PEP-CMV Vaccine Targeting CMV Antigen to Treat Newly Diagnosed Pediatric HGG and DIPG and Recurrent Medulloblastoma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 3 years to 39 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria for patients with recurrent /progressive medulloblastoma (stratum I)

1. Age: Patients must be ≥3 and ≤39 years of age at the time of study enrollment
2. Diagnosis: Patients must have a diagnosis of medulloblastoma that is recurrent, progressive or refractory. All patients must have histological verification of a medulloblastoma, at original diagnosis or relapse.

• Patients must have measurable disease defined as a lesion that can be measured in two perpendicular diameters on MRI.
3. Metastatic Disease: Patients with M+ disease are eligible.
4. Performance Status:

Karnofsky ≥ 50% for patients >16 years of age or Lansky ≥ 50 for patients ≤ 16 years of age. Patients who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.
5. Prior Therapy:

1. Radiotherapy: prior radiotherapy requirements Patients must have received prior disease-directed therapy including radiotherapy for their initial diagnosis of medulloblastoma unless patients are less than 4 years of age at the time of enrollment.

   For those less than 4 years of age at the time of enrollment, prior disease directed therapy does not have to include prior radiotherapy.

   Patients must have had their last fraction of:

   - Craniospinal irradiation, total body irradiation or radiation to ≥ 50% of pelvis > 3 months prior to enrollment.
   - Focal irradiation > 4 weeks prior to enrollment
2. Myelosuppressive anticancer therapy: Patients must have received their last dose of myelosuppressive anticancer therapy at least 21 days prior to enrollment
3. Immunotherapy: Patients must have received their last dose of any immunotherapy agents at least 30 days prior to enrollment
4. Non-myelosuppressive anticancer agents: Patients must have received their last dose of non-myelosuppressive anticancer agents at least 7 days prior to study enrollment.
5. Antibodies: Patients must have received their last dose of any antibodies at least 21 days prior to enrollment.
6. Hematopoietic growth factors: Patients must have received their last dose of hematopoietic growth factors at least 14 days prior to enrollment for a long-acting growth factor (e.g. pegfilgrastim) or 7 days prior to enrollment for short-acting growth factor.
7. Autologous stem cell infusion: At least 90 days must have elapsed after an autologous stem cell infusion

    1. Organ Function Requirements:
8. Adequate bone marrow function defined as:

* ANC (Absolute neutrophil count) ≥ 1000/µl.
* Platelets ≥ 100,000/µl. (may be supported)
* Hemoglobin \> 8 g/dL. (may be supported)

1. Adequate Renal Function defined as: Creatinine clearance or radioisotope GFR ≥ 70ml/min/1.73 m2 or A serum creatinine based on age/gender as follows:

   Age: Maximum Serum Creatinine (mg/dL)

   - 2 to < 6 years: 0.8 (Male) 0.8 (Female)
   - 6 to < 10 years: 1 (Male) 1 (Female)
   - 10 to < 13 years: 1.2 (Male) 1.2 (Female)
   - 13 to < 16 years: 1.5 (Male) 1.4 (Female)
   - ≥ 16 years: 1.7 (Male) 1.4 (Female)
2. Adequate Liver Function Defined as

* Total bilirubin ≤1.5 times institutional ULN
* AST(SGOT) ≤3 × institutional upper limit of normal
* ALT(SGPT) ≤3 × institutional upper limit of normal

1. Adequate Neurological Function Defined as

* Patients with neurological deficits should have deficits that are stable for a minimum of 2 weeks prior to enrollment

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* Patients with current seizure disorders may be enrolled if seizures are well- controlled on antiepileptic therapies.

1. Patients of childbearing or child-fathering potential must be willing to use a medically acceptable form of birth control, which includes abstinence, while being treated on this study and for three months after drug cessation.
2. Signed informed consent according to institutional guidelines must be obtained prior to enrollment.

Inclusion Criteria for Patients with Newly-Diagnosed High-Grade Gliomas (HGG) (stratum II, CLOSED on 19Aug2026) and Newly-Diagnosed (DIPG) (stratum III)

1. Age: Patients must be ≥3 and ≤39 years of age at the time of study enrollment
2. Diagnosis

    1. Stratum II [CLOSED on 19Aug2026]: patients must have histologically confirmed, newly-diagnosed HGG (such as anaplastic astrocytoma, glioblastoma, H3K27-altered DMG).

* Patients with a newly-diagnosed HGG must enroll within 6 weeks of their final dose of standard radiation therapy with or without chemotherapy.
* Patients with primary spinal cord tumors are eligible

1. Stratum III: Patients with a newly-diagnosed DIPG:

* Patients with a radiographically typical DIPG, defined as a tumor with a pontine epicenter and diffuse involvement of more than 2/3 of the pons, are eligible wit hout histologic confirmation.
* Patients with brainstem lesions that do not meet these radiographic criteria will be eligible if there is histologic confirmation of an infiltrating astrocytoma WHO grades II-IV.

1. Metastatic Disease: Patients with M+ disease are eligible.
2. Performance Status:

Karnofsky ≥ 50 for patients > 16 years of age and Lansky ≥ 50 for patients ≤ 16 years of age (See Appendix I). Patients who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.
5. Prior Therapy requirements: Patients must have received no prior therapy other than surgery, radiation, chemotherapy during radiotherapy and/or steroids (dexamethasone with goal to wean dexamethasone throughout protocol therapy).

