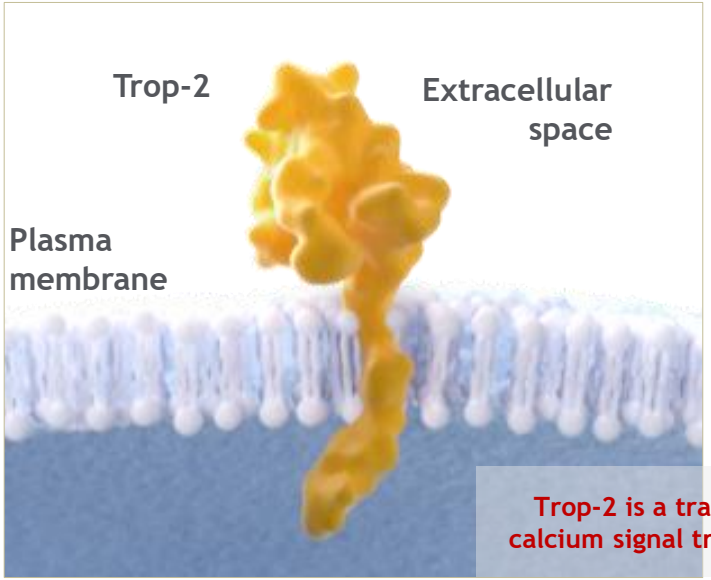
SACITUZUMAB GOVITECAN : Mas allá del ASCENT ….

- **INTRODUCCIÓN**
- **DATOS DE RWE**
- **NUEVAS INDICACIONES : TROPICS-02**
  Estudios en marcha
- **Mas allá del cáncer de mama.**

Trop-2 Protein Localized at the Cellular Membrane[1]



Strong IHC Staining (% of Normal vs Cancer Tissue)	
Breast	36% vs 62%[2]
Ovarian	15% vs 92%[3]
Colorectal	0% vs 21%[4]
Gastric	0% vs 22%[5]
Oral	0% vs 12%[6]
Pancreatic	0%[a] vs 29%[7]

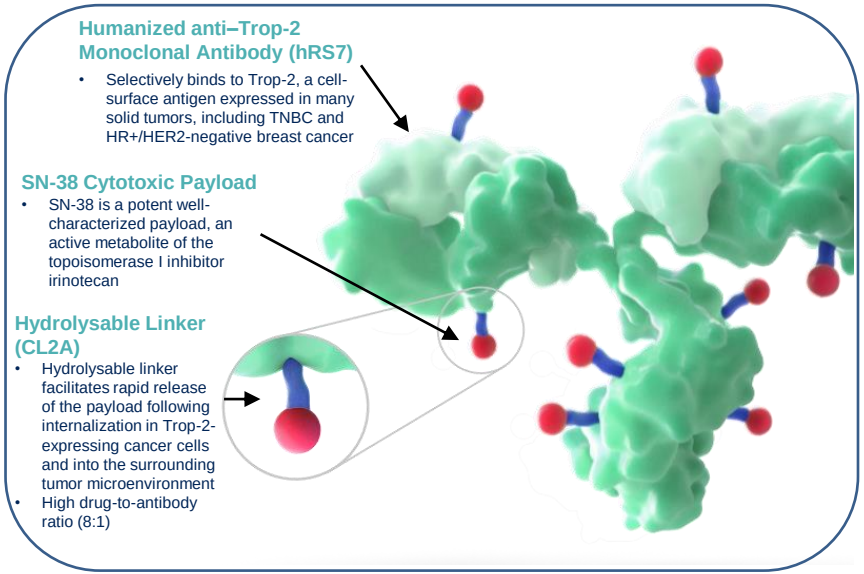
Trop-2 is a transmembrane glycoprotein expressed in various epithelial cancers as a tumor-associated calcium signal transducer that is functionally linked to cell migration and anchorage-independent growth[1]

- IHC, immunohistochemistry; Trop-2, trophoblast cell-surface antigen 2.

1. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512; 2. Zhao W, et al. *Oncol Rep*. 2018;40:759-766; 3. Bignotti E, et al. *Eur J Cancer*. 2010;46:944-953; 4. Ohmachi T, et al. *Clin Cancer Res*. 2006;12:3057-3063; 5. Mühlmann G, et al. *J Clin Pathol*. 2009;62:152-158; 6. Fong D, et al. *Mod Pathol*. 2008;21:186-191;
7. Fong D, et al. *Br J Cancer*. 2008;99:1290-1295.

Sacituzumab Govitecan Is a First-in-Class Trop-2–Directed Antibody-Drug Conjugate[1-5]

- Trop-2 is a transmembrane calcium signal transducer commonly expressed in multiple subtypes of breast cancer, and has been linked to tumor progression and poor outcomes[1,2]
- SG is a first-in-class Trop-2–directed ADC that selectively delivers SN-38, an active metabolite of irinotecan[3]
- SG is approved for 2L and later mTNBC in multiple countries.



2L, second line; ADC, antibody-drug conjugate; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor-positive; IC50, half maximal inhibitory concentration; mBC, metastatic breast cancer; mTNBC, metastatic triple-negative breast cancer; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

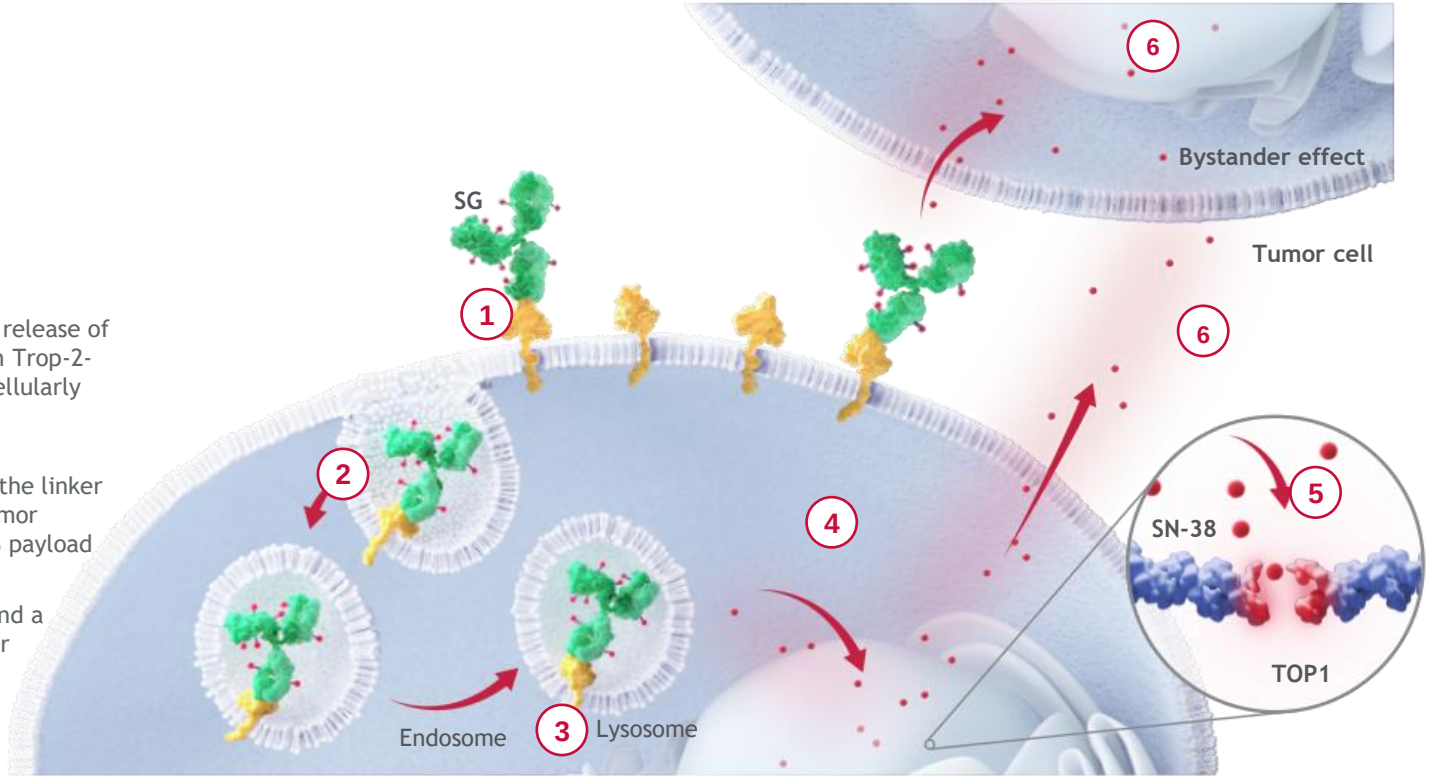
1. Ambrogi F, et al. PLoS One. 2014;9:e96993. 2. Trerotola M, et al. Oncogene. 2013;32(2):222-233. 3. Goldenberg DM, et al. Oncotarget. 2015;6:22496-22512. 4. Kopp A, et al. Mol Cancer Ther. 2023;22:102-111. 5. Brenner AJ, et al. Abstract presented at San Antonio Breast Cancer Symposium; December 8-11, 2020; Virtual. Abstract PD13-05.

SG Is a First-in-Class Trop-2-Directed ADC That Concentrates SN-38 Payload Intracellularly and in the Surrounding Tumor Microenvironment[a,1-3]

1) **Binding**
2) **Internalization**
3) **Intracellular trafficking**
4) **Lysosomal degradation**
5) **Cell cytotoxicity**
6) **Bystander effect**

- Rapid internalization and efficient release of the SN-38 payload intracellularly in Trop-2-expressing cancer cells and extracellularly into the surrounding tumor microenvironment[1-3]
- Before internalization of the ADC, the linker can be cleaved at the pH of the tumor microenvironment, releasing SN-38 payload outside the targeted tumor cell[2,3]
- DNA damage to the targeted cell and a bystander effect on adjacent tumor cells that may not express Trop-2[2]

Tumor cell



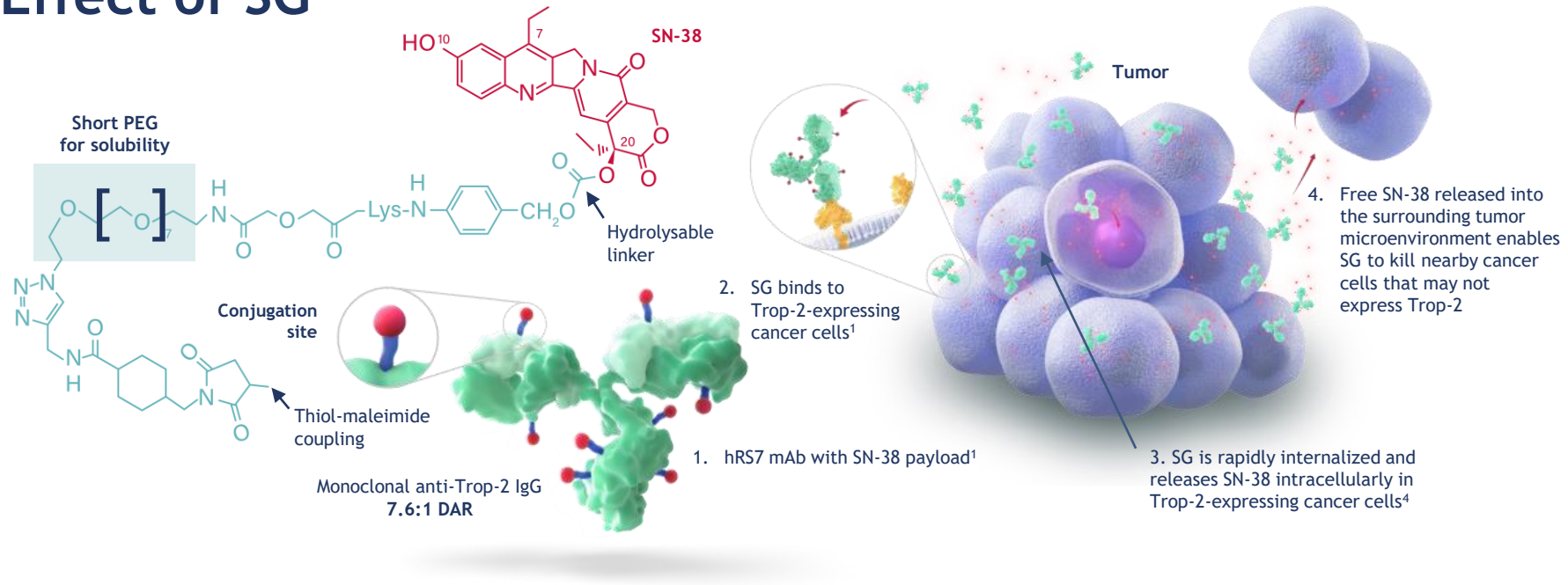
Cell death due to DNA damage

[a]Adapted from Rugo HS, et al.[2]

ADC, antibody–drug conjugate; DNA, deoxyribonucleic acid; SG, sacituzumab govitecan; TOP1, topoisomerase I; Trop-2, trophoblast cell-surface antigen 2.

1. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512; 2. Rugo HS, et al. *Future Oncol*. 2020;16:705-715; 3. Kopp A, et al. *Mol Cancer Ther*. 2023;22:102-111.

Bystander Effect May Contribute to the Potent Antitumor Effect of SG[1-4]

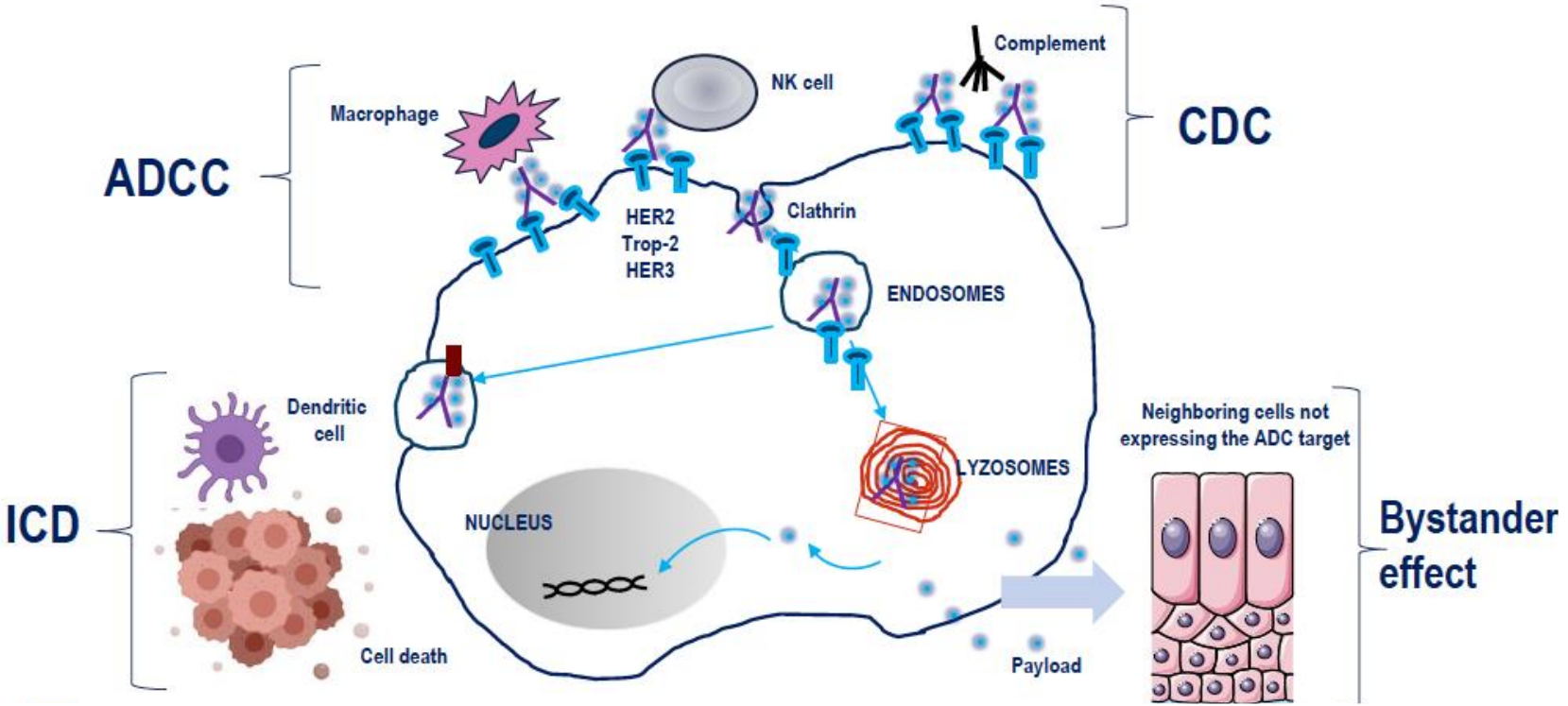


Hydrolysable linker facilitates rapid internalization and efficient release of the SN-38 payload in Trop-2-expressing cancer cells and into the surrounding tumor microenvironment, contributing to the bystander killing of neighboring cells[1-4]

ADC, antibody–drug conjugate; DAR, drug-to-antibody ratio; hRS7, humanized anti-Trop-2 monoclonal antibody; IgG, immunoglobulin G; mAb, monoclonal antibody; PEG, polyethylene glycol; SG, sacituzumab govitecan; Trop-2, trophoblast cell-surface antigen 2.

1. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512; 2. Cardillo TM, et al. *Bioconjugate Chem*. 2015;26:919-931; 3. Goldenberg DM et al. *MAbs*. 2019;11:987-995; 4. Kopp A, et al. *Mol Cancer Ther*. 2023;22:102-111.

Other mechanisms of action beyond the direct cytotoxicity



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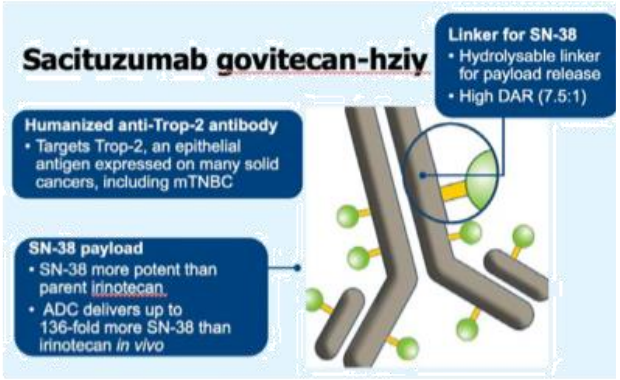
Sacituzumab Govitecan en CMTN metastásico

Estudio ASCENT



Anti Trop-2 antibody SN38 payload

ASCENT: A Phase 3 Study of Sacituzumab Govitecan in mTNBC

Metastatic TNBC
(per ASCO/CAP)
2 or more lines for advanced disease
[no upper limit; 1 of the required prior regimens could be progression occurred within a 12-month period after completion of (neo)adjuvant therapy)]
N=529

NCT02574455

R 1:1

Sacituzumab Govitecan (SG)
10 mg/kg IV
days 1 & 8, every 21-day cycle
(n=267)

Treatment of Physician's Choice (TPC)*
(n=262)

Continue treatment until progression or unacceptable toxicity

Endpoints

Primary
- PFS[9]

Secondary
- PFS for the full population[9]
- OS, ORR, DOR, TTR, safety

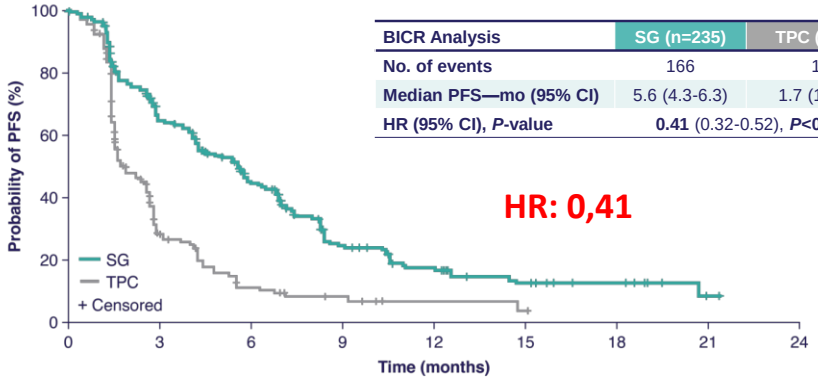
Data cutoff: March 11, 2020

Stratification factors
- Number of prior chemotherapies (2-3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (yes/no)

Bardia et al. ESMO 2021. Bardia et al NEJM 2021

SG CMTN metastásico
Estudio ASCENT

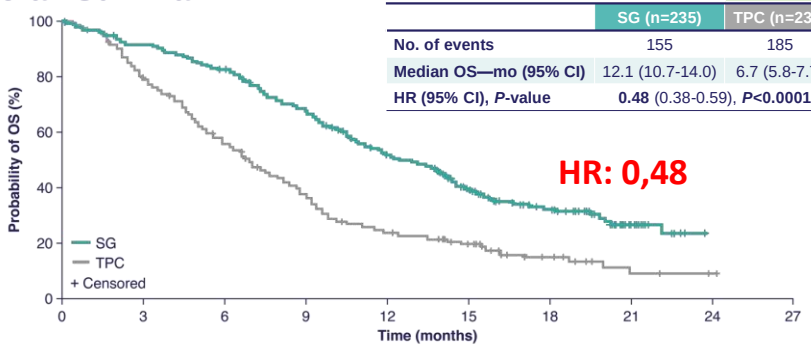
Progression-Free Survival (BICR Analysis)



BICR Analysis	SG (n=235)	TPC (n=233)
No. of events	166	150
Median PFS—mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P*-value	**0.41** (0.32-0.52), ***P*<0.0001**	

