# Progression-Free Survival After Next Line of Treatment (PFS2) and Subsequent Therapies in the ASCENT-04 Study of Participants With Previously Untreated PD-L1+ Metastatic Triple-Negative Breast Cancer Treated With Sacituzumab Govitecan Plus Pembrolizumab vs Chemotherapy Plus Pembrolizumab

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# Key Takeaway Points: ASCENT-04 PFS2 and Subsequent Therapies

In the ASCENT-04 study, PFS2 was longer in the SG + pembro group compared with the chemo + pembro group, indicating sustained long-term benefit beyond first progression

Despite the high rate of crossover from the control group to SG, time to first and second subsequent therapies suggest that participants receiving 1L SG + pembro experience longer initial disease control and delayed need for subsequent therapy

These results support SG + pembro as a new 1L standard of care for patients with PD-L1+ mTNBC

**1L**, first line; **chemo**, chemotherapy; **mTNBC**, metastatic triple-negative breast cancer; **PD-L1**, programmed death ligand 1; **pembro**, pembrolizumab; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

# Background

- SG + pembro demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo + pembro in participants with previously untreated PD-L1+ advanced TNBC[1]

**PFS by BICR**

HR, 0.65; 95% CI, 0.51-0.84; *P* < .001

- OS data were immature at the primary analysis; however, a trend in improvement was observed for SG + pembro vs chemo + pembro[1]

OS maturity rate, 26% (as of Mar 2025)

- SG was provided on-study as crossover following PD on chemo + pembro and may have also been received commercially[1]

96 of 119 pts with subsq tx (**81%**) from the chemo + pembro group received SG in any subsq line

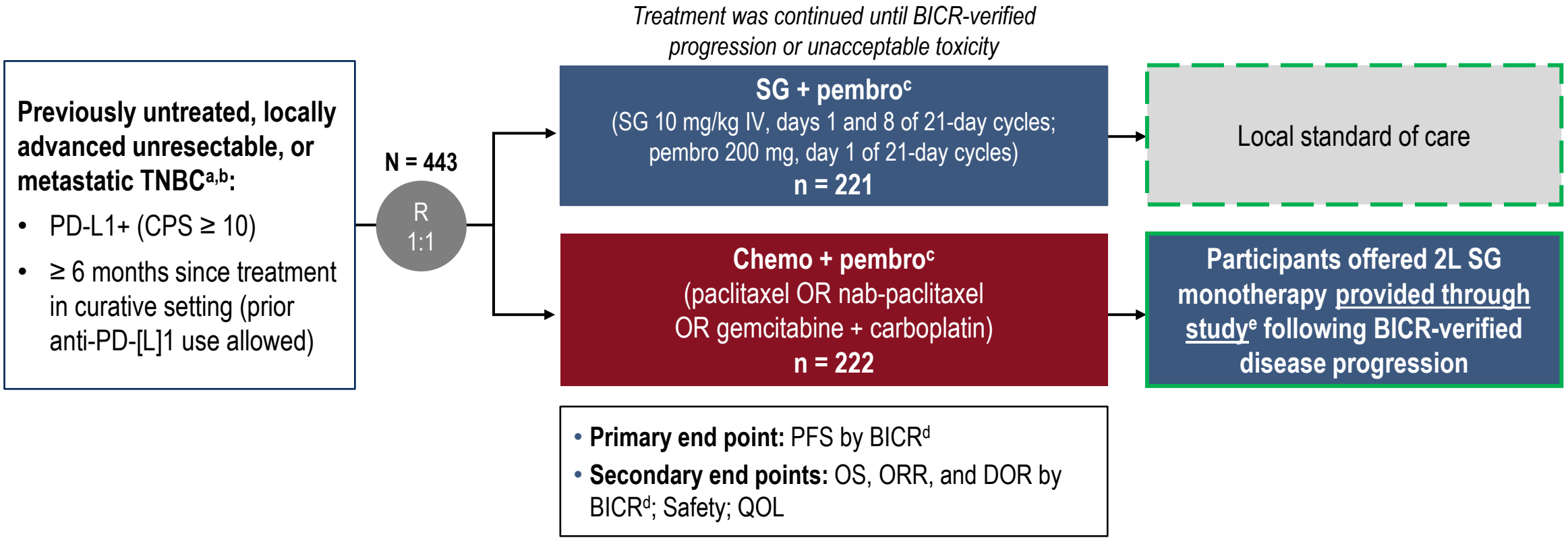
- PFS2 can be used to measure long-term clinical benefit in the absence of mature OS data and is particularly valuable when OS is confounded by a crossover design[2-4]

