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A Global Study of Midostaurin in Combination With Chemotherapy to Evaluate Safety, Efficacy and Pharmacokinetics in Newly Diagnosed Pediatric Patients With FLT3 Mutated AML

Last Update: Jul 22, 2025
A Phase II, Open-label, Single Arm Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Twice Daily Midostaurin (PKC412) Combined With Standard Chemotherapy and as a Single Agent Post-consolidation Therapy in Children With Untreated FLT3-mutated AML
ClinicalTrials.gov Identifier:
NCT03591510
Novartis Reference Number:CPKC412A2218
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All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

This study will evaluate the safety, efficacy and pharmacokinetics of midostaurin in combination with standard chemotherapy in pediatrics patients with newly diagnosed FLT3-mutated Acute Myeloid Leukemia. The study has two parts: Part 1 to define the Recommended Phase 2 Dose, and Part 2 to evaluate safety and tolerability and efficacy of midostaurin. Both parts will consist of 2 induction blocks, 3 consolidation blocks, 12 cycles of post-consolidation consisting of continuous therapy with midostaurin, and a follow-up phase. This trial is an open label, multi center single arm study to evaluate twice daily oral midostaurin with standard induction, consolidation chemotherapy with sequential midostaurin therapy for 5 treatment blocks (2 induction blocks, 3 consolidation blocks, followed by single agent midostaurin post consolidation therapy for 12 cycles).

The total maximum planned duration on treatment is 17 cycles (5 blocks and 12 cycles). A block is defined as the time from start of study treatment to the time of hematopoietic recovery, at the latest at Day (D) 42, or determination of persistent disease, whichever occur first.

In both Part 1 and Part 2, patients will receive the first course of induction chemotherapy according to local standard and duration is from 8 to 12 days. Upon FLT3 mutation confirmation, patients will receive midostaurin for 14 days. After determination of remission and hematopoietic recovery, patients will receive Block 2.

In Part 1:

* Block 2 FLADx treatment duration is D1 to D6, and midostaurin from D8 to D21. Patients who achieve documented CR (and hematopoietic recovery at the latest at D42 from the first day of Block 2) will receive Block 3.
* Block 3 consolidation HAM treatment duration is D1 to D4, followed by midostaurin D8 to D21. Patients who achieve hematopoietic recovery at the latest at D42 from the first day of Block 3 will receive Block 4. Patients who relapse will discontinue further study treatment.

* Block 4 HA3E treatment duration is D1 to D5 followed by midostaurin D8 to D21. Patients who achieve hematopoietic recovery at the latest at D42 from the first day of Block 4 will receive Block 5.
* Block 5 HiDAC treatment duration is D1 to D3 followed by midostaurin D8 to D21. Patients who relapse will discontinue further study treatment.

Patients in continuous remission with hematopoietic recovery will receive continuous post consolidation therapy of midostaurin, during 12 cycles (28 days per cycle).

In Part 1 of the study, patients in cohorts of 3 will receive sequential midostaurin administered at 30mg/m2bid. If the 30mg/m2 bid is well tolerated as measured by the Dose Limited Toxicity (DLT) rate during Bock 1, additional patients in cohort of 3 will be treated with sequential midostaurin at 60mg/m2 bid. When the recommended phase 2 dose (RP2D) is confirmed, subsequent patients will be treated in Part 2 of the study at the RP2D.

In Part 2:

* Block 2 HAM treatment duration is D1 to D4 and midostaurin from D8 to D21. Patients who achieve documented CR (and hematopoietic recovery at the latest at D42 from the first day of Block 2) will receive Block 3.
* Block 3 consolidation HA3E treatment duration is D1 to D5, followed by midostaurin D8 to D21. Patients who achieve hematopoietic recovery at the latest at D42 from the first day of Block 3 will receive Block 4. Patients who relapse will discontinue further study treatment.
* Block 4 HAM treatment duration is D1 to D4 followed by midostaurin D8 to D21. Patients who achieve hematopoietic recovery at the latest at D42 from the first day of Block 4 will receive Block 5.
* Block 5 HiDAC treatment duration is D1 to D3 followed by midostaurin D8 to D21. Patients who relapse will discontinue further study treatment.

Patients in continuous remission with hematopoietic recovery will receive continuous post consolidation therapy of midostaurin, during 12 cycles (28 days per cycle). Patients who relapse will discontinue further study treatment.

Condition
FLT3-mutated Acute Myeloid Leukemia
Phase
Phase2
Overall Status
Recruiting
Number of Participants
20
Start Date
Mar 13, 2019
Completion Date
Oct 31, 2030
Gender
All
Age(s)
3 Years - 17 Years (Child)

Interventions

Drug

Cytarabine

Part 1: 2000mg/m2/day D1 to D5 of Block 2 FLADx 1000mg/m2 every 12 hours D1 to D3 Block 3 HAM 3000mg/m2 every 12 hours D1 to D3 Block 4 HA3E 3000mg/m2 every 12 hours D1 to D3 Block 5 HIDAC Part 2: 1000mg/m2 every 12 hours D1 to D3 Block 2 HAM 3000mg/m2 every 12 hours D1 to D3 Block 3 HA3E 1000mg/m2 every 12 hours D1 to D3 Block 4 HAM 3000mg/m2 every 12 hours D1 to D3 Block 5 HIDAC
Drug

Daunorubicin or idarubicin

daunorubicin 60 mg/m2/day OR idarubicin 12mg/m2/day On D2, D4, D6 of Block 2 FLADx
Drug

Etoposide

100mg/m2/day D1 to D5
Drug

Fludarabine

30mg/m2/day on D1-D5 of Block 2 FLADx
Drug

Midostaurin

midostaurin 30mg/m2 bid
Drug

Mitoxantrone

10mg/m2/day D3 and D4

Eligibility Criteria

Inclusion Criteria:

* Documented Diagnosis of previously untreated de novo AML according to WHO 2016 criteria
* Presence of a FLT3 mutation status as measured/confirmed by a designated lab with results available prior first dose of Midostaurin
* Patients with Lansky or Karnofsky performance status equal or superior to 60
* Patient with the following laboratory value : AST and ALT ≤ 3times ULN
* Serum Total bilirubin ≤ 1.5times ULN
* Estimated creatinine clearance ≥30ml/min

Exclusion Criteria:

* Any concurrent malignancy, AML with Philadelphia Chromosome, AML-DS, JMML
* Symptomatic leukemic CNS involvement
* Isolated extramedullary leukemia, secondary AML and MDS

* Acute Promyelocytic Leukemia with the PML RARA rearrangement
* Patient who have received prior treatment with a FLT3 inhibitor. However, up to 1 week of FLT3 inhibitor (except midostaurin) exposure prior to study enrollment is permissible.

Other protocol-defined inclusion/exclusion criteria may apply

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