Nivolumab, Ixazomib, Cyclophosphamide, and Dexamethasone in Relapsed/Refractory Myeloma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04119336	RECRUITING	OCTOBER 8, 2019	FEBRUARY 28, 2020

STUDY DESCRIPTION

Brief Summary

This research is being done to assess the effectiveness and safety of the combination of nivolumab with ixazomib, cyclophosphamide, and dexamethasone in relapsed and refractory multiple myeloma.

Condition or Disease: Relapsed Multiple Myeloma
Refractory Multiple Myeloma

Intervention/treatment: Drug: Nivolumab
Drug: Ixazomib
Drug: Dexamethasone
Drug: Cyclophosphamide

Phase: Phase 2

DETAILED DESCRIPTION

This research study is a phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational drug to learn whether the drug works in treating a specific disease. "Investigational" means that the drug is being studied.
- The U.S. Food and Drug Administration (FDA) has not approved nivolumab for relapsed and refractory Multiple Myeloma but it has been approved for other uses.
- The FDA has approved ixazomib and cyclophosphamide as treatment options for your disease.
- Nivolumab is a type of antibody (a protein that attaches to other cells to fight off infection and disease) that attaches to and inhibits a protein called PD-1.
-- PD-1 is a checkpoint protein on immune cells called T cells. It normally acts as a type of "off switch" that helps keep the T cells from attacking other cells in the body. Some cancer cells have large amounts of PD-L1 which binds to PD-1 and turns off the immune system. Nivolumab inhibits PD-1 and helps take the "brake" off the immune system. The investigators' hope that nivolumab will inhibit the PD-1 protein, thus allowing your immune cells to recognize and destroy cancer cells.
- Ixazomib is a type of inhibitor that blocks a protein in your cells called a proteasome. This protein is responsible for breaking down other proteins in your cells when they need to be disposed of. By blocking the proteasome from working, a buildup of proteins will be created in the cancer cells, which may lead to cell death.
- The investigators hope that the combination of ixazomib and nivolumab with standard of care chemotherapy cyclophosphamide and dexamethasone will work together with ixazomib and nivolumab to treat multiple myeloma.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 50 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase II Study of Nivolumab in Combination With Ixazomib, Cyclophosphamide, and Dexamethasone in Relapsed and Refractory Multiple Myeloma

Actual Study Start Date: January 2020

Estimated Primary Completion Date: March 2022

Estimated Study Completion Date: March 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment

Experimental: Nivolumab and Ixazomib - Participants will receive Nivolumab, Ixazomib, Cyclophosphamide, and Dexamethasone on a 28-day cycle. Oral: Ixazomib given weekly on days 1, 8, 15 Dexamethasone given weekly during cycle Infused: Nivolumab given once per cycle Cyclophosphamide given on days 1, 8, 15 during cycle	Drug: Nivolumab Given intravenously once per cycle Drug: Ixazomib Given orally on days 1, 8, 15. Drug: Dexamethasone Given orally on days 1, 8, 15, 22 Drug: Cyclophosphamide Given intravenously on days 1, 8, 15.

OUTCOME MEASURES

Primary Outcome Measures:	1. Objective response rate [Time Frame: 2 Years] Objective response rate per International Myeloma Working Group criteria.
Secondary Outcome Measures:	1. Progression Free Survival [Time Frame: The time from starting treatment to disease progression or death from any cause, for up to 10 years. Patients who have not progressed or died are censored at the date of last known progression-free.] Estimated using the Kaplan-Meier method

