Study of a Novel BET Inhibitor FT-1101 in Patients With Relapsed or Refractory Hematologic Malignancies

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT02543879	COMPLETED	SEPTEMBER 7, 2015	JUNE 26, 2019

STUDY DESCRIPTION

Brief Summary

This is an open-label, multicenter, dose-escalation Phase 1/1b study in patients with acute myelogenous leukemia (AML)/MDS or non-Hodgkin Lymphoma (NHL), intended to investigate safety, pharmacokinetics, and the pharmacodynamic effects of FT-1101 administered via one or more intermittent dosing schedules alone and in combination with azacitidine. Once the MTD has been established for a treatment cohort, up to 20 additional patients may be enrolled in up to 4 expansion cohorts each of select populations of patients with either AML/MDS or NHL at the recommended dose for future studies to confirm safety.

Condition or Disease: Acute Myeloid Leukemia
Acute Myelogenous Leukemia
Myelodysplastic Syndrome
Non-Hodgkin Lymphoma

Intervention/treatment: Drug: FT-1101
Drug: Azacitidine

Phase: Phase 1

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 94 participants

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1/1b Dose Escalation, Multicenter, Open-label, Safety, Pharmacokinetic and Pharmacodynamic Study of FT-1101 as a Single Agent and in Combination With Azacitidine in Patients With Relapsed or Refractory Hematologic Malignancies

Study Start Date: September 2015

Actual Primary Completion Date: March 2019

Actual Study Completion Date: March 2019

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Dose Escalation FT-1101 Following a 3+3 dose escalation strategy, the first cohort of patients will be administered FT-1101 at 10 mg, oral capsules, once weekly on a continuous basis. Subsequent cohorts dose and frequency will be determined by investigators and sponsor following observations of previous cohorts. Dose escalation will continue until the MTD is determined.	Drug: FT-1101 FT-1101 will be supplied as 5 mg, 20 mg or 100 mg capsules and will be administered per the protocol defined frequency and dose level
Experimental: Dose Escalation FT-1101 + azacitidine Following a 3+3 dose escalation strategy, the first cohort of AML/MDS patients will be administered FT-1101 at approximately 50% or lower than the MTD identified for the single agent FT-1101. Subsequent cohorts dose will be determined by investigators and sponsor following observations of previous cohorts. Dose escalation will not exceed the dose determined to be the single agent MTD for that schedule.	Drug: FT-1101 FT-1101 will be supplied as 5 mg, 20 mg or 100 mg capsules and will be administered per the protocol defined frequency and dose level Drug: Azacitidine Azacitidine will be administered per site's standard of care
Experimental: Dose Expansion FT-1101 Once the MTD is determined, the Recommended Phase 2 Dose (RP2D) will be identified. 3 Expansion cohorts of up to 20 patients each will be treated with the RP2D of FT-1101	Drug: FT-1101 FT-1101 will be supplied as 5 mg, 20 mg or 100 mg capsules and will be administered per the protocol defined frequency and dose level
Experimental: Dose Expansion FT-1101 + azacitidine Once the MTD is determined, the Recommended Phase 2 Dose (RP2D) will be identified. 1 Expansion cohorts of up to 20 AML/MDS patients each will be treated with the RP2D of FT-1101 in combination with azacitidine.	Drug: FT-1101 FT-1101 will be supplied as 5 mg, 20 mg or 100 mg capsules and will be administered per the protocol defined frequency and dose level Drug: Azacitidine Azacitidine will be administered per site's standard of care

OUTCOME MEASURES

Primary Outcome Measures:	1. Maximum Tolerated Dose (MTD) [Time Frame: Within first 4 weeks of treatment] 2. Dose Limiting Toxicities (DLT) [Time Frame: Within first 4 weeks of treatment] 3. Recommended Phase 2 Dose (RP2D) [Time Frame: Participants to be followed for duration of participation, an expected average of 12 weeks]
Secondary Outcome Measures:	1. Area under the plasma concentration versus time curve (AUC) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 2. Peak Plasma Concentration (Cmax) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 3. Time of peak plasma concentration (TMax) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 4. Time for half of the drug to be absent in blood stream following dose (T 1/2) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 5. Rate at which drug is removed from blood stream (CL/F) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 6. Rate of drug distribution within the blood stream (Vd/F) [Time Frame: PK collected at multiple visits during the first 30 days of treatment] 7. Observe patients for any evidence of anti-leukemic or anti-myelodysplastic activity of FT-1101 [Time Frame: Assessed for duration of participation, an expected average of 12 weeks]
Other Outcome Measures:	1. To evaluate PK/PD relationships in dose-escalation and dose-expansion cohorts [Time Frame: Assessed for duration of participation, an expected average of 12 weeks] 2. Assessment of on-target activity of FT-1101, as determined by changes in PD biomarkers in bone marrow aspirates and/or peripheral blood [Time Frame: Assessed for duration of participation, an expected average of 12 weeks] 3. To determine if there is any correlation between cancer-associated genetic alterations with response [Time Frame: Assessed for duration of participation, an expected average of 12 weeks]

