A Study of Selinexor in People With Wilms Tumors and Other Solid Tumors

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 1 year and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Age:

1. Age ≥ 6 at the time of informed consent
2. Age ≥ 2 years to < 6 years at time of informed consent (Refer to Section 4.3): If PK cohort 1 is open, patients in this age range may enroll onto this cohort. If PK cohort 1 has been completed and deemed sufficient to proceed, then such patients may enroll onto the phase 2.
3. Age ≥ 12 months to < 2 years at time of informed consent (Refer to Section 4.3):

If PK cohort 2 is open, patients in this age range may enroll onto this cohort. If PK cohort 2 has been completed and deemed sufficient to proceed, then such patients may enroll onto the phase 2.

- Consent: 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.
- Performance: Karnofsky ≥ 60% for patients > 16 years of age and Lansky ≥ 60 for patients ≤ 16 years of age.
- Diagnosis: Patients must enroll into one of the following cohorts:

1. Cohort A: Any type of Wilms tumor or nephroblastoma is eligible for this study provided they meet at least one of these criteria: (1) in their second or greater relapse, (2) refractory or in their first relapse with high risk histology (i.e., any anaplastic or blastemal-type after neoadjuvant chemotherapy), or (3) refractory or in first relapse without high risk histology but after having received chemotherapies other than the initial 4 agents used as current standard of care in the up-front setting for non-high risk cases - specifically vincristine, dactinomycin, doxorubicin, and irinotecan (i.e., any patient who relapses following an initial regimen more intense than EE4A, DD4A, VAD, AVD, or VIVA; for example, those including cyclophosphamide/etoposide - such as Regimen I, M, or MVI - or those additionally including carboplatin - such as Regimens UH-1, UH-2, or UH-3).
2. Cohort B: Any Rhabdoid tumor is eligible for this cohort. This includes, but is not limited to, related subtypes of rhabdoid tumors such as atypical teratoid rhabdoid tumors (ATRT), malignant rhabdoid tumors of the kidney (MRTK), malignant rhabdoid tumors of the soft tissue and liver, small cell undifferentiated hepatoblastomas (SCUH), and small-cell carcinoma of the ovary of hypercalcemic type (SCCOHT). Patients must have failed to respond to at least 1 line of systemic therapy prior to enrollment.
3. Cohort C: Patients with progressive, relapsed, unresectable or metastatic MPNST, are eligible for this cohort. Patients must have failed to respond to at least 1 line of systemic therapy prior to enrollment.
4. Cohort D: Patients must not qualify for Cohorts A, B, or C but have a solid tumor (no hematologic malignancies including lymphoma) for which there is specific evidence that this particular patient's tumor may benefit from selinexor.

Patients must have failed to respond to at least 1 line of systemic therapy prior to enrollment. Examples of evidence are listed below. All patients in this cohort require approval of study principal investigator and must provide documentation of specific supporting evidence. i. Tumor XPO1 Dependency: Defined as either Darwin OncoTarget demonstrating XPO1 as aberrantly activated or Darwin OncoTreat demonstrating context-specific tumor checkpoint inversion with Selinexor, both of which must be significant at a -log10 (Bonferroni corrected p-value) of 5 or greater. ii. Tumor XPO1 Activation: Defined as the detection of a gain of function mutation in XPO1, specifically E571K. Additionally, detection of elevated transcriptomic or proteomic expression of XPO1 in the tumor via RNAseq or IHC, respectively, would be considered sufficient for treatment.

iii. Preclinical Tumor Testing: Defined as testing of Selinexor on patient derived cell line, organoid, or xenograft models of the patient's tumor (or other related tumors) performed in a laboratory context and for which, in the investigator's opinion, demonstrates promising activity. Testing may include commercial testing as well as academic laboratory testing.

- Cohort E: Patients must have a solid tumor with an activating genomic alteration (e.g. fusion or internal tandem duplication) involving BCOR. Specific examples of qualifying alterations including BCOR-ITD, BCOR-CCNB3, BCOR-MAML3 and ZC3H7B-BCOR; Other potentially qualifying BCOR alterations require approval of study principal investigator; note that loss of function alterations of BCOR would not qualify.
- Disease Status: Patients on the phase II portion of the study must have measurable disease whereas patients on the PK cohorts can have either evaluable or measurable disease as measured by the revised Response Evaluation Criteria in Solid Tumors (RECIST) guideline (Version 1.1).

a. Primary Brain Tumors: Patients with primary brain tumors are eligible and must also have measurable disease for the phase II (as well as evaluable or measurable for the PK cohorts), but this can be defined as at least equal or greater than twice the slice thickness in two perpendicular diameters on MRI OR diffuse leptomeningeal disease OR clear MRI evidence of disease that may not be measurable in two perpendicular diameters OR positive CSF cytology alone.
* Prior Therapy: Patients must have fully recovered from the acute toxic effects of all prior anti-cancer therapy and meet minimum washout durations (shown below) from prior therapy.

