**Trial Description:** In this phase III study, patients who have had any type of positive response to induction therapy followed by high-dose therapy with stem cell transplant will be randomly assigned by a computer to receive either a placebo (a capsule that looks like ixazomib but has no active ingredient) or ixazomib, an oral proteasome inhibitor, as maintenance therapy. This is a double-blind study, meaning that neither the patient, nor the caregiver, nor the doctor, nor those who evaluate the trial outcome know if the patient is receiving ixazomib or placebo.

**Trial Objectives:** To determine the effect of ixazomib maintenance therapy on progression-free survival (PFS), defined as the time from the date a patient is randomized to the date that disease progression is first documented, compared to placebo. Key secondary objectives including determining 1) overall survival (OS) rates for a period of up to 110 months; 2) time to disease progression; 3) time to the end of the next line of therapy; 4) time to the second disease progression; 5) time to the end of the next line of therapy after the study treatment; 6) duration of the next line of therapy after the study treatment; 7) percentage of patients who develop a new primary malignancy; 8) percentage of participants who convert from minimal residual disease (MRD) positive to MRD negative; 9) correlation of MRD status with PFS and OS; and 10) percentage of participants with adverse events (AEs, or unfavorable and unintended signs or symptoms associated with ixazomib or placebo).

**Trial Arms:**
- **Arm 1 (experimental arm)**
  - Cycles 1 through 4: Ixazomib 3 mg capsule orally, once daily, on days 1, 8, and 15 of a 28-day cycle.
  - Cycles 5–26: Ixazomib 3 or 4 mg capsule orally, once daily, on days 1, 8, and 15 of a 28-day cycle.
  - Patients experiencing AEs attributed to the study drug during any cycle may continue in the study but may have doses of the study drug held or reduced by at least one dose level.
- **Arm 2 (placebo comparator arm)**
  - Cycles 1 through 4: Placebo capsule matching the 3 mg ixazomib capsule orally, once daily, on days 1, 8, and 15 of a 28-day cycle.
  - Cycles 5–26: Placebo capsule matching the 3 mg or 4 mg ixazomib capsule orally, once daily, on days 1, 8, and 15 of a 28-day cycle.
  - Patients experiencing AEs attributed to the study drug during any cycle may continue in the study but may have doses of the study drug held or reduced by at least one dose level.
- **Other requirements:** The time commitment for this study is up to 24 months. Participants will be required to make 28 visits to the clinic where they are being treated during the treatment period, and will continue to make follow-up visits every four weeks until the next line of therapy begins. Participants will also be contacted by telephone every 12 weeks after the last treatment visit for a follow-up assessment.

*(continues on back side)*
Clinicaltrials.gov Identifier: NCT02181413

A Study of Oral Ixazomib Citrate (MLN9708) Maintenance Therapy in Patients with Multiple Myeloma Following Autologous Stem Cell Transplant

**Key Eligibility Criteria:**

- Documented evidence of cytogenetics and FISH testing obtained at any time before transplant, and ISS staging at the time of diagnosis.
- Induction therapy must have been standard of care and have included a proteasome inhibitor (PI) and/or an immunomodulating drug (IMiD) followed by a single autologous stem cell transplant with high-dose melphalan conditioning, within 12 months of diagnosis. VAD is not an acceptable induction therapy for this trial.
- Cannot have started screening for the trial before 75 days after transplant and cannot be randomized for the trial later than 115 days after transplant.
- No post-ASCT consolidation therapy.
- Documented response to ASCT of at least PR (50% drop in monoclonal protein) according to IMWG criteria.
- Female patients of childbearing potential must, from the time they sign a consent form until 90 days after they have their last dose of study drug, practice 2 effective, acceptable methods of contraception at the same time.
- Male patients, even post vasectomy, must practice effective barrier contraception from the time of signing the consent form until 90 days after their last dose of study drug.

**Key Exclusion Criteria:**

- Multiple myeloma that has relapsed following primary therapy or did not respond to primary therapy. For this study, stable disease after stem cell transplant is considered non-responsive to primary therapy.
- Tandem (double) transplant.
- Radiation therapy, major surgery, or infection requiring intravenous antibiotics within two weeks before randomization.
- Myeloma involvement in the central nervous system.
- Uncontrolled cardiovascular conditions, including uncontrolled hypertension, cardiac arrhythmias, congestive heart failure, or myocardial infarction within the past 6 months.
- Peripheral neuropathy that is Grade 1 with pain or Grade 2 or higher of any cause.
- Treatment with any investigational products within 60 days before the first dose of the study drug regimen.

