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Efficacy analysis and updated safety from the phase 2 PRIMED study of prophylactic granulocyte-colony stimulating factor (G-CSF) and loperamide for patients with HER2-negative advanced breast cancer treated with sacituzumab govitecan

José Manuel Pérez-García[1,2], María Gion [1,3,4], Manuel Ruiz-Borrego[5], Isabel Blancas[6,7,8], Elena López-Miranda[1,3], Salvador Blanch[9], Sabela Recalde[10], Lourdes Calvo[11], Xavier González[12], Nerea Ancizar[13], Serafin Morales[14], Patricia Cortez[4,15], Zuzanna Piwowarska[1], Eileen Shimizu[1], José Antonio Guerrero[1], Miguel Sampayo-Cordero[1], Alejandro Martínez-Bueno[15], Javier Cortés[1,2,4,17], Antonio Llombart-Cussac[1,18,19]

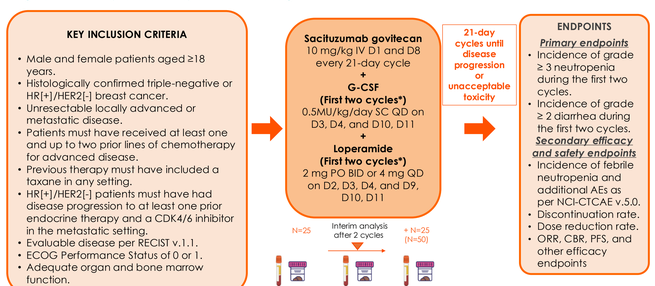
1. Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil); 2. International Breast Cancer Center (IBCC), Pangaea Group, Quiron Group, Barcelona, Spain ; 3. Hospital Universitario Ramón y Cajal, Madrid, Spain ; 4. IOB Madrid, Hospital Beata María Ana, Madrid, Spain 5. Hospital Universitario Virgen del Rocío, Sevilla, Spain; 6. Hospital Universitario Clínico San Cecilio, Granada, Spain 7. Medicine Department, Granada University, Granada, Spain; 8. Instituto de Investigación Biosanitaria de Granada, Granada, Spain; 9. Instituto Valenciano de Oncología, Valencia, Spain; 10. Institut Català d'Oncologia Hospitalet- Hospital Moises Broggi, Barcelona, Spain; 11. Complejo Hospitalario Universitario A Coruña, Coruña, Spain; 12. Institut Oncològic Dr. Rosell, Hospital General de Catalunya, Sant Cugat del Vallès, Spain; 13. Hospital Universitario de Donostia, San Sebastián, Spain; 14. Hospital Universitario de Arnau de Villanova de Lleida, Lleida, Spain; 15. IOB Institute of Oncology, Hospital Ruber Internacional, Quiron Group, Madrid, Spain; 16. Instituto Oncológico Dr. Rosell, Hospital Quiron Dexeus, Barcelona, Spain 17. Universidad Europea de Madrid, Faculty of Biomedical and Helath Sciences, Department of Medicine, Madrid, Spain; 18. Arnau de Vilanova, Valencia, Spain; 19. Universidad Católica de Valencia, Valencia, Spain

BACKGROUND

- Sacituzumab govitecan is a Trop-2-directed antibody drug conjugate that has shown a statistically significant and clinically meaningful overall survival benefit for patients with HER2[-] advanced breast cancer in two phase III trials: ASCENT and TROPiCS-02[1-4].
- The most common treatment-emergent adverse events of any grade associated with sacituzumab govitecan are neutropenia (~60-70%) and diarrhea (~60%), which can lead to dose reductions and treatment interruptions/discontinuations[2-3].
- Previously, the PRIMED study demonstrated that primary prophylactic administration of G-CSF and loperamide resulted in a clinically meaningful reduction of neutropenia and diarrhea during the first two treatment cycles of sacituzumab govitecan [5].
- Herein we report the extended safety follow-up and secondary efficacy endpoints.

STUDY DESIGN

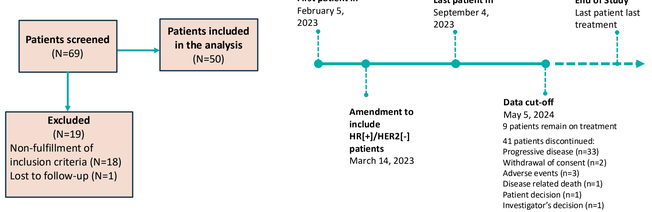
Figure 1. PRIMED (NCT05520723) clinical trial design



*Continuation of G-CSF and loperamide was at physician's discretion after cycle 2

PATIENT RECRUITMENT

Figure 2. PRIMED patient recruitment and timeline



RESULTS

1. Efficacy Results

- Between February 2023 and September 2023, 50 patients were enrolled (Figure 2): 32 patients with TNBC and 18 patients with HR[+]/HER2[-] breast cancer.
- At data cut-off (May 5, 2024), with a median follow-up of 9.0 months (range; 0.2-13.5), 9 patients remained on treatment (Figure 2).
- The median PFS for patients with TNBC was 6.4 months (95%CI; 6.1-10.3) and for patients with HR[+]/HER2[-] tumors was 5.8 months (95%CI; 4.2-NA) (Figure 3).
- The ORR and CBR were 34.4% and 71.9% for TNBC, and 16.7% and 44.4% for HR[+]/HER2[-] patients, respectively (Table 2).

