Nab-paclitaxel plus capecitabine as first-line treatment for patients with recurrence or metastatic biliary tract cancer


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Background: Gemcitabine-based and fluoropyrimidine-based regimens demonstrated activity in phase II trials. Nab-paclitaxel plus gemcitabine was found well tolerated and superior to gemcitabine monotherapy in recurrent or metastatic biliary tract cancer leading to the current phase III trial.

Methods: Patients with histopathology or cytology confirmed recurrence or metastatic biliary tract cancer [including intrahepatic cholangiocarcinoma (ICC), extrapancreatic cholangiocarcinoma (ECC), gallbladder carcinoma (GC), with ECOG PS 0-1 and adequate major organ function, were enrolled and treated with Nab-paclitaxel (125mg/m², d1, q4d) plus capecitabine (2g/m²,d1-d17; q4d) until disease progression or unacceptable toxicity. The primary endpoint was ORR. The secondary endpoints were PFS, OS and safety. This study was registered with Chinese Clinical Trial Registry, number ChiCTR1900025004.

Results: Data cutoff for this analysis was May 16, 2020. We recruited 18 patients, 12 (66.7%) were males, median age was 64 years (range 35-74 years), ICC/ECC/GC/NE were 4 (22.2%) / 5 (27.8%) / 8 (44.4%) / 1 (5.6%) respectively. The median treatment cycle was 6 cycles (range 1-9). 15 patients were evaluable for efficacy. The ORR and DCR were 26.7% and 80%. The median follow-up was 8.3 months (range 4.3-13.6 months), the median PFS was 6.2 months (95% CI 3.1-NE months) and median OS was not reached. Common AEs were: leucopenia 7 (38.9%), neutropenia 5 (27.8%), ALT increase 3 (16.7%), AST increase 3 (16.7%), blood bilirubin increased 5 (5.6%). Most were grade 1/2.

Conclusions: Nab-paclitaxel plus capecitabine presented a clinically meaningful efficacy and a favorable safety profile as first-line treatment for recurrence or metastatic biliary tract cancer.

Clinical trial identification: ChiCTR1900025004.

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GLOW: Phase III study of first-line zolbetuximab and CAPOX versus placebo and CAPOX in Claudin18.2+ HER2- advanced metastatic gastric or gastroesophageal junction adenocarcinoma (G/GJE)


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Background: Capecitabine + oxaliplatin (CAPOX) is a standard first-line treatment for advanced gastric cancer. Claudin (CLDN)18.2 is a promising targetable biomarker. In healthy tissue, CLDN18.2, a tight junction protein, is confined to gastric mucosa (ie, cells in the pit and base regions of gastric glands). Upon malignant transformation, structural loss in G/GEI cells may allow antibodies more access to previously unavailable CLDN18.2. Zolbetuximab, a chimeric IgG1 monoclonal antibody, specifically binds to CLDN18.2 and mediates cell death through antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. Phase II (NCT01630083) results showed prolonged survival of patients with CLDN18.2-positive (CLDN18.2+) advanced G/GJE treated with zolbetuximab + epirubicin, oxaliplatin, and capecitabine (EOX) vs EOX alone.

Trial design: GLOW (NCT03653507) will enroll ~500 adults from global sites, including China, Japan, Korea, Malaysia, and Thailand. Patients must have CLDN18.2+ human epidermal growth factor receptor 2-negative (HER2-) locally advanced unresectable or metastatic G/GJE that is radiographically evaluable per RECIST v1.1. Prior treatment with chemotherapy for advanced/metastatic G/GJE is not permitted. Patients will be randomized 1:1 to zolbetuximab + CAPOX or placebo + CAPOX.