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

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

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)

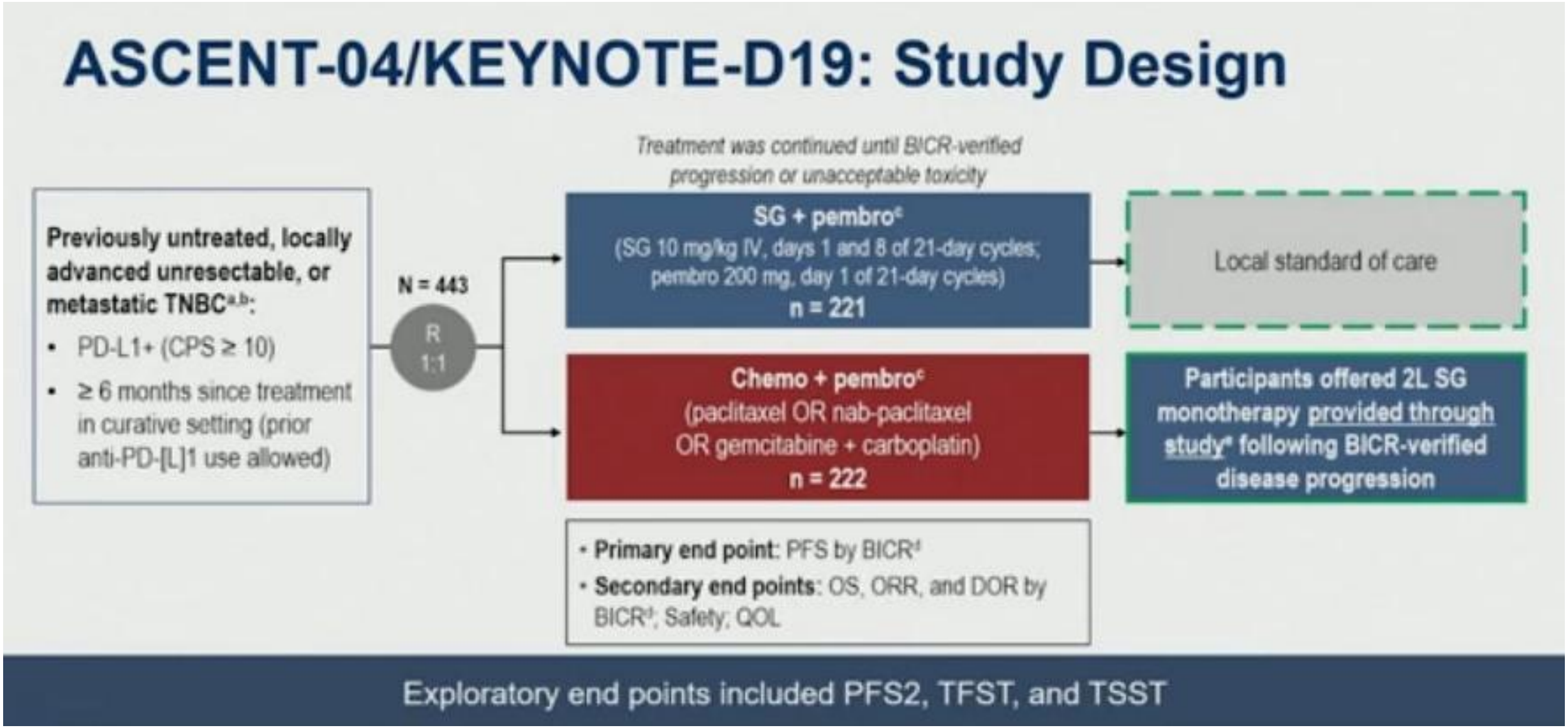
- SG was provided on-study as crossover following PD on chemo + pembro and may have also been received commercially[1]

