

Trial record **1 of 1** for: EZH-102

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A Phase 1 Study of the EZH2 Inhibitor Tazemetostat in Pediatric Subjects With Relapsed or Refractory INI1-Negative Tumors or Synovial Sarcoma

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified November 2016 by Epizyme, Inc.

Sponsor:

Epizyme, Inc.

Information provided by (Responsible Party):

Epizyme, Inc.

ClinicalTrials.gov Identifier:

NCT02601937

First received: October 21, 2015

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[No Study Results Posted](#)

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Purpose

This is a Phase I, open-label, dose escalation and dose expansion study with a BID oral dose of tazemetostat. Subjects will be screened for eligibility within 14 days of the planned first dose of tazemetostat. A treatment cycle will be 28 days. Response assessment will be evaluated after 8 weeks of treatment and subsequently every 8 weeks while on study.

The study has two parts: Dose Escalation and Dose Expansion.

Dose escalation for subjects with the following relapsed/refractory malignancies:

- Rhabdoid tumors:
- Atypical teratoid rhabdoid tumor (ATRT)
- Malignant rhabdoid tumor (MRT)
- Rhabdoid tumor of kidney (RTK)
- Selected tumors with rhabdoid features
- INI1-negative tumors:
- Epithelioid sarcoma
- Epithelioid malignant peripheral nerve sheath tumor
- Extraskeletal myxoid chondrosarcoma
- Myoepithelial carcinoma
- Renal medullary carcinoma
- Other INI1-negative malignant tumors (e.g., dedifferentiated chordoma) (with Sponsor approval)
- Synovial Sarcoma with a SS18-SSX rearrangement

Dose Expansion at the MTD or the RP2D, for subjects with rhabdoid tumors (MRT/ATRT/RTK/selected tumors with rhabdoid features).

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
Rhabdoid Tumors INI1-negative Tumors Synovial Sarcoma Malignant Rhabdoid Tumor of Ovary	Drug: Tazemetostat	Phase 1

Study Type: Interventional

Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase 1 Study of the EZH2 Inhibitor Tazemetostat in Pediatric Subjects With Relapsed or Refractory INI1-Negative Tumors or Synovial Sarcoma

Resource links provided by NLM:

[Genetics Home Reference](#) related topics: [ovarian cancer](#)

[MedlinePlus](#) related topics: [Soft Tissue Sarcoma](#)

[Genetic and Rare Diseases Information Center](#) resources: [Ovarian Cancer](#) [Rhabdoid Tumor](#) [Malignant Mesenchymal Tumor](#)
[Soft Tissue Sarcoma](#) [Synovial Sarcoma](#)

[U.S. FDA Resources](#)

Further study details as provided by Epizyme, Inc.:

Primary Outcome Measures:

- To determine the MTD or the RP2D (Dose Escalation) [Time Frame: 1 cycle/28 days] [Designated as safety issue: No]
The incidence and severity of treatment-emergent adverse events (AEs) qualifying as protocol-defined DLTs in Cycle 1 will guide establishment of the protocol defined RP2D and/or MTD
- Dose expansion: Number of subjects with objective response using disease appropriate standardized response criteria [Time Frame: Assessed every 8 weeks for duration of study participation which is estimated to be 24 months] [Designated as safety issue: No]

Secondary Outcome Measures:

- Dose escalation: Number of subjects with objective response using disease appropriate standardized response criteria [Time Frame: Assessed every 8 weeks for duration of study participation which is estimated to be 24 months] [Designated as safety issue: No]
- Dose Expansion: Progression-free survival (PFS) [Time Frame: At 24 and 56 weeks post treatment using Kaplan-Meier method] [Designated as safety issue: No]
- Dose Expansion: Overall Survival (OS) [Time Frame: At 24 and 56 weeks post treatment using Kaplan-Meier method] [Designated as safety issue: No]
- Incidence of treatment-emergent adverse events as a measure of safety and tolerability [Time Frame: Adverse events assessed from first dose through 30 days post last dose] [Designated as safety issue: Yes]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): Cmax [Time Frame: Days 1 and 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): Tmax [Time Frame: Days 1 and 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): AUC(0-t) [Time Frame: Days 1 and 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): AUC(0-12) [Time Frame: Days 1 and 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): t1/2 [Time Frame: Days 1 and 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): CL/F [Time Frame: Day 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): Vd/F [Time Frame: Day 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): Ka [Time Frame: Day 15] [Designated as safety issue: No]
- Pharmacokinetics profile of tazemetostat and its metabolite (plasma): Ctrough [Time Frame: Day 1 of cycles 2, 3 and 4] [Designated as safety issue: No]

