TPS4222 Poster Session

# Trial in progress: A phase Ib/II study to evaluate the safety and efficacy of atezolizumab plus bevacizumab as adjuvant therapy following carbon ion radiotherapy in hepatocellular carcinoma (VANGUARD trial).

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**Background:** While hepatic resection remains the standard curative treatment for hepatocellular carcinoma (HCC), many cases are ineligible due to impaired liver function or patient-related factors. Percutaneous ablation is an option for small HCC but is limited by tumor size. Carbon ion radiotherapy (C-ion RT) has emerged as a promising modality, characterized by superior biological efficacy and dose distribution compared to conventional radiotherapy. Although HCC is relatively radiosensitive, conventional radiotherapy has limited efficacy due to low radiation tolerance of surrounding liver tissue. C-ion RT achieves effective treatment while minimizing radiation exposure through the superior dose localization of the carbon ion beam's Bragg peak. The establishment of adjuvant systemic therapy to prevent recurrence remains an urgent unmet need in HCC management. The IMbrave050 trial demonstrated the efficacy of combined atezolizumab and bevacizumab (Atezo+Bev) after resection or ablation, but recent analyses suggest diminishing long-term benefits. The combination of immune checkpoint inhibitors (ICIs) and radiotherapy has shown promise in several malignancies, with preclinical studies demonstrating synergistic enhancement of ICI efficacy through radiation-induced immunogenic cell death. Additionally, carbon ion radiation induces stronger immune responses compared to proton therapy. Based on these findings, we designed a phase Ib/II study to evaluate sequential C-ion RT followed by ICI as a novel therapeutic approach. **Methods:** This multicenter, open-label, single-arm phase Ib/II study evaluates the safety and efficacy of Atezo+Bev as adjuvant therapy following C-ion RT for HCC. Key inclusion criteria include treatment-naïve, Child-Pugh class A, maximum intrahepatic tumor diameter $\geq$4 cm and $\leq$3 intrahepatic tumors. After initial enrollment, patients undergo C-ion RT followed by a two-week observation period with eligibility screening for second enrollment. Eligible patients receive atezolizumab (1200 mg) and bevacizumab (15 mg/kg) every 3 weeks for up to 48 weeks, with radiological assessments every 3 months. The Phase Ib part will enroll six patients to evaluate dose-limiting toxicities. Secondary endpoints include adverse events (AEs) and serious AEs for safety and 1-year RFS, overall survival (OS) and 6-month OS rates for efficacy. If tolerability is confirmed, the trial will proceed to Phase II. Clinical trial information: jRCT2031240284. Research Sponsor: Chugai Pharmaceutical Co., Ltd.