Tipifarnib for the Treatment of Advanced Solid Tumors, Lymphoma, or Histiocytic Disorders With HRAS Gene Alterations, a Pediatric MATCH Treatment Trial

Status: Recruiting
System ID: NCT04284774
Sex: All
Age: 12 Months to 21 Years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Contact(s): sfinder@umn.edu
Phase: Phase 2
IRB Number:

Conditions & Interventions

Interventions:
Drug: Tipifarnib

Conditions:

Eligibility Criteria
Inclusion Criteria:

• Patient must have enrolled onto APEC1621SC and must have been given a treatment assignment to MATCH to APEC1621M based on the presence of an actionable mutation

• Patients must have a body surface area >= 0.29 m^2 at enrollment

• Patients must have radiographically measurable disease at the time of study enrollment. Patients with neuroblastoma who do not have measurable disease but have metastadobenzylguanidine (MIBG) positive (+) evaluable disease are eligible. Measurable disease in patients with CNS involvement is defined as tumor that is measurable in two perpendicular diameters on magnetic resonance imaging (MRI) and visible on more than one slice

• Note: The following do not qualify as measurable disease:
  - Malignant fluid collections (e.g., ascites, pleural effusions)
  - Bone marrow infiltration except that detected by MIBG scan for neuroblastoma
  - Lesions only detected by nuclear medicine studies (e.g., bone, gallium or positron emission tomography [PET] scans) except as noted for neuroblastoma
  - Elevated tumor markers in plasma or cerebral spinal fluid (CSF)
  - Previously radiated lesions that have not demonstrated clear progression post radiation
  - Leptomeningeal lesions that do not meet the measurement requirements for Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.
  - Karnofsky => 50 for patients > 16 years of age and Lansky => 50 for patients <= 16 years of age. Note: Neurologic deficits in patients with CNS tumors must have been relatively stable for at least 7 days prior to study enrollment. 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
  - Patients must have fully recovered from the acute toxic effects of all prior anti-cancer therapy and must meet the following minimum duration from prior anti-cancer directed therapy prior to enrollment. If after the required timeframe, the numerical eligibility criteria are met, e.g. blood count criteria, the patient is considered to have recovered adequately
    - Cytotoxic chemotherapy or other anti-cancer agents known to be myelosuppressive.
    - >= 21 days after the last dose of cytotoxic or myelosuppressive chemotherapy (42 days if prior nitrosourea)
    - Anti-cancer agents not known to be myelosuppressive (e.g. not associated with reduced platelet or absolute neutrophil count [ANC] counts): >= 7 days after the last dose of agent.
    - Antibodies: >= 21 days must have elapsed from infusion of last dose of antibody, and toxicity related to prior antibody therapy must be recovered to grade <= 1
    - Corticosteroids: If used to modify immune events related to prior therapy, >= 14 days must have elapsed since last dose of corticosteroid
    - Hematopoietic growth factors: >= 14 days after the last dose of a long-acting growth factor (e.g. pegfilgrastim) or 7 days for short-acting growth factor. For growth factors that have known adverse events occurring beyond 7 days after administration, this period must be extended beyond the time during which adverse events are known to occur. The duration of this interval must be discussed with the study chair and the study-assigned research coordinator
    - Interleukins, interferons and cytokines (other than hematopoietic growth factors): >= 21 days after the completion of interleukins, interferon or cytokines (other than hematopoietic growth factors)
    - Stem cell infusions (with or without total body irradiation [TBI]):
      - Autologous (non-autologous) bone marrow or stem cell transplant, or any stem cell infusion including donor lymphocyte infusion (DLI) or boost infusion: => 84 days after infusion and no evidence of graft versus host disease (GVHD)
      - Autologous stem cell infusion including boost infusion: => 42 days
    - Cellular therapy: => 42 days after the completion of any type of cellular therapy (e.g. modified T cells, natural killer [NK] cells, dendritic cells, etc.)
    - Radiation therapy (XRT)/external beam irradiation including protons: => 14 days after local XRT; => 150 days after TBI, craniospinal XRT or if radiation to => 50% of the pelvis; => 42 days after systemically administered radio-pharmaceutical therapy
    - Patients must not have received prior exposure to tipifarnib
    - For patients with solid tumors without known bone marrow involvement (within 7 days prior to enrollment):
      - Peripheral absolute neutrophil count (ANC) => 1000/mm^3
      - For patients with solid tumors without known bone marrow involvement (within 7 days prior to enrollment):
        - Platelet count => 100,000/mm^3 (transfusion independent, defined as not receiving platelet transfusions for at least 7 days prior to enrollment)
        - Patients with known bone marrow metastatic disease will be eligible for study provided they meet the blood counts (may receive transfusions provided they are not known to be refractory to red cell or platelet transfusions). These patients will not be evaluable for hematologic toxicity
        - A serum creatinine based on age/gender as follows (within 7 days prior to enrollment):
          - Age: Maximum serum creatinine (mg/dL):
            - 1 to < 2 years: male (0.6), female (0.5)
            - 2 to < 6 years: male (0.8), female (0.8)
            - 6 to < 10 years: male (1), female (1)
            - 10 to < 13 years: male (1.2), female (1.2)
            - 13 to < 16 years: male (1.5), female (1.4)
            - >= 16 years: male (1.7), female (1.4)
        - Bilirubin (sum of conjugated + unconjugated) =< 1.5 x upper limit of normal (ULN) for age (within 7 days prior to enrollment)
Serum glutamate pyruvate transaminase (SGPT) (alanine aminotransferase [ALT]) =< 135 U/L. (For the purpose of this study, the ULN for SGPT is 45 U/L.) (within 7 days prior to enrollment)

