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Patient-Reported Outcomes With Sacituzumab Govitecan Plus Pembrolizumab vs Chemotherapy Plus Pembrolizumab in Patients With Previously Untreated PD-L1+ Metastatic Triple-Negative Breast Cancer in the Phase 3 ASCENT-04/KEYNOTE-D19 Study

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Monday, October 20, 2025; 10:15 – 10:20 AM

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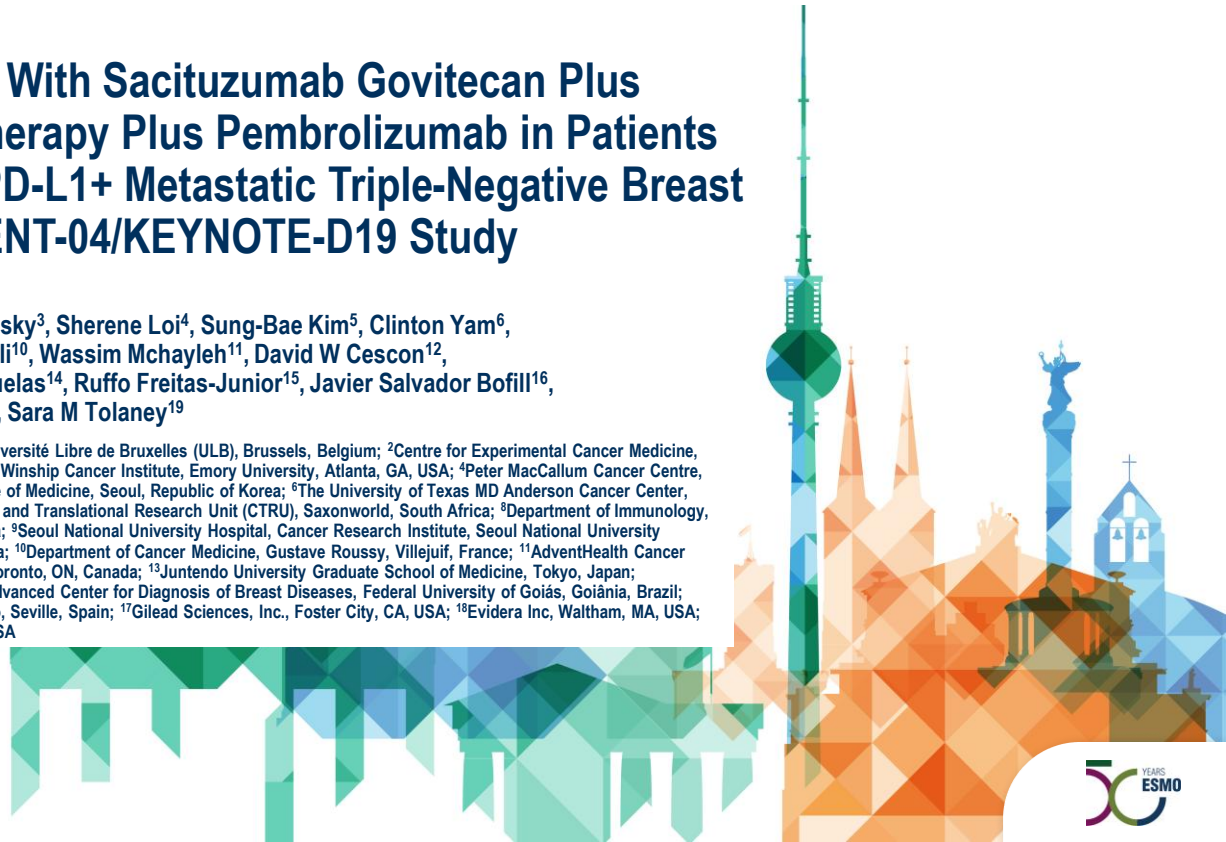

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Declaration of Interests

Evandro de Azambuja, MD, PhD

Advisory Boards: Gilead Sciences, MSD, Novartis, Roche/Genentech, and Seagen

Invited Speaker: AstraZeneca, Eli Lilly, Gilead Sciences, Libbs, Pierre Fabre, and Zodiac

Institutional Research Funding: AstraZeneca, GlaxoSmithKline/Novartis, Pfizer, Roche/Genentech, and Servier

Travel Support: AstraZeneca, Gilead Sciences, and Roche/Genentech

Other Financial Interests: Gilead Sciences and Roche/Genentech

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Addressing the Unmet Need in 1L mTNBC Treatment