We report PFS2 and subsequent therapies from the ASCENT-04 study

**BICR**, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **OS**, overall survival; **PD**, progressive disease; **PD-L1**, programmed death-ligand 1; **pembro,** pembrolizumab**; PFS**, progression-free survival; **PFS2**, progression-free survival 2; **pts**, participants; **SG**, sacituzumab govitecan; **subsq**, subsequent; **TNBC**, triple-negative breast cancer; **tx**, treatment.

1. Tolaney S, et al. *N Engl J Med*. 2026;394:354-66. 2. Chowdhury S, et al. *Front.Oncol*. 2020;10:1349. 3. Filis P, et al. *ESMO Open*. 2026;11:106062. 4. Woodford RG, et al. *Cancer*. 2022;128:1449-57.

# ASCENT-04/KEYNOTE-D19: Study Design

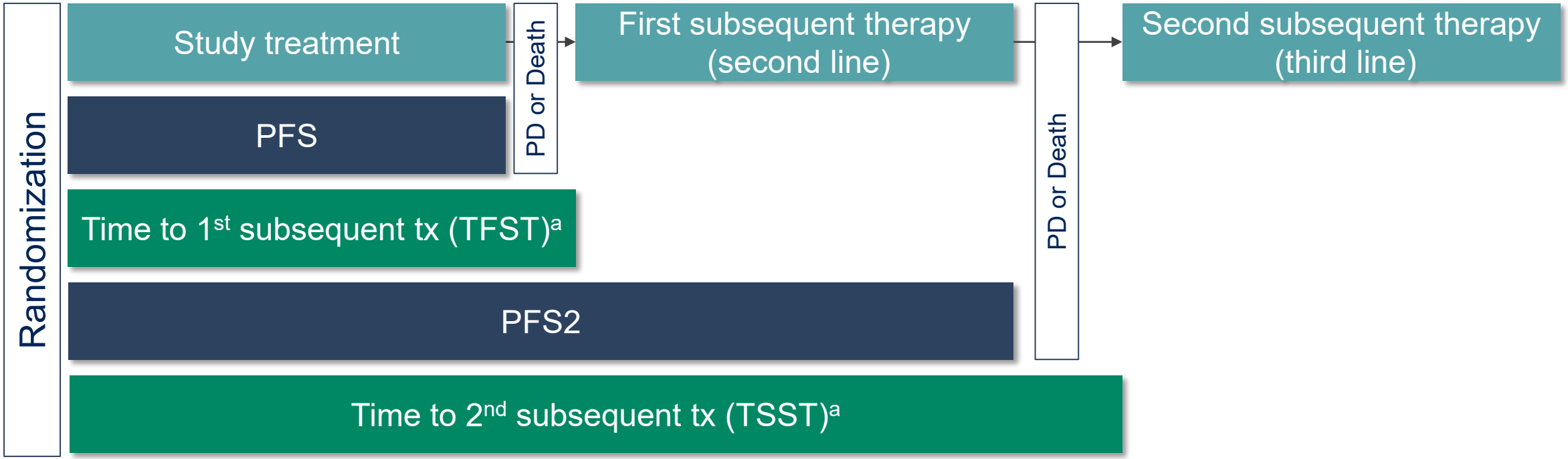



Exploratory end points included PFS2, TFST, and TSST

ClinicalTrials.gov identifier: NCT05382286. [a]TNBC status determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]Up to 35% de novo mTNBC. [c]Pembro was administered for a maximum of 35 cycles. [d]Per RECIST v1.1. [e]Participants could have also received SG in any subsequent line commercially; other subs treatments per local practice were also permitted.

