

Subgroup Analysis From the ASCENT-04/KEYNOTE-D19 Study of Sacituzumab Govitecan + Pembrolizumab vs Chemotherapy + Pembrolizumab in Previously Untreated Metastatic Triple-Negative Breast Cancer: PFS by Preselected Chemotherapy, Disease Status, and Brain and Visceral Metastases

Evandro de Azambuja¹, Peter Schmid², Kevin Kalinsky³, Sherene Loi⁴, Sung-Bae Kim⁵, Clinton Yam⁶, Bernardo Rapoport^{7,8}, Seock-Ah Im⁹, Barbara Pistilli¹⁰, Wassim Mchayleh¹¹, David W Cescon¹², Junichiro Watanabe¹³, Manuel Alejandro Lara Banuelas¹⁴, Ruffo Freitas-Junior¹⁵, Alain Lortholary¹⁶, Maryam Afshari¹⁷, Ann Chen¹⁷, Danjie Zhang¹⁷, Sara M Tolaney¹⁸

Evandro de Azambuja¹, Peter Schmid², Kevin Kalinsky³, Sherene Loi⁴, Sung-Bae Kim⁵, Clinton Yam⁶, Bernardo Rapoport^{7,8}, Seock-Ah Im⁹, Barbara Pistilli¹⁰, Wassim Mchayleh¹¹, David W Cescon¹², Junichiro Watanabe¹³, Manuel Alejandro Lara Banuelas¹⁴, Ruffo Freitas-Junior¹⁵, Alain Lortholary¹⁶, Maryam Afshari¹⁷, Ann Chen¹⁷, Danjie Zhang¹⁷, Sara M Tolaney¹⁸

1Institut Jules Bordet, Hôpital Universitaire de Bruxelles (HUB) and Université Libre de Bruxelles (ULB), Brussels, Belgium; 2Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; 3Winship Cancer Institute, Emory University, Atlanta, GA, USA; 4Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia; 5Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 6University of Texas MD Anderson Cancer Center, Houston, TX, USA; 7Medical Oncology Centre of Rosebank, Clinical and Translational Research Unit, Saxonwold, South Africa; 8Department of Immunology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa; 9Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; 10Department of Cancer Medicine, Gustave Roussy, Villejuif, France; 11AdventHealth Cancer Institute, Orlando, FL, USA; 12Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; 13Juntendo University Graduate School of Medicine, Tokyo, Japan; 14SCIENTIA Investigación Clínica, Chihuahua, Mexico; 15Araujo Jorge Cancer Hospital, Goias Anticancer Association, Goiânia, Brazil; 16Department of Medical Oncology, Hopital Privé du Confluent, Nantes, France; 17Gilead Sciences, Inc., Foster City, CA, USA; 18Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Poster 4648P

ASCENT-04/
KEYNOTE-D19

Copies of this poster obtained through QR, AR and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.

Conclusions

- Consistent with the overall results of the ASCENT-04 study, first-line (1L) sacituzumab govitecan (SG) + pembrolizumab demonstrated clinical benefit vs chemotherapy (chemo) + pembrolizumab in this clinical subgroup analysis of participants with programmed death ligand 1-positive (PD-L1+) metastatic triple-negative breast cancer (mTNBC)
 - The benefit was observed across key clinical subgroups, including preselected chemo, disease status, and presence of brain and visceral metastases at baseline
- A progression-free survival (PFS) benefit was observed with SG + pembrolizumab across all assessed subgroups by blinded independent central review (BICR) and investigator assessment
- Fewer participants developed new visceral lesions with SG + pembrolizumab vs chemo + pembrolizumab at time of progression
- Findings from this exploratory analysis in participants with PD-L1+ mTNBC in ASCENT-04, in conjunction with results from the ASCENT-03 study of SG monotherapy vs chemo for PD-(L)1 inhibitor–ineligible mTNBC,¹ support the use of 1L SG as the backbone of care for patients with previously untreated, locally advanced unresectable or mTNBC, regardless of PD-L1 status

