FAST FACTS

Pharmacokinetic Guided Dose Escalation and Dose Confirmation With Oral Decitabine and Oral CDAi in Patients With MDS
ASTX727-01

Sponsor: *ASTEX Pharmaceuticals.*

Information provided by: *ASTEX Pharmaceuticals, ClinicalTrials.gov*

ClinicalTrials.gov Identifier: *NCT02103478*

Study Title: A Phase1-2 Pharmacokinetic Guided Dose-Escalation and Dose-Confirmation Study of ASTX727, a Combination of the Oral Cytidine Deaminase Inhibitor (CDAi) E7727 With Oral Decitabine in Subjects With Myelodysplastic Syndromes (MDS

Subject Population: IPSS low, intermediate -1, intermediate-2, or high risk MDS (including CMML) in Dose Escalation and Dose Confirmation-Randomization; only intermediate-2, or high risk MDS in Dose Confirmation-Open Label

Currently accepting participants? *Yes patients needed for enrollment*

Contact: **MDS FOUNDATION: www.mds-foundation.org**
Phone within the US: 1-800-MDS-0839
Outside the US only: 1-609-298-1035

ASTEX Pharmaceuticals Contact: Roya Nawabi roya.nawabi@astx.com

ASTX727 is an oral dose combination investigational drug, of oral decitabine + E7727, an inhibitor of the metabolism of decitabine. ASTX727 is designed to allow for efficient oral delivery of decitabine at low doses. Intravenous decitabine is one of the approved drugs by the FDA for this use. The trial is designed to define the doses of both drugs so that the blood levels of decitabine after oral administration look like what is seen with IV decitabine.

Primary Objectives This 2-stage, open-label study will evaluate safety and pharmacokinetics of ASTX727, as well as determine the dose for the study's second stage. In the second stage the selected dose will be confirmed and evaluated for clinical activity, including response rate and duration.

Who can participate?

INCLUSION CRITERIA:
(See protocol for additional inclusion criteria)

- Men or women more than 18 years of age.
- IPSS low, intermediate -1, intermediate-2, or high risk MDS (including CMML) in Dose Escalation and Dose Confirmation-Randomization; only intermediate-2, or high risk MDS in Dose Confirmation-Open Label
- Performance status of 0 to 2 by the Eastern Cooperative Oncology Group (ECOG) scale.
- No major surgery within 2 weeks of starting study treatment
- No cytotoxic chemotherapy within 2 weeks of starting study treatment
- Able to swallow pills

EXCLUSION CRITERIA:
(See protocol for additional exclusion criteria)

- Previous treatment with 2 or more courses of decitabine (all stages) or azacitidine (Dose Confirmation stage only)
- Treatment with investigational therapy within 2 weeks of study treatment
- Uncontrolled medical disease(s) or active, uncontrolled infection
- Diagnosed with AML
- Active uncontrolled gastric or duodenal ulcer
- Known history of HIV or hepatitis C or B

Detailed Study Description:

Approximately 150 MDS subjects who are defined as; IPSS low, intermediate - 1, intermediate-2, or high risk MDS (including CMML) in Dose Escalation and Dose Confirmation-Randomization; only intermediate-2, or high risk MDS in Dose Confirmation-Open Label will be enrolled.

Drug: ASTX727 *(Combination of the Oral Cytidine Deaminase Inhibitor (CDAi) E7727 With Oral Decitabine)*

Treatment ARM:

Experimental: ASTX 727 Dose Escalation
ASTX727 is given by mouth daily X 5 consecutive days. Dosing details will vary in the first 3 courses of therapy for pharmacokinetic measurements. Based on safety and pharmacokinetic results the dose will be modified for subsequent cohorts. Dose escalation will continue until target pharmacokinetics are achieved or until a safe dose is exceeded.

ASTX727 Dose Confirmation-Randomization
After completion of dose escalation, subjects will be randomized to receive either IV decitabine or oral ASTX727 for course 1 (days 1-5) and cross over to receive the other regimen in course 2. Beginning with course 3 all subjects will receive ASTX727 orally days 1-5

Experimental: ASTX727-01 Dose Confirmation Open Label
All subjects will receive ASTX727-01 days 1-5 for all courses.