**2L**, second-line; **BICR**, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **DOR**, duration of response; **IV**, intravenously; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-(L)1**, programmed cell death (ligand) 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **PFS2,** progression-free survival 2; **QOL**, quality of life; **R**, randomized; **RECIST v1.1**, Response Evaluation Criteria in Solid Tumors, version 1.1; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TNBC**, triple-negative breast cancer; **TSST**, time to second subsequent therapy.

# Methods




- ASCENT-04 *post hoc* analysis
  - The data cutoff date was March 3, 2025; at this time, the median follow-up was 14.0 months (range, 0.1-28.6)
  - Two-sided *P* value was calculated using the stratified log-rank test and the hazard ratio with 95% CIs was calculated using a Cox proportional hazards model adjusted for randomization stratification factors
  - PFS2 is defined as time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first

[a]Time to first or second subsequent therapy is defined as time from randomization to the start of the first or second subsequent treatment or death due to any cause, whichever occurred first.
**PD,** progressive disease**; PFS**, progression-free survival; **PFS2**, progression-free survival 2; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy; **tx**, treatment.

# Demographics and Baseline Characteristics

| ITT Population | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Female sex, n (%)** | 221 (100) | 222 (100) |
| **Median age (range), years** | 54 (23-88) | 55 (27-82) |
| ≥ 65 years, n (%) | 58 (26) | 57 (26) |
| **Race or ethnic group,[a] n (%)** | | |
| White | 139 (63) | 118 (53) |
| Asian | 43 (19) | 63 (28) |
| Black | 13 (6) | 11 (5) |
| Other/not specified | 26 (12) | 30 (14) |
| **Geographic region, n (%)** | | |
| United States/Canada/Western Europe | 85 (38) | 85 (38) |
| Rest of the world[b] | 136 (62) | 137 (62) |
| **ECOG PS at baseline,[c] n (%)** | | |
| 0 | 156 (71) | 154 (69) |
| 1 | 65 (29) | 67 (30) |
| **PD-L1 CPS ≥ 10,[d] n (%)** | 221 (100) | 222 (100) |

| ITT Population | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Curative treatment-free interval, n (%)** | | |
| De novo | 75 (34) | 75 (34) |
| Recurrent within 6-12 months | 40 (18) | 40 (18) |
| Recurrent > 12 months | 106 (48) | 107 (48) |
| **Metastatic sites, n (%)** | | |
| Lymph node | 159 (72) | 154 (69) |
| Lung | 111 (50) | 95 (43) |
| Bone | 61 (28) | 45 (20) |
| Liver | 55 (25) | 57 (26) |
| Brain | 8 (4) | 6 (3) |
| Other[e] | 81 (37) | 71 (32) |
| **Chemo selected prior to randomization,[f] n (%)** | | |
| Taxane | 116 (52) | 114 (51) |
| Gemcitabine/carboplatin | 105 (48) | 108 (49) |
| **Prior anti–PD-(L)1 therapy,[g] n (%)** | 9 (4) | 11 (5) |

As previously reported, participant demographics were consistent between treatment groups

Data cutoff date: March 3, 2025. [a]As reported by the participants; "other" includes American Indian or Alaska Native, other, and not permitted. [b]Rest of the world includes Argentina, Australia, Brazil, Chile, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Singapore, South Africa, South Korea, Taiwan, and Türkiye. [c]One participant in the chemo + pembro group had an ECOG PS ≥ 2. [d]PD-L1 status assessed using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies) at the time of enrollment. [e]Other metastatic sites includes pleura, pleural effusion, skin, soft tissue, chest wall, and muscle. [f]Actual chemo received was consistent with what was selected prior to randomization; however, 2 participants were randomized but did not receive treatment. [g]While 20 participants were included in the stratified subgroup of prior exposure to anti–PD-(L)1 therapy (yes) per the IRT system, only 6 participants received prior treatment with anti–PD-(L)1 agents per the clinical database.
**Chemo**, chemotherapy; **CPS**, combined positive score; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **IHC**, immunohistochemistry; **IRT**, interactive response technology; **ITT**, intent-to-treat; **PD-(L)1**, programmed cell death (ligand) 1; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan.