UNMET NEED

- ~50% of patients who receive 1L treatment do not receive 2L+ treatment[1]
- There is a substantial deterioration in QOL with each line of therapy[2]
- 1L treatment is an important opportunity to control disease without worsening QOL

CLINICAL IMPACT OF ASCENT-04/ KEYNOTE-D19

- 1L SG + pembro led to a statistically significant improvement in PFS vs chemo + pembro (median, 11.2 vs 7.8 months; HR, 0.65; *P* < .001), with no new safety concerns in patients with PD-L1+ (CPS ≥ 10) mTNBC[3]
- PROs provide insights on impact of treatment on QOL, including symptom burden and functional status

We present the PRO data from the ASCENT-04/KEYNOTE-D19 study

1L, first-line; **2L+**, second-line or later; **chemo**, chemotherapy; **CI**, confidence interval; **CPS**, combined positive score; **HR**, hazard ratio; **mTNBC**, metastatic triple-negative breast cancer; **PD-L1**, programmed cell death-ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **PRO**, patient-reported outcome; **QOL**, quality of life; **SG**, sacituzumab govitecan.

1. Punie K, et al. *Oncologist*. 2025;30:oyaf034. 2. Zhang Y, et al. *Value Health.* 2025;28:S359-60. 3. Tolaney SM, et al. *J Clin Oncol*. 2025;43(suppl 17; abstr LBA109).

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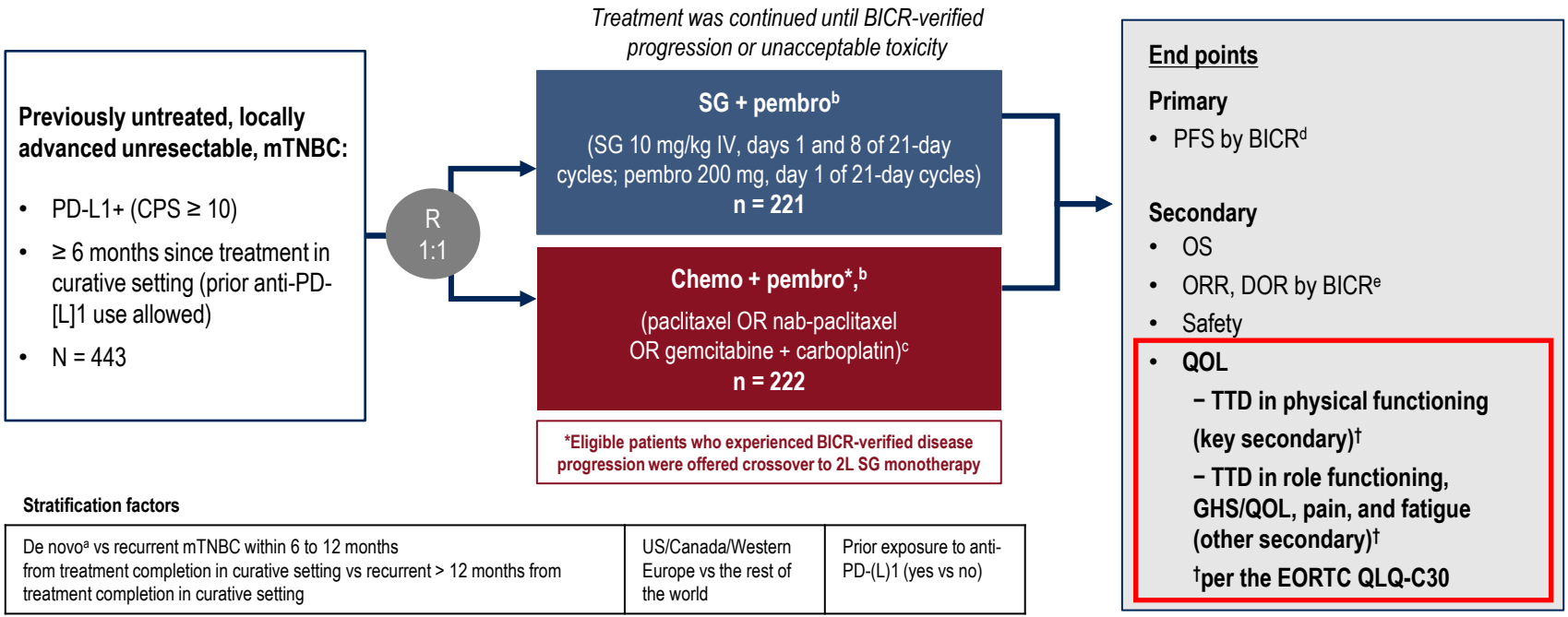
ASCENT-04/KEYNOTE-D19: Study Design



