Version 02/27/24

NCI National Clinical Trials Network

EAF223/GABLE

For Patients with Newly Diagnosed Glioblastoma

EAF223 Available Through the ECOG-ACRIN Cancer Research Group

Phase II Glioblastoma Accelerated Biomarkers Learning Environment Trial (GABLE)

Patient Population

See Section 3 for Complete Eligibility Details

- ≥ 18 years of age
- Karnofsky Performance Status ≥ 60%
- Must have newly diagnosed glioblastoma (GBM) (must be IDH wild type), with pathologic proof, based on WHO 2021 criteria
- Must be planning to receive standard-of-care treatment for newly diagnosed GBM
  - ◊ Patients who are planning to receive radiotherapy: protons, stereotactic radiosurgery, or abbreviated hypofractionated regimens are not eligible
- Must have completed an MRI prior to the diagnostic surgery for GBM and have images available for upload into TRIAD
- Must have diagnostic surgery for GBM within 7 weeks prior to registration
- Must not have any additional planned surgery for GBM prior to initiating RT/TMZ
- Must have O6-Methylguanine-DNA Methlytransferase (MGMT) methylation status ordered at time of registration
- Must have a post-op MRI completed within 3 weeks after diagnostic surgery for GBM and have images available for TRIAD
- No contraindications to MRI, including injection of gadolinium-based contrast agents, and demonstrated ability to tolerate MRI on pre-surgical imaging
- No allergies to agents that may potentially be used for non-standard of care imaging (18F-fluciclovine, MR contrast)
- Not pregnant or breast-feeding
- Patients with prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible

Treatment Plan

See Section 5 for Complete Treatment Details

- Patients with newly diagnosed GBM will be registered within 7 weeks after diagnostic surgery and prior to the start of treatment
- EAF223 treatment: Concomitant temozolomide and radiation followed by maintenance temozolomide, with or without Optune
  - ◊ Standard treatment includes radiotherapy administered at 1.8-2.0 Gy per day to a total dose of 59.4-60 Gy (+/- 5%)
  - ◊ Temozolomide will be 75 mg/m²/day or per institutional guidelines
- Only patients with 3DCRT/IMRT will be evaluable for the biomarker evaluation endpoints
- MRI imaging must be completed at the following times:
  - ◊ Pre-operative (prior to diagnostic surgery)
  - ◊ Post-operative (within 3 weeks after diagnostic surgery)
  - ◊ Time point 1: 4 (+/- 2) weeks after completing radiation
  - ◊ Time point 2: 12 (+/- 2) weeks after completing radiation
  - ◊ Time point 3: 12-22 weeks after completing radiation
- Patients showing progressive enhancement by central review will be scheduled for a single non-standard of care imaging study (1st cohort is 18F-flucivlovine PET, 2nd cohort is MR spectroscopy)
- Neurological Assessment in Neuro-Oncology (NANO) will require completion by a clinician at the clinical visit corresponding to/closest to time point 1 and 2 MRI, and any unscheduled MRI within 12 weeks post-XRT. Then, for patients with progressive enhancement, every clinical visit thereafter