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
- Previously treated relapsed and refractory multiple myeloma per International Myeloma Working Group consensus criteria (Rajkumar et al., 2011).
- Patients must have received at least three prior lines of therapy, including an immunomodulatory drug (e.g. lenalidomide, pomalidomide), a proteasome inhibitor (e.g. bortezomib, carfilzomib), and anti-CD38 monoclonal antibody (e.g. daratumumab)
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (see Appendix A).
- Age ≥ 18 years
- All laboratory assessments for eligibility should be performed within 21 days of initiation of protocol therapy unless otherwise specified.
- Measurable disease of multiple myeloma as defined by at least one of the following (IgD and IgA with monoclonal protein < 0.5 g/dL may be permitted after discussion with PI): - Serum monoclonal protein ≥ 0.5 g/dL (or quantitative IgA ≥ 1000 mg/dL), or - ≥ 200 mg of monoclonal protein in the urine on 24-hour urine protein electrophoresis, and/or - Serum free light chain ≥ 100 mg/L (10 mg/dL) and abnormal serum free kappa to serum free kappa light chain ratio - ANC ≥ 1000/µL. G-CSF is not permitted within 14 days of screening. - Platelet count ≥ 75,000/µL. Platelet transfusions are not permitted within 7 days of screening. - Hemoglobin ≥ 8 g/dL. Red blood cell transfusions are permitted to meet eligibility criteria. - Calculated creatinine clearance of ≥ 30 mL/min according to Cockroft-Gault equation. - Adequate hepatic function, as evidenced by each of the following: - Serum aspartate transaminase (ALT) and/or aspartate transaminase (AST) values < 3 × the institutional upper limit of normal (ULN). - Serum bilirubin values 2 medications for adequate control; diabetes mellitus with > 2 episodes of ketoacidosis in the preceding 12 months; or chronic obstructive pulmonary disease (COPD) requiring > 2 hospitalizations in the preceding 12 months.
3.2.15 Autoimmune disease: patients with a history of inflammatory bowel disease, including ulcerative colitis and Crohn's disease, are excluded from this study, as are patients with a history of symptomatic disease (e.g., rheumatoid arthritis, systemic progressive sclerosis [scleroderma], systemic lupus erythematosus, autoimmune pneumonitis, autoimmune vasculitis (e.g., Wegener's granulomatosis) and motor neuropathy considered of autoimmune origin (e.g. Guillain-Barré syndrome and myasthenia gravis). Patients with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
- Patients with history of interstitial lung disease and/or pneumonitis, or pulmonary hypertension.
- Major surgery within 14 days prior to study registration.
- Central nervous system involvement.
- Infection requiring systemic antibiotic therapy or other serious infection within 14 days prior to study registration
- Systemic treatment with strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of St. John's wort within 14 days prior to C1D1.
- Receipt of a live or attenuated vaccine within 30 days of C1D1.
- Any serious medical of psychiatric illness that could, in the investigator's opinion, potentially interfere with the completion of treatment according to this protocol.
- Known allergy to any study medications, their analogs, or excipients in the various formulations of any agent.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Massachusetts	Massachusetts General Hospital Cancer Center	Boston
United States, Massachusetts	Mass General/North Shore Cancer Center	Danvers
United States, Massachusetts	Massachusett General Hopsital at Newton Wellsley Hospital	Newton

Sponsors and Collaborators

Andrew Yee, MD

Bristol-Myers Squibb

Takeda Pharmaceuticals North America, Inc.

Investigator

Principal Investigator :	Andrew Yee, MD	Massachusetts General Hospital

---

MORE INFORMATION

Responsible Party :	Andrew Yee, MD
ClinicalTrials.gov Identifier :	NCT04119336
Other Study ID Numbers :	19-283
First Posted :	October 8, 2019
Last Update Posted :	February 28, 2020
Last Verified :	February 2020
Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	Yes
Plan Description:	The Dana-Farber / Harvard Cancer Center encourages and supports the responsible and ethical sharing of data from clinical trials. De-identified participant data from the final research dataset used in the published manuscript may only be shared under the terms of a Data Use Agreement. Requests may be directed to: [contact information for Sponsor Investigator or designee]. The protocol and statistical analysis plan will be made available on Clinicaltrials.gov only as required by federal regulation or as a condition of awards and agreements supporting the research.
Supporting Materials:	Study Protocol, Statistical Analysis Plan (SAP), Informed Consent Form (ICF)
Time Frame:	Data can be shared no earlier than 1 year following the date of publication
Access Criteria:	MGH - Contact the Partners Innovations team at http://www.partners.org/innovation
URL:	http://www.partners.org/innovation
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Andrew Yee, MD:	*Refractory Multiple Myeloma Relapsed Multiple Myeloma*
Additional relevant MeSH terms :	*Multiple Myeloma* *Neoplasms, Plasma Cell*