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80MO

Durvalumab (D) plus tremelimumab (T) in advanced biliary tract carcinoma (BTC) patients (Pts) after failure of platinum-based chemotherapy (CTx): Final results of the IMMUNOBIL GERCOR D18-1 PRODIGE-57 phase II trial

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Background

FOLFOX provides limited efficacy in second-line of BTC. Durvalumab (anti-PDL1) + tremelimumab (anti-CTLA-4) immunotherapy showed positive results in hepato-biliary cancers.

Methods

The single-arm IMMUNOBIL study included two consecutive cohorts of Pts with recurrent/advanced BTC (intrahepatic cholangiocarcinoma [iCCA]/extrahepatic cholangiocarcinoma [eCCA]/gallbladder cancer [GC]), ECOG PS 0-1, pretreated with platinum-based CTx but no immunotherapy. Arm A received D (1500 mg Q4W) + T (75 mg Q4W for 4 cycles [T75]). The study was further amended (Arm A [Aam]) to modify T to 300 mg at cycle 1 (T300), STRIDE regimen. The primary endpoint: 6-month (mo) overall survival (M6 OS) in Arm Aam (D + T300), with a Fleming 2-stage design (H0: 50%, H1: 65%, 1-sided α: 5%, ß: 10%, efficacy threshold ≥59%).

Results

From 12/2018 to 11/2021, 212 Pts were included (106/arm); 104 (Arm Aam) and 103 (Arm A) were evaluable for M6 OS. Pts characteristics seemed similar between Arm A and Arm Aam and were in overall population: median age 66, 48% male, 55% ECOG PS 0, 65%/20%/15% with iCCA/eCCA/GC, 69% metastatic, and 35% prior resection. First-line CTx: GEMCIS/GEMOX/other in 69%/21%/10%. 60 Pts (58% [95% CI 49.2–65.9]) in Arm Aam and 60 (58% [95% CI 49.7–66.5]) in Arm A were alive at M6. Other efficacy outcomes are in table. Lack of progression at first CT-scan after 2 cycles (33%) correlated with longer OS (18.5 vs 4.8 mo [Arm Aam] and 18.3 vs 4.1 [Arm A]). A PD-L1 CPS (available in 102 of Pts) ≥5 (17% of Pts) was associated with longer OS (12.8 vs 6.4 mo).Table: 80MO

	Arm Aam	Arm A
Median OS, mo	6.7 (95% CI 5.1–7.8)	7.5 (95% CI 5.3–10.4)
Median PFS, mo	1.8 (95% CI 1.8–1.9)	2.0 (95% CI 1.9–2.2)
Complete Response	2%	2%
Partial Response	10%	8%
Stable Disease	17%	28%
Objective Response Rate	12%	10%

	Arm Aam	Arm A
Disease Control Rate	29%	38%
Safety		
≥1 G3–5 AE	66%	70%
≥1 G3–5 TRAE	17%	22%
Most common G3–4 AEs (both arms)	Abdominal pain (9%), fatigue (8%), diarrhea (5%)	
Most common G3–4 TRAEs	Diarrhea (4%), fatigue (2%)	

Conclusions

The STRIDE regimen did not meet the primary endpoint although it was very close to the efficacy threshold. A subset of Pts appeared to benefit from immunotherapy, not fully explained by PDL1. Results from additional tumor and blood ancillary program are pending.

Clinical trial identification

NCT03704480.

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