HR: 0,41

Overall Survival



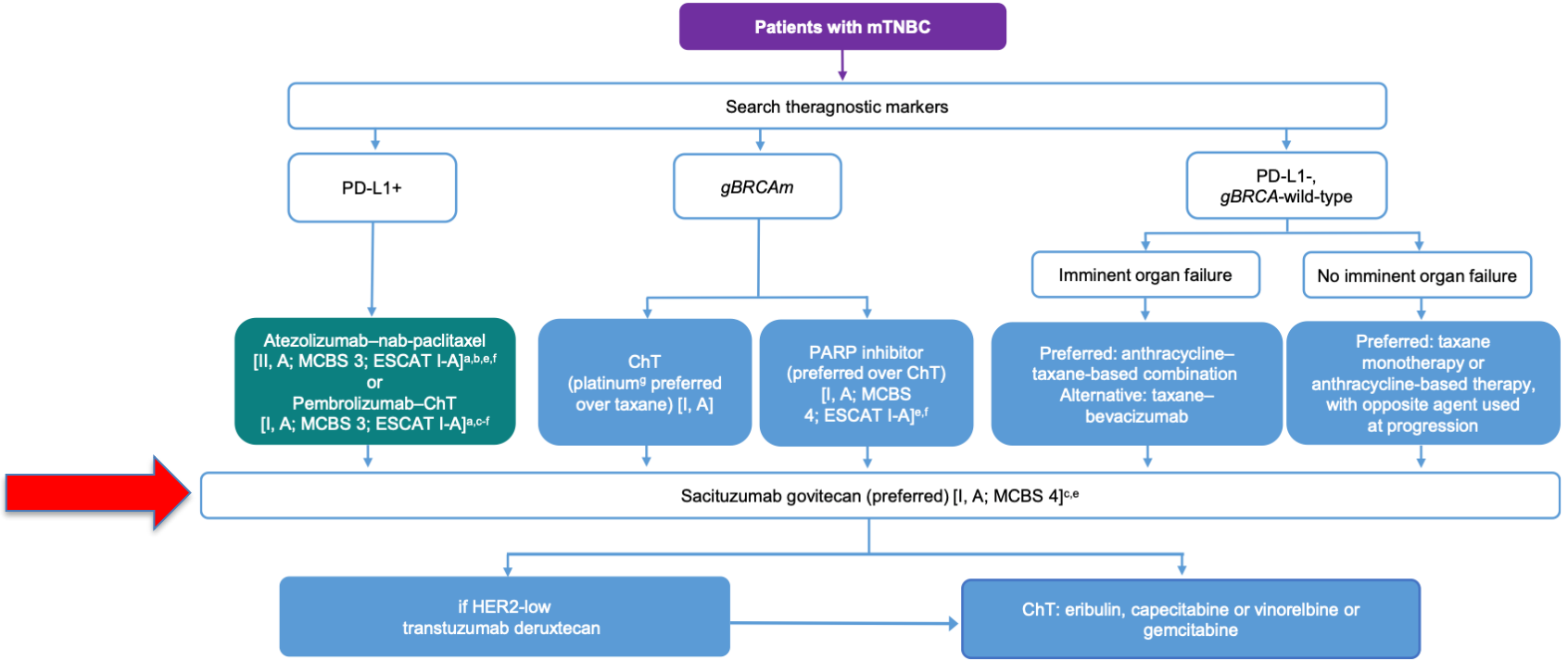
	SG (n=235)	TPC (n=233)
No. of events	155	185
Median OS—mo (95% CI)	12.1 (10.7-14.0)	6.7 (5.8-7.7)
HR (95% CI), *P*-value	**0.48** (0.38-0.59), ***P*<0.0001**	

HR: 0,48

Bardia et al. ESMO 2021. Bardia et al NEJM 2021

Algoritmo terapéutico para CMTNm

ESMO guidelines (Gennari et al, 2021)



SACITUZUMAB GOVITECAN (Trodelvy)

REAL WORLD EVIDENCE

- Real World Study of SG in mTNBC in the UK
- Single US Institution Experience (Roswell Park) – SG in mTNBC
- SG in patients with mTNBC treated through the French Early Access Program
- Real-world outcomes of SG in 2L+ mTNBC in the United States

foro debate oncología

Real World Study of Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer in the UK

- D. Hanna[1], S. Merrick[2], A. Ghose[1], D. Yang[3], E. Phillips[3], N. Chopra[4], K. Ross[5], Z.Y. Boh[6], A. Swampillai, T. Robinson[10], L. Germain[11], C. Atkinson[12],A.A. Konstantis[2,13], P. Riddle[14], N. Cresti[15],J.D. Naik[16], A. Borley[17], A. Guppy[18],P. Schmid[1], M. Phillips[1]

[1]St. Bartholomew's, Barts Health NHS trust, London, [2]UCLH NHS foundation trust, London, [3]The Royal Marsden NHS foundation trust London and Sutton, [4]The Royal Free, London NHS foundation trust, [5]BWSCC -Beatson West of Scotland Cancer Centre, Glasgow, [6]NHS Lothian, Edinburgh, [7]Guy's and St Thomas' NHS foundation trust, [10]Bristol Haematology and Oncology Centre- NHS foundation trust, Bristol, [11]Leeds Cancer Centre, Leeds, [12]Taunton and Somerset NHS foundation trust, Taunton, [13]Princess Alexander Hospital, London, [14]Chelsea and Westminster, London, [15]The Freeman hospital, Northern Centre for Cancer Care, Newcastleupon-Tyne, [16]Harrogate

Real World Study of Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer in the UK

Barts Health NHS Trust

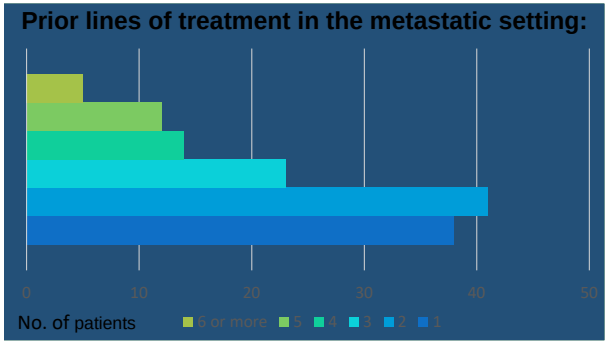
132 patients

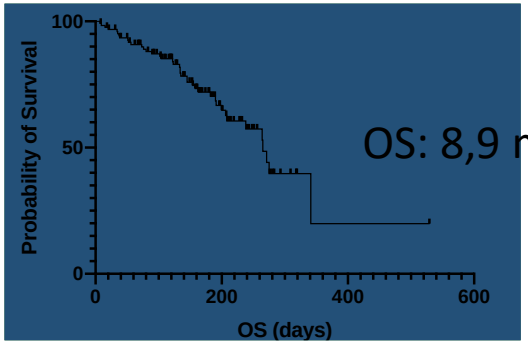
Performance status
0: 39 pts
1: 76 pts
2: 16 pts
3: 1 pt

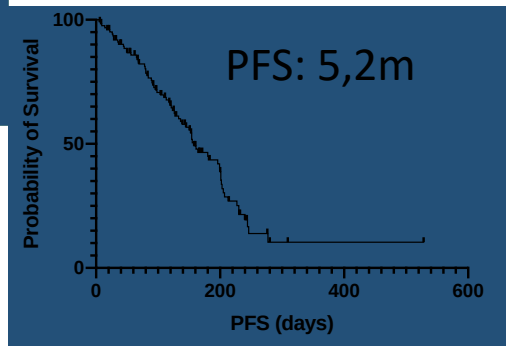
99 pts with visceral metastases

24 pts with CNS metastases (18%)

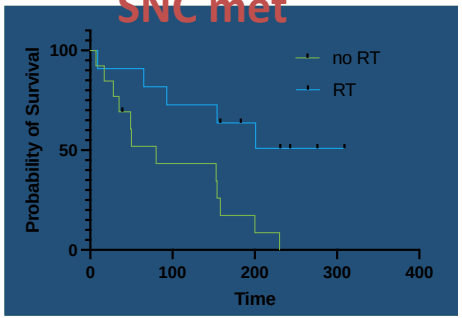
11 pts treated with RT to brain metastasis







SNC met

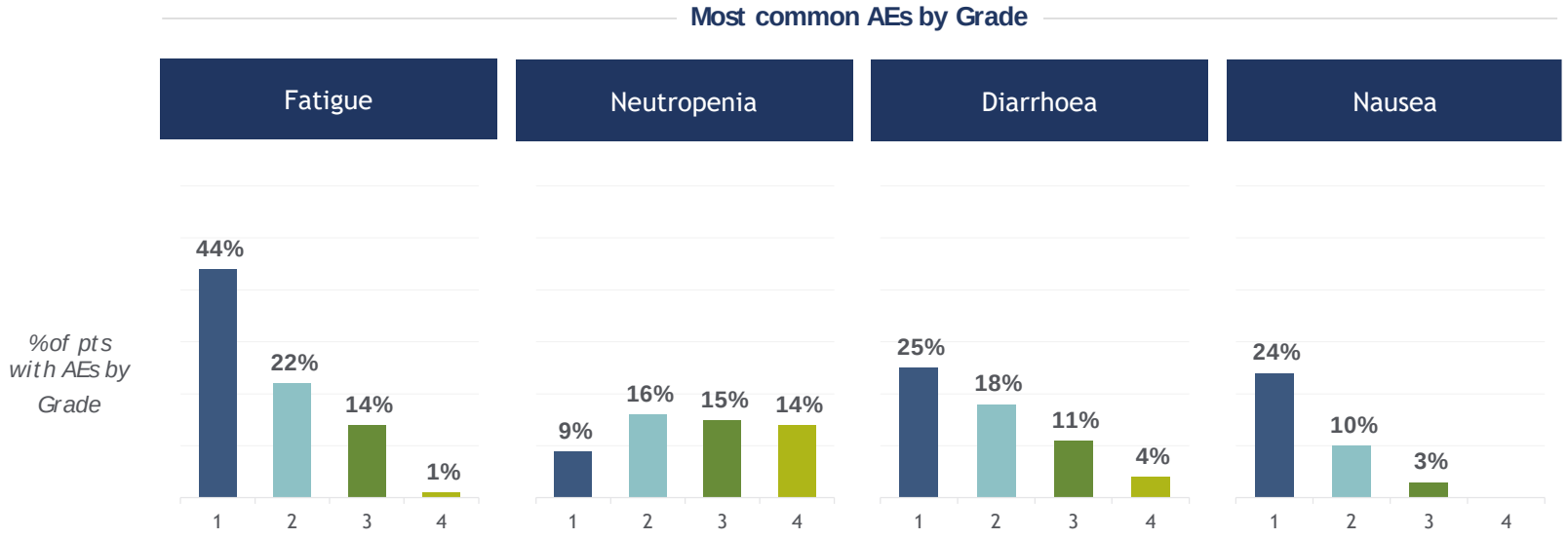


PFS: 5,1m
(No RT PFS: 1,6m)

This study provides the first real-world experience of sacituzumab govitecan in the UK, confirming substantial anti-tumour activity in pre-treated metastatic TNBC.
•The safety profile is consistent with clinical trial experience.

Results

- SG dose reduction occurred 54% of patients due to adverse event
- Most common AEs (All Grade) were fatigue (82%), neutropenia (55%), diarrhoea (58%), and nausea (38%)



AEs, adverse events

Hanna D, et al. Presented at ESMO Breast Cancer Congress; May 11-13, 2023; Berlin, Germany. Poster 232P.

