Rituximab Plus Lenalidomide for Patients With Relapsed / Refractory Indolent Non-Hodgkin’s Lymphoma (Follicular Lymphoma and Marginal Zone Lymphoma) (AUGMENT)

Purpose

This double-blind randomized, parallel group study will evaluate the efficacy and safety of lenalidomide (Revlimid, CC-5013) in combination with rituximab (MabThera/Rituxan) in patients with relapsed or refractory follicular lymphoma or marginal zone lymphoma. Patients will be randomized to receive either lenalidomide or placebo for twelve 28-day cycles in combination with rituximab. Anticipated time on study treatment is 1 year.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma, Non-Hodgkin</td>
<td>Drug: Rituximab Drug: Lenalidomide Drug: Placebo</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

Study Type: Interventional
Study Design: Allocation: Randomized Intervention Model: Parallel Assignment Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) Primary Purpose: Treatment

Official Title: A Phase 3, Double-blind, Randomized Study to Compare the Efficacy and Safety of Rituximab Plus Lenalidomide (CC-5013) Versus Rituximab Plus Placebo in Subjects With Relapsed/Refractory Indolent Lymphoma

Primary Outcome Measures:
- Progression free survival (PFS) for indolent lymphoma (Follicular lymphoma and Marginal zone lymphoma [ Time Frame: Up to 8 years ] [ Designated as safety issue: No ]

Progression-free survival is defined as the time from date of randomization to the first observation of disease progression or death due to any cause as assessed by an independent review committee.
Secondary Outcome Measures:

- **Overall response rate for indolent lymphoma (Follicular lymphoma and Marginal zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Overall response rate is defined as proportion of subjects with best response of at least partial remission during the trial without administration of new anti-lymphoma therapy.

- **Durable complete response rate for indolent lymphoma (Follicular lymphoma and Marginal zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Rate of durable complete response defined as complete response of at least 1 year's duration.

- **Complete response rate for indolent lymphoma (Follicular lymphoma and Marginal zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Complete response rate is defined as proportion of subjects with disappearance of all evidence of disease during the trial without administration of new anti-lymphoma therapy.

- **Duration of response for indolent lymphoma (Follicular lymphoma and Marginal Zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Duration of response is defined as time from initial response of at least a partial remission to documented progression/relapse.

- **Duration of complete response for indolent lymphoma (Follicular lymphoma and Marginal Zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Duration of complete response is defined as time from initial response of a complete remission to documented progression/relapse.

- **Overall survival for indolent lymphoma (Follicular lymphoma and Marginal zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Overall survival is defined as time from date of randomization to death from any cause.

- **Safety in indolent lymphoma (Follicular lymphoma and Marginal Zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: Yes]
  Incidence of Adverse Events (AEs). An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values, regardless of etiology. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a pre-existing condition) should be considered an AE.

- **Event Free Survival for indolent lymphoma (Follicular lymphoma and Marginal Zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  Event-free survival is defined as the time from the date of randomization to the first observation of disease progression, institution of new anti-lymphoma treatment, or death due to any cause.

- **Time to next anti-lymphoma therapy (TTNLT) for indolent lymphoma (Follicular lymphoma and Marginal Zone lymphoma)** [Time Frame: Up to 8 years]
  [Designated as safety issue: No]
  TTNLT is defined as the time from date of randomization to institution of new anti-lymphoma treatment.

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**Estimated Enrollment:** 350

**Study Start Date:** November 2013

**Estimated Study Completion Date:** December 2021

**Estimated Primary Completion Date:** March 2017 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
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<tbody>
<tr>
<td><strong>Experimental: Rituximab and Lenalidomide</strong></td>
<td>Drug: Rituximab 375mg/m² IV every week in Cycle 1 (Days 1, 8, 15 and 22) on Day 1 of every 28 day cycle from Cycles 2 to 5</td>
</tr>
</tbody>
</table>
Lenalidomide 20mg by mouth (PO) QD on Days 1 to 21 every 28 days up to 12 cycles
Other Name: CC-5013, Revlimid

Active Comparator: Rituximab and Placebo

Drug: Rituximab
Rituximab 375mg/m² IV every week in Cycle 1 (Days 1, 8, 15 and 22) on Day 1 of every 28 day cycle from Cycles 2 to 5
Other Name: Rituxan
Drug: Placebo
Placebo (identical matched capsule) PO QD Days 1 to 21 every 28 days

Detailed Description:
Indolent lymphoma is a slow growing but incurable lymphoma which includes follicular lymphoma and marginal zone lymphoma. Follicular Lymphoma and Marginal zone lymphoma are cancers of the B lymphocyte, a type of white blood cell. Lenalidomide is an immunomodulatory drug (a drug that affects the immune system) which alters the body's immune system and it may also interfere with the development of tiny blood vessels involved in tumor growth. Therefore, lenalidomide may reduce or prevent the growth of cancer cells. Lenalidomide has also been shown to restore the immune cells' ability to attack and kill tumor cells, an ability that may be inhibited by follicular lymphoma and other lymphomas. The combination of rituximab and lenalidomide may eliminate the cancer while restoring the immune system's ability to attack tumor cells.