*(trial sites on next page)*
Clinicaltrials.gov Identifier: NCT02181413

A Study of Oral Ixazomib Citrate (MLN9708) Maintenance Therapy in Patients with Multiple Myeloma Following Autologous Stem Cell Transplant

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
Morgantown, West Virginia (not yet recruiting)

AUSTRALIA
Adelaide (not yet recruiting)
Auchenflower
Heidelberg
Kogarah (not yet recruiting)
Prahran
Waratah
Woodville South (not yet recruiting)

AUSTRIA
Vienna

BELGIUM
Antwerp
Brugge (not yet recruiting)
Gent (not yet recruiting)
La Louviere (not yet recruiting)

CZECH REPUBLIC
Brno (not yet recruiting)
Hradec Kralove (not yet recruiting)
Olomouc (not yet recruiting)
Ostrava
Praha 2
Praha 10 (not yet recruiting)

DENMARK
Aalborg (not yet recruiting)
Aarhus C
Copenhagen
Herlev (not yet recruiting)
Odense
Roskilde
Vejle (not yet recruiting)

FRANCE
Clamart (not yet recruiting)
Lille (not yet recruiting)
Nantes
Paris

GERMANY
Berlin
Bonn
Darmstadt (not yet recruiting)
Dresden
Essen (not yet recruiting)
Frankfurt Am Main (not yet recruiting)
Hagen (not yet recruiting)
Hamburg
Hannover (not yet recruiting)
Heidelberg
Köln (not yet recruiting)
Ludwigshafen (not yet recruiting)
Mainz
Mannheim
München
Oldenburg
Tübingen
Würzburg (not yet recruiting)

GREECE
Athens
Thessaloniki (not yet recruiting)

HUNGARY
Budapest
Debrecen (not yet recruiting)
Kaposvar (not yet recruiting)
Szeged

ISRAEL
Haifa (not yet recruiting)
Jerusalem (not yet recruiting)
Naharia (not yet recruiting)
Petah-Tiqwa (not yet recruiting)
Ramat-Gan (not yet recruiting)
Rehovot (not yet recruiting)
 Safed (not yet recruiting)
Tel Aviv (not yet recruiting)

ITALY
Ancona
Bologna (not yet recruiting)
Brescia (not yet recruiting)
Firenze (not yet recruiting)
Meldola (not yet recruiting)
Milano (not yet recruiting)
Rimini (not yet recruiting)
Rionero in Vulture
Roma (not yet recruiting)
Terni (not yet recruiting)
Torino (not yet recruiting)

KOREA, REPUBLIC OF
Daejeon (not yet recruiting)
Goyang-SI
Incheon
Seoul

NETHERLANDS
Amsterdam
Dordrecht (not yet recruiting)
Groningen (not yet recruiting)
Utrecht (not yet recruiting)

NORWAY
Gjettum (not yet recruiting)
Oslo
Stavanger (not yet recruiting)
Trondheim (not yet recruiting)

POLAND
Brzozow (not yet recruiting)
Chorzow (not yet recruiting)
Lodz

PORTUGAL
Braga (not yet recruiting)
Coimbra (not yet recruiting)
Porto

SINGAPORE
Singapore

SOUTH AFRICA
Johannesburg
Pretoria

SPAIN
Badalona
Barcelona (not yet recruiting)
Cordoba (not yet recruiting)
Girona (not yet recruiting)
Madrid
Salamanca (not yet recruiting)
Sevilla (not yet recruiting)

SWEDEN
Göteborg
Helsingborg (not yet recruiting)
Lund
Stockholm
Uppsala

TAIWAN
Kaohsiung (not yet recruiting)
Taipei (not yet recruiting)
Taoyuan County (not yet recruiting)

THAILAND
Bangkok

TURKEY
Ankara (not yet recruiting)

UNITED KINGDOM
Leeds (not yet recruiting)
Leicester
London (not yet recruiting)
Oxford
Sutton (not yet recruiting)
Swansea (not yet recruiting)