Plain Language Summary

- This additional analysis from the ASCENT-04 study explored how the treatment combination of sacituzumab govitecan (SG) + pembrolizumab worked compared with chemotherapy + pembrolizumab in different groups of participants with advanced triple-negative breast cancer whose tumors make a protein called PD-L1, including those whose cancer had returned and those whose cancer had spread to the brain or other organs at the time of enrollment in the study
- Across these groups, SG + pembrolizumab generally helped participants live longer without their cancer getting worse or without them dying compared with chemotherapy + pembrolizumab
- When their cancer worsened, fewer participants treated with SG + pembrolizumab developed new areas with cancer in organs, such as the lungs or liver, compared with those treated with chemotherapy + pembrolizumab
- The results were consistent with results from the overall population in the study and support the use of SG + pembrolizumab as a first treatment option for patients with advanced triple-negative breast cancer

Introduction

- TNBC is a heterogeneous and aggressive subtype of breast cancer associated with poor outcomes²
 - Outcomes are particularly unfavorable in certain patient subgroups (eg, those defined by disease recurrence or sites of metastasis)^{2,3} due to poor prognosis and limited treatment options
- The Trop-2–targeted antibody-drug conjugate, SG, in combination with pembrolizumab was recently approved in the European Union, United States, and other regions based on the results of the phase 3 ASCENT-04 study⁴⁻⁶ and is recommended globally in multiple treatment guidelines as a preferred 1L option for patients with unresectable locally advanced or mTNBC whose tumors express PD-L1 (combined positive score [CPS] ≥ 10)^{7,8}
- In the PFS primary analysis from ASCENT-04 of SG + pembrolizumab vs chemo + pembrolizumab:
 - Median PFS by BICR was 11.2 months vs 7.8 months (stratified hazard ratio [HR], 0.65; 95% CI, 0.51-0.84) and by investigator assessment was 11.3 months vs 8.3 months (stratified HR, 0.67; 95% CI, 0.52-0.87)⁴
 - Overall survival (OS) data were immature (at 26% maturity), and median OS was not reached in either group⁴
- Given the demonstrated clinical benefit of 1L SG + pembrolizumab, evaluating treatment outcomes across clinically relevant patient subgroups may provide insights into SG efficacy across diverse patient populations
- Here, the efficacy results in subgroups of clinical interest from ASCENT-04 are presented

Methods

- Participants were randomized 1:1 to SG + pembrolizumab or chemo (taxanes [paclitaxel, nab-paclitaxel] or gemcitabine + carboplatin [gem/carbo]) + pembrolizumab
- The primary end point was PFS by BICR
- An analysis was conducted in the following prespecified subgroups:
 - Chemo selected prior to randomization (taxane, gem/carbo)
 - Disease status (de novo metastatic, recurrent disease within 6-12 months and > 12 months)
 - Presence of brain metastases at baseline (yes/no)
- A post hoc analysis by presence of visceral metastases at baseline (yes/no) was also conducted
- These analyses were not powered to detect statistically significant differences between subgroups

Results

- In total, 443 participants were enrolled and randomly assigned (intent-to-treat [ITT] population) to receive SG + pembrolizumab (n = 221) or chemo + pembrolizumab (n = 222)
- Baseline characteristics were generally well balanced between the SG + pembrolizumab and chemo + pembrolizumab groups, both overall and within each assessed subgroup (**Table 1**)
 - Median age was generally consistent across subgroups, ranging from 48 to 60 years, with approximately one-quarter of participants aged ≥ 65 years
 - The majority of participants had an Eastern Cooperative Oncology Group performance status of 0 at baseline, irrespective of the subgroup
 - Recurrent disease was more common than de novo metastatic disease, with approximately half of participants experiencing disease recurrence > 12 months after prior treatment in the curative setting
 - Consistent with contemporary clinical practice, preselected chemotherapy varied by disease setting; there was a higher proportion of participants with recurrent disease preselected for gem/carbo and a higher proportion of participants with de novo disease preselected for taxane treatment