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

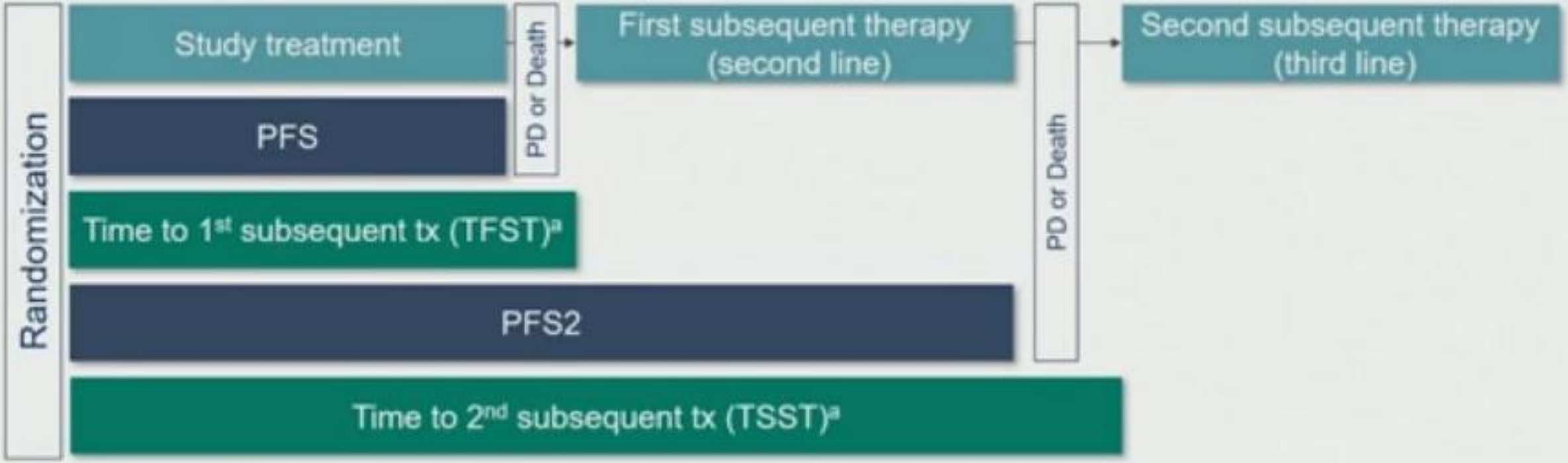
- PFS2 can be used to measure long-term clinical benefit in the absence of mature OS data and is particularly valuable when OS is confounded by a crossover design[2-4]

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

ASCENT-04/KEYNOTE-D19: Study Design



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

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

Participant Disposition and Subsequent Treatment

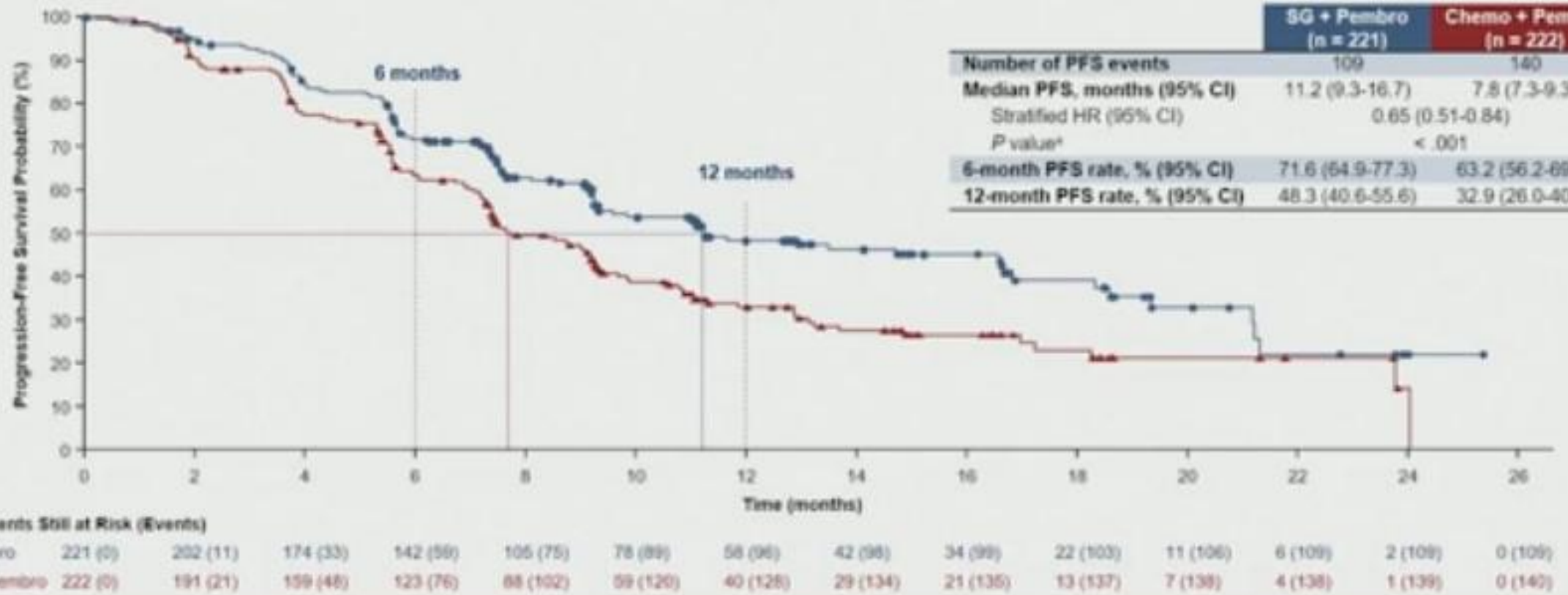
Participant Disposition, n (%)	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Remaining on study treatment	95 (43)	52 (23)
Discontinued treatment[a]	125 (57)	170 (77)
Progressive disease[b]	84 (67)	138 (81)

