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A randomized trial of paclitaxel ± tovecimig in previously treated patients with advanced biliary tract cancer

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Background

Patients (pts) with biliary tract cancer (BTC) who have been previously treated have a poor prognosis with median overall survival (OS) of ~6 months. Tovecimig [T] is a bispecific antibody to delta-like ligand-4 (DLL4) and VEGF-A that inhibits the Notch 1 and VEGFR signaling pathways. COMPANION-002 is an open-label, phase 2/3 randomized, controlled study in pts with advanced or metastatic BTC who have received one prior therapy.

Methods

Eligible pts had advanced BTC with disease progression after first-line therapy. All pts received paclitaxel [P] (80 mg/m² on days 1, 8 & 15 of each 28-day cycle). Combination arm pts also received T (10 mg/kg on days 1 & 15 of each 28-day cycle). Primary objective was objective response rate (ORR) assessed by blinded independent central review (BICR) using RECIST v1.1. Key secondary objectives include progression-free survival (PFS) & OS. Crossover was permitted in the P arm following BICR confirmed progressive disease (PD). Prespecified secondary objective was PFS2 for those who crossed over to receive T + P.

Results

Between Apr 2023 and Aug 2024, 168 patients were randomized 2:1 to T + P (n=111) vs. P (n=57). Baseline demographics were well balanced. T + P resulted in statistically significant improvements in both BICR assessed ORR (17.1% vs 5.3%, p=0.031) and PFS (4.7 months (mos) vs 2.6 mos; HR=0.44, p<0.0001) compared to P alone. T + P also had a statistically significant improvement in mPFS2 of 3.5 mos after addition of T compared with mPFS1 of 1.9 mos for P alone in the same pts (HR=0.36, p=0.0016). 31 of 57 (54%) of P pts crossed over to receive T + P. Overall, no difference in OS (HR=1.05, p=0.78). Most common T + P TEAEs were hypertension [HTN] (69%) and fatigue (67%) and related ≥ grade 3 TEAEs included HTN (44%) and neutropenia (36%). T + P had more related SAEs (40% vs 19%) & TEAE leading to discontinuation (40% vs 15%) than P, respectively. TEAE leading to death were comparable, 6% in T + P vs 2% with P.

Conclusions

T + P was generally well tolerated and demonstrated a statistically significant advantage in BICR assessed ORR and PFS. Crossover pts derived clinical benefit based on PFS2. The OS analysis was confounded by high crossover (with 85% of all pts receiving T + P), precluding a meaningful comparison.

Clinical trial identification

NCT05506943.

Legal entity responsible for the study

Compass Therapeutics.

Funding

Compass Therapeutics.

Disclosure

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