GRAVITAS-119: Itacitinib in Combination With Calcineurin Inhibitor-Based Interventions for the Prophylaxis of Graft-Versus Host Disease

NCT-Nummer:
NCT03320642

Studienbeginn:
Februar 2018

Letztes Update:
16.02.2021

Wirkstoff:
Itacitinib, Calcineurin inhibitor
Indikation (Clinical Trials):
Graft vs Host Disease, Hematologic Neoplasms

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 1

Sponsor:
Incyte Corporation

Collaborator:
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Studien-Informationen

Brief Summary:

The purpose of this study is to assess the impact and safety of itacitinib in combination

with calcineurin inhibitor (CNI)-based interventions for the prophylaxis of

graft-versus-host-disease (GVHD).

Ein-/Ausschlusskriterien

Inclusion Criteria:

- Subjects with acute leukemia, chronic myelogenous leukemia, or myelodysplasia with no circulating blasts and < 5% blasts in the bone marrow.

- Subjects with non-Hodgkin lymphoma, including but not limited to chronic lymphocytic leukemia/small lymphocytic lymphoma, follicular, marginal zone, diffuse large B cell, or mantle cell lymphoma must have chemosensitive disease at time of transplant. Subjects with Hodgkin lymphoma with chemosensitive disease at the time of transplant.

- Must be candidates for reduced-intensity conditioning regimens.

- Must be candidates for peripheral blood stem cell transplants.

- Karnofsky Performance Status score ≥ 70% or Eastern Cooperative Oncology Group Performance Status score of 0 to 2.

- Serum creatinine ≤ 2.0 mg/dL or creatinine clearance ≥ 40 mL/min measured or calculated by Cockcroft-Gault equation.

- Be willing to avoid pregnancy or fathering children.

Exclusion Criteria:

- Has previously received an allogenic hematopoietic stem cell transplant.

- Presence of an active uncontrolled infection.

- Known HIV infection.

- Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection that requires treatment or at risk for HBV reactivation.

- Prior malignancies.

- Severe organ dysfunction.

- Prior treatment with a JAK inhibitor or with an investigational agent, device, or

procedure within 21 days of enrollment.

- Currently breastfeeding.

- Known allergies, hypersensitivity, or intolerance to any of the study medications.

- Receipt of live (including attenuated) vaccines during the study, or anticipation of

need for such a vaccine during the study.

- History of primary idiopathic myelofibrosis or any severe marrow fibrosis that would

prolong neutrophil engraftment to > 28 days after transplant.

- Post-transplant maintenance therapy for the hematologic malignancy or plans to

initiate maintenance therapy during study treatment.

Studien-Rationale

Primary outcome:

1. Proportion of participants with hematologic recovery when itacitinib is added to GVHD prophylaxis treatment (Time Frame - Day 28):
Hematologic recovery defined as demonstrating both neutrophil recovery (ANC ≥ 500/mm^3 for 3 consecutive measurements) and platelet recovery (platelet count ≥ 20,000/mm^3 with no requirement for platelet transfusion in the preceding 3 days).

Secondary outcome:

1. GVHD relapse-free survival rate (Time Frame - Days 100, 180 and 365):
Defined as the proportion of subjects who do not experience Grade III-IV acute GVHD (aGVHD), chronic GVHD (cGVHD) requiring systemic therapy, malignancy relapse or progression, or death due to any cause.

2. Relapse-free survival (Time Frame - Up to 1 year):
Defined as the interval between enrollment and malignancy relapse or progression, or death, whichever occurs first.

3. Transplant-related mortality (Time Frame - Up to 1 year):
Defined as the proportion of subjects who die due to causes other than malignancy relapse or progression.

4. Median time to neutrophil and platelet engraftment (Time Frame - Up to Day 28):
Defined as the median time to achieve neutrophil and platelet engraftment.

5. Percentage of participants who achieve neutrophil and platelet engraftment (Time Frame - Up to Day 28):
Defined as the median time to achieve engraftment and hematologic recovery at prespecified

time points.

6. Donor Chimerism (Time Frame - Up to Day 28)

7. Proportion of subjects who are diagnosed with Grade II-IV aGVHD, by each grade and by Grade III/IV (Time Frame - Days 100 and Days 180):
Measured to assess the incidence of aGVHD.

8. Proportion of subjects who are diagnosed with cGVHD by grade (mild, moderate, or severe) (Time Frame - Up to 1 year):
Measured to assess the incidence of cGVHD.

9. Infection rate (Time Frame - Up to 1 year):
Defined as the proportion of subjects who demonstrate an infection and/or cytomegalovirus reactivation.

10. Overall survival (Time Frame - Up to 1 year):
Defined as the interval between enrollment and death due to any cause.

11. Participants with Grade 3-5 treatment-emergent adverse events (TEAEs) (Time Frame - Up to approximately 200 days):
TEAE is defined as either an adverse event (AE) reported for the first time or worsening of a pre-existing condition after the first dose of study treatment.

Geprüfte Regime

- Itacitinib (INCB039110):
  Itacitinib administered orally once daily at the protocol-defined dose.
- Calcineurin inhibitor:
  The CNI-based prophylaxis regimen will be identified by the investigator before the subject's enrollment and will consist of the combination of tacrolimus/methotrexate, cyclosporine A/mycophenolate mofetil or tacrolimus plus post-treatment cyclophosphamide. Antithymocyte globulin may be included at the treating investigator's discretion with the tacrolimus/methotrexate or cyclosporine A/mycophenolate mofetil combinations.

Studienleiter

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Quelle: ClinicalTrials.gov