Estimated Enrollment: 44
Study Start Date: December 2015
Estimated Study Completion Date: January 2018
Estimated Primary Completion Date: October 2017 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Open-label Tazemetostat Level 1 (Starting Dose) Oral Tazemetostat 240 mg/m ² BID; Level 2 Oral Tazemetostat 300 mg/m ² BID; Level 3 Oral Tazemetostat 400 mg/m ² BID; Level 4 Oral Tazemetostat 520 mg/m ² BID	Drug: Tazemetostat Tazemetostat (EPZ-6438) is a selective small molecule inhibitor of the histone-lysine methyltransferase EZH2 gene. Other Names: <ul style="list-style-type: none">• EPZ-6438• E7438

▶ Eligibility

Ages Eligible for Study: 6 Months to 21 Years (Child, Adult)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Age (at the time of consent/assent): ≥ 6 months to ≤ 21 years
2. Performance Status:
 - If < 12 years of age: Lansky Performance Status $> 50\%$
 - If ≥ 12 years of age: Karnofsky Performance Status $> 50\%$
3. Has a life expectancy of > 3 months
4. Has relapsed or refractory disease and no standard treatment options as determined by locally or regionally available standards of care and treating physician's discretion
5. Is ineligible or inappropriate for other treatment regimens known to have effective potential
6. Has a documented local diagnostic pathology of original biopsy confirmed by a Clinical Laboratory Improvement Amendments (CLIA)/College of American Pathologists (CAP) or equivalent laboratory certification
7. Has completed a prior therapy (ies) according to the criteria below:
 - Other investigational study agent (any medicinal product that is not approved in the country of treatment for any indication, adult or pediatric) (At least 30 days or five half-lives, whichever is longer, since last dose prior to the first dose of tazemetostat)
 - Chemotherapy: cytotoxic (At least 21 days since last dose of chemotherapy prior to first dose of tazemetostat)
 - Chemotherapy: nitrosoureas (At least 6 weeks since last dose of nitrosoureas prior to first dose of tazemetostat)
 - Chemotherapy: non-cytotoxic (e.g., small molecule inhibitor) (At least 14 days since last dose of non-cytotoxic chemotherapy prior to first dose of tazemetostat)
 - Monoclonal antibody (ies) (At least 3 half-lives since the last dose of any monoclonal antibody prior to first dose of tazemetostat)
 - Immunotherapy (e.g., tumor vaccine) At least 6 weeks since last dose of immunotherapy agent(s) prior to first dose of tazemetostat)
 - Radiotherapy (RT) (At least 14 days from last local site RT prior to first dose of tazemetostat/At least 21 days from stereotactic radiosurgery prior to first dose of tazemetostat/At least 12 weeks from craniospinal, $\geq 50\%$ radiation of pelvis, or total body irradiation prior to first dose of tazemetostat)
 - Hematopoietic growth factor (At least 14 days from last dose of hematopoietic growth factor prior to first dose of tazemetostat)
 - Hematopoietic cell transplantation (At least 60 days from infusion of hematopoietic cells prior to first dose of tazemetostat)
8. Has adequate hematologic (bone marrow and coagulation factors), renal and hepatic function as defined by criteria below:
 - Hematologic (BM Function):
 - Hemoglobin ≥ 8 mg/dL
 - Platelets $\geq 100,000/\text{mm}^3$ ($\geq 100 \times 10^9/\text{L}$)
 - ANC $\geq 1,000/\text{mm}^3$ ($\geq 1.0 \times 10^9/\text{L}$)
 - Hematologic (Coagulation Factors):
 - PT ≤ 1.5 ULN
 - PTT ≤ 1.5 ULN
 - Fibrinogen ≥ 0.75 LLN
 - Renal Function (creatinine clearance or serum creatinine):
 - Calculated creatinine clearance ≥ 60 mL/min/1.73m²
 - Serum creatinine 6 months to 1 year: male 0.6 mg/dL (53 $\mu\text{mol}/\text{L}$) female 0.5 mg/dL (44 $\mu\text{mol}/\text{L}$)
 - Serum creatinine 1 to < 2 years: male 0.6 mg/dL (53 $\mu\text{mol}/\text{L}$) female 0.6 mg/dL (53 $\mu\text{mol}/\text{L}$)
 - Serum creatinine 2 to < 6 years: male 0.8 mg/dL (71 $\mu\text{mol}/\text{L}$) female 0.8 mg/dL (71 $\mu\text{mol}/\text{L}$)
 - Serum creatinine 6 to < 10 years: male 1 mg/dL (88 $\mu\text{mol}/\text{L}$) female 1 mg/dL (88 $\mu\text{mol}/\text{L}$)
 - Serum creatinine 10 to < 13 years: male 1.2 mg/dL (106 $\mu\text{mol}/\text{L}$) female 1.2 mg/dL (106 $\mu\text{mol}/\text{L}$)
 - Serum creatinine 13 to < 16 years: male 1.5 mg/dL (133 $\mu\text{mol}/\text{L}$) female 1.4 mg/dL (125 $\mu\text{mol}/\text{L}$)
 - Serum creatinine ≥ 16 years: male 1.7 mg/dL (150 $\mu\text{mol}/\text{L}$) female 1.4 mg/dL (125 $\mu\text{mol}/\text{L}$)
 - Hepatic Function:
 - Conjugated bilirubin < 1.5 x ULN
 - ALT or AST < 3 x ULN
9. For subjects with CNS involvement: Subjects must have deficits that are stable for a minimum of 14 days prior to enrollment, or seizures that are stable, not increasing in frequency or severity and controlled on current anti-seizure medication(s) for a minimum of 7 days prior to enrollment NOTE: Subjects with leptomeningeal disease or brain tumors with positive cerebral spinal fluid cytology are eligible for this study. Subjects may receive glucocorticoids (at stable or tapering dose) to control CNS symptoms prior to enrollment; however, subjects should receive a stable or tapering dose for at least 7 days prior to enrollment.
10. Has a shortening fraction of $> 27\%$ or an ejection fraction of $\geq 50\%$ by echocardiogram or multi-gated acquisition scan
11. Has a QT interval corrected by Fridericia's formula (QTcF) ≤ 450 msec
12. Is able to swallow and retain orally administered medication and does not have any uncontrolled gastrointestinal (GI) condition such as nausea, vomiting, or diarrhea, or any clinically significant GI abnormalities that may alter absorption such as malabsorption syndromes, hereditary fructose intolerance, glucose-galactose malabsorption, sucrose-isomaltase insufficiency, or major resection of stomach and/or bowels

