BARCELONA 2024 ESMO congress

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Iparomlimab and tuvonralimab (QL1706) with bevacizumab and/or chemotherapy in first-line (1L) treatment of advanced hepatocellular carcinoma (aHCC): A randomized, open-label, phase II/III study (DUBHE-H-308)

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Background

QL1706, a single bifunctional MabPair product consisting of two engineered monoclonal antibodies (anti-PD-1 and anti-CTLA-4), plus bevacizumab (bev) as 1L therapy in aHCC showed promising antitumor activity and favorable safety profile in a Phase 1b/2 study. Thus the Phase 2 part of DUBHE-H-308 study (NCT05976568) investigating QL1706 with bev and/or chemotherapy (chemo) for 1L treatment of aHCC was conducted and the results were reported here.

Methods

Patients (pts) were randomly assigned (1:1:1:1) to the arm 1 QL1706 (7.5 mg/kg, Q3W) + bev (15 mg/kg, Q3W)+chemo (aHCC regimen, namely oxaliplatin 85 mg/m^2 plus capecitabine 1000 mg/m^2, Q3W, up to 4 cycles), the arm 2 QL1706 + bev, the arm 3 QL1706 + chemo, or the arm 4 another PD-1 antibody sintilimab (200 mg, Q3W)+ bev. Primary endpoints for this Phase 2 study included ORR by investigator per RECIST v1.1, and safety.

Results

In total, 120 pts were enrolled. As of data cutoff (12 Jul 2024), median follow-up was 6.7 months. The baseline characteristics were generally balanced across 4 arms. ORR and DCR were showed in the table. At this time progression free survival (PFS) was not mature. The 6-month PFS rate was 78.5%, 64.3%, 53.8% and 50.3% in the above 4 arms, respectively. Grade ≥3 treatment-related AEs in 4 arms occurred in 46.7%, 50.0%, 46.7% and 37.9% of pts, respectively. Only one pt died due to treatment-related hepatic failure in the arm 4.Table: LBA38

The efficacy of 4 arms

	QL1706+bev+chemo (Arm 1, n=31)	QL1706+bev (Arm 2, n=30)	QL1706+chemo (Arm 3, n=30)	Sintilimab+bev(Arm 4, n=29)
Best overall response, n (%)				
CR	1 (3.2)	0	0	0
PR	10 (32.3)	11 (36.7)	11 (36.7)	4 (13.8)
SD	16 (51.6)	13 (43.3)	15 (50.0)	17 (58.6)
PD	2 (6.5)	5 (16.7)	3 (10.0)	5 (17.2)
Not done	2 (6.5)	1 (3.3)	1 (3.3)	3 (10.3)
ORR, % (95% CI)	35.5 (19.2-54.6)	36.7 (19.9-56.1)	36.7 (19.9-56.1)	13.8 (3.9-31.7)

	QL1706+bev+chemo (Arm 1, n=31)	QL1706+bev (Arm 2, n=30)	QL1706+chemo (Arm 3, n=30)	Sintilimab+bev(Arm 4, n=29)
DCR, % (95% CI)	87.1 (70.2-96.4)	80.0 (61.4-92.3)	86.7 (69.3-96.2)	72.4 (52.8-87.3)

Conclusions

In the Phase 2 part of DUBHE-H-308 study, QL1706 plus bev with chemo showed encouraging preliminary efficacy and a manageable safety profile in 1L treatment of aHCC. QL1706 + bev + XELOX was selected as study arm by Independent Data Monitoring Committee for future Phase 3 study.

Clinical trial identification

NCT05976568.

Legal entity responsible for the study

Qilu Pharmaceutical Co., Ltd.

Funding

Qilu Pharmaceutical Co., Ltd.

Disclosure

L. Li, P. Shao, X. Kang: Personal, Full or part-time Employment: Qilu Pharmaceutical Co., Ltd. All other authors have declared no conflicts of interest.