# Participant Disposition and Subsequent Treatment

| Participant Disposition, n (%) | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Remaining on study treatment** | 95 (43) | 52 (23) |
| **Discontinued treatment**[a] | 125 (57) | 170 (77) |
| Progressive disease[b] | 84 (67) | 138 (81) |

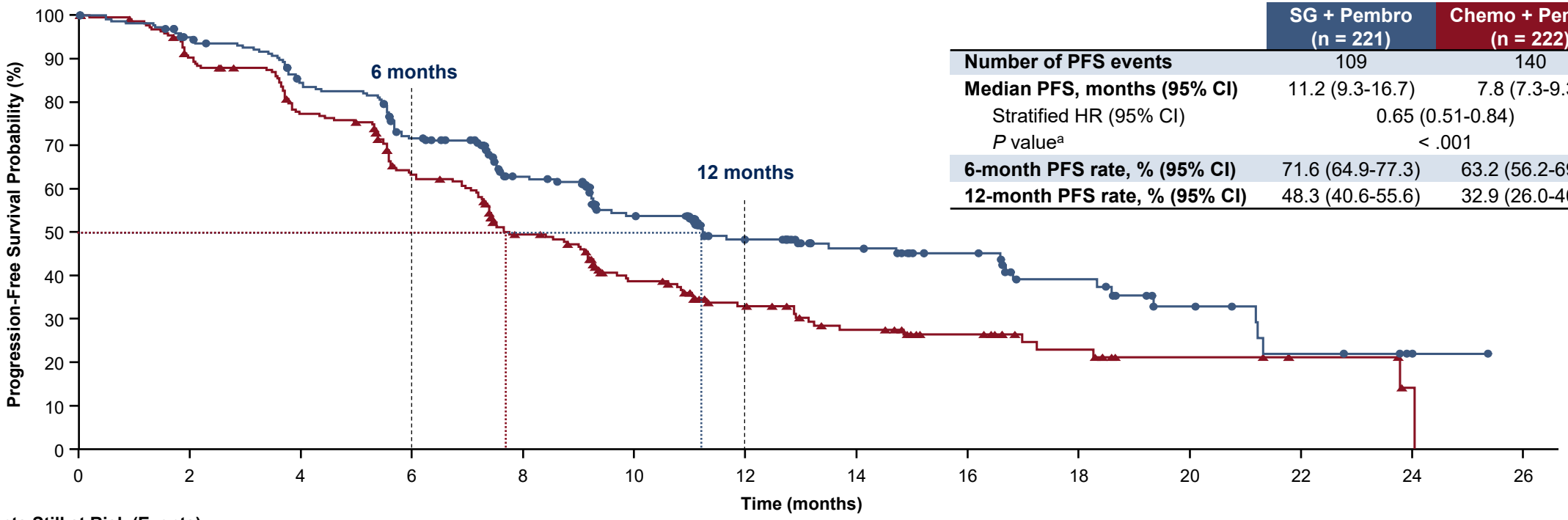
| Participants who discontinued first-line treatment,* n (%) | SG + Pembro (n = 125) | Chemo + Pembro (n = 170) |
|---|---|---|
| **Received second-line or later therapy** | 69 (55) | 119 (70) |
| Received any subsequent ADC[c] | 13 (19) | 97 (82) |
| Received any subsequent SG[c] | 3 (4) | 96 (81) |
| **Received third-line therapy** | 18 (14) | 29 (17) |

*Data are based on the primary analysis data-cut and follow-up is ongoing.

Almost twice as many participants in the SG + pembro group (43%) remained on study treatment compared with the chemo + pembro group (23%) at the time of data cutoff

[a]In the SG + pembro group, treatment discontinuation was also due to participant decision (n = 20); adverse events (n = 11); death (n = 6); investigator choice (n = 3); and non-compliance with study drug (n = 1); in the chemo + pembro group, treatment discontinuation was due to adverse events (n = 14); participant decision (n = 13); non-compliance with study drug and death (n = 2 each); and investigator choice (n = 1). [b]Percentages are calculated based on the number of participants who discontinued treatment. [c]Percentages are calculated based on the number of participants who received second-line or later therapy.
**ADC,** antibody-drug conjugate; **chemo,** chemotherapy; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan.