Single US Institution Experience of Sacituzumab Govitecan

Rowswell Park Comprehensive Cancer Center

This was a retrospective case series of patients with metastatic breast cancer in the US who received sacituzumab govitecan between 01/01/2021 to 12/31/2022

Alaklabi S, et al. Poster presented at: 40th Annual Miami Breast Cancer Conference; March 2-5, 2023; Miami Beach, FL

Single US Institution Experience of Sacituzumab Govitecan Rowswell Park (US) Comprehensive Cancer Center

Demographic and Clinical Characteristics

Characteristic, n (%)	Sacituzumab Govitecan (N=24)
Median age, years	**58 (29-84)**
ECOG	
0	8 (33.3)
1	14 (58.3)
2	1 (4.2)
3	1 (4.2)
Site of metastases	
Lung	11 (45.8)
Liver	16 (66.7)
Bone	16 (66.7)
Brain	7 (29.2)
Lymph Nodes	7 (29.2)
Other	1 (4.2)
Median number of cycles	**5.5 (1-18)**
Number of previous therapies	
<3	6 (25.0)
≥3	18 (75.0)

Characteristic, n (%)	Sacituzumab Govitecan (N=24)
Previous Therapies	
Endocrine therapy	3 (13.0)
Taxane	17 (70.8)
Anthracycline	6 (25.0)
Carboplatin	2 (8.3)
Capecitabine	11 (45.8)
PARP inhibitor	3 (12.5)
PD-1/PD-L1 inhibitor	14 (58.3)
BRCA1/2(+)	**3 (12.5)**
TNBC	22 (91.7)
HR+	2 (8.3)
HER-2 IHC score	
0	5 (20.8)
1-2	19 (79.2)
Starting dose	
10 mg/kg	21 (87.5)
7.5 mg/kg	2 (8.3)
5 mg/kg	1 (4.2)

BRCA, BReast CAncer gene; ECOG, Eastern Cooperative Oncology Group Performance Status, HER-2, human epidermal growth factor receptor 2; HR, hormone receptor; PARP, poly ADP ribose polymerase; PD-(L)1, programmed death (ligand) 1; TNBC, triple negative breast cancer

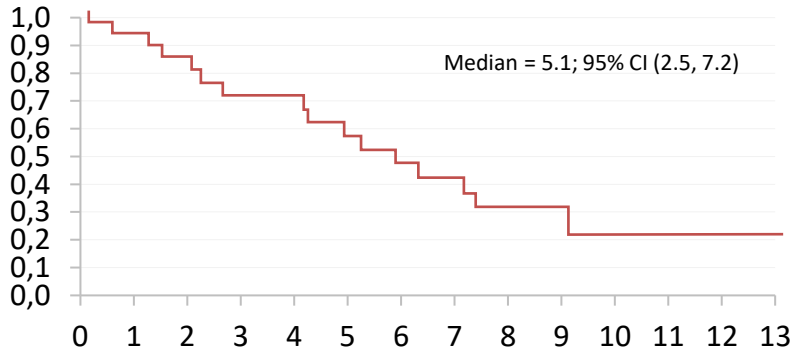
Alaklabi S, et al. Poster presented at: 40th Annual Miami Breast Cancer Conference; March 2-5, 2023; Miami Beach, FL

Results

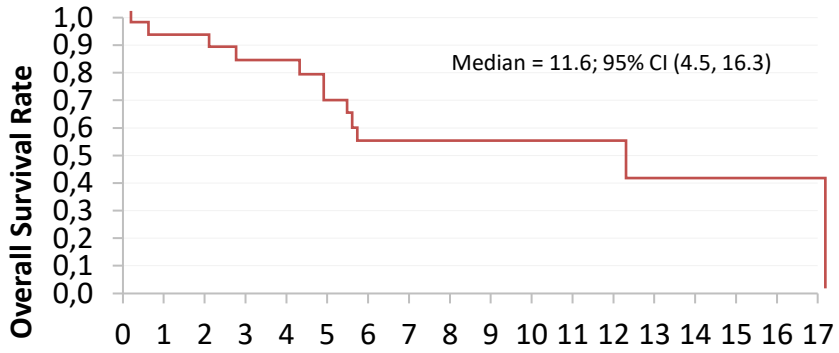
Clinical Outcomes

Outcomes	Sacituzumab Govitecan (N=24)
Best response*	
PR	11/18 (61.1%)
SD	4/18 (22.2%)
PD	3/18 (16.7%)
Not assessed	6/24 (25.0%)
ORR*	**11/18 (61.1%)**
Median duration of response, months	**6.5 (3-13)**

Progression Free Survival



Overall Survival



*6 patients were not evaluated for response; response was calculated based on 18 patients whose response was assessed
ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease
Alaklabi S, et al. Poster presented at: 40th Annual Miami Breast Cancer Conference; March 2-5, 2023; Miami Beach, FL

Results

Clinical Outcomes and Adverse Events

Adverse Events, n (%)	Sacituzumab Govitecan (N=24)
Nausea/vomiting	16 (66.7)
Diarrhea	12 (50.0)
Mucositis	5 (20.8)
Fatigue	14 (60.9)
Alopecia	4 (16.7)
Anemia	1 (4.2)
Neutropenia	10 (41.7)
Febrile neutropenia	12 (50.0)
Treatment discontinuation due to AEs	**2 (8.7)**
Dose reduction due to AEs	14 (60.9)
Median relative dose intensity, %	**80 (30-100)**

AE, adverse event;
Alaklabi S, et al. Poster presented at: 40th Annual Miami Breast Cancer Conference; March 2-5, 2023; Miami Beach, FL

Conclusion

- Approximately 30% of patients in this cohort presented with brain metastases and results in this cohort showed comparable clinical outcomes to the ASCENT trial.
- In a heavily pretreated mTNBC population comparable disease response and tolerability were seen in patients treated with SG, and patients received a similar relative dose intensity.
- Limitations of this study include that it was a single center study, included a small sample size, and there was variability in provider documentation

HER2, human epidermal growth factor receptor 2; mTNBC, metastatic triple negative breast cancer; SG, sacituzumab govitecan

Alaklabi S, et al. Poster presented at: 40th Annual Miami Breast Cancer Conference; March 2-5, 2023; Miami Beach, FL

Sacituzumab govitecan experience in patients with metastatic triple negative breast treated through the French Early Access Program

An ambispective bicentric cohort study was conducted to assess the real-world effectiveness and safety of SG in patients with mTNBC. This study included patients treated through the French Early Access Program (EAP) from May 2021 to January 2023.

Delphine L, et al. Poster presented at: ESMO Breast Cancer 2023; May 11-13, 2023; Berlin, Germany. Abstract #216P

Sacituzumab govitecan in metastatic triple negative breast cancer : Efficacy -with a focus on brain metastases- and Toxicity in a real-world cohort

ESMO Breast 2023
Abstract #216P

Université Paris Cité

PATIENTS CHARACTERISTICS

	n=103
Female, n (%)	**103 (100%)**
Median age, years (range)	**55 (26-89)**
ECOG PS, n (%)	
0-1	83 (80.6%)
[illegible]	17 (16.5%)
NA	3 (2.9%)
Number of prior lines of treatment in advanced setting, median (range)	**2 (1-10)**
1-2, n (%)	66 (64.1%)
>2, n (%)	37 (35.9%)
Previous use of PARP inhibitors, n (%)	**6 (5.8%)**
Previous use of anti-PD-1/PD-L1, n (%)	**29 (28.2%)**
BRCA1/2 germline mutational status, n (%)	
Mutated	8 (7.8%)
Non-mutated	86 (83.5%)
NA	9 (8.7%)
***De novo* metastatic disease**	**15 (14.6%)**
Brain metatases	**32 (31.1%)**
Visceral metastases	**82 (79.6%)**
Liver metastases	**45 (43.7%)**

RESULTS : Efficacy

	All patients (n=103)	Brain metastases cohort (n=32)
Median PFS, mo (95%CI)	**4.0 (3.5-5.3)**	**3.7 (2.6-6.2)**
Median OS, mo (95%CI)	**9.2 (7.2-NR)**	**6.7 (56.3-NR)**
Median duration of SG exposure, mo (range)	3.4 (0.3-15.4)	3.1(0.3-9.5)
ORR, n (%)	**31 (30.1%)**	**6 (19.8%)**
Complete response	2 (1.9%)	0 (0%)
Partial response	29 (28.2%)	6 (19.8%)

Toxicity

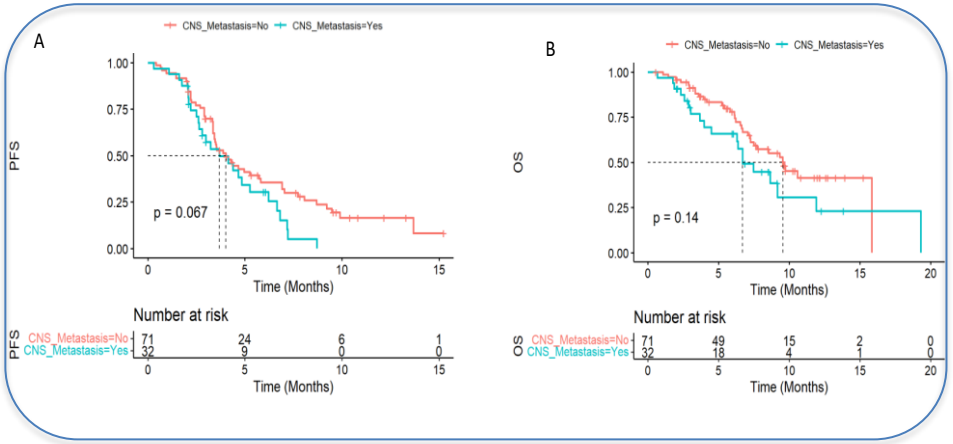
SG discontinuation causes

	All cohort (n=103)	Brain metastases cohort (n=32)
SG discontinuation	**78 (75.7%)**	**26 (81.2%)**
Progressive disease, n (%)	73 (93.6%)	24 (92.3%)
Toxicity, n (%)	1 (1.3%)	0 (0%)
Physical deterioration, n (%)	3 (3.8%)	2 (7.7%)
[illegible] request, n (%)	1 (1.3%)	0 (0%)

SG toxicity leading to dose reduction

	All cohort (n=103)	Brain metastases cohort (n=32)
SG dose reduction	**19 (16.4%)**	**4 (12.5%)**
Gastrointestinal toxicity, n (%)	6 (31.6%)	1 (25%)
Hematological toxicity, n (%)	8 (42.1%)	2 (50%)
Liver enzyme elevation, n (%)	1 (5.3%)	0 (0%)
Febrile neutropenia, n (%)	3 (26.3%)	1 (25%)
Physical deterioration, n (%)	1 (5.3%)	0 (0%)
SG related deaths	**0 (0%)**	**0 (0%)**

· **Progression-free (A) and overall survival (B) for patients without or with brain metastases**

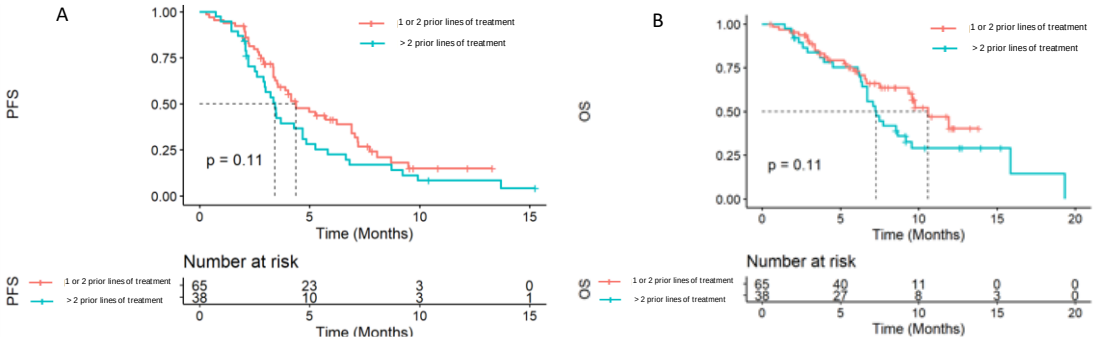


Our real-world data in mTNBC pts are consistent with results of the ASCENT trial in terms of ORR and safety, but observed median PFS (4 mo.) and median OS (9.2 mo.) are numerically shorter. Characteristics of our cohort population including pts with brain metastases (31,1%) and impaired performance status could explained shorter PFS and OS.

Progression-free (A) and overall survival (B) according number of prior lines of treatment

-In ASCENT :stable brain metastases (n=32) (6,8%)
PFSm 2.8 mo. (95% CI, 1.5- 3.9)
OSm 6.8 mo. (95% CI, 4.7-14.1)

-In our cohort of 32 pts including pts with active or stable CNS metastases, median PFS was 3.7 mo. and median OS 6.7 mo. This finding confirms that ***SG could be considered for pts with active CNS, in absence of available CNS local treatment***.