Study Chair:
Daniel Barboriak, MD

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org/open

Protocol Information

ECOG-ACRIN Operations - Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

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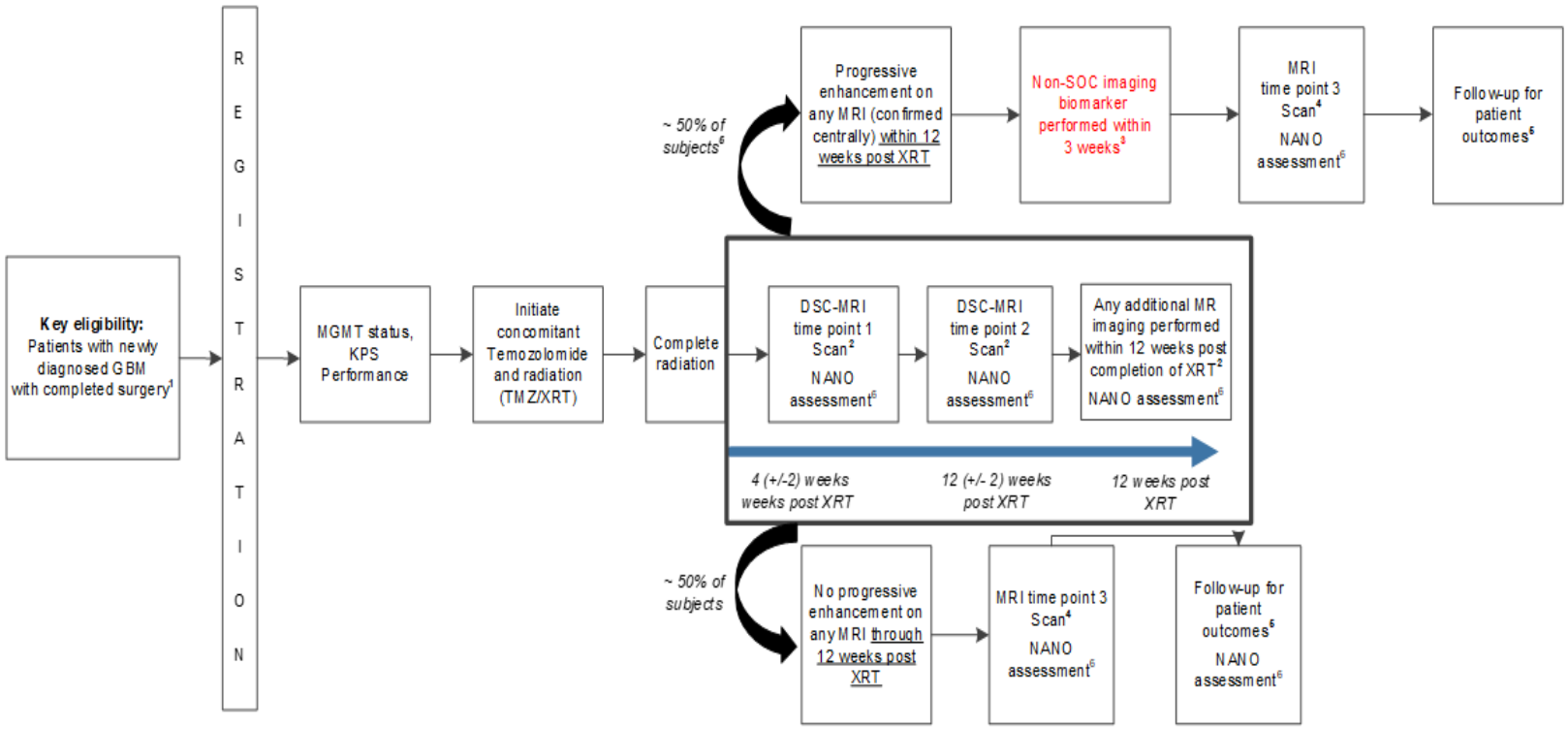
ECOG-ACRIN cancer research group

EAF223

Schema



1. Patients must have had surgery within 7 weeks of enrollment and a post-operative MRI completed within 3 weeks of surgery. Both pre- and post-operative MRIs must be available for submission to TRIAD after patient enrollment. Treatment for GBM cannot start prior to registration.
2. MRI time point 1 scan to be performed 4 (+/- 2) weeks after completing radiation. Time point 2 scan to be performed 12 (+/- 2) weeks after completing radiation. Both scans are required and should be submitted via TRIAD. Any additional MR imaging performed as clinically indicated within 12 weeks post completion of radiation must also be submitted via TRIAD. All MR imaging performed within 12 weeks post radiation will be read centrally to confirm presence or absence of progressive enhancement. All MR imaging must be submitted within 3 business days of acquisition. The time point 1 and time point 2 scans should have DSC sequencing completed. All MRIs should be Brain Tumor Imaging Protocol compliant.
3. Subjects with progressive enhancement on MRI at any time within 12 weeks post completion of radiation (confirmed centrally) will receive one non-SOC imaging test at the time of progressive enhancement (within 3 weeks of central confirmation of progressive enhancement).The first imaging biomarker cohort will receive ^{18}F-fluciclovine PET, and the second will receive MR spectroscopy.
4. MRI time point 3 (Brain Tumor Imaging Protocol compliant) scan to be performed 12 weeks (up to 22 weeks) after completion of radiation and after time point 2.
5. Subjects will be followed for a minimum of 12 months from the last patient enrollment (per non-SOC biomarker) and up to a maximum of six years.
6. Neurological Assessment in Neuro-Oncology (NANO): NANO will be done at the clinical visits closest to the time point 1 MRI, the time point 2 MRI, and any unscheduled MRI that is within 12 weeks post-XRT. In addition, NANO will be done at every clinical visit thereafter for patients demonstrating progressive enhancement.

For each non-SOC imaging biomarker (Fluciclovine PET or MRS), we anticipate that an accrual of 220 subjects will be necessary in order to achieve 100 subjects in the progressive enhancement pathway. However, for each non-SOC imaging biomarker, an interim analysis for efficacy and futility will be performed once 60 subjects with progressive enhancement are reached. Thus, up to 440 participants are expected to be enrolled to the trial; however, the total sample size could be larger or smaller depending on the observed rate of progressive enhancement and if accrual to one or more biomarkers is stopped early at the respective interim analysis.