LBA109

Oral Abstract Session

Sacituzumab govitecan (SG) + pembrolizumab (pembro) vs chemotherapy (chemo) + pembro in previously untreated PD-L1–positive advanced triple-negative breast cancer (TNBC): Primary results from the randomized phase 3 ASCENT-04/KEYNOTE-D19 study.

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Background: Although PD-1/PD-L1 inhibitors plus chemo have expanded treatment options for previously untreated PD-L1–positive advanced TNBC, there still remains a critical unmet need to improve outcomes. SG previously demonstrated significant clinical benefit in pretreated metastatic TNBC (mTNBC). We report results from the ASCENT-04/KEYNOTE-D19 study in patients with previously untreated, PD-L1–positive (CPS ≥ 10; 22C3 assay) locally advanced unresectable or mTNBC. **Methods:** Patients were randomized 1:1 to SG (10 mg/kg IV, day 1 & 8) + pembro (200 mg, day 1, max 35 cycles) in 21-day cycles or chemo (gemcitabine + carboplatin, paclitaxel, nab-paclitaxel) + pembro until disease progression or unacceptable toxicity. Randomization was stratified by curative treatment-free interval, geography, and prior exposure to anti–PD-(L)1 therapy in the curative setting. Primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR). Key secondary endpoints include overall survival (OS); objective response rate (ORR) and duration of response (DOR) by BICR; and safety. **Results:** 443 patients were randomized at a 1:1 ratio: 221 to SG + pembro and 222 to chemo + pembro. The median follow-up was 14 mo. SG + pembro showed a significant improvement in PFS by BICR compared with chemo + pembro (hazard ratio [HR], 0.65; 95% CI, 0.51-0.84; P = .0009; Table). Median DOR was 16.5 mo for SG + pembro vs 9.2 mo for chemo + pembro (Table). Although OS data were immature, a positive early trend in OS improvement was also noted. The most frequent (≥ 10% of patients) grade ≥ 3 treatment-emergent adverse events (TEAEs) with SG + pembro were neutropenia (43%) and diarrhea (10%); and with chemo + pembro were neutropenia (45%), anemia (16%), and thrombocytopenia (14%). **Conclusions:** SG + pembro led to a statistically significant and clinically meaningful improvement in PFS vs chemo + pembro with durable responses, no new safety concerns for SG or pembro, and a lower rate of treatment discontinuation due to TEAEs in patients with previously untreated, PD-L1–positive advanced TNBC. These data support the use of SG + pembro as a potential new standard of care treatment in this patient population. Clinical trial information: NCT05382286. Research Sponsor: Gilead Sciences, Inc.

Efficacy, BICR, intent-to-treat	SG + pembro (n = 221)	Chemo + pembro (n = 222)
Median PFS (95% CI), mo	11.2 (9.3-16.7)	7.8 (7.3-9.3)
HR (95% CI); *P*-value (adjusted for randomization stratification factors)	0.65 (0.51-0.84); *P* = .0009	
ORR (95% CI), %	59.7 (52.9-66.3)	53.2 (46.4-59.9)
Median DOR (95% CI), mo	16.5 (12.7-19.5)	9.2 (7.6-11.3)
Safety (TEAEs), all treated, n (%)	**n = 221**	**n = 220**
Any grade; grade ≥ 3	220 (> 99); 158 (71)	219 (> 99); 154 (70)
Led to dose reduction	78 (35)	96 (44)
Led to any treatment discontinuation	26 (12)	68 (31)