# Progression-Free Survival by BICR




| | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Number of PFS events** | 109 | 140 |
| **Median PFS, months (95% CI)** | 11.2 (9.3-16.7) | 7.8 (7.3-9.3) |
| Stratified HR (95% CI) | 0.65 (0.51-0.84) | |
| *P* value[a] | < .001 | |
| **6-month PFS rate, % (95% CI)** | 71.6 (64.9-77.3) | 63.2 (56.2-69.4) |
| **12-month PFS rate, % (95% CI)** | 48.3 (40.6-55.6) | 32.9 (26.0-40.0) |

**No. of Patients Still at Risk (Events)**

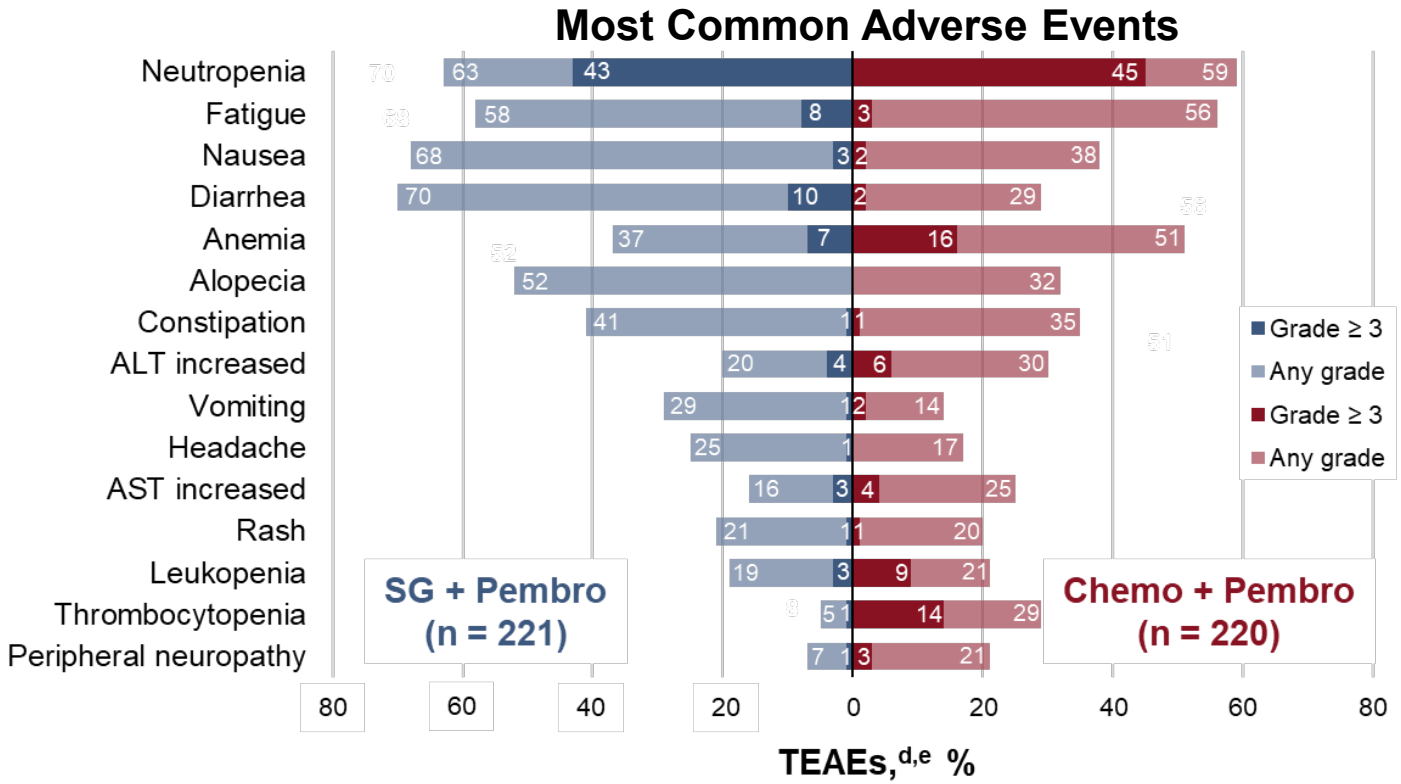
| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SG + pembro | 221 (0) | 202 (11) | 174 (33) | 142 (59) | 105 (75) | 78 (89) | 58 (96) | 42 (98) | 34 (99) | 22 (103) | 11 (106) | 6 (109) | 2 (109) | 0 (109) |
| Chemo + pembro | 222 (0) | 191 (21) | 159 (48) | 123 (76) | 88 (102) | 59 (120) | 40 (128) | 29 (134) | 21 (135) | 13 (137) | 7 (138) | 4 (138) | 1 (139) | 0 (140) |