Figure 1. Progression-Free Survival by BICR Across Subgroups

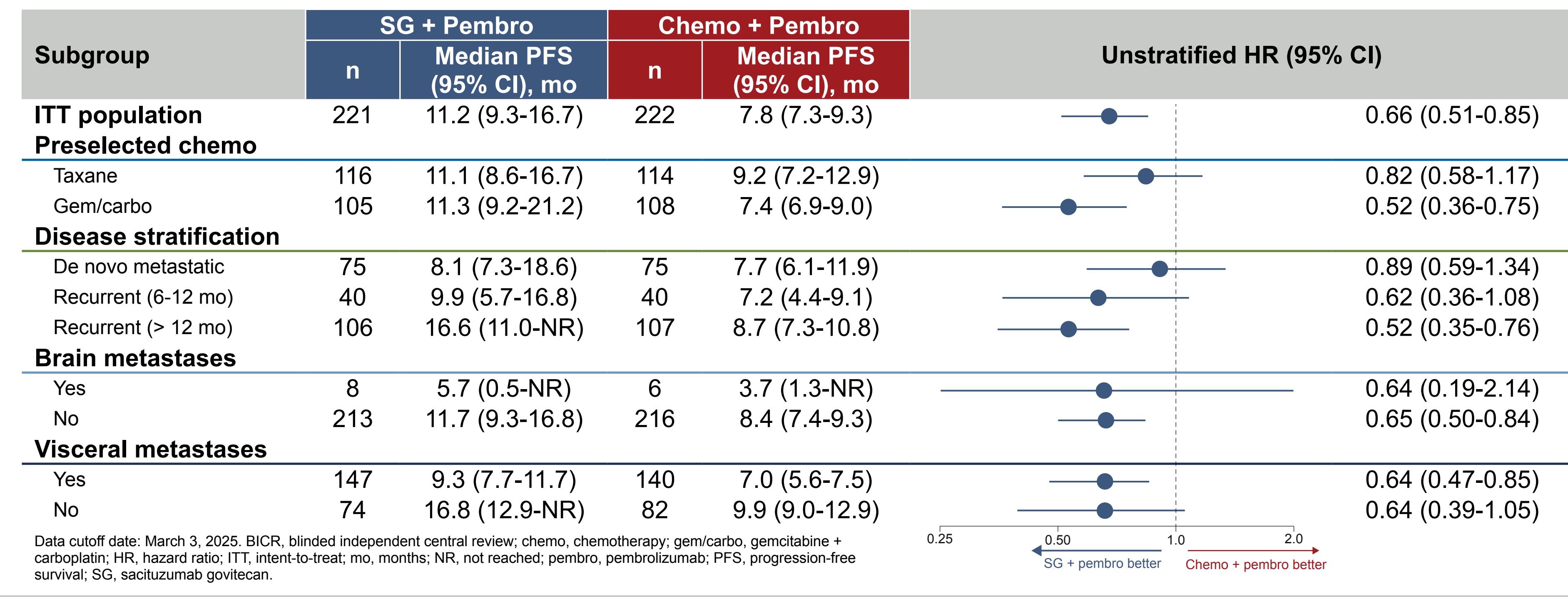


Figure 2. Progression-Free Survival by Investigator Assessment Across Subgroups

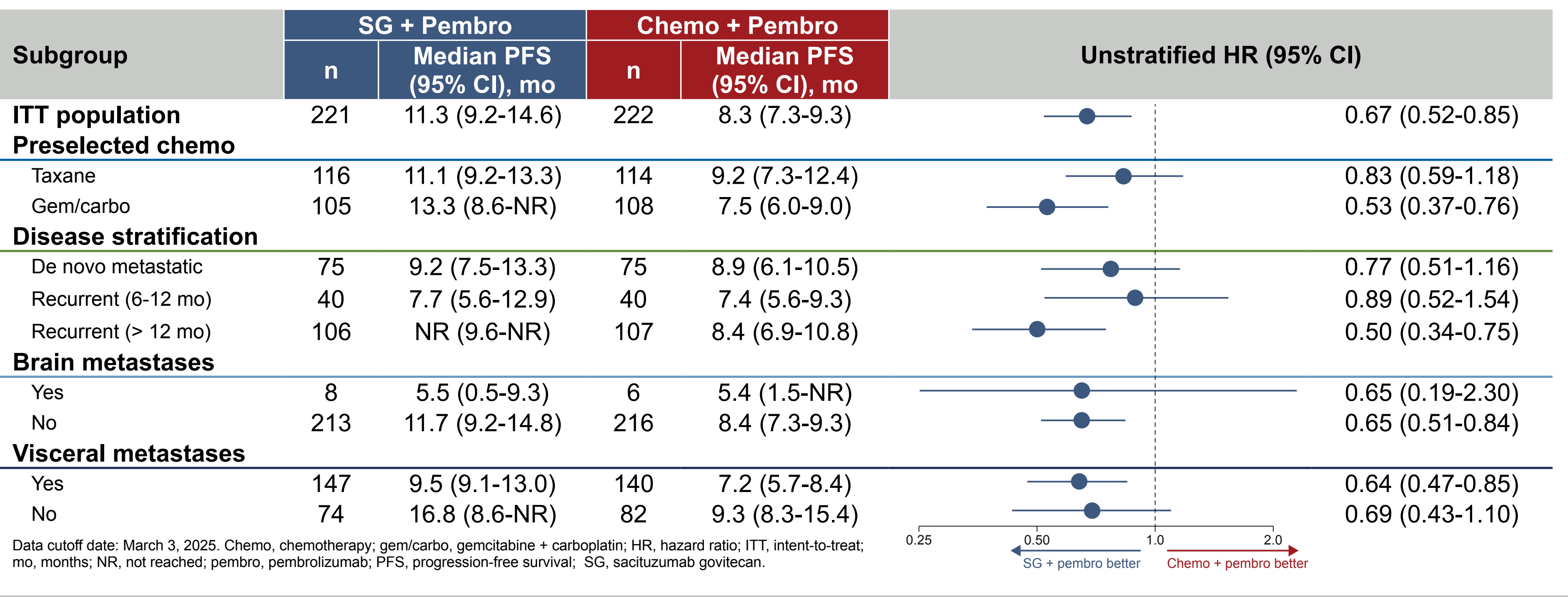


Table 1. Demographic and Baseline Characteristics of Participants Across Subgroups

