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Title: Phase 3 stage 1 randomized controlled trial of gotistobart vs. docetaxel in patients with metastatic squamous cell lung cancer who have progressed on PD-(L)1 inhibitors

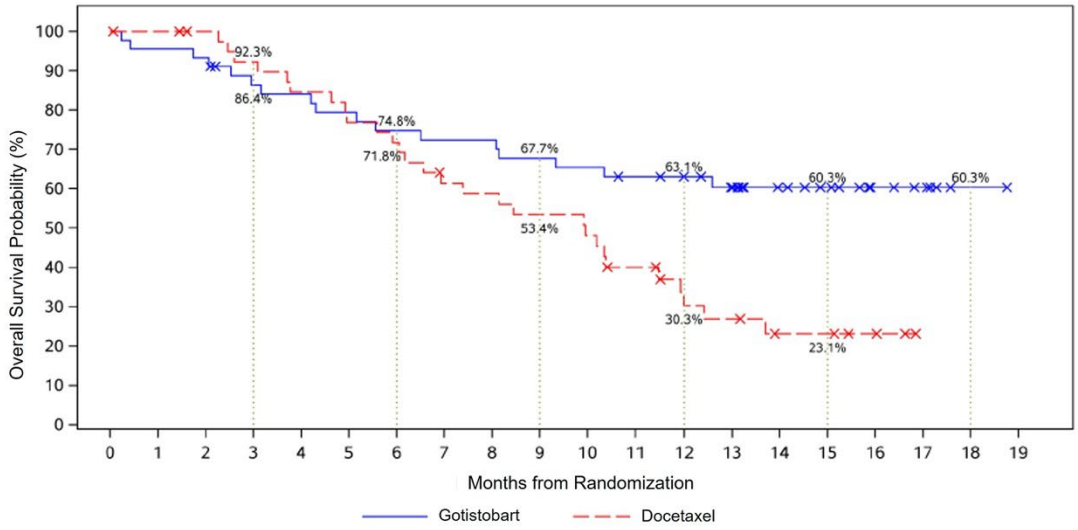
Background: Patients with metastatic squamous non-small cell lung cancer (sqNSCLC) who progress on PD-(L)1 inhibitors and platinum-based chemotherapy have poor prognosis. Multiple recent Phase 3 studies showed that the median overall survival (mOS) for 2L+ sqNSCLC is less than 11 months regardless of experimental or control chemotherapy arms. The Phase 3 PRESERVE-003 (NCT05671510) randomized seamless 2-stage trial evaluates safety and efficacy of gotistobart (ONC-392/BNT316), an investigational pH-sensitive anti-CTLA-4 mAb, in NSCLC patients who had progressed on PD-(L)1 inhibitors. Stage 1 is the dose-confirming part including all NSCLC patients. The pivotal stage 2 part is actively enrolling patients with sqNSCLC at 160 sites globally. Here, we report the Stage 1A/1B results from patients with sqNSCLC.

Methods: The phase 3 trial primary endpoint is OS. In Stage 1A, patients were randomized in a 1:1:1 ratio to gotistobart 3 mg/kg Q3W, 6 mg/kg with two 10 mg/kg loading doses Q3W, or docetaxel 75 mg/m^2 Q3W. In Stage 1B, patients were randomized in 1:1 to gotistobart 6 mg/kg with two 10 mg/kg loading doses Q3W or docetaxel 75 mg/m^2 Q3W.

Results: As of August 8, 2025, a total of 217 patients were enrolled in Stage 1A/1B. 87 patients with sqNSCLC were randomized to gotistobart 6 mg/kg with two 10 mg/kg loading doses Q3W (N=45) or docetaxel 75 mg/m^2 Q3W (N=42) with median follow up of 14.5 months. With 45 OS events, mOS was not reached in gotistobart (NE, 95% CI: 9.33, NE) and 9.95 m in docetaxel (9.95 m, 95% CI: 6.18, 11.93) with the HR = 0.46 (95% CI: 0.25, 0.84), nominal p=0.0102 (2-sided). Demographics, safety and OS data are shown in Table 1 and Figure 1.

Conclusion: Gotistobart treatment demonstrated a clinically meaningful OS benefit compared to docetaxel in patients with sqNSCLC who had progressed following PD-(L)1 inhibitors and platinum-based chemotherapy.

Additional Parameters	Gotistobart (N = 45)	Docetaxel (N=42)
Median age, years (range)	64 (39–86)	68.5 (43–84)
Gender (female/male), n (%)	9 (20) / 36 (80)	4 (9.5) /38 (90.5)
ECOG PS score = 1, out of 0 or 1, n (%)	36 (80)	35 (83.3)
Prior treatment ≥ 2 lines, n (%)	15 (33.3)	12 (28.6)
Brain Metastasis / Liver Metastasis, n (%)	6 (13.3) / 6 (13.3)	4 (9.5) / 2 (4.8)
TEAEs Gr ≥ 3, n (%)	30 (66.7)	26 (63.4)
Study drug related TEAEs Gr ≥ 3, n (%)	19 (42.2)	20 (48.8)
Diarrhea/Colitis, Gr ≥ 3, n (%)	2 (4.4) / 4 (8.9)	0
Overall Survival Rate at 12m, % (95% CI)	63.1 (46.9, 75.5)	30.3 (16.2, 45.6)



Number at Risk (censored)

Gotistobart, 6 mg/kg	45(0)	43(0)	42(0)	37(2)	36(2)	34(2)	32(2)	31(2)	31(2)	29(2)	28(2)	26(3)	24(5)	21(7)	15(13)	12(16)	7(21)	5(23)	1(27)	0(28)
Docetaxel, 75 mg/m^2	42(0)	41(1)	39(3)	36(3)	33(3)	30(3)	28(3)	23(4)	22(4)	20(4)	18(4)	14(5)	9(7)	8(7)	5(9)	5(9)	3(11)	0(14)		