CLINICAL TRIAL FACT SHEET

Clinicaltrials.gov Identifier: NCT02046070

The Oral Combination of Ixazomib with Cyclophosphamide and Dexamethasone in Patients with Newly Diagnosed or Relapsed and/or Refractory Multiple Myeloma

Trial Description: A phase II trial for approximately 148 patients with either newly diagnosed or relapsed and/or refractory myeloma in which response rates and safety of the all-oral combination therapy of ixazomib (an oral proteasome inhibitor), cyclophosphamide (an alkylating chemotherapy agent), and dexamethasone (a synthetic steroid) will be assessed. Newly diagnosed patients will be randomly assigned by a computer to receive one of two different dosing regimens (only the dose of cyclophosphamide will vary), and relapsed/refractory patients will be assigned to a third group.

Trial Objectives: The primary goal of this study is to measure response to this combination therapy over a period of 13 28-day cycles (up to 1 year). Both the rate of complete response (stringent complete response, complete response, and very good partial response) and the overall response rate (complete response, very good partial response, and partial response) will be measured. Key secondary goals include assessing the following:

- The rate and severity of adverse events (side effects), and the rate at which these events cause patients to have dose reductions or to discontinue the trial;
- The amount of time it takes newly diagnosed and relapsed/refractory patients to respond to therapy;
- The time it takes newly diagnosed and relapsed/refractory patients to relapse when measured from 1) trial enrollment and from 2) first response;
- Changes, whether positive or negative, in quality of life;
- The overall response rate of patients remaining on the trial after 13 28-day cycles.

Trial Arms:

- **Arm 1 (newly diagnosed patients)**

  Ixazomib 4.0 mg capsules orally on days 1, 8, and 15 of a 28-day cycle until progressive disease or unacceptable side effects (13 cycles in the induction phase and continuing in the maintenance phase for up to 36 months);

  Cyclophosphamide 300 mg/m^2 tablets orally on days 1, 8, and 15 of a 28-day cycle (for 13 cycles or until progressive disease or unacceptable side effects);

  Dexamethasone 40 mg tablets orally on days 1, 8, 15, and 22 (dose reduced to 20 mg for patients >75 years) of a 28-day cycle (for 13 cycles or until progressive disease or unacceptable side effects)

- **Arm 2 (newly diagnosed patients)**

  Ixazomib 4.0 mg capsules orally on days 1, 8, and 15 of a 28-day cycle until progressive disease or unacceptable side effects (13 cycles in the induction phase and continuing in the maintenance phase for up to 36 months);

  Cyclophosphamide 400 mg/m^2 tablets orally on days 1, 8, and 15 of a 28-day cycle (for 13 cycles or until progressive disease or unacceptable side effects);

  Dexamethasone 40 mg tablets orally on days 1, 8, 15, and 22 (dose reduced to 20 mg for patients >75 years) of a 28-day cycle (for 13 cycles or until progressive disease or unacceptable side effects).

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(continued)

- **Arm 3 (relapsed/refractory patients)**

  Ixazomib 4.0 mg capsules orally on days 1, 8, and 15 of a 28-day cycle;

  Cyclophosphamide 300 mg/m^2 tablets orally on days 1, 8, and 15 of a 28-day cycle;

  Dexamethasone 40 mg tablets orally on days 1, 8, 15, and 22 (dose reduced to 20 mg for patients >75 years) of a 28-day cycle (until progressive disease or unacceptable side effects).

Key Eligibility Criteria:

- **Newly diagnosed patients (NDMM)**
  - Must be 18 years or older with a confirmed diagnosis of myeloma
  - Must be ineligible for high-dose therapy with stem cell transplant either because the participant is 65 years of age or older or because the participant is less than 65 but has a significant medical condition that would make high-dose therapy with stem cell transplant an inappropriate option
- **Patients with relapsed/refractory myeloma (RRMM)**
  - Must be at least 18 years old with a confirmed diagnosis of myeloma either currently or at the time of diagnosis
  - Must have relapsed or refractory disease after 1-3 lines of prior therapy (induction, stem cell transplant, and maintenance therapy are considered one line of therapy)
  - Must have no evidence of graft-versus-host disease (GVHD) if patient has undergone allogeneic stem cell transplant
- **All NDMM patients and all patients with RRMM**
  - Must have measurable disease
  - Female patients must be post-menopausal, or must be surgically sterile, or must agree to practice true abstinence AND must adhere to the guidelines of the lenalidomide pregnancy prevention program
  - Male patients, if not surgically sterile, must agree to practice effective barrier contraception or true abstinence through the entire study period and for 90 days after the last dose of study drug
  - Patients must meet the clinical laboratory criteria set forth in the treatment protocol

Key Exclusion Criteria:

- Prior treatment for multiple myeloma
- Diagnosis of smoldering myeloma, Waldenström's macroglobulinemia, POEMS syndrome, plasma cell leukemia, primary amyloidosis, myelodysplastic syndrome, or myeloproliferative syndrome
- Central nervous system involvement
- Diagnosed or treated for another malignancy within two years before first dose or any evidence of residual disease other than non-melanoma skin cancer that has been completely resected
- Peripheral neuropathy Grade 1 with pain or Grade 2 or higher
- Known gastrointestinal (GI) disease or procedure that could interfere with oral absorption and tolerance of the study drug
- Female patients who are pregnant or lactating
- Ongoing or active infection
- Use of certain medications as well as St. John's wort or ginko biloba within 14 days of the first dose of study treatment

(trial sites on next page)

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Sites that are or will be recruiting patients

(For the latest updates, contact the Takeda Study Registration Call Center at 877-825-3327 or medicalinformation@tpna.com)

USA

Kentucky
Hazard

Minnesota
Rochester

Missouri
St. Louis

New York
Rochester
(not yet recruiting)

AUSTRALIA

Adelaide
Camperdown
Concord
Heidelberg
Prahran
Waratah

GREECE

Athens
Patras
Thessaloniki

POLAND

Chorzow
Gdansk
Lodz
Lublin
Warszawa

SWEDEN

Helsingborg
Lund
Stockholm