Stratification factors

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

ClinicalTrials.gov identifier: NCT05382286; Data cutoff was March 3, 2025

[a]Up to 35% de novo mTNBC. [b]Pembro was administered for a maximum of 35 cycles. [c]Administered per country-specific prescribing information. [d]Per Response Evaluation Criteria in Solid Tumors, version 1.1.

2L, second-line; **BICR**, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **DOR**, duration of response; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **GHS**, global health status; **IV**, intravenously; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-L1**, programmed cell death-ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **PRO**, patient-reported outcome; **QOL**, quality of life; **R**, randomization; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

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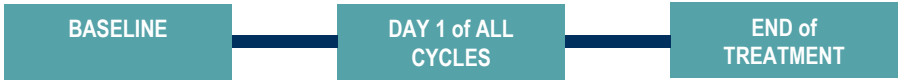
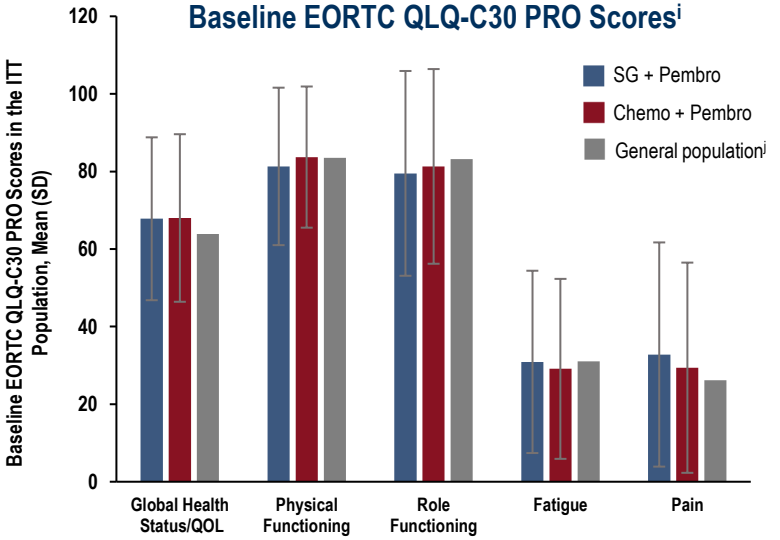
PRO End Points and Baseline PRO Scores

Outcome Using the EORTC QLQ-C30 Questionnaire[a,b]	Clinically Meaningful Threshold[c]
TTD[d] in physical functioning (key secondary end point)	≥ 13.33 points[e]
TTD[d] in all remaining domains	≥ 10 points[1,2]
TTD[d] in physical functioning at a higher threshold[f]	≥ 20 points
Time to confirmed deterioration[f,g] in physical functioning	≥ 13.33 points[e]
Time to confirmed deterioration[g] in all remaining domains	≥ 10 points
Overall LS mean changes from baseline in scores	0.3 × SD[h]

PRO Assessment Schedule for EORTC QLQ-C30 (All Randomized Patients)





At the primary analysis, all PRO results, including TTD in the physical functioning domain of EORTC QLQ-C30, are descriptive; baseline EORTC QLQ-C30 domain scores were consistent between treatment groups and with general population scores for most domains

[a]Functional domains = physical, role, emotional, cognitive, and social functioning. [b]Symptom domains = fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties. [c]Defined as MWPC from baseline. [d]TTD in each EORTC QLQ-C30 domain, defined as the time between randomization and the assessment at which a patient first experienced a worsening exceeding prespecified MWPC from BL or death [e]Physical functioning scores change in 6.67 increments so 13.33 ≡ 10-point threshold. [f]Prespecified sensitivity analysis. [g]Deterioration from BL confirmed by a next scheduled visit or followed by missing PRO visit or death < 42 days after last PRO assessment or death < 42 days after randomization if BL/post-BL assessments were missing. [h]Minimally important difference was estimated using 0.3 of the SD for EORTC QLQ-C30 scores at baseline. [i]Key and other secondary end points shown, similar results observed for remaining domains. [j]Norm scores were from general population data,[3] reweighted by the age and sex distributions of the ITT population.
BL, baseline; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **ITT**, intent-to-treat; **LS**, least squares; **MWPC**, meaningful within-patient change; **pembro**, pembrolizumab; **PRO**, patient-reported outcome; **QOL**, quality of life; **SD**, standard deviation; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.
1. Osoba D, et al. *J Clin Oncol.* 1998;16:139-44; 2. Coon CD, et al. *Patient.* 2022;15:691-702; 3. Nolte S, et al. *Eur J Cancer.* 2019;107:153-63.