Eligibility

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

Criteria

Inclusion Criteria:

- Age ≥18 years at the time of signing the informed consent document.
- Understand and voluntarily sign an informed consent document prior to any study related assessments/procedures are conducted.
- Histologically confirmed marginal zone lymphoma or follicular lymphoma (grade 1, 2 or 3a; CD20+ by flow cytometry or histochemistry).
- Previously treated with at least one prior systemic chemotherapy, immunotherapy or chemoimmunotherapy and have received at least 2 previous doses of rituximab.
- Documented relapsed, refractory or progressive disease after treatment with systemic therapy and must not be Rituximab-refractory.
- Investigator considers rituximab monotherapy appropriate.
- Bi-dimensionally measurable disease on cross sectional imaging by X-ray Computed Tomography (CT) or Magnetic Resonance Imaging (MRI).
- Need of treatment for relapsed, progressed or refractory disease as assessed by the investigator.
- Eastern Cooperative Oncology Group (ECOG) Performance status ≤ 2.
- Adequate bone marrow function.
- Willingness to follow study visit schedule, pregnancy precautions and other protocol requirements.

Exclusion Criteria:

- Histology other than follicular or marginal zone lymphoma or clinical evidence of transformation or Grade 3b follicular lymphoma.
- Subjects taking corticosteroids during the last week prior to study treatment, unless administered at a dose equivalent to < 20 mg/day prednisone or prednisolone.
- Systemic anti-lymphoma therapy within 28 days or use of antibody agents within 8 weeks use of radioimmunotherapy within 6 months.
- Known seropositive for or active viral infection with hepatitis B virus (HBV) or/and human immunodeficiency virus (HIV).
- Known hepatitis C virus (HCV) positive with chronic HCV or active viral infection with HCV hepatitis requiring anti-viral medication (at time of randomization).
- Life expectancy < 6 months.
- Known sensitivity or allergy to murine products.
- Prior history of malignancies, other than follicular or marginal zone lymphoma, unless the subject has been free of the disease for ≥ 5 years.
- Prior use of lenalidomide.
- Known allergy to thalidomide.
- Neuropathy > Grade 1.
- Presence or history of central nervous system involvement by lymphoma.
- Subjects who are at a risk for a thromboembolic event and are not willing to take prophylaxis for it.
Uncontrolled intercurrent illness.
Any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent document.
Pregnant or lactating females.
Any condition that places the subject at unacceptable risk if he/she were to participate in the study or that confounds the ability to interpret data from the study.

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: NCT01938001

Contacts
Contact: Emmanuel Ryembault, MS Neuropsychopharmacology  clinicaltrialdisclosure@celgene.com
Contact: Kenichi Takeshita, MD  clinicaltrialdisclosure@celgene.com

Show 141 Study Locations

Sponsors and Collaborators
Celgene Corporation

Investigators
Study Director: Barbara Amoroso, MD  Celgene Corporation

More Information
No publications provided

Responsible Party: Celgene Corporation
ClinicalTrials.gov Identifier: NCT01938001  History of Changes
Other Study ID Numbers: CC-5013-NHL-007
Study First Received: September 5, 2013
Last Updated: January 26, 2016
Health Authority:
United States: Food and Drug Administration
Belgium: Federal Agency for Medicinal Products and Health Products
Czech Republic: State Institute for Drug Control
France: Agence Nationale de Sécurité du Médicament et des produits de santé
Germany: Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
Italy: Agenzia Italiana del Farmaco
Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Portugal: INFARMED - Autoridade Nacional do Medicamento e Produtos de Saúde IP Direcção de Avaliação de Medicamentos Parque da Saúde de Lisboa
Spain: Agencia Española de Medicamentos y Productos Sanitarios
United Kingdom: Medicines and Healthcare Products Regulatory Agency
Israel: Israeli Health Ministry Pharmaceutical Administration
Russia: Ministry of Healthcare of the Russian Federation
Brazil: Agência Nacional de Vigilância Sanitária (ANVISA)
Turkey: T.R.Ministry of Health, Turkish Drug&Medical Device Agency, Drug, Biologic&Medical Products Presidency,
China: Food and Drug Administration
Japan: Pharmaceuticals and Medical Devices Agency

Keyw ords provided by Celgene Corporation:
Non-Hodgkins Follicular lymphoma, Non-Hodgkins Marginal zone lymphoma, treatment for follicular lymphoma, treatment for Marginal zone lymphoma

Additional relevant MeSH terms:
Lymphoma  Angiogenesis Inhibitors
Lymphoma, B-Cell, Marginal Zone  Angiogenesis Modulating Agents