TPS2102 **Poster Session**

Regorafenib versus local standard of care in patients with grade 2-3 meningioma no longer eligible for loco-regional treatments: The MIRAGE trial.

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Background: Meningiomas are the most common intracranial tumors. Standard treatment involves surgical resection with curative intent. When gross total resection is not achievable, or in case of recurrence, RT is frequently utilized. On the other hand, the role of systemic treatments remains poorly supported by evidence.Regorafenib is an oral multi-tyrosine kinase (RTK) inhibitor. It exhibits high selectivity for VEGFR1/2/3, while also inhibiting PDGFRβ, FGFR1, and c-RAF/RAF1 and BRAF pathways, highly expressed in high-grade meningiomas. **Methods:** TheMIRAGE Trial (NCT06275919) is a multicenter, open-label, randomized phase 2 clinical trial evaluating grade 2/3 meningioma pts who have progressed following surgery and RT. A total of 94 pts are being randomized (1:1) to receive either Regorafenib (160 mg orally for 3 weeks on, 1 week off) or local standard-of-care therapies (e.g., bevacizumab, hydroxyurea, somatostatin analogues).Major inclusion criteria include histological confirmation of WHO 2021 grade 2-3 meningioma, radiologically documented progression at least 24 weeks from RT (estimated planar growth $>$ 25% in two dimensional tumor areas within the prior 12 months or development of a new lesion) with at least 1 measurable lesion (minimum 10 x 10 mm) on baseline MRI, ineligibility for further surgery and/or radiotherapy, absence of extracranial lesions and a WHO performance status of 0-1.The primary endpoint is 6-month PFS (6m-PFS). Assuming a 6m-PFS of 20% in the control arm and 40% in the regorafenib arm (corresponding to a HR = 0.57) with a = 5%, b = 85%, 104 patients are needed to assess the targeted efficacy. Response to treatment will be assessed by using RANO criteria. Secondary endpoints include OS, ORR, DCR, volumetric analysis of the target lesions, safety and health-related quality of life. Multi-omics exploratory analysis will also be performed to investigate possible prognostic and predictive biomarkers. Radiomics analysis will also be performed. MIRAGE, initiated in September 2024, is an academic trial promoted by the Istituto Oncologico Veneto, IOV-IRCCS and will recruit patients across 15 neuro-oncology Centers in Italy with an estimated study duration of 18 months. Discussion: MIRAGE is the first randomized phase 2 trial analyzing the role of a RTK inhibitor (regorafenib) in prolonging PFS in pts with grade 2-3 meningioma who are ineligible for further surgery and/or radiotherapy. Clinical trial information: NCT06275919. Research Sponsor: None.