Real-world outcomes in patients with metastatic triple-negative breast cancer with sacituzumab govitecan in 2L+ in the United States

Kalinsky K, et al. Presented at ASCO 2023. Abstract #e18879.

Baseline Characteristics

- In total, 230 pts met the eligibility criteria and were included for analysis.

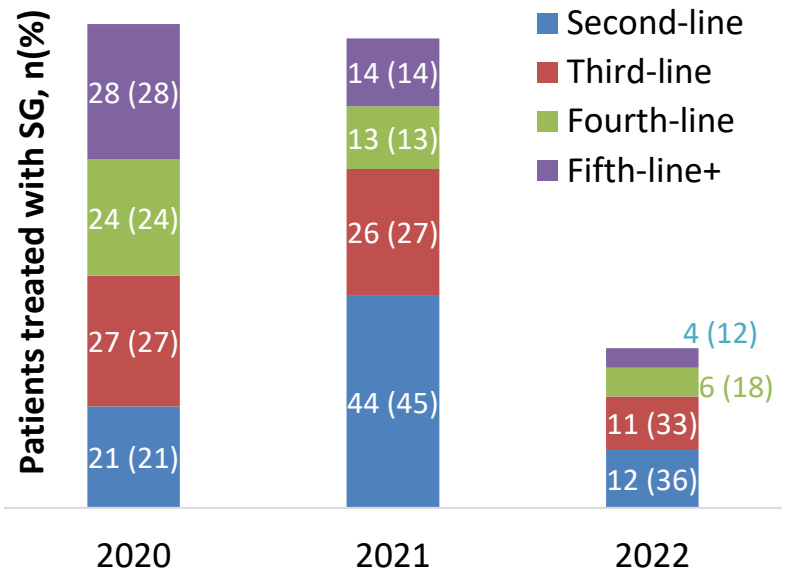
	Sacituzumab Govitecan N=230
Female	100%
Median age	60 years (IQR, 49–69)
Race	
White	64%
Black	26%
ECOG PS 0-1	71%
Treatment in community setting	66%
Median time from diagnosis of Stage 4 to initiation on sacituzumab govitecan	11.8 months (IQR, 7.6–19.2)
Visceral metastases at baseline	71%
Brain metastases at baseline	7%
Line of therapy on sacituzumab govitecan	
2L	34%
3L	28%
4L	19%
>5L	20%

ECOG, Eastern Cooperative Oncology Group; mBC, metastatic breast cancer; SG, Sacituzumab govitecan.
Kalinsky K, et al. Presented at ASCO 2023. Abstract #e18879.

Results

- Median starting dose was 10 mg/kg (IQR, 9.8-10.1)
- Between 2020-2022, there was a trend in the distribution of SG use shifting to earlier line settings (Figure 1)

SG use by line of therapy by index year



2L, second-line; 3L+, third-line and later; rwOS, real world overall survival; SG, Sacituzumab govitecan;
Kalinsky K, et al. Presented at ASCO 2023. Abstract #e18879.

Median Real World Overall Survival in Patients Treated with Sacituzumab Govitecan

	Median rwOS (95% CI) from index date
All patients	10 months (8.3 — 11.1)
2L	13.9 months (9.79 — not estimable)
3L+	8.4 months (7.7 — 10.3)

Patients who were treated with SG in routine clinical practice in the US showed similar survival benefit to those patients enrolled in ASCENT (despite an older and with worse performance status.)
The proportion of patients treated with SG in the 2L metastatic mTNBC setting increased from 2020 to 2022, reflecting post approval drug uptake in routine practice

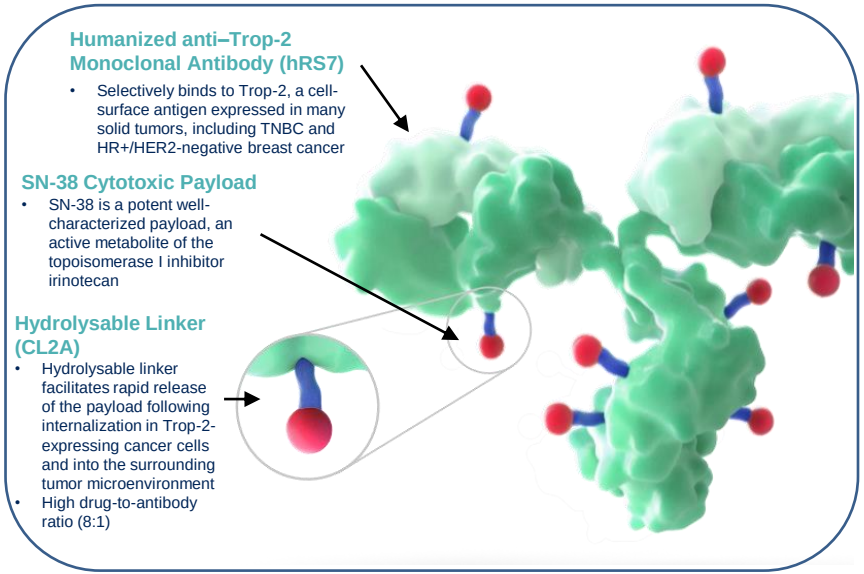
SACITUZUMAB GOVITECAN : Mas allá del ASCENT ….

- INTRODUCCIÓN
- DATOS DE RWE
- **NUEVAS INDICACIONES : TROPICS-02**

  Estudios en marcha
- Mas allá del cáncer de mama.

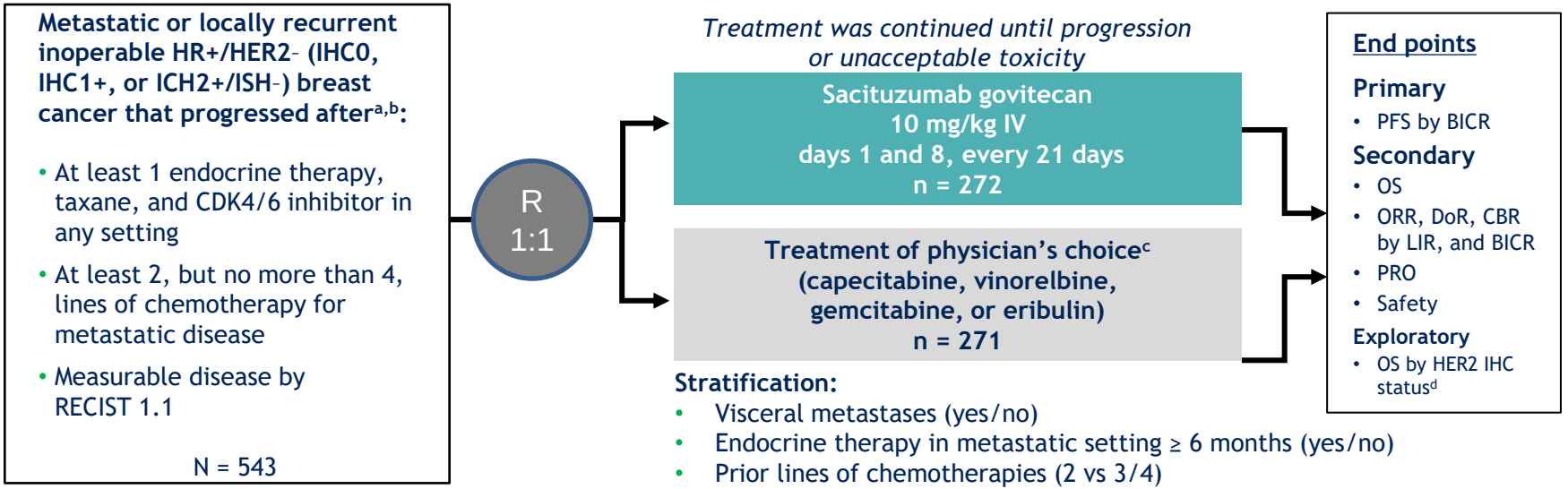
Sacituzumab Govitecan Is a First-in-Class Trop-2–Directed Antibody-Drug Conjugate

- **SG is approved for 2L and later mTNBC in multiple countries.**
- **For HR+/HER2- mBC in the US /EMA based on the results of the TROPiCS-02 trial**
- Received accelerated approval in 2L metastatic urothelial cancer in the US[1,2,3]



. 1 TRODELVY® (sacituzumab govitecan-hziy) [package insert]. Foster City, CA: Gilead Sciences,Inc.; April 2023. 2. European Medicines Agency: Trodelvy, INN-sacituzumab govitecan, https://www.ema.europa.eu/en/documents/product-information/trodelvy-epar-product-information_en.pdf, April 2023; 3. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

TROPiCS-02: Phase 3 Study SG in Patients with HR+/HER2– mBC



ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CBR, clinical benefit rate; CDK, cyclin-dependent kinase; DoR, duration of response; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor-positive; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenously; LIR, local investigator review; ORR, objective response rate; OS, overall survival; PFS, progression-free survival, PRO, patient-reported outcomes; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

[a]ClinicalTrials.gov. NCT03901339. [b]Disease histology based on the ASCO/CAP criteria. [c]Single-agent standard-of-care treatment of physician's choice was specified prior to randomization by the investigator. [d]HER2-low was defined as IHC score of 1+, or score of 2+ with negative ISH result; HER2 IHC0 was defined as IHC score of 0.

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

Demographics and Baseline Characteristics[1]

	SG (n = 272)	TPC (n = 271)
Female, %	99	99
Median age, (range) y	57 (29-86)	55 (27-78)
< 65 y, %	73	75
≥ 65 y, %	27	25
Race or ethnic group, %		
White	68	66
Black	3	5
Asian	4	2
Other[a]/Not reported[b]	25	28
Geographic region, %		
North America	42	42
Europe	58	58
ECOG PS, %		
0	43	46
1	57	54
Visceral metastases at baseline, %	95	95
Liver metastases,[c] %	84	87
De novo metastatic breast cancer, %	29	22

	SG (n = 272)	TPC (n = 271)
Median time from initial metastatic diagnosis to randomization, (range) mo	48.5 (1.2-243.8)	46.6 (3.0-248.8)
Prior chemotherapy in (neo)adjuvant setting, %	64	68
DFI < 12 mo, %	8	8
Prior endocrine therapy use in the metastatic setting ≥ 6 mo, %	86	86
Prior CDK4/6 inhibitor use, %		
≤ 12 months	59	61
> 12 months	39	38
Unknown	2	1
Number of prior lines of chemotherapy, %		
≤ 2	42	44
≥ 3	58	56
Median prior chemotherapy regimens in the metastatic setting, n (range)[d]	3 (0-8)	3 (1-5)

CDK, cyclin-dependent kinase; DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status, (neo)adjuvant, neoadjuvant or adjuvant; RECIST, Response Evaluation Criteria In Solid Tumors; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

[a]Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander. [b]Not reported indicates local regulators did not allow collection of race or ethnicity information. [c]Presence of baseline target/non-target liver metastases per RECIST 1.1 by local investigator review. [d]The reported number of prior therapies was miscounted at screening for some patients; 9 patients received prior chemotherapy regimens in the metastatic setting outside the per-protocol range for inclusion criteria and were included in the intent-to-treat population.