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

Progression-Free Survival by BICR

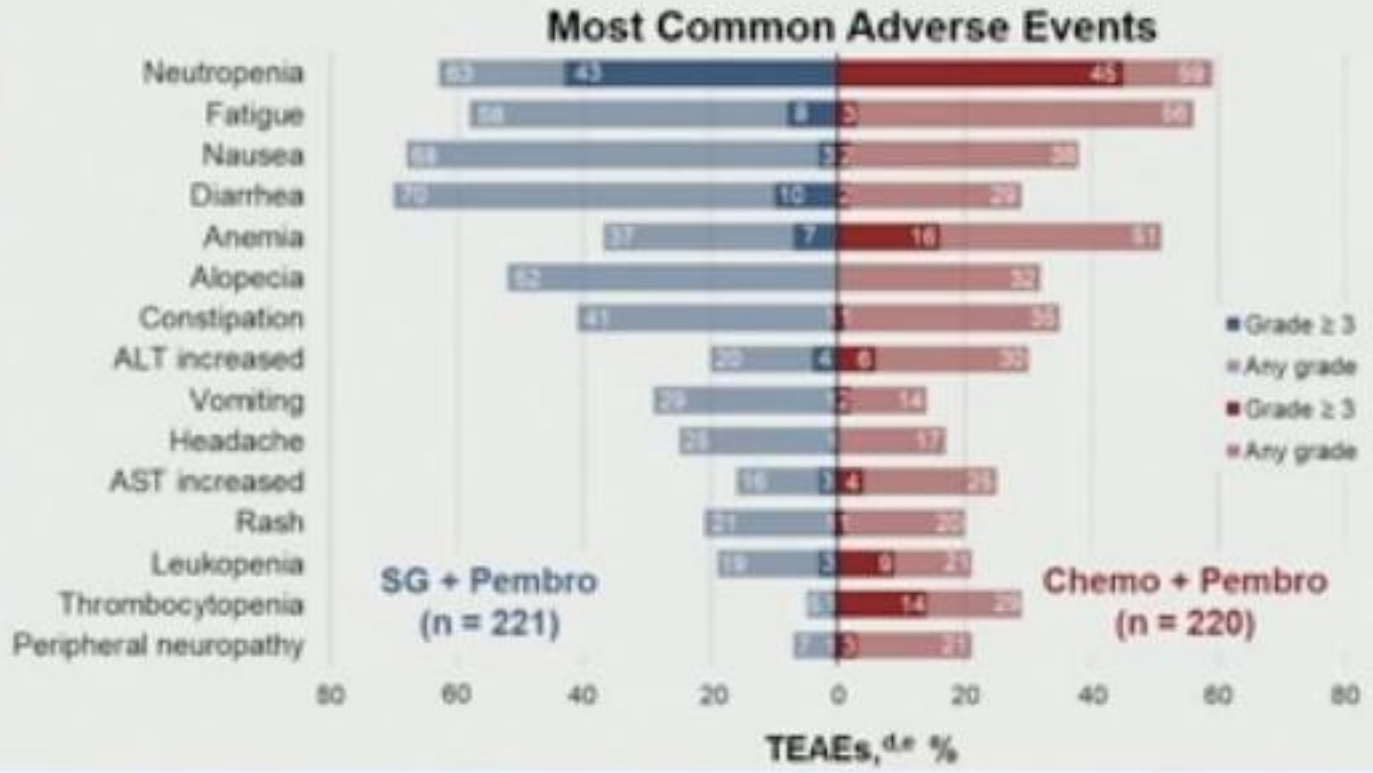


	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Number of PFS events	109	140
Median PFS, months (95% CI)	11.2 (9.3-16.7)	7.8 (7.3-9.3)
Stratified HR (95% CI)	0.65 (0.51-0.84)	
P value*	< .001	
6-month PFS rate, % (95% CI)	71.6 (64.9-77.3)	63.2 (56.2-69.4)