Table 1. Patient baseline demographics

Patient characteristics, n (%)	TNBC (N = 32)	HR[+]/HER2[-] (N = 18)	Overall (N = 50)
Age in years, Median (Min; Max)	51.0 (31;74)	53.5 (37;72)	52.0 (31;74)
ECOG			
0	18 (56.3%)	12 (66.7%)	30 (60.0%)
1	14 (43.8%)	6 (33.3%)	20 (40.0%)
Visceral disease			
Yes	20 (62.5%)	15 (83.3%)	35 (70.0%)
No	12 (37.5%)	3 (16.7%)	15 (30.0%)
Prior chemotherapy in the (neo)adjuvant setting			
Yes	19 (59.4%)	5 (27.8%)	24 (48.0%)
No	13 (40.6%)	13 (72.2%)	26 (52.0%)
Prior chemotherapy regimens for advanced disease			
0*	8 (25.0%)	2 (11.1%)	10 (20.0%)
1	18 (56.3%)	11 (66.1%)	29 (58.0%)
2	6 (18.8%)	5 (27.8%)	11 (22.0%)

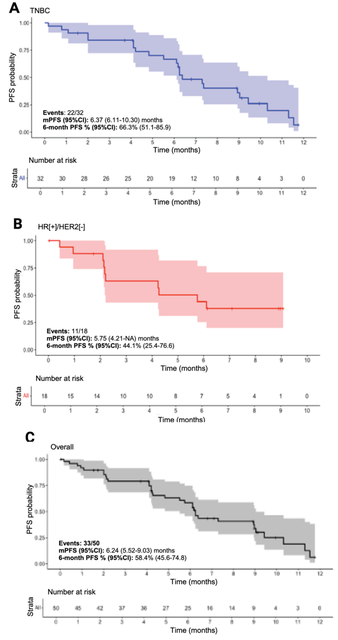
*Earlier systemic treatment in the curative setting was considered as one line of therapy if the development of unresectable locally advanced or metastatic disease occurred within a 12-month period after completion of chemotherapy or immunotherapy

Table 2. Secondary efficacy endpoints

n (%)	TNBC (N=32)	HR[+]/HER2[-] (N=18)	Overall (N=50)
CR	1 (3.2%)	0 (0%)	1 (2.0%)
PR	10 (31.2%)	3 (16.7%)	13 (26.0%)
SD≥24w	12 (37.5%)	5 (27.8%)	17 (34.0%)
SD<24w	3 (9.4%)	3 (16.7%)	6 (12.0%)
PD	4 (12.5%)	6 (33.3%)	10 (20.0%)
Not performed*	2 (6.2%)	1 (5.6%)	3 (6.0%)
ORR, 95%CI	11 (34.4%) (19.1-53.2)	3 (16.7%) (4.4-42)	14 (28.0%) (16.7-42.7)
CBR, 95%CI	23 (71.9%) (53.3-65.8)	8 (44.4%) (21.5-69.2)	31 (62.0%) (47.2-75.4)

*Patient stopped treatment before first post-baseline tumor assessment

Figure 3. Progression-free survival in (A) TNBC, (B) HR[+]/HER2[-], and (C) all patients



2. Extended Safety Results

- Previously safety analysis had a median follow-up of 4.3 months (range; 0.2-8.6).
- For the extended analysis, with a median follow-up of 9.0 months (range; 0.2-13.5), the incidence of any grade (G) neutropenia and diarrhea were 42.0% and 44.0%, respectively (Table 3).
- A total of 12 patients (24.0%) had ≥ G3 neutropenia (18.0% G3; 6.0% G4; with no febrile neutropenia) and 9 patients (18.0%) had ≥ G2 diarrhea (4.0% G3, with no G4).
- The overall rate of all AEs associated with dose reductions and treatment interruptions was 22.0% and 50.0%, respectively (Table 4).
- Four patients discontinued due to AEs, two of which were sacituzumab govitecan-related (G2 enteritis and G3 diarrhea).
- TEAEs were consistent with the known safety profile of sacituzumab govitecan (Table 5).
- Constipation was higher in PRIMED, which was manageable and expected given the prophylactic use of loperamide and occurred in 56.0% of patients (Table 5).