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Key Inclusion Criteria:
- Single agent (SA) Dose Escalation: Histologically or cytologically proven acute leukemia or high-risk MDS as defined by the World Health Organization (WHO) criteria and IPSS-R, respectively, that is relapsed or refractory (R/R) to standard therapy or for whom standard treatments are contraindicated, OR
- Mature B-Cell non-Hodgkin Lymphoma that is Relapsed/Refractory to standard therapy
- AML SA expansion group 1: histologically or cytologically proven AML with a FLT3 ITD or TKD mutation previously determined by local testing that is R/R to standard therapy or for whom standard treatments are contraindicated
- AML SA expansion group 2: histologically or cytologically proven AML with intermediate or unfavorable risk cytogenetics in the absence of a detectable FLT3 ITD or TKD mutation as previously determined by local testing that is R/R to standard therapy or for whom standard treatments are contraindicated
- NHL SA expansion: Mature B-cell NHL with the following histologies: primary mediastinal lymphoma, DLBCL, and B-cell lymphoma not specified that is R/R to standard therapy and for whom standard treatments are contraindicated or unavailable
- AML/MDS combination treatment (dose escalation and expansion): histologically or cytologically proven AML or MDS as defined by WHO criteria and IPSS-R, respectively, that is: R/R to standard therapy, or AML: who are unfit for, or unwilling to receive standard induction therapy, or MDS: eligible to receive azacitidine
- Patients ≥ 18 years old
- Good kidney and liver function
- No prior organ allograft
- For fertile men and women, agreement to use effective contraceptive methods duration of study participation and 90 days after

Key Exclusion Criteria:
- History of prior malignancy unless disease free for > or equal to 12 months or considered surgically cured.
- Patients with symptomatic central nervous system (CNS) metastases or other tumor location (such as spinal cord compression, other compressive mass, uncontrolled painful lesion, bone fracture, etc.) necessitating an urgent therapeutic intervention, palliative care, surgery or radiation therapy
- Treatment with major surgery (requiring general anesthesia) within one month prior to study entry
- Previous treatment with any prior BET inhibitor therapy
- Patients unable to swallow oral medications, or patients with gastrointestinal conditions (e.g. malabsorption, gastric or small bowel resection, etc.) deemed to jeopardize intestinal absorption
- Congestive heart failure (New York Heart Association Class III or IV) or unstable angina pectoris. Previous history of myocardial infarction within 1 year prior to study entry, uncontrolled hypertension or uncontrolled arrhythmias
- Pulmonary disease (e.g. COPD, asthma, etc) that is not controlled (moderate to severe symptoms) with current medication
- Known HIV positivity
- Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic therapy

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CONTACTS AND LOCATIONS

Contacts

Locations

United States, California	Cedars Sinai	Los Angeles
United States, Florida	Florida Cancer Specialists	Sarasota
United States, Florida	Moffitt Cancer Center	Tampa
United States, Illinois	Northwestern University	Chicago
United States, Maryland	University of Maryland, Greenebaum Comprehensive Cancer Center	Baltimore
United States, North Carolina	Levine Cancer Institute	Charlotte
United States, Tennessee	Sarah Cannon Research Institute	Nashville

United States, Texas	MD Anderson Cancer Center	Houston

Sponsors and Collaborators

Forma Therapeutics, Inc.

Investigator

Study Director :	Patrick Kelly, MD	Forma Therapeutics, Inc.

MORE INFORMATION

Responsible Party :	Forma Therapeutics, Inc.
ClinicalTrials.gov Identifier :	NCT02543879
Other Study ID Numbers :	1101-HEM-101
First Posted :	September 7, 2015
Last Update Posted :	June 26, 2019
Last Verified :	June 2019
Keywords provided by Forma Therapeutics, Inc.:	*BET Inhibitor* *FT-1101* *Acute Leukemia* *Myelodysplastic Syndrome NHL* *Non-Hodgkin Lymphoma* *AML*
Additional relevant MeSH terms :	*Myelodysplastic Syndromes* *Leukemia* *Leukemia, Myeloid, Acute* *Preleukemia* *Lymphoma, Non-Hodgkin* *Hematologic Neoplasms*