12-month PFS rate, % (95% CI)	48.3 (40.6-55.6)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

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]

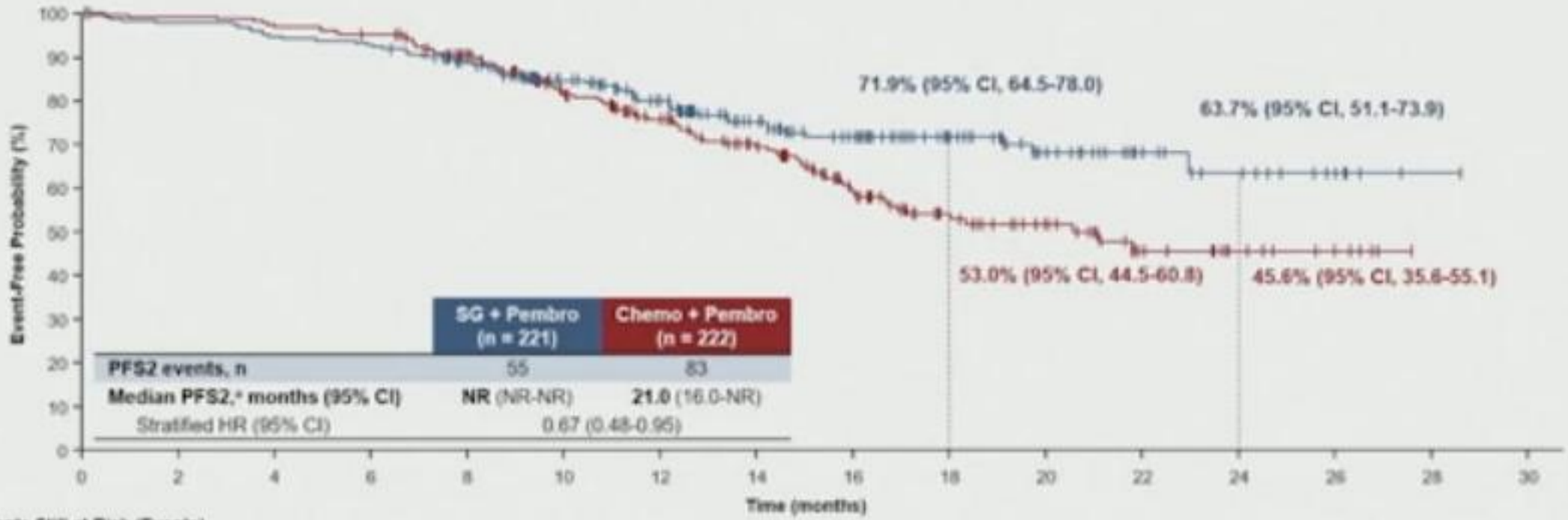
Safety Summary

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]

PFS After Next Line of Treatment (PFS2)



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

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

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