SG + pembro demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo + pembro by BICR analysis, with a 35% reduction in risk of disease progression or death[1]

Data cutoff date: March 3, 2025. [a]Two-sided *P*-value from stratified log-rank test.
**BICR**, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.
1. Tolaney S, et al. *N Engl J Med*. 2026;394:354-66.

# Safety Summary

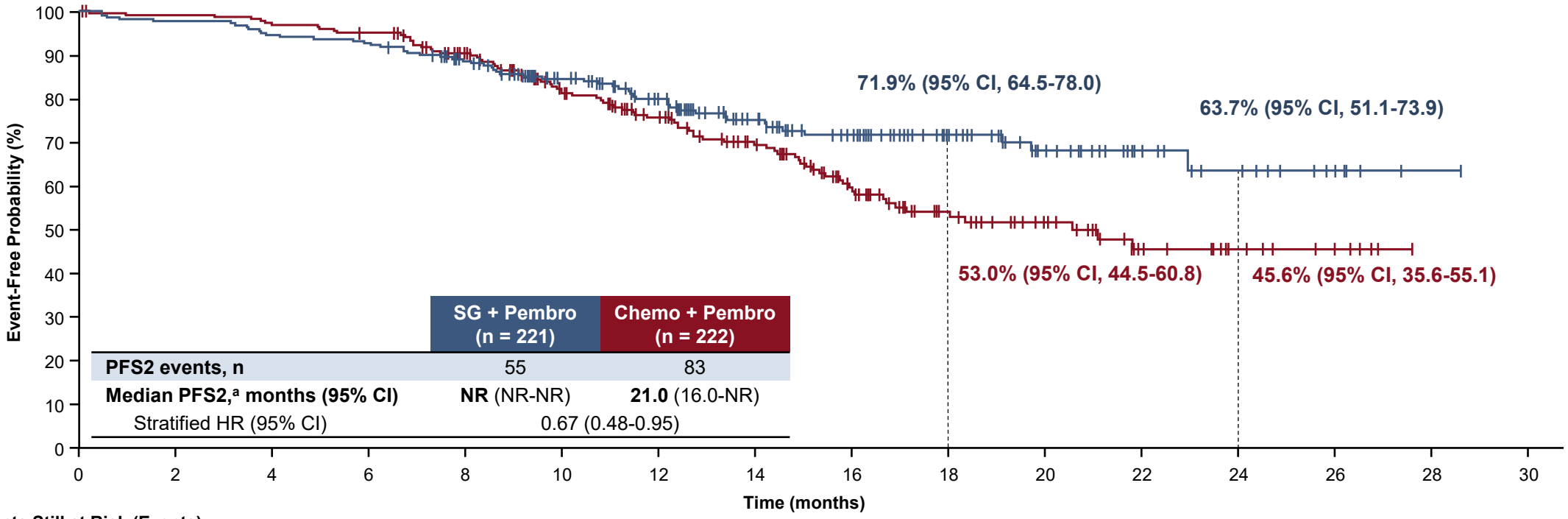
| n (%) | SG + Pembro (n = 221) | Chemo + Pembro (n = 220) |
|---|---|---|
| **Any TEAE** | 220 (> 99) | 219 (> 99) |
| Grade ≥ 3 | 158 (71) | 154 (70) |
| **Treatment-emergent SAE** | 84 (38) | 68 (31) |
| Treatment-related | 61 (28) | 42 (19) |
| **TEAEs leading to treatment discontinuation[a]** | 26 (12) | 68 (31) |
| **TEAEs leading to dose interruption** | 171 (77) | 162 (74) |
| **TEAEs leading to dose reduction** | 78 (35) | 96 (44) |
| **TEAEs leading to death[c]** | 7 (3) | 6 (3) |
| Treatment-related | 3 (1) | 1 (< 1) |