Serum albumin = 2 g/dL (within 7 days prior to enrollment)

Patients with seizure disorder may be enrolled if on anticonvulsants and well controlled

Nervous system disorders (Common Terminology Criteria for Adverse Events [CTCAE] version [v] 5.0) resulting from prior therapy must be =< grade 2

Patients must be able to swallow intact tablets or crushed tablets mixed in water, orange juice, apple juice, tomato juice, ginger ale, applesauce, yogurt, protein shake, or a dietary supplement drink (such as Ensure). Percutaneous endoscopic gastrostomy (PEG)-tube or nasogastric tube administration is permitted

All patients and/or their parents or legally authorized representatives must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines

Exclusion Criteria:

Pregnant or breast-feeding women will not be entered on this study due to risks of fetal and teratogenic adverse events as seen in animal/human studies. Pregnancy tests must be obtained in girls who are post-menarchal. Males or females of reproductive potential may not participate unless they have agreed to use two effective contraceptive methods for the duration of study treatment. Both female subjects and male subjects with female partners of child-bearing potential must agree to use a highly effective method of contraception for 2 weeks prior to protocol therapy, during, and at least 4 weeks after last dose of tipifarnib. In addition, since tipifarnib could induce toxicity of male reproductive organs and cause impairment of fertility, sperm cryopreservation should be recommended for male subjects wishing to preserve their fertility following tipifarnib treatment

Patients receiving corticosteroids who have not been on a stable or decreasing dose of corticosteroid for at least 7 days prior to enrollment are not eligible. If used to modify immune adverse events related to prior therapy, => 14 days must have elapsed since last dose of corticosteroid

Patients who are currently receiving another investigational drug are not eligible

Patients who are currently receiving other anti-cancer agents are not eligible

Patients who are receiving cyclosporine, tacrolimus or other agents to prevent graft-versus-host disease post bone marrow transplant are not eligible for this trial

Patients who are currently receiving drugs that are strong inducers or inhibitors of CYP3A4/5 or UGT are not eligible. Strong inducers or inhibitors of CYP3A4/5 or UGT should be avoided from 14 days prior to the 1st dose of tipifarnib to the end of the study. In addition, patients receiving agents that are sensitive or narrow therapeutic range substrates of CYP3A4/5 are not eligible. Note: CYP3A4/5 inducing anti-epileptic drugs and dexamethasone for CNS tumors or metastases, on a stable dose, are allowed

Patients with uncontrolled infection are not eligible

Patients who have received a prior solid organ transplantation are not eligible

Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study are not eligible

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