13. Has sufficient tumor tissue (slides or blocks) available for central confirmatory testing of immunohistochemistry and/or cytogenetics/fluorescence in situ hybridization (FISH) and/or deoxyribonucleic acid mutation analysis (required for study entry but enrollment based on local results)

For Dose Escalation Only:

1. Has evaluable disease as defined as lesions that can be accurately measured at least in one dimension by radiographic examination or physical examination and other lesions such as bone lesions, leptomeningeal disease, ascites, hepatosplenomegaly from disease.
2. Has one of the following histologically confirmed tumors: (NOTE: Evidence of diagnostic pathology of original biopsy confirmed by a CLIA/CAP certified laboratory must be available)
 - Rhabdoid tumor:
 - ATRT
 - MRT
 - RTK
 - Selected tumors with rhabdoid features
 - INI1-negative tumor:
 - Epithelioid sarcoma
 - Epithelioid malignant peripheral nerve sheath tumor
 - Extraskelatal myxoid chondrosarcoma
 - Myoepithelial carcinoma
 - Renal medullary carcinoma
 - Other INI1-negative malignant tumors (e.g., dedifferentiated chordoma) with Sponsor approval
 - Synovial sarcoma with SS18-SSX rearrangement
3. For subjects with ATRT, MRT, RTK, or selected tumors with rhabdoid features only, the following test results must be available: Morphology and immunophenotypic panel consistent with rhabdoid tumor and loss of INI1 or SMARCA4 confirmed by IHC, or molecular confirmation of tumor bi-allelic INI1 or SMARCA4 loss/mutation when INI1 or SMARCA4 IHC is equivocal or unavailable
4. For subjects with INI1 negative tumor only, the following test results must be available: Morphology and immunophenotypic panel consistent with INI1-negative tumors, and loss of INI1 confirmed by IHC, or molecular confirmation of tumor bi-allelic INI1 loss/mutation when INI1 IHC is equivocal or unavailable
5. For subjects with synovial sarcoma only, the following test results must be available: Morphology consistent with synovial sarcoma, and cytogenetics or FISH and/or molecular confirmation (e.g., DNA sequencing) of SS18 rearrangement t(X;18)(p11;q11)

