TPS1139 Poster Session

Efficacy and safety of disitamab vedotin in combination with RC148 versus albumin-bound paclitaxel ± toripalimab for patients with HR-negative HER2-low-expressing unresectable locally advanced or metastatic breast cancer: An open-label, randomized, controlled phase II study.

Jiayu Wang, Quchang Ouyang, Xiying Shao, Wenbin Zhou, Yongsheng Wang, Weimin Xie, Jingfen Wang, Aimei Jiang, Changwen Li, Zerui Qu, Chenran Han, Bo Yang, Jianmin Fang, Binghe Xu; Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; Hunan Cancer Hospital, Changsha, China; Zhejiang Cancer Hospital, Hangzhou, China; Jiangsu Province Hospital, Suzhou, China; Breast Cancer Center, Shandong Cancer Hospital, Shandong University, Jinan, China; Guangxi Medical University Cancer Hospital, Nanning, China; Linyi Cancer Hospital, Linyi, China; The First Affiliated Hospital of Kunming Medical University, Kunming, China; Xuzhou Central Hospital, Xuzhou, China; RemeGen Co., Ltd., Yantai, China; RemeGen Co., Ltd, Yantai, China; School of Life Science and Technology, Tongji Univesity, Shanghai, China; Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China

Background: Patients (pts) with hormone receptor (HR)-negative and HER2-low-expressing (defined as IHC 1+, or IHC 2+/ISH-) advanced breast cancer have poor prognosis and more effective treatment options are needed. Disitamab vedotin (DV) is a novel humanized anti-HER2 antibody conjugated with monomethyl auristatin E (MMAE) via a cleavable linker. DV alone or in combination with a PD-1 inhibitor showed encouraging antitumor activities with manageable safety in pts with HER2-low-expressing (IHC 1+, or IHC 2+/ISH-) advanced or metastatic breast cancer, gastric cancer and other solid tumors (Wang J., et al., *Cancer Commun*, 2024; Wang Y., et al., *eClinicalMedicine*, 2024). RC148 is a bispecific monoclonal antibody directed against programmed death receptor-1 and vascular endothelial growth factor receptor. DV+RC148 combination is expected to exert a synergistic antitumor effect by improving the tumor immune microenvironment. We aim to evaluate the efficacy and safety of DV plus RC148 versus albumin-bound paclitaxel ± toripalimab in pts with HR-negative HER2-low-expressing advanced breast cancer in this randomized phase II trial (NCT06642545). **Methods:** The key eligibility criteria are pts aged 18 years or older with unresectable stage III or stage IV breast cancer, negative HR status, low HER2 expression (defined as IHC1+, or IHC2+/ISH-), no previous chemotherapy for locally recurrent or metastatic disease, and no disease recurrence within 6 months after treatment completion (within 12 months if using taxanes) if with radical treatment. Pts who previously received anti-HER2 therapy or immunotherapy are excluded (except pts receiving neoadjuvant/adjuvant PD-[L]1 inhibitors 12 months prior to recurrence or progression). Pts will be randomized (stratified by PD-L1 expression status: positive or negative) in a ratio of 1:1 to receive DV (2.0 mg/kg) plus RC148 (20 mg/kg) intravenously once every two weeks or to receive albumin-bound paclitaxel (125 mg/m^2 day 1 and day 8) ± toripalimab (240 mg day 1) intravenously every three weeks until occurrence of disease progression or intolerable toxicity. The primary endpoint is objective response rate (ORR) in all pts per investigator's assessment according to RECIST v1.1. The secondary endpoints are ORR in the PD-L1-positive pts; investigator-assessed progression-free survival, disease control rate, duration of response, and overall survival in all pts and the PD-L1-positive pts. This study was initiated in August 2024. Clinical trial information: NCT06642545. Research Sponsor: RemeGen Co., Ltd.