TPS4217 Poster Session

A randomized phase 2 study of casdozokitug, an IL-27 targeting antibody, in combination with toripalimab plus bevacizumab in patients with unresectable and/or locally advanced or metastatic hepatocellular carcinoma.

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Background: IL-27 is a heterodimerized cytokine, a member of the IL-12/IL-23 cytokine family, and an immunoregulatory cytokine expressed by myeloid cells that dampens T and NK effector function. IL-27 is highly expressed by tumor-associated macrophages in several cancers, including hepatocellular carcinoma (HCC) and non-small cell lung cancer (NSCLC), and suppresses antitumor immune responses. Casdozokitug (Casdozo) is the only clinical-stage IL-27 targeting antibody and it increases IFN-g and T and NK cell activation in preclinical/clinical studies. A phase 1 study (NCT04374877) demonstrated a favorable safety profile and antitumor activity of casdozo as monotherapy and in combination with PD-1 blockade in indications, including HCC, with known high levels of IL-27 activation signature (Marron T, et al. *Ann Oncol*. 2023). A phase 3 study of toripalimab (tori) + bevacizumab (bev) demonstrated significant improvements in efficacy (overall survival [OS], progression-free survival [PFS], and objective response rate [ORR]) compared to sorafenib (Yinghong S, et al. CSCO 2024) in HCC. A phase 2 study of casdozo + atezolizumab + bev showed an acceptable safety profile and antitumor activity (ORR 38%, CR 17.2%, mPFS 8.1 mo) (Li D, et al. ASCO GI 2025). CHS-388-202 (NCT06679985) will evaluate the efficacy, safety, and biomarkers of tori + bev ± casdozo and optimize the dose for casdozo in combination with tori + bev as first-line treatment for patients (pts) with unresectable and/or locally advanced/metastatic HCC. **Methods:** CHS-388-202 is a Phase 2, open-label, randomized study and will enroll up to 72 pts randomized (1:1:1) to 1 of 3 treatment arms (IV Q3W): Arm A (tori 240 mg + bev 15 mg/kg + casdozo 700 mg), Arm B (tori 240 mg + bev 15 mg/kg + casdozo 1400 mg), Arm C (tori 240 mg + bev 15 mg/kg). Key eligibility criteria include treatment-naïve unresectable metastatic HCC with ≥1 measurable lesion; not suitable for surgical or local therapy; Child-Pugh A; ECOG PS 0 or 1; controlled hepatitis B virus or cured hepatitis C virus. Pts will be stratified by geographic region (Asia excluding Japan vs the rest of the world) and macrovascular invasion or extrahepatic spread of disease (presence vs absence). Primary endpoints are ORR by investigator review according to RECIST v1.1 and safety. Secondary endpoints are ORR by investigator review according to HCC modified RECIST (mRECIST) criteria; duration of response, PFS, and disease control rate by investigator review according to RECIST v1.1 and mRECIST criteria; OS, pharmacokinetics. A safety run-in evaluation will be conducted after the first ~6 pts are enrolled in Arms A and B, with ≥3 from each arm completing 1 cycle of treatment. Pts will remain on study treatment for ≤2 years or until documented disease progression or unacceptable toxicity. Enrollment is ongoing. Clinical trial information: NCT06679985. Research Sponsor: Coherus BioSciences.