1. Rugo HS, et al. J Clin Oncol. 2022;40:3365-3376; 2. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor-positive/HER2-negative (HR+/HER2-) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

SG vs TPC in HR+/HER2- mBC

- In the primary analysis of the phase 3 randomized TROPiCS-02 trial of patients with pretreated, endocrine-resistant HR+/HER2- mBC, SG vs TPC demonstrated significantly improved PFS, longer median OS and median DoR, and higher ORR with a well characterized safety profile[1]
- At the second interim analysis of OS (final OS analysis per protocol), SG continued to demonstrate clinically meaningful improvement in efficacy vs TPC with manageable safety[2]

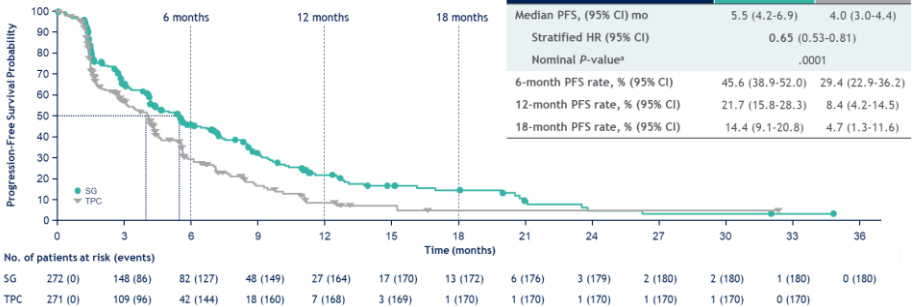
Patients, ITT[2]	SG (n = 272)	TPC (n = 271)
Median PFS,[a] mo	5.5 (4.2-7.0)	4.0 (3.1-4.4)
HR (95% CI), *P*-value	0.66 (0.53-0.83), *P* = .0003	
Median OS, mo	14.4 (13.0-15.7)	11.2 (10.1-12.7)
HR (95% CI), *P*-value	0.79 (0.65-0.96), *P* = .020	
ORR,[a] %	21%	14%
Odds ratio (95% CI), *P*-value	1.63 (1.03-2.56), *P* = .035	
Median DoR,[a] mo (95% CI)	8.1 (6.7-8.9)	5.6 (3.8-7.9)

BICR, blinded independent central review; CBR, clinical benefit rate; CI, confidence interval; DoR, duration of response; HER2-, human epidermal growth factor receptor 2-negative; HR, hazard ratio; HR+, hormonal receptor-positive; mBC, metastatic breast cancer; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]BICR investigation.
1. Rugo HS, et al. J Clin Oncol. 2022;40:3365-3376. 2. Rugo HS, et al. Oral presentation at ESMO Congress; September 9-13, 2022; Paris, France. Abstract LBA7; 3. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3).

ASCO 2023 Present efficacy and safety from TROPiCS-02 with additional follow-up

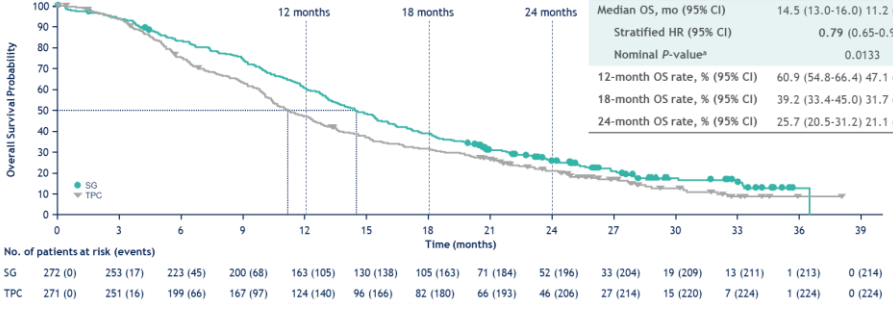
Progression-Free and Overall Survival

Progression-Free Survival



BICR analysis	SG (n = 272)	TPC (n = 271)
Median PFS, (95% CI) mo	5.5 (4.2-6.9)	4.0 (3.0-4.4)
Stratified HR (95% CI)	0.65 (0.53-0.81)	
Nominal *P*-value[a]	.0001	
6-month PFS rate, % (95% CI)	45.6 (38.9-52.0)	29.4 (22.9-36.2)
12-month PFS rate, % (95% CI)	21.7 (15.8-28.3)	8.4 (4.2-14.5)
18-month PFS rate, % (95% CI)	14.4 (9.1-20.8)	4.7 (1.3-11.6)

Overall Survival



	SG (n = 272)	TPC (n = 271)
Median OS, mo (95% CI)	14.5 (13.0-16.0)	11.2 (10.2-12.6)
Stratified HR (95% CI)	0.79 (0.65-0.95)	
Nominal *P*-value[a]	0.0133	
12-month OS rate, % (95% CI)	60.9 (54.8-66.4)	47.1 (41.0-53.0)
18-month OS rate, % (95% CI)	39.2 (33.4-45.0)	31.7 (26.2-37.4)
24-month OS rate, % (95% CI)	25.7 (20.5-31.2)	21.1 (16.3-26.3)

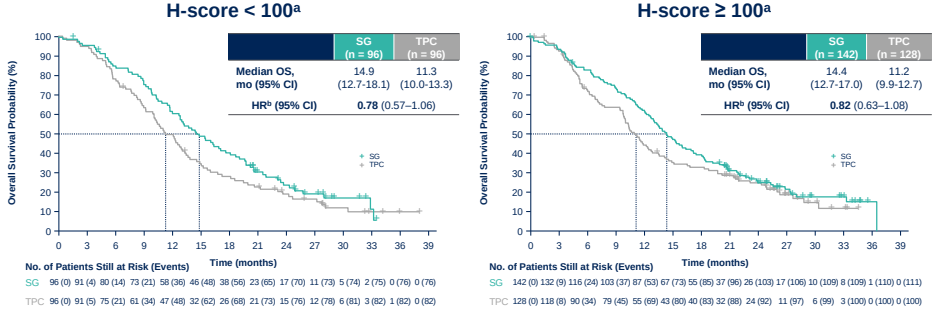
SG continued to demonstrate improvement in PFS vs TPC at longer follow-up, with 35% reduction in risk of disease progression or death, and a higher proportion of patients remained alive and progression-free at each landmark

SG continued to demonstrate improvement in OS vs TPC at longer follow-up, with 21% reduction in risk of death and a higher proportion of patients remaining alive at each landmark

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

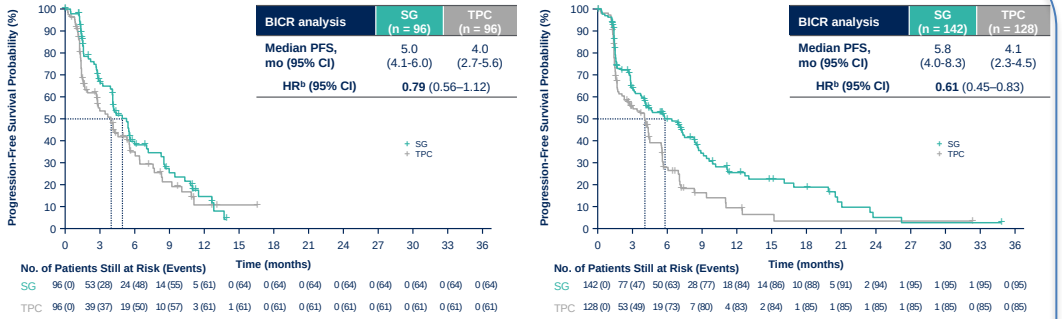
Trop-2 Expression Level

Overall Survival



OS benefit was observed with SG over TPC in the H-score < 100 and the H-score ≥ 100 groups with longer follow-up, consistent with a previous analysis[2]

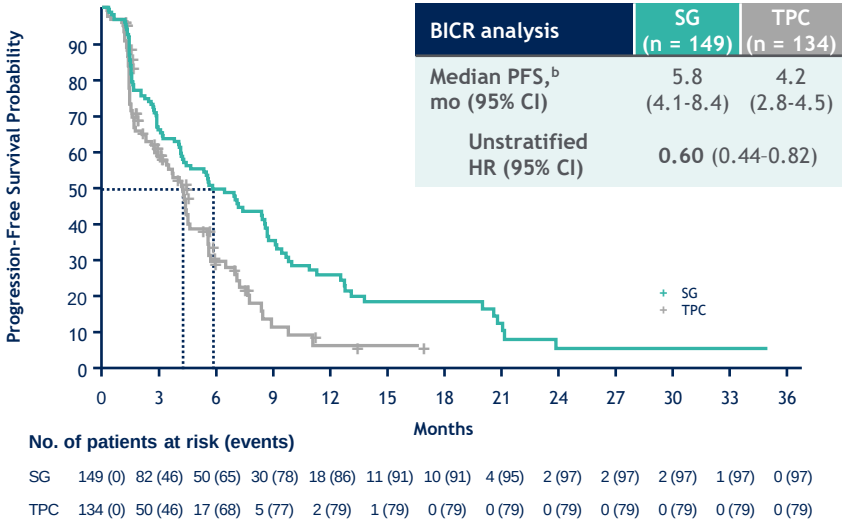
Progression-Free Survival



PFS outcome favored SG over TPC in the H-score < 100 and the H-score ≥ 100 groups with longer follow-up, consistent with a previous analysis[1]

Progression-Free Survival by HER2 IHC Status

HER2-low (IHC1+, IHC2+/ISH-)[a]

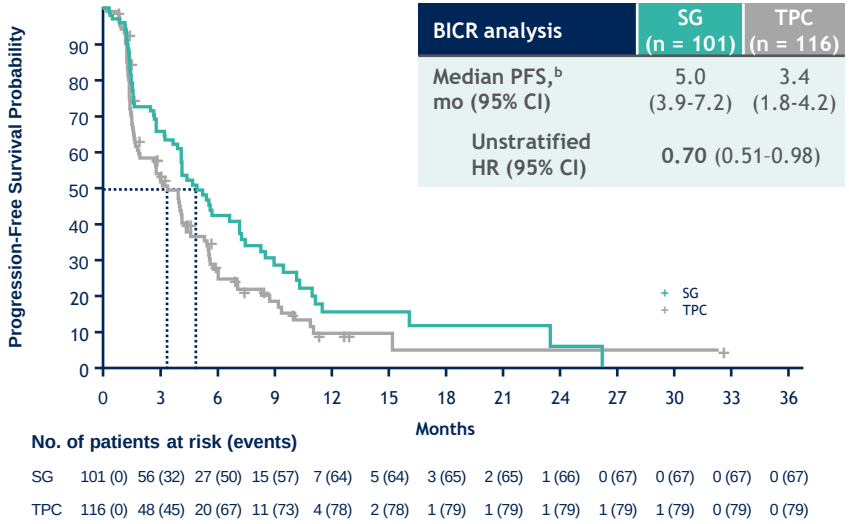


BICR analysis	SG (n = 149)	TPC (n = 134)
Median PFS,[b] mo (95% CI)	5.8 (4.1-8.4)	4.2 (2.8-4.5)
Unstratified HR (95% CI)	**0.60** (0.44-0.82)	

No. of patients at risk (events)

SG	149 (0)	82 (46)	50 (65)	30 (78)	18 (86)	11 (91)	10 (91)	4 (95)	2 (97)	2 (97)	2 (97)	1 (97)	0 (97)
TPC	134 (0)	50 (46)	17 (68)	5 (77)	2 (79)	1 (79)	0 (79)	0 (79)	0 (79)	0 (79)	0 (79)	0 (79)	0 (79)

HER2 IHC0[a]



BICR analysis	SG (n = 101)	TPC (n = 116)
Median PFS,[b] mo (95% CI)	5.0 (3.9-7.2)	3.4 (1.8-4.2)
Unstratified HR (95% CI)	**0.70** (0.51-0.98)	

No. of patients at risk (events)