1. Anti-cancer agents not known to be myelosuppressive: ≥ 7 days
2. Anti-cancer and cytotoxic agents known to be myelosuppressive: ≥ 21 days
3. Immunotherapies (including antibodies, interleukins, interferons, etc.): ≥ 21 days

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4. Adoptive cellular therapies (including modified T cells, vaccines, etc.): ≥ 42 days
5. Autologous stem cell infusion (boost, no conditioning): ≥ 21 days
6. Autologous stem cell transplantation (with conditioning): ≥ 42 days
7. Allogeneic bone marrow transplantation: ≥ 84 days
8. Focal external beam radiation (e.g., limited sites of disease): ≥ 14 days
9. Substantial external beam radiation (e.g. whole lung or abdomen): ≥ 42 days
10. Radiopharmaceutical therapy (e.g., radiolabeled antibody or MIBG): ≥ 42 days

    - Hepatic Function: Adequate function (within 14 days prior to C1D1), defined as:

11. Total bilirubin < 1.5 × upper limit of normal (ULN) (except patients with Gilbert's syndrome, who must have a total bilirubin of <3 × ULN)
12. Alanine aminotransferase (ALT) < 3 × ULN
13. Serum albumin ≥ 2 g/dL

    - Renal Function: Adequate function (within 14 days prior to C1D1) defined as a GFR

≥ 50 ml/min/1.73 m2 determined via any of these methods:
1. Nuclear radioisotope
2. 24 hr urine creatinine clearance
3. Serum cystatin c
4. Serum creatinine using the Schwartz formula for estimating creatinine clearance (Schwartz et al. J Peds, 106:522, 1985)
* Hematologic Function: Adequate function (within 14 days prior to C1D1), defined as:

1. Absolute neutrophil count (ANC) ≥ 1000/mm3
2. Platelet count ≥ 100,000/mm3
3. Note: patients may not receive platelet transfusions nor hematopoietic growth factor support, including granulocyte-colony stimulating factor (e.g. filgrastim) and platelet stimulators (e.g. romiplostim) for at least 7 days prior to demonstrating adequate hematologic function.

Exclusion Criteria:

- Prior Therapy: Has received selinexor or another XPO1 inhibitor previously.
- Infection: Patients who have an uncontrolled infection are not eligible. Patients on prophylactic antibiotics or with a controlled infection within 1 week prior to C1D1 are acceptable
- Transplants: Patients who have received allogeneic bone marrow transplant are potentially eligible unless they are being actively treated for GvHD. Patients who have had a prior solid organ transplantation are not eligible.
- Compliance: Patients who as a result of serious medical, psychiatric, and/or social situation(s), in the opinion of the investigator, may not be able to comply with supportive care, safety monitoring, or any other key requirements of the study protocols are not eligible.
- Pregnancy and Breast-feeding: Pregnant or breast-feeding women will not be entered on this study because there is yet no available information regarding human fetal or teratogenic toxicities. Pregnancy tests must be obtained in girls who are post-menarchal.
- Contraception: Males or females of reproductive potential may not participate unless they have agreed to use two effective methods of birth control, including a medically accepted barrier or contraceptive method (e.g., male or female condom) for the duration of the study. Abstinence is an acceptable method of birth control.

Conditions & Interventions

Interventions:
DRUG: Selinexor
Conditions:
Wilms Tumor, Rhabdoid Tumor, Malignant Peripheral Nerve Sheath Tumors, MPNST, Nephroblastoma, XPO1 Gene Mutation, Solid Tumor
Keywords:
Wilms Tumor, Rhabdoid Tumor, Malignant Peripheral Nerve Sheath Tumors, MPNST, Nephroblastoma, XPO1, Selinexor, Memorial Sloan Kettering Cancer Center, 22-393, Solid Tumor

More Information

Description:
The purpose of this study is to find out whether selinexor is an effective treatment for people who have a relapsed/refractory Wilms tumor, rhabdoid tumor, MPNST, BCOR-driven sarcoma, or another solid tumor that makes a higher than normal amount of XPO1 or has genetic changes that increase the activity of XP01.

Contact(s): - cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE2
IRB Number:
System ID: NCT05985161