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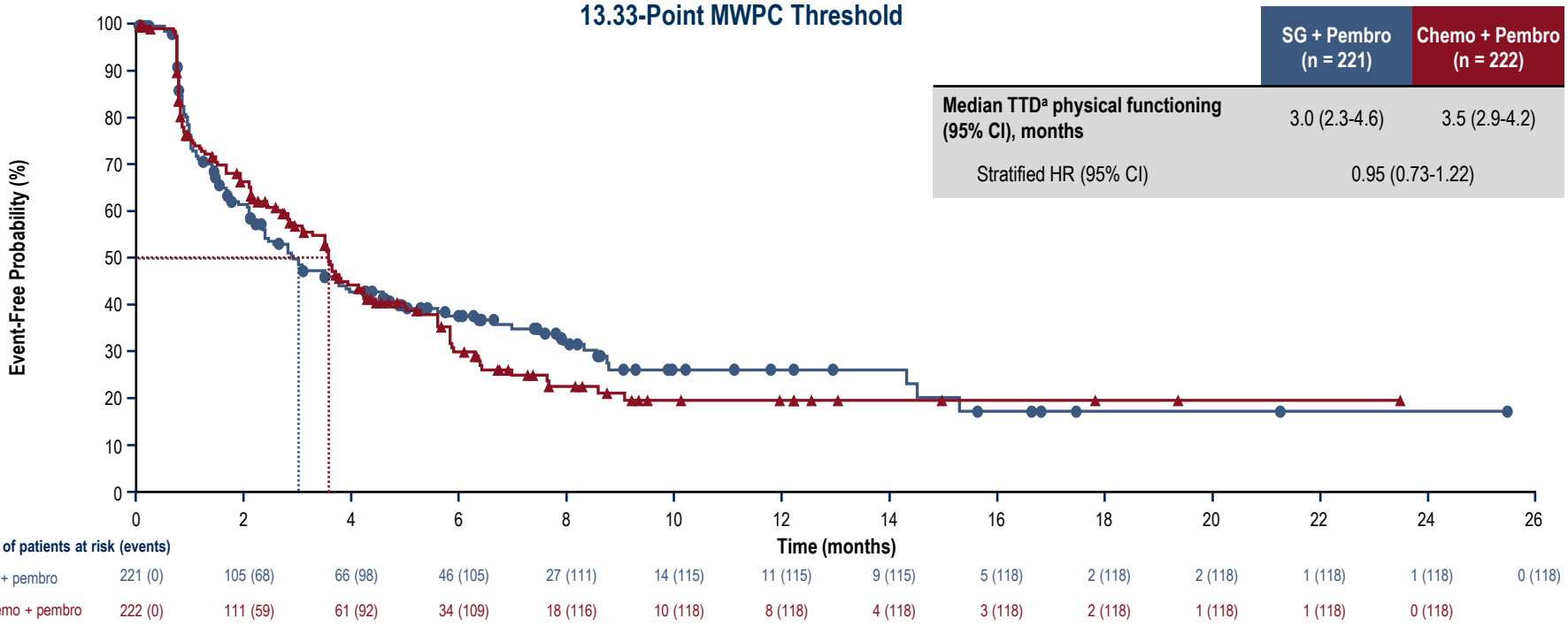
Time to First Deterioration in Physical Functioning



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Median TTD[a] physical functioning (95% CI), months	3.0 (2.3-4.6)	3.5 (2.9-4.2)
Stratified HR (95% CI)	0.95 (0.73-1.22)	

No. of patients at risk (events)														
SG + pembro	221 (0)	105 (68)	66 (98)	46 (105)	27 (111)	14 (115)	11 (115)	9 (115)	5 (118)	2 (118)	2 (118)	1 (118)	1 (118)	0 (118)
Chemo + pembro	222 (0)	111 (59)	61 (92)	34 (109)	18 (116)	10 (118)	8 (118)	4 (118)	3 (118)	2 (118)	1 (118)	1 (118)	0 (118)	