Characteristics	ITT Population		Preselected Chemo				Disease Stratification								Brain Metastases				Visceral Metastases			
	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)	SG + Pembro (n = 116)	Chemo + Pembro (n = 116)	SG + Pembro (n = 105)	Chemo + Pembro (n = 105)	SG + Pembro (n = 75)	Chemo + Pembro (n = 75)	SG + Pembro (n = 40)	Chemo + Pembro (n = 40)	SG + Pembro (n = 106)	Chemo + Pembro (n = 107)	SG + Pembro (n = 8)	Chemo + Pembro (n = 6)	SG + Pembro (n = 213)	Chemo + Pembro (n = 216)	SG + Pembro (n = 147)	Chemo + Pembro (n = 140)	SG + Pembro (n = 74)	Chemo + Pembro (n = 82)
Median age (range), years	54 (23-88)	55 (27-82)	56 (23-83)	60 (28-82)	52 (24-88)	53 (27-79)	54 (23-83)	53 (28-78)	48 (25-77)	55 (27-79)	57 (28-88)	56 (28-82)	51 (37-75)	49 (38-68)	54 (23-88)	55 (27-82)	53 (23-88)	54 (27-82)	56 (25-77)	56 (28-79)		
≥ 65 years, n (%)	58 (26)	57 (26)	32 (28)	36 (32)	26 (25)	21 (19)	21 (28)	15 (20)	7 (18)	9 (23)	30 (28)	33 (31)	2 (25)	2 (33)	56 (26)	55 (25)	38 (26)	37 (26)	20 (27)	20 (24)		
Race or ethnic group,* n (%)																						
White	139 (63)	118 (53)	86 (74)	67 (59)	53 (50)	51 (47)	40 (53)	39 (52)	28 (70)	23 (58)	71 (67)	56 (52)	8 (100)	4 (67)	131 (62)	114 (53)	97 (66)	79 (56)	42 (57)	39 (48)		
Asian	43 (19)	63 (28)	16 (14)	30 (26)	27 (26)	33 (31)	18 (24)	23 (31)	3 (8)	8 (20)	22 (21)	32 (30)	0	1 (17)	43 (20)	62 (29)	23 (16)	33 (24)	20 (27)	30 (37)		
Black	13 (6)	11 (5)	6 (5)	4 (4)	7 (7)	7 (6)	3 (4)	4 (5)	4 (10)	2 (5)	6 (6)	5 (5)	0	0	13 (6)	11 (5)	8 (5)	7 (5)	5 (7)	4 (5)		
Other or not specified	26 (12)	30 (14)	8 (7)	13 (11)	18 (17)	17 (16)	14 (19)	9 (12)	5 (13)	7 (18)	7 (7)	14 (13)	0	1 (17)	26 (12)	29 (13)	19 (13)	21 (15)	7 (9)	9 (11)		
Geographic region, n (%)																						
Canada/United States/Western Europe	85 (38)	85 (38)	48 (41)	52 (46)	37 (35)	33 (31)	32 (43)	31 (41)	13 (33)	12 (30)	40 (38)	42 (39)	3 (38)	3 (50)	82 (38)	82 (38)	64 (44)	58 (41)	21 (28)	27 (33)		