**The AEs observed were consistent with the known profiles of both SG and pembro, with no new safety concerns[1]**

Data cutoff date: March 3, 2025. TEAEs were defined as any adverse events that began or worsened on or after the first dose date of study drug up to 30 days (or up to 90 days for SAEs) after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurred first. [a]The most common any-grade TEAEs that led to treatment discontinuation were pneumonitis (1%) for the SG + pembro group and neuropathy peripheral (5%), pneumonitis (3%), and thrombocytopenia (3%) for the chemo + pembro group. [b]There was no dose reduction for pembro per the protocol. [c]TEAEs leading to death were pneumonia, sepsis, neutropenic sepsis, pulmonary embolism, and suicide (1 each), as well as 2 deaths of unknown cause in the SG + pembro group, and cardiac arrest, large intestine perforation, pneumonia, sepsis, post-procedural complication, and death of unknown cause (1 each) in the chemo + pembro group. [d]TEAEs were included if they occurred in ≥ 20% of patients in either arm. [e]Combined preferred terms of Neutropenia includes neutrophil count decreased, Leukopenia includes white blood cell count decreased, Anemia includes hemoglobin decreased and red blood cell count decreased, Thrombocytopenia includes platelet count decreased, and Fatigue includes asthenia. **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **chemo**, chemotherapy; **pembro**, pembrolizumab; **SAE**, serious adverse event; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event. 1. Tolaney S, et al. *N Engl J Med*. 2026;394:354-66.

# PFS After Next Line of Treatment (PFS2)




**No. of Patients Still at Risk (Events)**

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SG + pembro | 221 (0) | 216 (5) | 209 (12) | 205 (16) | 186 (25) | 154 (33) | 128 (41) | 97 (48) | 76 (52) | 48 (52) | 31 (54) | 17 (54) | 12 (55) | 5 (55) | 1 (55) | 0 (55) |
| Chemo + pembro | 222 (0) | 218 (2) | 213 (7) | 208 (11) | 186 (21) | 154 (39) | 129 (49) | 101 (59) | 70 (74) | 46 (79) | 32 (80) | 16 (83) | 10 (83) | 5 (83) | 0 (83) | |

PFS2 was longer in the SG + pembro group compared with the chemo + pembro group despite the high rate of crossover in the chemo + pembro group, with a 33% reduction in risk of a PFS2 event with SG + pembro

[a]PFS2 is defined as time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first.
**Chemo**, chemotherapy; **HR**, hazard ratio; **NR**, not reached; **pembro**, pembrolizumab; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

# Subsequent Therapy

## Subsequent Therapies in the Second Line

| | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Any subsequent therapy, n** | 69 | 119 |
| **Any subsequent therapy in 2L,[a] n (%)** | 68 (99)[b] | 119 (100) |
| Taxanes | 23 (33) | 8 (7) |
| Platinum agents | 18 (26) | 3 (3) |
| ADC | 7 (10) | 94 (79) |
| Trastuzumab deruxtecan | 5 (7) | 2 (2) |
| Sacituzumab govitecan | 2 (3) | 92 (77)[c] |
| PD-(L)1 inhibitors | 6 (9) | 7 (6) |
| Anthracyclines | 4 (6) | 5 (4) |
| PARPi | 3 (1) | 1 (1) |
| Other[d] | 40 (58) | 14 (12) |
| **Median TFST, months (95% CI)** | 17.3 (12.7-NR) | 9.8 (8.7-10.9) |
| Stratified HR (95% CI) | 0.59 (0.46-0.76) | |