TTD in physical functioning was maintained in the SG + pembro group and comparable between treatment groups

[a]TTD defined as the time between randomization and the assessment at which a patient first experienced a worsening exceeding prespecified MWPC from BL or death.
BL, baseline; **chemo**, chemotherapy; **CI**, confidence interval; **HR**, hazard ratio; **MWPC**, meaningful within-patient change; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

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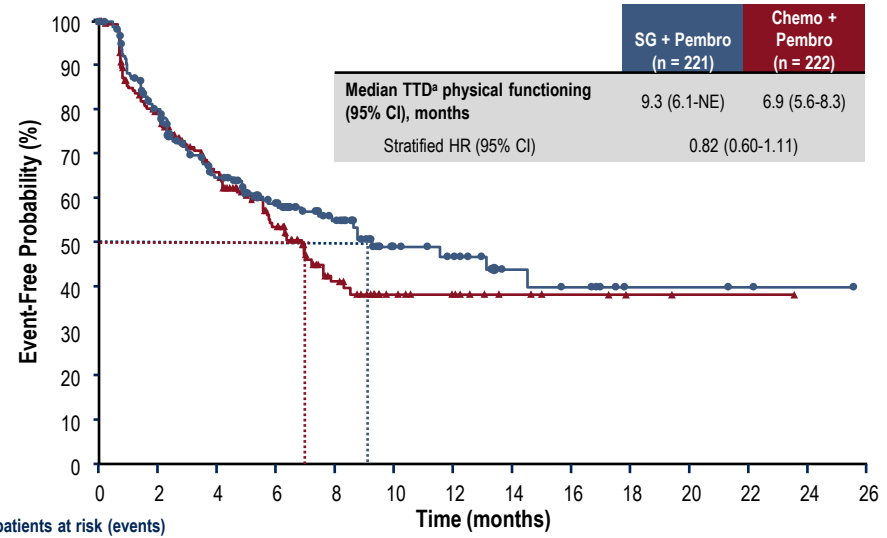
Time to Deterioration in Physical Functioning

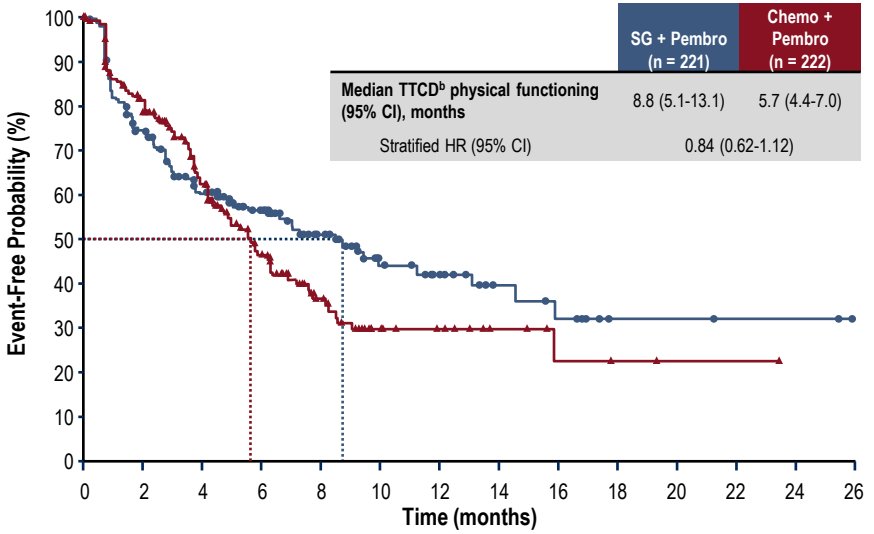
Sensitivity Analysis - Time to first deterioration
20-Point MWPC Threshold



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Median TTD[a] physical functioning (95% CI), months	9.3 (6.1-NE)	6.9 (5.6-8.3)
Stratified HR (95% CI)	0.82 (0.60-1.11)	