For Dose Expansion Only:

1. Has measurable disease
2. Has one of the following histologically confirmed rhabdoid tumors:
 - ATRT
 - MRT
 - RTK
 - Selected tumors with rhabdoid features
3. Has the following test results available: Morphology and immunophenotypic panel consistent with rhabdoid tumor, and loss of INI1 or SMARCA4 confirmed by IHC, or molecular confirmation of tumor bi-allelic INI1 or SMARCA4 loss/mutation when INI1 or SMARCA4 IHC is equivocal or unavailable

Exclusion Criteria:

1. Has had prior exposure to tazemetostat or other inhibitor(s) of EZH2
2. Is being actively treated for another concurrent malignancy or is less than five years from completion of treatment for another malignancy
3. Has participated in another interventional clinical study and received investigational drug within 30 days or 5 half-lives, whichever is longer, prior to the planned first dose of tazemetostat
4. Has had major surgery within 2 weeks prior to enrollment
5. Is unwilling to exclude grapefruit juice, Seville oranges and grapefruit from the diet and all foods that contain those fruits from time of enrollment to while on study
6. Has clinically active heart disease including prolonged corrected QT interval
7. Is currently taking any prohibited medication(s)
8. Has an active infection requiring systemic treatment
9. Is immunocompromised (i.e. congenital immunodeficiencies), including subjects known history of infection with human immunodeficiency virus
10. Has known history of chronic infection with hepatitis B virus (hepatitis B surface antigen positive) or hepatitis C virus (detectable HCV RNA)
11. Has had a symptomatic venous thrombosis within the 3 months prior to study enrollment - NOTE: Subjects with a history of a deep vein thrombosis >3 months prior to study enrollment who are on anticoagulation therapy with low molecular weight heparin are eligible for this study
12. For subjects with CNS involvement (primary tumor or metastatic disease): Have ≥3 foci of punctate hemorrhage, any active bleeding, or intratumoral hemorrhage at time of enrollment or known bleeding diathesis or treatment with anti-platelet or anti-thrombotic agents

▶ Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see [Learn About Clinical Studies](#).

Please refer to this study by its ClinicalTrials.gov identifier: NCT02601937

Contacts

Contact: Maria Roche, NP 855-500-1011 clinicaltrials@epizyme.com

Contact: Peter Ho, MD, PhD 855-500-1011 clinicaltrials@epizyme.com

+ Show 31 Study Locations

Sponsors and Collaborators

Epizyme, Inc.

▶ More Information

Responsible Party: Epizyme, Inc.
ClinicalTrials.gov Identifier: [NCT02601937](#) [History of Changes](#)
Other Study ID Numbers: **EZH-102**
Study First Received: October 21, 2015
Last Updated: November 22, 2016
Health Authority: United States: Food and Drug Administration

Additional relevant MeSH terms:

Neoplasms	Endocrine Gland Neoplasms
Sarcoma	Neoplasms by Site
Sarcoma, Synovial	Ovarian Diseases
Rhabdoid Tumor	Adnexal Diseases
Ovarian Neoplasms	Genital Diseases, Female
Neoplasms, Connective and Soft Tissue	Genital Neoplasms, Female
Neoplasms by Histologic Type	Urogenital Neoplasms
Neoplasms, Connective Tissue	Endocrine System Diseases
Neoplasms, Complex and Mixed	Gonadal Disorders

ClinicalTrials.gov processed this record on November 23, 2016