Rest of the world ^b	136 (62)	137 (62)	68 (59)	62 (54)	68 (65)	75 (69)	43 (57)	44 (59)	27 (68)	28 (70)	66 (62)	65 (61)	5 (63)	3 (50)	131 (62)	134 (62)	83 (56)	82 (59)	53 (72)	55 (67)		
ECOG PS, ^c n (%)																						
0	156 (71)	154 (69)	84 (72)	80 (70)	72 (69)	74 (69)	54 (72)	53 (71)	30 (75)	29 (73)	72 (68)	72 (67)	4 (50)	2 (33)	152 (71)	152 (70)	101 (69)	93 (66)	55 (74)	61 (74)		
1	65 (29)	67 (30)	32 (28)	33 (29)	33 (31)	34 (31)	21 (28)	22 (29)	10 (25)	11 (28)	34 (32)	34 (32)	4 (50)	4 (67)	61 (29)	63 (29)	46 (31)	46 (33)	19 (26)	21 (26)		
Disease stratification, n (%)																						
De novo	75 (34)	75 (34)	41 (35)	50 (44)	34 (32)	25 (23)	75 (100)	75 (100)	0	0	0	0	1 (13)	1 (17)	74 (35)	74 (34)	53 (36)	44 (31)	22 (30)	31 (38)		
Recurrent within 6-12 months	40 (18)	40 (18)	20 (17)	11 (10)	20 (19)	29 (27)	0	0	40 (100)	40 (100)	0	0	3 (38)	1 (17)	37 (17)	39 (18)	24 (16)	27 (19)	16 (22)	13 (16)		
Recurrent > 12 months	106 (48)	107 (48)	55 (47)	53 (46)	51 (49)	54 (50)	0	0	0	0	106 (100)	107 (100)	4 (50)	4 (67)	102 (48)	103 (48)	70 (48)	69 (49)	36 (49)	38 (46)		
Metastatic sites, n (%)																						
Lung	111 (50)	95 (43)	60 (52)	45 (39)	51 (49)	50 (46)	32 (43)	20 (27)	20 (50)	22 (55)	59 (56)	53 (50)	7 (88)	3 (50)	104 (49)	92 (43)	111 (76)	95 (68)	0	0		
Liver	55 (25)	57 (26)	25 (22)	30 (26)	30 (29)	27 (25)	28 (37)	26 (35)	10 (25)	6 (15)	17 (16)	25 (23)	3 (38)	2 (33)	52 (24)	55 (25)	55 (37)	57 (41)	0	0		
Brain	8 (4)	6 (3)	7 (6)	4 (4)	1 (1)	2 (2)	1 (1)	1 (1)	3 (8)	1 (3)	4 (4)	4 (4)	8 (100)	6 (100)	0	0	8 (5)	6 (4)	0	0		
Chemo selected prior to randomization, n (%)																						
Taxane	116 (52)	114 (51)	116 (100)	114 (100)	0	0	41 (55)	50 (67)	20 (50)	11 (28)	55 (52)	53 (50)	7 (88)	4 (67)	109 (51)	110 (51)	77 (52)	71 (51)	39 (53)	43 (52)		
Gemcitabine plus carboplatin	105 (48)	108 (49)	0	0	105 (100)	108 (100)	34 (45)	25 (33)	20 (50)	29 (73)	51 (48)	54 (50)	1 (13)	2 (33)	104 (49)	106 (49)	70 (48)	69 (49)	35 (47)	39 (48)		