Table 3. Rates of neutropenia and diarrhea during the first two cycles and until data cut-off

	Neutropenia						Diarrhea					
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade	n (%)	Grade 1	Grade 2	Grade 3	Any Grade
After two cycles	2 (4.0%)	4 (8.0%)	6 (12.0%)	2 (4.0%)	14 (28.0%)	**After two cycles**	9 (18.0%)	6 (12.0%)	2 (4.0%)	17 (34.0%)
Data cut-off	4 (8.0%)	5 (10.0%)	9 (18.0%)	3 (6.0%)	21 (42.0%)	**Data cut-off**	13 (26.0%)	7 (14.0%)	2 (4.0%)	22 (44.0%)

Table 4. Dose reductions, treatment interruptions, and permanent discontinuations due to adverse events during the first two cycles and until data cut-off

n (%)	Dose Reductions	Treatment Interruptions	Permanent Discontinuations
After two cycles	7 (14.0%)	15 (30.0%)	0 (0.0%)
Data cut-off	11 (22.0%)	25 (50.0%)	4 (8.0%)

Table 5: TEAEs occurring in ≥20% of patients or grade 3 or more until data cut-off

	Any grade	Grade 1	Grade 2	Grade ≥3
All TEAEs, n (%)	50 (100%)	46 (92.0%)	37 (74.0%)	26 (52.0%)
Gastrointestinal Disorders	47 (94.0%)	43 (86.0%)	16 (32.0%)	6 (12.0%)
- Constipation	28 (56.0%)	23 (46.0%)	5 (10.0%)	0 (0.0%)
- Nausea	27 (54.0%)	24 (48.0%)	3 (6.0%)	0 (0.0%)
- Diarrhea	22 (44.0%)	13 (26.0%)	7 (14.0%)	2 (4.0%)
- Abdominal Pain Upper	9 (18.0%)	7 (14.0%)	0 (0.0%)	2 (4.0%)
- Intestinal Obstruction	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
- Neutropenic Colitis	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
General Disorders and Administration Site Conditions	38 (76.0%)	22 (44.0%)	16 (32.0%)	8 (16.0%)
- Asthenia	35 (70.0%)	13 (26.0%)	15 (30.0%)	7 (14.0%)
- Pain	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
Blood and Lymphatic System Disorders	32 (64.0%)	18 (36.0%)	10 (20.0%)	13 (26.0%)
-Anemia	24 (48.0%)	15 (30.0%)	7 (14.0%)	2 (4.0%)
-Neutropenia	21 (42.0%)	4 (8.0%)	5 (10.0%)	12 (24.0%)
Infections and Infestations	23 (46.0%)	16 (32.0%)	8 (16.0%)	1 (2.0%)
- Acute Pyelonephritis	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
Skin and Subcutaneous Tissue Disorders	30 (60.0%)	17 (34.0%)	16 (32.0%)	5 (10.0%)
- Alopecia	20 (40.0%)	2 (4.0%)	14 (28.0%)	4 (8.0%)
- Urticaria	2 (4.0%)	0 (0.0%)	1 (2.0%)	1 (2.0%)
Investigations	14 (28.0%)	13 (26.0%)	2 (4.0%)	2 (4.0%)
- Increased Gamma-Glutamyltransferase	6 (12.0%)	4 (8.0%)	0 (0.0%)	2 (4.0%)
Hepatobiliary Disorders	5 (10.0%)	3 (6.0%)	1 (2.0%)	1 (2.0%)
- Hepatic Failure	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)

CONCLUSIONS

- The efficacy results of sacituzumab govitecan in the PRIMED study are consistent with previously reported data.
- PRIMED had lower rates of all grade and ≥G3 neutropenia and diarrhea compared to the ASCENT and TROPICS02 trials, with fewer dose reductions and treatment interruptions.
- G-CSF and loperamide should be considered as primary prophylactic treatment for patients receiving sacituzumab govitecan.

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CONTACT INFORMATION

José Manuel Pérez-García, MD

jose.perez@medsir.org

Abbreviations: **AEs:** adverse events; **BID:** twice a day; **CBR:** clinical benefit rate; **CR:** complete response; **D:** days; **ECOG**: Eastern Cooperative Oncology Group; **G:** grade; **G-CSF**: granulocyte-colony stimulating factor; **HR[+]/HER2[-]:** hormone receptor-positive/HER2-negative; **IV:** intravenous; **n(%):** number of patients (percentage of patients); **NA:** not available; **NCI-CTCAE:** National Cancer Institute-Common Terminology Criteria for Adverse Events; **ORR:** objective response rate; **PD:** progressive disease; **PFS:** progression-free survival; **PO**: orally; **PR:** partial response; **QD:** daily; **QoL**: quality of life; **RECIST V.1.1**: Response Evaluation Criteria In Solid Tumors version 1.1; **SC**: subcutaneous; **SD:** stable disease; **TEAEs:** treatment emergent adverse events; **TNBC**: triple-negative breast cancer; **Trop-2**: trophoblast cell surface antigen 2