ID #950 CURE-ETMR, a prospective, international, molecularly guided trial utilizing centralized screening and risk-adapted assignment for infants with rare embryonal brain tumors [Abstract]

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ID #950 CURE-ETMR, A PROSPECTIVE, INTERNATIONAL, MOLECULARLY GUIDED TRIAL UTILIZING CENTRALIZED SCREENING AND RISK-ADAPTED ASSIGNMENT FOR INFANTS WITH RARE EMBRYONAL BRAIN TUMORS

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Embryonal tumors with multilayered rosettes (ETMR) are rare, highly aggressive tumors of infancy with extremely poor outcomes and no established standard of care therapy. ETMRs were recognized as a distinct molecular entity in 2016, however, the absence of prospective, biology-driven clinical trials has limited translation of these insights into standardized, risk-adapted treatment approaches for this vulnerable population.

To address this gap, the Collaborative Network for Neuro-oncology Clinical Trials (CONNECT) developed *CURE*(Clinical trial advancing Understanding of Rare Embryonal Brain Tumors), an international, multi-institutional, molecularly guided umbrella trial. All patients enroll through the centralized **CURE-Screening** protocol, which provides rapid comprehensive molecular profiling with real-time central pathology, molecular, and radiographic review to confirm diagnosis, define molecular subtype, and determine eligibility and assignment to disease-specific treatment arms. **CURE-ETMR represents the first disease-specific arm to open within this platform.**

Following centralized screening, children with newly diagnosed ETMR are assigned to clinically defined risk strata using integrated molecular, radiographic, and clinical criteria. Patients will be treated using a risk-adapted multimodal approach in which we prioritize maximal safe surgical resection with consideration of second-look surgery based on centralized imaging review; administer induction chemotherapy followed by consolidation with high-dose chemotherapy and autologous hematopoietic cell rescue or dose-intensified chemotherapy, selectively incorporate radiation sparing approach or early focal radiotherapy for patients with unresectable residual disease or brainstem involvement; deliver intrathecal chemotherapy for leptomeningeal prophylaxis; and include biologically informed maintenance therapy.

In parallel, protocol-required longitudinal collection of tumor tissue, cerebrospinal fluid, blood, and advanced neuroimaging supports integrated molecular, liquid biopsy, and imaging biomarker analyses to identify predictors of treatment response, resistance, and relapse. Primary objectives include evaluation of feasibility, safety, progression-free survival, and overall survival compared with molecularly annotated historical cohorts. This centralized screening to assignment framework establishes a scalable model for prospective, biology-driven trials in rare embryonal brain tumors.