Purpose

This pivotal phase III trial (CINC424B2301) is designed to compare the efficacy and safety of INC424 to Best Available Therapy (BAT) in subjects with polycythemia vera (PV) who are resistant to or intolerant of hydroxyurea (HU).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycythemia Vera</td>
<td>Drug: INC424 tablets Other: Best Available Therapy (BAT)</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>
Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Randomized, Open Label, Multicenter Phase III Study of Efficacy and Safety in Polycythemia Vera Subjects Who Are Resistant to or Intolerant of Hydroxyurea: JAK Inhibitor INC424 Tablets Versus Best Available Care

Resource links provided by NLM:

Genetics Home Reference related topics: polycythemia vera

Drug Information available for: Hydroxyurea

Genetic and Rare Diseases Information Center resources: Chronic Myeloproliferative Disorders Polycythemia Vera

U.S. FDA Resources

Further study details as provided by Incyte Corporation:

Primary Outcome Measures:
- To compare the efficacy of INC424 to Best Available Therapy as assessed by both the absence of phlebotomy eligibility and reduction in spleen volume. [ Time Frame: 32 Weeks ] [ Designated as safety issue: No ]

Secondary Outcome Measures:
- To compare the proportion of subjects randomized to INC424 vs. Best Available Therapy achieving both durable absence of phlebotomy eligibility and durable spleen volume reduction. [ Time Frame: 48 Weeks. ] [ Designated as safety issue: No ]
- To compare the proportion of subjects randomized to INC424 vs. Best Available Therapy achieving complete hematological remission. [ Time Frame: 32 Weeks ] [ Designated as safety issue: No ]
- To determine the proportion of subjects achieving a durable spleen volume reduction [ Time Frame: 48 Weeks ] [ Designated as safety issue: No ]
- To estimate the proportion of subjects achieving a durable complete hematological remission [ Time Frame: 48 Weeks ] [ Designated as safety issue: No ]
- To estimate the proportion of subjects achieving a durable phlebotomy independence [ Time Frame: 48 Weeks ] [ Designated as safety issue: No ]
- To estimate the duration of both the absence of phlebotomy eligibility and reduction in spleen volume [ Time Frame: Through study ]
To determine the overall clinicohematologic response rate [ Time Frame: 32 Weeks ] [ Designated as safety issue: No ]

To estimate the proportion of subjects achieving a durable complete or partial clinicohematologic response [ Time Frame: 48 Weeks ] [ Designated as safety issue: No ]

To estimate the duration of the overall clinicohematologic response [ Time Frame: Through study completion ] [ Designated as safety issue: No ]

To estimate the proportion of subjects achieving both durable absence of phlebotomy eligibility and durable spleen volume reduction 48 weeks after the response was initially documented [ Time Frame: Through study completion. ] [ Designated as safety issue: No ]

Safety and tolerability of INC424 as measured by adverse events, laboratory assessments, physical examination, vital signs, and ECG measurements. [ Time Frame: Through study completion ] [ Designated as safety issue: No ]

Estimated Enrollment: 200
Study Start Date: October 2010
Estimated Study Completion Date: September 2014
Primary Completion Date: February 2014 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>Experimental: INC424 tablets</td>
<td>Drug: INC424 tablets</td>
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<tr>
<td>Starting dose of 10 mg BID with individualized dose titration ranging from 5 mg QD to 25 mg BID based on safety and efficacy</td>
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</tr>
<tr>
<td>Best Available Therapy</td>
<td>Other: Best Available Therapy (BAT)</td>
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<tr>
<td>Best Available Therapy (BAT) will be selected by the Investigator for each subject. BAT may not include experimental agents (i.e. those not approved for the treatment of any indication) as well as a limited number of other selected drugs.</td>
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<td>Other Names:</td>
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<tr>
<td>BAT:</td>
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<tr>
<td>1. Hydroxyurea</td>
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<tr>
<td>2. IFN/PEG-IFN</td>
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<td>3. Pipobroman</td>
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<td>4. Anagrelide</td>
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<td>5. IMIDs</td>
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Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
- Subjects diagnosed with PV for at least 24 weeks prior to screening according to the 2008 World Health Organization criteria
- Subjects resistant to or intolerant of hydroxyurea
- Subjects with a phlebotomy requirement
- Subjects with a palpable splenomegaly and a spleen volume of greater than or equal to 450 cubic centimeters
- Subjects with an ECOG performance status of 0, 1 or 2

Exclusion Criteria:
- Women who are pregnant or nursing
- Subjects with inadequate liver or renal function
- Subjects with significant bacterial, fungal, parasitic, or viral infection requiring treatment
- Subjects with an active malignancy within the past 5 years, excluding specific skin cancers
- Subjects with known active hepatitis or HIV positivity
- Subjects who have previously received treatment with a JAK inhibitor
- Subjects being treated with any investigational agent

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: NCT01243944
Show 160 Study Locations

Sponsors and Collaborators
Incyte Corporation
Novartis Pharmaceuticals

Investigators
Study Director: Srdan Verstovsek, MD,PhD  M.D. Anderson Cancer Center
Study Director: Mark Jones, MD  Incyte Corporation

More Information

Additional Information:

Related Info  exit

No publications provided

Responsible Party: Incyte Corporation
ClinicalTrials.gov Identifier: NCT01243944  History of Changes
Other Study ID Numbers: CINC424B2301
Study First Received: November 17, 2010
Last Updated: March 12, 2014
Health Authority: United States: Food and Drug Administration

Keywords provided by Incyte Corporation:
INCB018424

Additional relevant MeSH terms:
Polycythemia  Antisickling Agents
Polycythemia Vera  Enzyme Inhibitors
Bone Marrow Diseases  Hematologic Agents
Hematologic Diseases  Molecular Mechanisms of Pharmacological Action
Myeloproliferative Disorders  Nucleic Acid Synthesis Inhibitors
Hydroxyurea  Pharmacologic Actions