Patients with a newly diagnosed high-grade glioma or DIPG must enroll within 6 weeks of their final dose of standard of care radiation therapy with or without chemotherapy.
1. Patients with HGG or DIPG are permitted, but not required, to have received chemotherapy during radiation. Bevacizumab is permitted prior to enrollment in patients with DIPG or HGG. Patients must have received their last dose of bevacizumab at least 14 days prior to enrollment.
2. For HGG patients, Patients must have received radiotherapy at a standard dose of 54-59.4 Gy in 1.8 Gy fractions for approximately 6 weeks with an acceptable variance of 10%. Radiation therapy must have begun no later than 42 days after the date definitive surgery.
3. For patients with DIPG, Patients must have received radiotherapy at a standard dose of radiotherapy of 54 Gy in 1.8 Gy daily fractions for approximately 6 weeks with an acceptable variance rate of 10%. Radiation therapy must have begun no later than 42 days after the date of radiographic diagnosis or biopsy
4. For patients with spinal cord HGG: Patients must have received radiotherapy at a standard dose of 45-54 Gy in 1.8 Gy fractions for approximately 6-7 weeks with an acceptable variance of 10%
5. For patients with metastatic disease: Patients may have received standard dose CSI
6. Organ Function Requirements:

1. Adequate bone marrow function defined as • ANC (Absolute neutrophil count) ≥ 1000/µl.

    • Platelets ≥ 100,000/µl. (may be supported)

    • Hemoglobin > 8 g/dL. (may be supported)

2. Adequate Renal Function defined as: Creatinine clearance or radioisotope GFR ≥ 70ml/min/1.73 m2 or A serum creatinine based on age/gender as follows:

    Age: Maximum Serum Creatinine (mg/dL)

    • 2 to < 6 years: 0.8 (Male) 0.8 (Female)

    • 6 to < 10 years: 1 (Male) 1 (Female)

    • 10 to < 13 years: 1.2 (Male) 1.2 (Female)

    • 13 to < 16 years: 1.5 (Male) 1.4 (Female)

    • ≥ 16 years: 1.7 (Male) 1.4 (Female)

3. Adequate Liver Function Defined as:

    • Total bilirubin ≤1.5 times institutional ULN

        - AST(SGOT) ≤3 × institutional upper limit of normal
        - ALT(SGPT) ≤3 × institutional upper limit of normal
4. Adequate Neurological Function Defined as:

Patients with neurological deficits should have deficits that are stable for a minimum of 1 week prior to enrollment.

d. Patients of childbearing or child-fathering potential must be willing to use a medically acceptable form of birth control, which includes abstinence, while being treated on this study.

e. Signed informed consent according to institutional guidelines must be obtained prior to registration and for 3 months after drug cessation.

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Exclusion Criteria for all strata:

1. Pregnancy or Breast-Feeding:
    1. Pregnant or breast-feeding women will not be entered on this study due to known or unknown risks of fetal and teratogenic adverse events as seen in animal/human studies. Pregnancy tests must be obtained in girls who are post-monarchal. Males or females of reproductive potential may not participate unless they have agreed to use an effective contraceptive method.
    2. Pregnancy Prevention Patients of childbearing or child fathering potential must be willing to use a medically acceptable form of birth control, which includes abstinence, while being treated on this study and for 3 months after drug cessation.
2. Study Specific:
    1. Active infection requiring treatment
    2. Patients with malignancy related to HIV or solid organ transplant: known history of HIV, HBV surface antigen positivity or positive HCV antibody are not eligible. Viral testing is not required unless clinically indicated in patients without a known history
    3. Known immunosuppressive disease
    4. Patients with active renal, cardiac (congestive cardiac failure, myocardial infarction, myocarditis), or moderate to severe pulmonary problems generally defined by need for medical intervention (e.g., oxygen, medications) and/or limiting activities of daily living (generally CTCAE Grade 2 or higher) or shortness of breath with limited exertion are not eligible. Pulmonary conditions include (but are not limited to) COPD, asthma, and hemi-pneumectomy
    5. Patients receiving concomitant immunosuppressive agents for medical conditions; inhaled corticosteroids for asthma are allowed.
    6. Patients receiving concomitant tumor-directed therapy
    7. Patients receiving any other investigational drug therapy.
    8. Patients on dexamethasone > 0.1 mg/Kg/day up to maximum dose of 4 mg/day or equivalent.
    9. Patients with any clinically significant unrelated systemic illness (serious infections or significant cardiac, pulmonary, hepatic or other organ dysfunction).
    10. Patients with inability to return for follow-up visits or obtain follow-up studies required to assess toxicity to therapy
    11. Patients at high risk for imminent neurologic decline due to extensive bulk disease, midline shift, or herniation on MRI. These patients should be discussed with the study chairs.

Conditions & Interventions

Interventions:
BIOLOGICAL: PEP-CMV, DRUG: Temozolomide, BIOLOGICAL: Tetanus Diphtheria Vaccine
Conditions:
High Grade Glioma, Diffuse Intrinsic Pontine Glioma, Recurrent Medulloblastoma
Keywords:
High Grade Glioma, Diffuse Intrinsic Pontine Glioma, Recurrent Medulloblastoma, Immunotherapy

More Information

Description:
This study will address the question of whether targeting CMV antigens with PEP-CMV can serve as a novel immunotherapeutic approach in pediatric patients with newly-diagnosed high-grade glioma (HGG) or diffuse intrinsic pontine glioma (DIPG) as well as recurrent medulloblastoma (MB). PEP-CMV is a vaccine mixture of a peptide referred to as Component A. Component A is a synthetic long peptide (SLP) of 26 amino acid residues from human pp65. The SLPs encode multiple potential class I, class II, and antibody epitopes across several haplotypes. Component A will be administered as a stable water:oil emulsion in Montanide ISA 51. Funding Source - FDA OOPD

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