TPS3634 Poster Session

Alliance A022101/NRG-GI009: A pragmatic randomized phase III trial evaluating total ablative therapy for patients with limited metastatic colorectal cancer—Evaluating radiation, ablation, and surgery (ERASur).

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Background: For patients with oligometastatic colorectal cancer (CRC), aggressive local therapy of isolated metastases, particularly in the liver, has been associated with long-term progression-free and overall survival (OS) primarily based on retrospective evidence. However, in patients with limited metastatic CRC that is deemed inoperable or those with additional disease outside of the liver or lungs, the role of local ablative therapies, including microwave ablation (MWA) and stereotactic body radiation therapy (SBRT), to render patients disease free is less clear. Despite the long history of treating oligometastatic CRC with local therapy, which is largely provider biased, questions remain regarding the benefit of extending the paradigm of metastatic directed therapy to patients with more extensive disease. This trial seeks to use a pragmatic multimodality approach that mirrors the current clinical dilemma. This study is designed to evaluate the safety and efficacy of adding total ablative therapy (TAT) of all sites of disease to standard of care systemic treatment in those with limited metastatic CRC. **Methods:** A022101/NRG-GI009 is a National Clinical Trials Network randomized phase III study planned to enroll 364 patients with newly diagnosed metastatic CRC (BRAF wild-type, microsatellite stable) without peritoneal metastasis or liver-only disease on baseline imaging. Patients receive first-line systemic therapy for 12-39 weeks. Patients with ≤4 sites of metastatic disease following initial systemic therapy that are amenable to any combination of surgical resection, MWA, and/or SBRT are then randomized 1:1, stratified by number of metastatic organ sites (1-2 vs. 3-4), timing of metastatic disease diagnosis (de novo vs. secondary), and presence of metastatic disease outside the liver/lungs in at least 1 site. Patients in Arm 1 will receive TAT consisting of treatment of all metastatic sites with SBRT, MWA, and/or surgical resection followed by standard of care systemic therapy. Patients in Arm 2 will continue with standard of care systemic therapy alone. The primary endpoint is OS. Secondary endpoints include event-free survival, treatment-related toxicities, and local recurrence with exploratory biomarker analyses. The study needs 346 evaluable patients combined in the 2 arms to demonstrate an improvement in OS with a hazard ratio of 0.7 to provide 80% power with a one-sided alpha of 5%. The trial utilizes a group sequential design with two interim analyses (25% and 50% of events) for futility. The trial activated in January 2023 and recruitment is ongoing. Support: U10CA180821, U10CA180882; https://acknowledgments.alliancefound.org. U10CA180820 (ECOG-ACRIN); U10CA180868 (NRG); U10CA180888 (SWOG); Clinical trial information: NCT05673148. Research Sponsor: U.S. National Institutes of Health.