No. of patients at risk (events)															
SG + pembro	221 (0)	137 (35)	98 (60)	75 (68)	48 (72)	24 (76)	20 (77)	11 (78)	8 (79)	3 (79)	3 (79)	2 (79)	1 (79)	0 (79)	
Chemo + pembro	222 (0)	133 (36)	91 (57)	59 (72)	30 (83)	16 (85)	12 (85)	6 (85)	4 (85)	2 (85)	1 (85)	1 (85)	0 (85)		

Sensitivity Analysis - Time to confirmed deterioration
13.33-Point MWPC Threshold



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Median TTCD[b] physical functioning (95% CI), months	8.8 (5.1-13.1)	5.7 (4.4-7.0)
Stratified HR (95% CI)	0.84 (0.62-1.12)	

221 (0)	128 (45)	92 (68)	72 (73)	45 (79)	26 (84)	20 (85)	12 (86)	8 (88)	3 (88)	3 (88)	2 (88)	2 (88)	0 (88)		
222 (0)	137 (33)	88 (61)	53 (81)	29 (91)	15 (96)	12 (96)	6 (96)	3 (97)	2 (97)	1 (97)	1 (97)	0 (97)			

Both sensitivity analyses consistently showed that SG + pembro has a numerically longer time to deterioration and may delay the onset of decline in physical functioning

[a]TTD defined as the time between randomization and the assessment at which a patient first experienced a worsening exceeding prespecified MWPC from BL or death. [b]Deterioration from BL confirmed by a next scheduled visit or followed by missing PRO visit or death < 42 days after last PRO assessment or death < 42 days after randomization if BL/post-BL assessments were missing.

BL, baseline; **chemo**, chemotherapy; **CI**, confidence interval; **HR**, hazard ratio; **MWPC**, meaningful within-patient change; **NE**, not estimable; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan; **TTCD**, time to confirmed deterioration; **TTD**, time to first deterioration.

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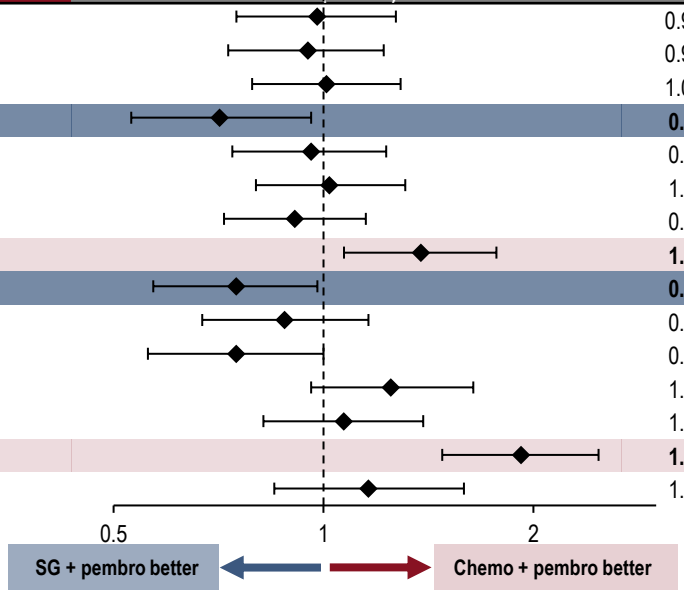
Time to First Deterioration in EORTC QLQ-C30 Domains

ITT Population	Median (95% CI) TTD,[a] Months SG + Pembro (n = 221)	Median (95% CI) TTD,[a] Months Chemo + Pembro (n = 222)	HR (95% CI)[b]
Global health status/QOL	2.2 (2.1-3.3)	3.5 (2.3-4.2)	0.98 (0.75-1.27)
Physical functioning	3.0 (2.3-4.6)	3.5 (2.9-4.2)	0.95 (0.73-1.22)
Role functioning	1.7 (1.1-2.2)	1.5 (1.4-2.3)	1.01 (0.79-1.29)
Emotional functioning	**9.3 (5.9-NE)**	**4.9 (3.5-6.3)**	**0.71 (0.53-0.96)**
Cognitive functioning	2.3 (1.5-3.5)	2.9 (2.2-3.5)	0.96 (0.74-1.23)
Social functioning	1.9 (1.5-2.2)	2.2 (1.5-3.3)	1.02 (0.80-1.31)
Fatigue	1.1 (1.0-1.4)	1.0 (0.9-1.4)	0.91 (0.72-1.15)
Nausea/vomiting	**1.5 (1.0-2.2)**	**3.5 (2.1-4.4)**	**1.38 (1.07-1.77)**
Pain	**4.3 (2.4-5.7)**	**3.2 (2.2-4.2)**	**0.75 (0.57-0.98)**
Dyspnea	4.7 (3.1-6.7)	3.7 (2.8-5.6)	0.88 (0.67-1.16)
Insomnia	5.6 (3.7-10.8)	3.5 (2.8-4.4)	0.75 (0.56-1.00)
Appetite loss	2.2 (1.7-3.0)	4.2 (2.9-5.6)	1.25 (0.96-1.64)
Constipation	2.8 (2.1-3.5)	3.7 (2.4-5.1)	1.07 (0.82-1.39)
Diarrhea	**1.4 (1.0-1.8)**	**5.3 (3.1-6.9)**	**1.92 (1.48-2.48)**
Financial difficulties	7.6 (4.2-13.6)	9.3 (5.7-NE)	1.16 (0.85-1.59)



