BACKGROUND: Brain metastases represent the most common intracranial tumor in adults, occurring in 10-40% of cancer patients. Most patients undergo multimodal treatment approaches and post-treatment follow-up with conventional MRI (CE-T1-weighted and FLAIR/T2-weighted) of the brain is performed to monitor for disease recurrence. However, owing to the similar appearance of treatment-related changes like radiation necrosis with that of true recurrence, conventional MRI alone suffers from low specificity. Given the high mortality of patients with brain metastases and the considerable treatment-associated morbidity, a need remains for an imaging modality that accurately differentiates recurrence from treatment-related changes. Accurate imaging is key to preventing unnecessary surgery or changes in effective therapy in patients mistaken for disease progression as well as prevent continuation of ineffective therapy if radiation necrosis is incorrectly diagnosed. To this end, 18F-fluciclovine is a synthetic amino acid-based PET imaging agent that has potential to evaluate primary and metastatic brain cancers owing to its low normal background uptake in the brain and increased uptake in brain tumors. METHODS: NCCT0413067 is a prospective, open-label, single-arm, single-dose (185 MBq ± 20%) study with a primary objective to establish visual image interpretation criteria for 18F-fluciclovine PET studies of recurrent brain metastases. Forty subjects with solid tumor brain metastases who have undergone radiation therapy will be enrolled across ~8 US sites if they have a reference lesion considered equivocal on MRI for recurrent disease and are planned for craniotomy. Subjects will undergo 18F-fluciclovine PET ~42 days after the MRI and 1–21 days before planned craniotomy. Outcome measures comprise the diagnostic performance of 18F-fluciclovine PET at different thresholds of 18F-fluciclovine uptake compared with histopathology, subject- and lesion-level diagnostic performance based on established image interpretation criteria, and safety evaluations. Enrollment began in August 2020 and the trial is open at the time of submission.

CLRM-03. BGB-290 AND TEMOZOLOMIDE IN TREATING ISOCITRATE DEHYDROGENASE (IDH)1/2-MUTANT GRADE I-V GLIOMAS – A NOVEL MODEL OF AYA TRIAL DESIGN AND DEPLOYMENT
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DESCRIPTION: The lack of enrollment of AYA patients on clinical trials is well documented and multivariant. Here we present the basic science, examination of its relevance to the AYA population specifically, and the parallel deployment of two international clinical trials via a pediatric neuro-oncology and adult brain tumor consortium. DISCUSSION: In February of 2017, the laboratory of Ranjit Bindra, MD, PhD, published a manuscript describing the finding that tumors with IDH1/2 mutations induce a proliferative state leading to PARP inhibitor (PARPi) sensitivity and synergistic interactions with temozolomide chemotherapy [2]. Despite IDH1/2 mutations being rare in the pediatric high-grade glioma population, three independent groups confirmed that the incidence is significantly increased to ~30% in the adolescent and young adult (AYA) population. Upon discovery of a high blood-brain-barrier penetrant, high potency PARPi by BeiGene Pharmaceuticals, an international trial was launched through the Pacific Pediatric Neuro-Oncology Consortium (PPONC) [3] to test this drug in an AYA specific trial recruiting patients ages 13 to 25; with a concurrent trial being run for patients older than 25 years of age through the Adult Brain Tumor Consortium (ABTC) [4].

While most trials that enroll AYA patients are forced to assess them as a unique cohort in post-analytical fashion, if at all, the PPONC trial mentioned above was designed from the ground up with the AYA population in mind. It allowed us to base initial dosing, recruitment strategies, psychosocial assessments, and outcomes, specifically on the AYA population. Ultimately, we expect their distinctive biology to yield unique results when compared to the ABTC trial.

We propose that this is a model that could potentially be replicated in other disease processes and early phase drugs with the buy-in of the pharmaceutical industry and early phase consortiums.

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CLRM-04. PHASE I/II SAFETY AND EFFICACY STUDY OF BET BROMODOMAIN INHIBITOR OTX-015 WITH OLPARIB AND LOMUSTINE IN PATIENTS WITH RECURRENT GLIOBLASTOMA
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Standard of care for patients with glioblastoma (GBM) includes resection with concurrent temozolomide (TMZ) and radiotherapy, with inevitable disease recurrence. Upon recurrence, tumors are often resistant to first-line therapies and/or have infiltrated eloquent or deep brain regions, precluding repeat resection. There is currently no standard of care for recurrent GBM and patients succumb to their disease burden within 12–15 months of their