SG	101 (0)	56 (32)	27 (50)	15 (57)	7 (64)	5 (64)	3 (65)	2 (65)	1 (66)	0 (67)	0 (67)	0 (67)	0 (67)
TPC	116 (0)	48 (45)	20 (67)	11 (73)	4 (78)	2 (78)	1 (79)	1 (79)	1 (79)	1 (79)	1 (79)	0 (79)	0 (79)

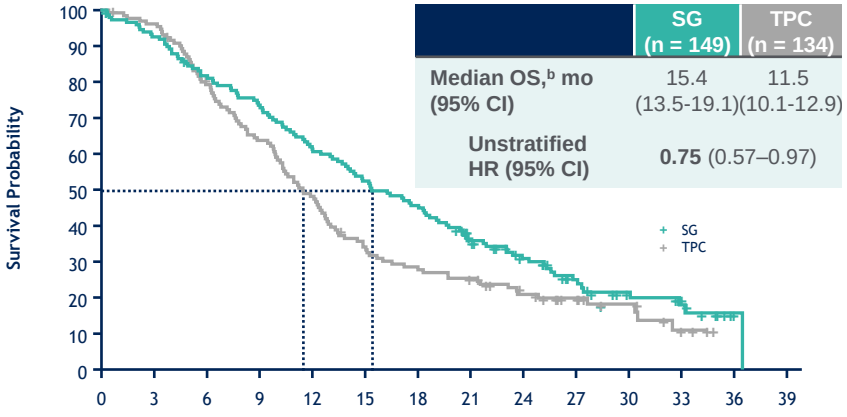
SG consistently improved PFS vs TPC in the HER2 low ((IHC1+, IHC2+/ISH-) and the HER2 IHC0 groups with longer follow-up, consistent with a previous analysis[1]

[a]HER2 IHC was determined by local assessment on last available pathology sample. 57% of patients were HER2-low (IHC1+, IHC2+/ISH-) and 43% were HER2 IHC0.

1. Schmid P, et al. Oral presentation at ESMO Congress; September 9-13, 2022; Paris, France. Abstract FPN 214MO; 2. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003

Overall Survival by HER2 IHC Status[1]

HER2-low (IHC1+, IHC2+/ISH-)[a]

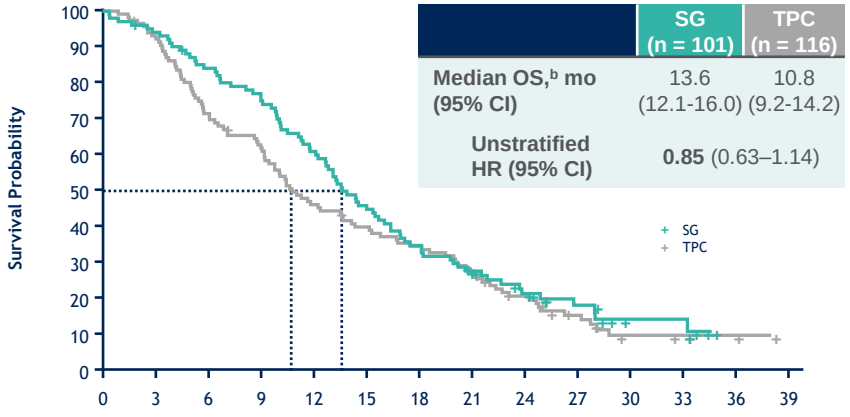


	SG (n = 149)	TPC (n = 134)
Median OS,[b] mo (95% CI)	15.4 (13.5-19.1)	11.5 (10.1-12.9)
Unstratified HR (95% CI)	**0.75** (0.57–0.97)	

No. of patients at risk (events)

SG	149	137	120	108	91	77	67	46	35	22	14	9	1	0
	(0)	(11)	(27)	(39)	(56)	(70)	(80)	(94)	(100)	(106)	(109)	(111)	(112)	(113)
TPC	134	126	102	82	62	43	36	31	22	13	9	3	0	0
	(0)	(5)	(27)	(47)	(67)	(85)	(92)	(96)	(101)	(102)	(103)	(106)	(106)	(106)

HER2 IHC0[a]



	SG (n = 101)	TPC (n = 116)
Median OS,[b] mo (95% CI)	13.6 (12.1-16.0)	10.8 (9.2-14.2)
Unstratified HR (95% CI)	**0.85** (0.63–1.14)	

No. of patients at risk (events)

SG	101	94	83	76	60	45	34	22	15	10	4	4	0	0
	(0)	(6)	(16)	(23)	(39)	(54)	(65)	(72)	(77)	(79)	(81)	(81)	(82)	(82)
TPC	116	107	82	71	52	44	38	29	20	12	5	4	1	0
	(0)	(8)	(33)	(43)	(62)	(69)	(75)	(83)	(90)	(95)	(99)	(99)	(99)	(99)

SG consistently improved OS vs TPC in the HER2 low (IHC1+, IHC2+/ISH-) and the HER2 IHC0 groups

[a]HER2 IHC was determined by local assessment on last available pathology sample. 57% of patients were HER2-low (IHC1+, IHC2+/ISH-) and 43% were HER2 IHC0.

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor-positive/HER2-negative (HR+/HER2-) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

GILEAD | Oncology

Responses

BICR analysis	SG (n = 272)	TPC (n = 271)
ORR, n (%)	58 (21)	38 (14)
Odds ratio (95% CI)	1.66 (1.06-2.61), *P* = .027	
Best overall response, n (%)		
CR	2 (1)	1 (<1)
PR	56 (21)	37 (14)
SD	141 (52)	106 (39)
SD ≥ 6 mo	34 (13)	22 (8)
PD	58 (21)	76 (28)
NE	15 (6)	51 (19)
CBR,[a] n (%)	92 (34)	60 (22)
Odds ratio (95% CI)	1.80 (1.23-2.63), *P* = .0025	
Median DoR,[b] mo (95% CI)	8.1 (6.7-8.9)	5.6 (3.8-7.9)

SG improved ORR and CBR with prolonged DoR compared with TPC at longer follow-up, consistent with previous analysis[1]

2.

[a]CBR is defined as the percentage of patients with a confirmed best overall response of CR, PR, and SD ≥ 6 months. [b]Number of responders, SG, n = 58; TPC, n = 38.

1. Rugo HS, et al. Oral presentation at ESMO Congress; September 9-13, 2022; Paris, France. Abstract LBA76; 2. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

Safety Summary[1]

TEAEs,[a] n (%)		SG (n = 268)		TPC (n = 249)	
		Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Hematologic	Neutropenia[b]	189 (71)	140 (52)	136 (55)	97 (39)
	Anemia[c]	98 (37)	20 (7)	69 (28)	8 (3)
	Thrombocytopenia[d]	17 (6)	1 (<1)	41 (16)	9 (4)
Gastrointestinal	Diarrhea	166 (62)	27 (10)	57 (23)	3 (1)
	Nausea	157 (59)	3 (1)	87 (35)	7 (3)
	Constipation	93 (35)	1 (<1)	61 (24)	0
	Vomiting	64 (24)	3 (1)	39 (16)	4 (2)
	Abdominal pain	53 (20)	10 (4)	34 (14)	2 (1)
Other	Alopecia	128 (48)	0	46 (18)	0
	Fatigue	105 (39)	16 (6)	82 (33)	9 (4)
	Asthenia	62 (23)	6 (2)	50 (20)	5 (2)
	Decreased appetite	57 (21)	4 (1)	52 (21)	2 (1)
	Dyspnea	49 (18)	5 (2)	39 (16)	11 (4)
	Headache	44 (16)	1 (<1)	36 (14)	2 (1)
	Pyrexia	39 (15)	2 (1)	45 (18)	0
	AST increased	33 (12)	4 (1)	44 (18)	8 (3)

The most common grade ≥ 3 TEAEs were neutropenia (52%), diarrhea (10%), and anemia (7%) in the SG group, and neutropenia (39%), thrombocytopenia (4%), fatigue (4%), and dyspnea (4%) in the TPC group

Overall, the safety profile of SG was consistent with that of previous studies of SG[1-4]; no new safety signals emerged with further follow-up

TEAE, treatment-emergent adverse event

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor-positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

Conclusions[1]

- In this exploratory analysis of the TROPiCS-02 phase 3 trial, extended follow-up of ~13 months demonstrated durable efficacy of SG vs TPC, with continued improvements in PFS and OS among patients with pretreated endocrine-resistant HR+/HER2– mBC
  - SG demonstrated median 1.5 months improvement in PFS with a 35% reduction in risk of progression or death, and median 3.3 months improvement in OS with a 21% reduction in risk of death
    - Improvement in PFS and OS were generally consistent across predefined subgroups
  - SG improved efficacy outcomes vs TPC irrespective of Trop-2 expression level and in both HER2-Low (IHC1+ or IHC2+/ISH-) and HER2 IHC0 HR+/HER2– mBC, consistent with the ITT population
- ORR and CBR were improved with SG vs TPC, and DoR was extended
- No new safety signals were identified with extended follow-up

Enduring benefit with SG vs TPC in the TROPiCS-02 trial with additional follow-up reinforces SG as an important novel therapy for patients with pretreated, -endocrine-resistant HR+/HER2– mBC

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 June 2023
EMA/319185/2023
Committee for Medicinal Products for Human Use (CHMP)

Extension of indication to include

Treatment of adult patients with unresectable or metastatic hormone receptor (HR)positive, (HER2)negative breast cancer who:

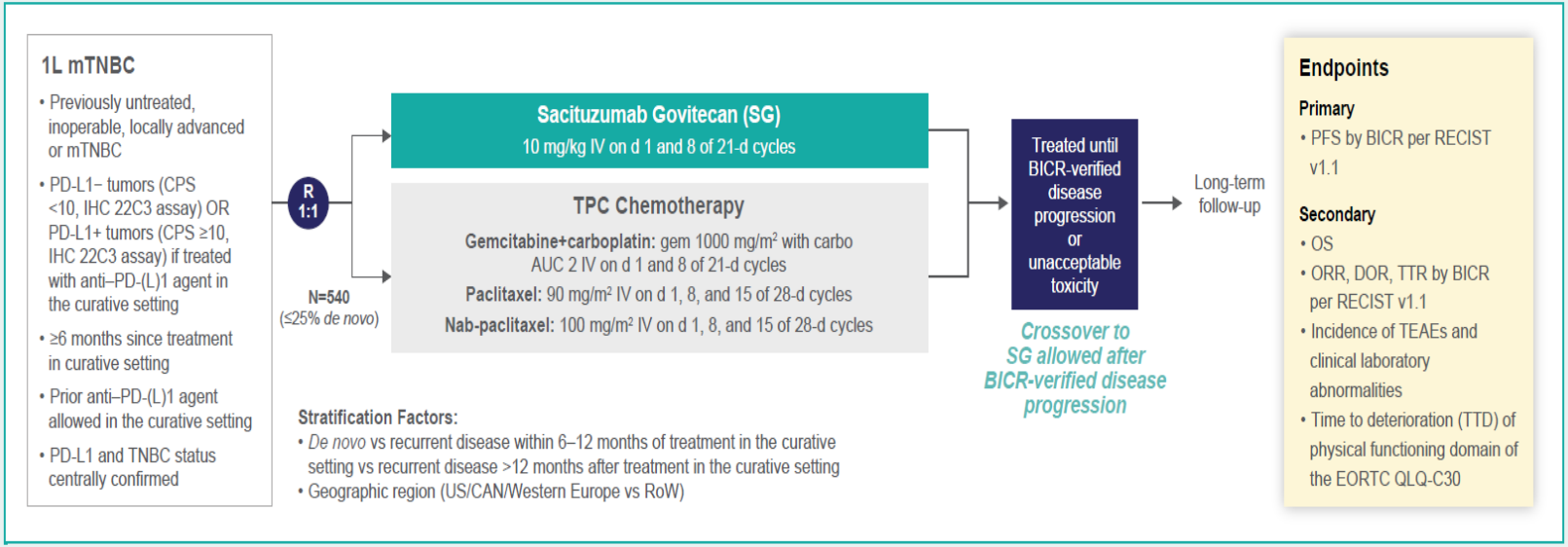
- Have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting, based on final results from study IMMU-132-09 (TROPiCS-02);

SACITUZUMAB GOVITECAN : Mas allá del ASCENT ….