QOL was generally maintained for a similar duration in both treatment groups; consistent results were observed in the analysis for TTCD[c]

[a]TTD in each EORTC QLQ-C30 domain, defined as the time between randomization and the assessment at which a patient first experienced a worsening exceeding prespecified MWPC from BL or death. [b]HR < 1 favors SG + pembro. [c]Deterioration from BL confirmed by a next scheduled visit or followed by missing PRO visit or death < 42 days after last PRO assessment or death < 42 days after randomization if BL/post-BL assessments were missing.

BL, baseline; **chemo**, chemotherapy; **CI**, confidence interval; **EORTC QLQ-C30**, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; **HR**, hazard ratio; **ITT**, intent-to-treat; **MWPC**, meaningful within-patient change; **NE**, not estimable; **pembro**, pembrolizumab; **QOL**, quality of life; **SG**, sacituzumab govitecan; **TTCD**, time to confirmed deterioration; **TTD**, time to first deterioration.

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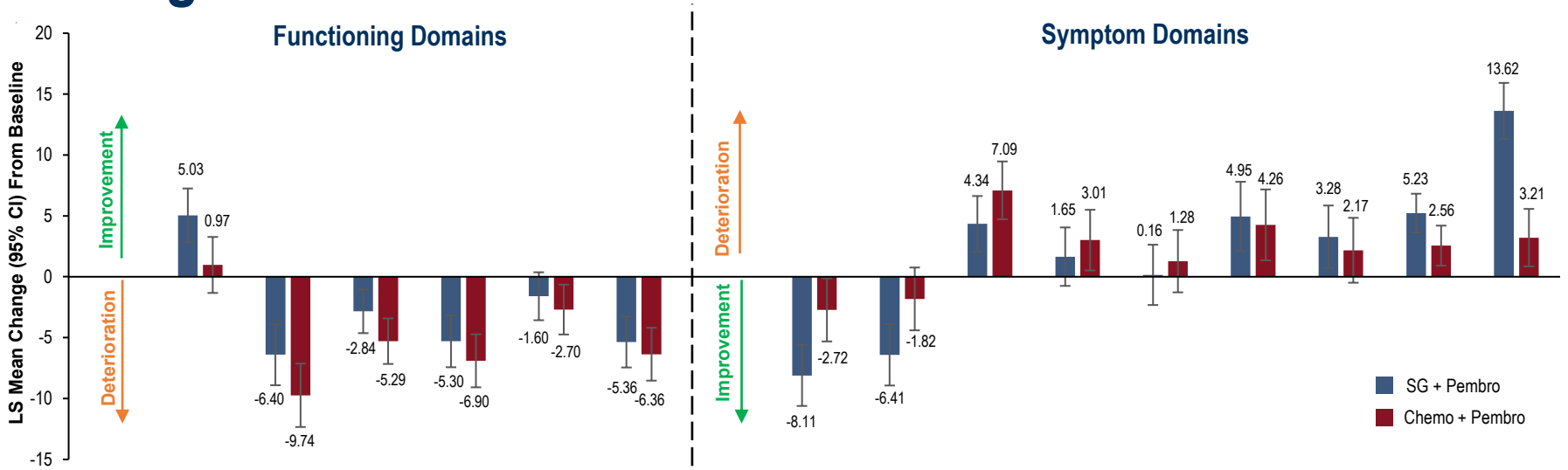
Change from Baseline in EORTC QLQ-C30 Scores