Data cutoff date: March 3, 2025. *As reported by the participants; other/not specified includes American Indian or Alaska Native, other races, and not provided/collection not permitted. ^bRest of the world includes Argentina, Australia, Brazil, Chile, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Singapore, Republic of Korea, South Africa, Taiwan, and Turkey. ^cOne participant in the chemo + pembro group assigned to taxane prior to randomization, with recurrent disease (> 12 months), with visceral metastasis, and with no brain metastasis had an ECOG PS of 2. Chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; gem/carbo, gemcitabine + carboplatin; ITT, intent-to-treat; pembro, pembrolizumab; SG, sacituzumab govitecan.

References: 1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25. 2. Hurvitz SA, et al. *NPJ Breast Cancer*. 2024;10:33. 3. Grinda T, et al. *Eur J Cancer*. 2023;189:112935. 4. Tolaney SM, et al. *N Engl J Med*. 2026;394:354-66. 5. TRODELVY® (sacituzumab govitecan-hzxy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; June 2026. 6. Gilead Sciences, Inc. European Commission expands role of Gilead's Trodelvy® in first-line metastatic triple-negative breast cancer across PD-L1 status. August 24, 2026. Accessed August 31, 2026. <https://www.gilead.com/news/news-details/2026/european-commission-expands-role-of-gileads-trodelvy-in-first-line-metastatic-triple-negative-breast-cancer-across-pd-l1-status>. 7. de Azambuja E, et al. *Ann Oncol*. 2026 May 29. Online ahead of print. doi: 10.1016/j.annonc.2026.05.707. 8. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. Version 4.2026. National Comprehensive Cancer Network. Accessed August 31, 2026. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Acknowledgments: We extend our thanks to the patients, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. Writing/editorial support was provided by Kanchan Bhatti, MPharm, of Parexel, and funded by Gilead Sciences, Inc.

Disclosures: EDA reports advisory board roles with Roche/Genentech, Novartis, Seagen, Eli Lilly, MSD, Gilead Sciences, Bayer, Boehringer Ingelheim, AstraZeneca, and Menarini; invited speaker roles with AstraZeneca, Boehringer Ingelheim, and Gilead Sciences; steering committee membership for Gilead Sciences, Roche, Breast International Group, and AstraZeneca; research grant support from Roche/Genentech, AstraZeneca, Gilead Sciences, Seagen, and GSK/Novartis; other financial interests with Gilead Sciences and Roche/Genentech; local or coordinating principal investigator roles for MSD, ABCSG, Nektar, Gilead Sciences, Immunomedics, Synthron, Odonate Therapeutics, Absynth, and Pfizer; travel grant support from Gilead Sciences and MSD; and nonfinancial advisory, editorial, and leadership roles with the European Organisation for Research and Treatment of Cancer (EORTC), KCE Belgium, ESMO Open, Anticancer Research, the Belgian Society of Medical Oncology, and the Breast International Group.

Correspondence: Evandro de Azambuja, evandro.deazambuja@hubruxelles.be