- INTRODUCCIÓN
- DATOS DE RWE
- **NUEVAS INDICACIONES** : TROPICS-02

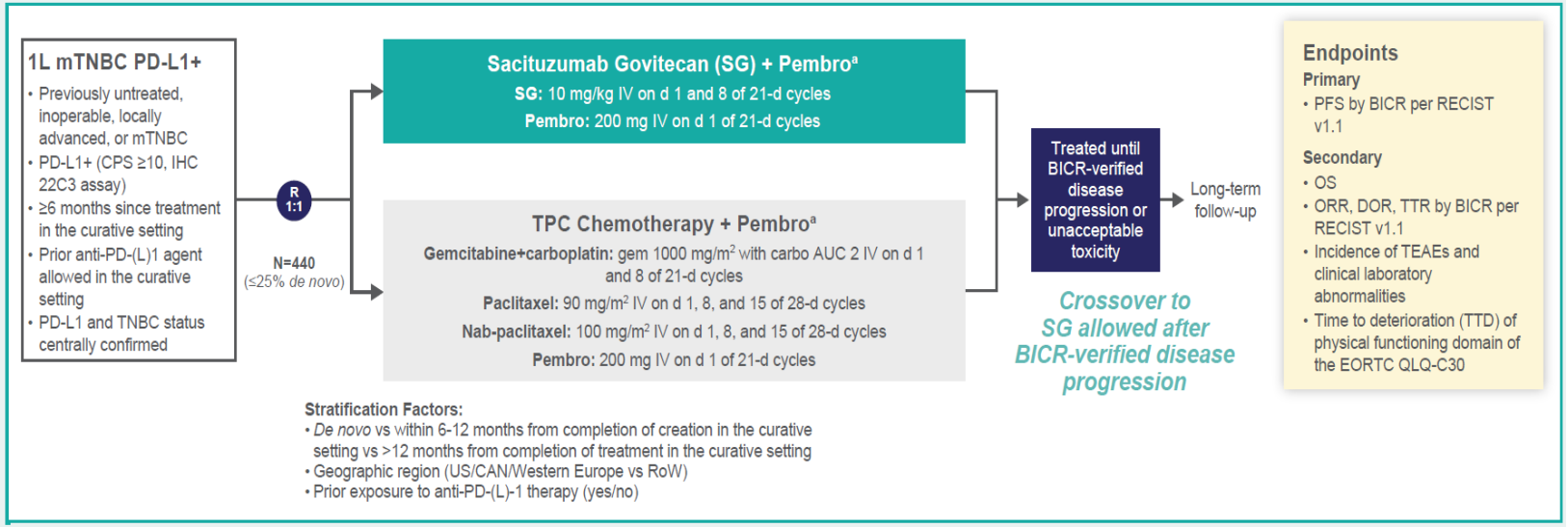
  Estudios en marcha
- Mas allá del cáncer de mama.

ASCENT-03 PD-L1 Negative Population: Study Design



1L, first-line; AUC, area under the curve; BICR, blinded independent central review; CAN, Canada; carbo, carboplatin; CPS, combined positive score; d, day; DOR, duration of response; EORTC, European Organisation for Research and Treatment of Cancer; gem, gemcitabine; IHC, immunohistochemistry; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire-Core 30; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors , version 1.1; RoW, rest of the world; SG, sacituzumab govitecan; TEAEs, treatment-emergent adverse events; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice; TTR, time to onset of response; US, United States.

ASCENT-04 PD-L1 Positive: Study Design



[a]Maximum of 35 pembro cycles.

AUC, area under the curve; BICR, blinded independent central review; CAN, Canada; carbo, carboplatin; CPS, combined positive score; d, day; DOR, duration of response; EORTC, European Organisation for Research and Treatment of Cancer; gem, gemcitabine; IHC, immunohistochemistry; IV, intravenous; mTNBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; Pembro, pembrolizumab; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire-Core 30; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid tumors, version 1.1; RoW, rest of the world; SG, sacituzumab govitecan; TEAEs, treatment-emergent adverse events; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice; TTR, time to onset of response; US, United States.

SACITUZUMAB GOVITECAN : Mas allá del ASCENT ….

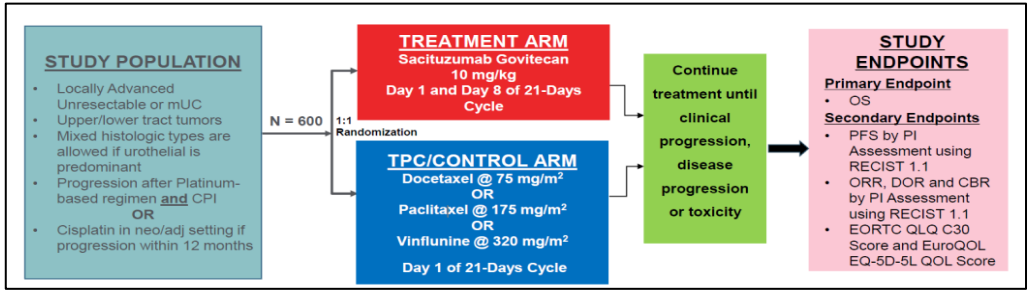
- INTRODUCCIÓN
- DATOS DE RWE
- NUEVAS INDICACIONES : TROPICS-02
  Estudios en marcha
- **Mas allá del cáncer de mama.**

Received accelerated approval in 2L metastatic urothelial cancer in the US[1,2]

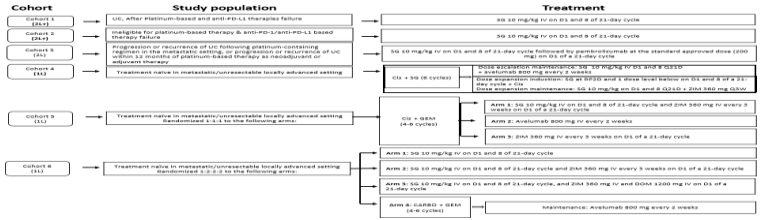
. 1 TRODELVY® (sacituzumab govitecan-hziy) [package insert]. Foster City, CA: Gilead Sciences,Inc.; April 2023. 2. European Medicines Agency: Trodelvy, INN-sacituzumab govitecan, https://www.ema.europa.eu/en/documents/product-information/trodelvy-epar-product-information_en.pdf, April 2023

GENITOURINARIO :Urothelial Cáncer (UC)

- IMMU-132-13 (TROPiCS 04): A Randomized Open-Label Phase III Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Subjects With Metastatic or Locally Advanced Unresectable Urothelial Cancer.

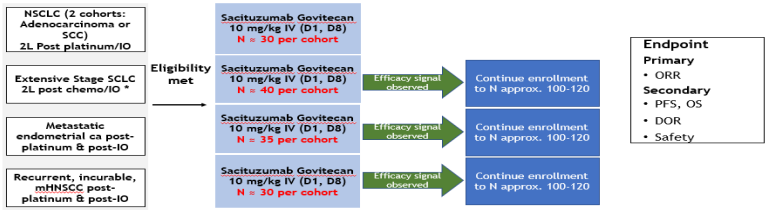


- TROPHY-U-01 Study: TROPHY-U-01, is an ongoing global, phase 2, open-label study of SG in participants with unresectable locally advanced/mUC, consisting of six treatment cohorts.

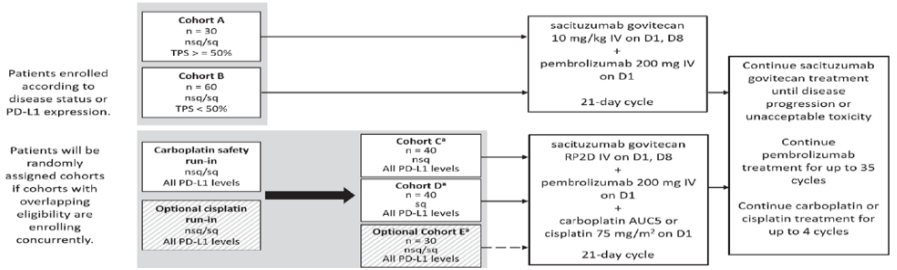


CÁNCER DE PULMÓN

IMMU-132-11 (TROPiCS 3): A Phase 2, Open-Label Study of Sacituzumab Govitecan (IMMU-132) in Subjects with Metastatic Solid Tumors



GS-US-576-6220 (EVOKE 2): An Open-label, Multicenter, Phase 2 Study of Sacituzumab Govitecan Combinations in First-line Treatment of Patients with Advanced or Metastatic Non−Small-Cell Lung Cancer (NSCLC) Without Actionable Genomic Alterations

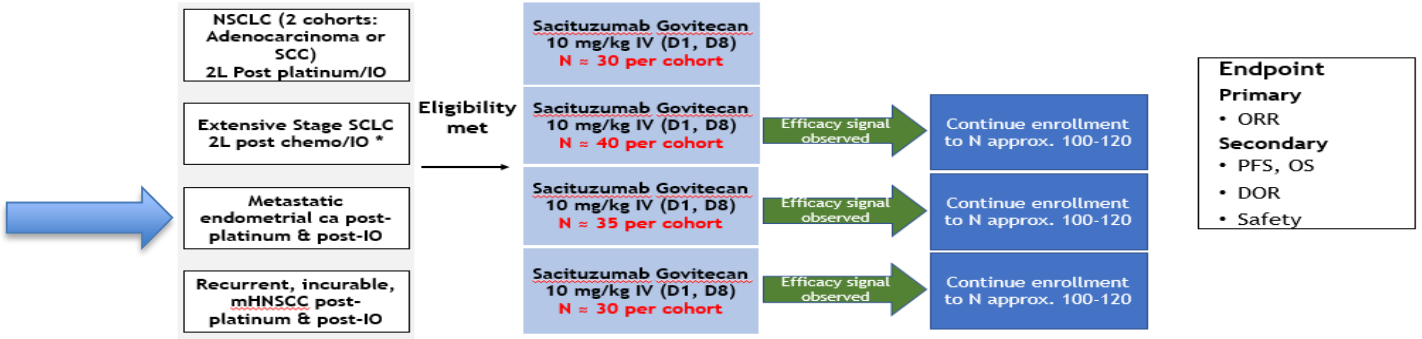


GS-US-577-6153 (EVOKE 1): Open-Label, Global, Multicenter, Randomized, Phase 3 Study of Sacituzumab Govitecan Versus Docetaxel in Patients with Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) With Progression on or After Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy

OTROS

IMMU-132-14**:** Open-label Rollover Study to Evaluate Long-Term Safety in Subjects with Metastatic Solid Tumors that are Benefiting from Continuation of Therapy with Sacituzumab Govitecan

IMMU-132-11 (TROPiCS 3): A Phase 2, Open-Label Study of Sacituzumab Govitecan (IMMU-132) in Subjects with Metastatic Solid Tumors



MUCHAS GRACIAS !!!!