EORTC QLQ-C30 Domain	Emotional Functioning	Role Functioning	Physical Functioning	Social Functioning	GHS/QOL	Cognitive Functioning	Pain	Insomnia	Fatigue	Dyspnea	Appetite Loss	Constipation	Financial Difficulties	Nausea/ Vomiting	Diarrhea
Difference	**4.07***	**3.34***	**2.45***	1.60	1.10	1.00	**-5.39***	**-4.59***	-2.75	-1.35	-1.13	0.69	1.11	**2.67***	**10.41***
95% CI	1.20 to 6.93	0.13 to 6.55	0.09 to 4.81	-1.15 to 4.34	-1.40 to 3.59	-1.63 to 3.63	-8.55 to -2.23	-7.70 to -1.48	-5.65 to 0.15	-4.29 to 1.59	-4.08 to 1.83	-2.76 to 4.14	-2.30 to 4.51	0.73 to 4.62	7.53 to 13.29
MID	7.00	7.72	5.78	7.49	6.38	5.20	8.42	8.86	7.00	6.91	7.09	6.88	8.73	4.23	4.31

Change from baseline favored SG + pembro for physical, role, and emotional functioning, and pain and insomnia

*Differences in overall LS mean change > 0 for functioning domains and < 0 for symptom domains are in favor of SG + pembro; differences > 0 for symptom domains are in favor of chemo + pembro.

Chemo, chemotherapy; **CI**, confidence interval; **EORTC QLQ-C30**, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; **GHS**, global health status; **LS**, least squares; **MID**, minimally important difference; **pembro**, pembrolizumab; **QOL**, quality of life; **SG**, sacituzumab govitecan.

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Conclusions

- Baseline QOL was generally maintained with SG + pembro, with benefits seen in several domains
- TTD in physical functioning was comparable between the groups, with **emotional functioning and pain** favoring SG + pembro vs chemo + pembro
- The sensitivity analyses to evaluate substantial and sustained changes showed that SG + pembro may delay the onset of decline in physical functioning, indicating a benefit in maintaining patients' ability to perform daily activities
- Mean changes from baseline favored SG + pembro for **physical, role, and emotional functioning,** as well as **pain and insomnia**
- There was worsening of symptoms such as **nausea/vomiting and diarrhea,** which are consistent with the safety profile of the SG + pembro group in the study, and can be managed by following established guidelines

SG + pembro maintained overall QOL, patients reported reduced symptom burden and improved functioning in multiple domains; these data complement the clinically meaningful improvement in PFS and support this treatment regimen as a potential new standard of care for patients with PD-L1+ mTNBC

Chemo, chemotherapy; **pembro**, pembrolizumab; **PFS**, progression-free survival; **QOL**, quality of life; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

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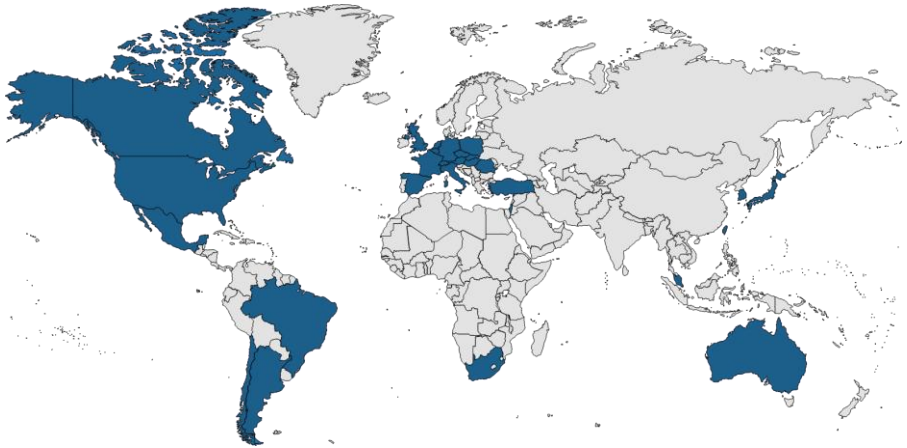

- We thank the patients and their caregivers for their participation and commitment to clinical research
- Thank you to the clinical trial investigators and their devoted team members for contributing to the ASCENT-04/KEYNOTE-D19 study
- This study is sponsored by Gilead Sciences, Inc., and is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA
- Medical writing and editorial support was provided by Sonal S. Joshi, PhD, of Parexel, and funded by Gilead Sciences, Inc.

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