TPS3639 **Poster Session**

Stereotactic body radiotherapy combined with PD-1 antibody in unresectable colorectal liver metastases: A prospective, multicenter, single-arm, phase II study (SPARKLE-L).

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Background: Colorectal cancer liver metastasis (CRLM) significantly decreases colorectal cancer (CRC) patient prognosis, affecting 30-50% of CRC patients at diagnosis or thereafter. Notably, up to 70%-90% CRLM are diagnosed as unresectable. Standard treatments include systemic chemotargeted-therapies (CT). However, only 10-30% CRLM can be converse to resectable state by CT, with an objective response rate (ORR) of just 15%-20% and a median overall survival (OS) of approximately 20-30 months. Improving prognosis of CRLM patients remains challenging. Stereotactic body radiation therapy (SBRT) combined with immunotherapy might offer promising alternatives. SBRT provides high-dose tumor control while protecting surrounding tissues better than conventional radiotherapy. It also facilitates the release of tumor-associated antigens, reshaping the immune microenvironment and inducing stronger immune responses. The combination of SBRT and PD-1 antibodies might synergistically enhance the anti-tumor efficacy. Despite SBRT's demonstrated efficacy in unresectable CRLM with few adverse reactions, no prospective studies have explored its combination with PD-1 antibodies. **Methods:** This is a multicenter, open-label, single-arm, phase II trial conducted in China. Patients will receive SBRT at 8-12 Gy per fraction over 5 fractions, combined with 5-FU-based CT and PD-1 antibody therapy before and after SBRT. Eight weeks ($\pm$2 weeks) post SBRT, imaging assessments or multi-point liver biopsies will be performed. Multidisciplinary teams (MDT) will determine subsequent plans: cCR/pCR patients will undergo maintenance CT or enter a watch-and-wait phase; non-cCR/pCR patients will continue maintenance CT or exit the study. This is the first study exploring whether SBRT combined with PD-1 monoclonal antibody can improve ORR, OS, quality of life (QOL) and potentially achieve no evidence of disease (NED) status for unresectable CRLM. Key inclusion criteria: pMMR/MSS CRC, MDT-assessed unresectability due to main portal vein invasion, multiple hepatic vein invasion or lack of R0 resection/ablation feasibility. Main exclusion criteria encompass active hepatitis, cirrhosis, Child-Pugh B/C, checkpoint inhibitor therapies history and ECOG performance status $\geq$2. Twenty-four patients are planned for enrollment, with two already enrolled as of January 25, 2025. The study is registered with ClinicalTrials.gov (NCT06794086) and is ongoing. Clinical trial information: NCT06794086. Research Sponsor: None.