## Subsequent Therapies in the Third Line

| | SG + Pembro (n = 221) | Chemo + Pembro (n = 222) |
|---|---|---|
| **Any subsequent therapy, n** | 69 | 119 |
| **Any subsequent therapy in 3L,[a] n (%)** | 18 (26)[b] | 29 (24) |
| Taxanes | 5 (7) | 3 (3) |
| Anthracyclines | 4 (6) | 2 (2) |
| Platinum agents | 3 (4) | 5 (4) |
| ADC | 2 (3) | 6 (5) |
| Trastuzumab deruxtecan | 2 (3) | 3 (3) |
| Sacituzumab govitecan | 0 (0) | 3 (3)[e] |
| PD-(L)1 inhibitors | 1 (1) | 2 (2) |
| PARPi | 0 (0) | 1 (1) |
| Other[f] | 11 (16) | 18 (15) |
| **Median TSST, months (95% CI)** | NR (22.9-NR) | 21.0 (16.6-NR) |
| Stratified HR (95% CI) | 0.82 (0.59-1.14) | |

The majority of participants on chemo + pembro received 2L SG; in the SG + pembro group, most received 2L chemo.

Long-term benefit was observed with SG + pembro vs chemo + pembro, with substantially longer median time to second subsequent treatment, despite high crossover rates

[a]Percentages are calculated based on the number of participants who received any subsequent therapy. [b]One participant who received any subsequent therapy did not have the line of therapy documented and was excluded from the second-line– and third-line–specific analyses. [c]Includes both commercial use of SG in 2L (n = 15) and crossover to SG on study (n = 77). [d]Includes capecitabine (n = 20); gemcitabine and bevacizumab (n = 7 each), cyclophosphamide (n = 3); eribulin (n = 2); eribulin mesylate, etoposide, gemcitabine hydrochloride, investigational agent, letrozole, ribociclib, trastuzumab, and vinorelbine (n = 1 each) in the SG + pembro group and cyclophosphamide (n = 6); capecitabine (n = 4); gemcitabine (n = 2); bevacizumab and eribulin mesylate (n = 1 each) in the chemo+ pembro group. [e]One patient in the chemo + pembro group received SG beyond 3L. [f]Includes cyclophosphamide (n = 3); capecitabine and bevacizumab (n = 2 each); and eribulin, gemcitabine, vinorelbine, eribulin mesylate, fluorouracil, pertuzumab/trastuzumab, and investigational drug (n = 1 each), in the SG + pembro group; and capecitabine and eribulin (n = 4 each); gemcitabine and cyclophosphamide (n = 2 each); and bevacizumab, vinorelbine, Bt 8009, gemcitabine hydrochloride, letrozole, regorafenib, and investigational agent (n = 1 each) in the chemo + pembro group. **2L**, second line; **3L**, third line; **ADC**, antibody-drug conjugate; **chemo**, chemotherapy; **HR**, hazard ratio; **NR**, not reached; **PARPi**, poly ADP-ribose polymerase inhibitor; **PD-(L)1**, programmed death (ligand) 1; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy.

# Conclusions

- PFS2 was improved in the SG + pembro group compared with the chemo + pembro group despite the high rate of crossover, indicating sustained long-term benefit beyond first progression

**Median PFS2**

NR vs 21.0 months
HR, 0.67 (95% CI, 0.48-0.95)

- The most frequent 2L+ subsequent therapy was chemo in the SG + pembro group and SG in the chemo + pembro group

**Subsequent therapy in any line**

Chemo + pembro group: SG (81%)
SG + pembro group: chemo (88%)

- Despite the high rate of crossover from the control group to SG, time to first and second subsequent therapies suggest that participants receiving 1L SG + pembro experience longer initial disease control and delayed need for subsequent therapy

**Median TFST & TSST**

TFST: 17.3 vs 9.8 months
TSST: NR vs 21.0 months

**These results from the ASCENT-04 study further support 1L SG + pembro use for patients with PD-L1+ mTNBC**

**1L**, first-line; **2L+,** second-line and later; **chemo**, chemotherapy; **HR**, hazard ratio; **mTNBC**, metastatic triple-negative breast cancer; **NR**, not reached; **PD-L1**, programmed cell death ligand 1; **pembro**, pembrolizumab; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy.

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