

The TOURMALINE Clinical Development Program:


An in-depth investigation of ixazomib in multiple myeloma and AL amyloidosis


Multiple myeloma is a rare form of cancer that starts in plasma cells, which are found in the bone marrow.¹ It is the second-most-common blood cancer and represents approximately 1 percent of all diagnosed cancers worldwide.² Despite treatment advances in the past decade, multiple myeloma remains a devastating, relapsing, and incurable cancer.


Long-term treatment is emerging as a standard of care in multiple myeloma because it has demonstrated the potential to improve clinical outcomes.³ In addition, proteasome inhibition is an established standard of care in the treatment of multiple myeloma.⁴ Ixazomib's TOURMALINE program is designed to evaluate whether sustained therapy with an oral proteasome inhibitor improves the outcomes for patients living with multiple myeloma and AL amyloidosis.


The TOURMALINE program is the result of Takeda's long-standing history of patient-centric innovation in multiple myeloma and the company's continuing commitment to individual patient needs in populations across the continuum of multiple myeloma care.


Takeda would like to express its appreciation for the patients, their families, and trial investigators participating in the TOURMALINE program, without whom this would not be possible.

TRIAL	DESCRIPTION
 <p>(NCT01564537)</p>	<p>A Phase 3 Study of Oral Ixazomib Plus Lenalidomide and Dexamethasone Versus Placebo Plus Lenalidomide and Dexamethasone in Adult Patients With Relapsed and/or Refractory Multiple Myeloma</p> <ul style="list-style-type: none"> » Initiated: August 2012 » Design: Global, randomized, double-blind, placebo-controlled, multi-center » Eligibility: Patients with relapsed/refractory multiple myeloma who have received 1 to 3 prior therapies » Primary Endpoint: Progression-free survival (PFS) » Enrollment: 722 patients worldwide; Completed » Status: This study met its primary endpoint at the first pre-specified interim analysis which became the final PFS analysis. Data were presented at the American Society of Hematology 2015 annual meeting. <p>https://clinicaltrials.gov/ct2/show/NCT01564537</p>

TRIAL	DESCRIPTION
 <p>(NCT01850524)</p>	<p>A Phase 3 Study of Oral Ixazomib Plus Lenalidomide and Dexamethasone Versus Placebo Plus Lenalidomide and Dexamethasone in Adult Patients With Newly Diagnosed Multiple Myeloma</p> <ul style="list-style-type: none"> » Initiated: May 2013 » Design: Global, randomized, double-blind, placebo-controlled, multi-center » Eligibility: Patients with newly diagnosed multiple myeloma ineligible for stem cell transplant » Primary Endpoint: PFS » Enrollment: Approximately 700 patients worldwide; Completed <p>https://clinicaltrials.gov/ct2/show/NCT01850524</p>

TRIAL	DESCRIPTION
 <p data-bbox="272 388 427 415">(NCT02181413)</p>	<p data-bbox="662 195 1458 249">A Phase 3 Study of Oral Ixazomib Maintenance Therapy in Patients With Multiple Myeloma Following Autologous Stem Cell Transplant</p> <ul style="list-style-type: none"> <li data-bbox="639 264 854 291">» Initiated: July 2014 <li data-bbox="639 302 1398 329">» Design: Global, randomized, double-blind, placebo-controlled, multi-center <li data-bbox="639 340 1414 394">» Eligibility: Patients with symptomatic multiple myeloma with prior induction therapy and ASCT and no post-ASCT consolidation therapy <li data-bbox="639 405 898 432">» Primary Endpoint: PFS <li data-bbox="639 443 1289 470">» Enrollment: Approximately 650 patients worldwide; Completed <p data-bbox="662 485 1049 512">https://clinicaltrials.gov/ct2/show/NCT02181413</p>

TRIAL	DESCRIPTION
 <p data-bbox="272 871 427 898">(NCT02312258)</p>	<p data-bbox="662 678 1446 732">A Phase 3 Study of Oral Ixazomib Maintenance Therapy in Patients With Newly Diagnosed Multiple Myeloma Not Treated With Stem Cell Transplantation</p> <ul style="list-style-type: none"> <li data-bbox="639 747 862 774">» Initiated: April 2015 <li data-bbox="639 785 1398 812">» Design: Global, randomized, double-blind, placebo-controlled, multi-center <li data-bbox="639 823 1479 877">» Eligibility: Patients with newly diagnosed multiple myeloma with response to prior induction therapy and not receiving stem-cell transplantation <li data-bbox="639 888 898 915">» Primary Endpoint: PFS <li data-bbox="639 926 1382 953">» Enrollment: Approximately 750 patients worldwide; Open for enrollment <p data-bbox="662 968 1057 995">https://clinicaltrials.gov/ct2/show/NCT02312258</p>

TRIAL	DESCRIPTION
 <p data-bbox="272 1365 427 1392">(NCT01659658)</p>	<p data-bbox="662 1171 1451 1226">A Phase 3 Study of Dexamethasone Plus Oral Ixazomib or Physicians Choice of Treatment in Relapsed or Refractory Systemic Light Chain (AL) Amyloidosis</p> <ul style="list-style-type: none"> <li data-bbox="639 1241 915 1268">» Initiated: December 2012 <li data-bbox="639 1278 1378 1306">» Design: Global, randomized, placebo-controlled, open-label, multi-center <li data-bbox="639 1316 1382 1371">» Eligibility: Biopsy-proven diagnosis of AL amyloidosis that is relapsed or refractory after 1 or 2 prior therapies <li data-bbox="639 1381 1401 1436">» Primary Endpoints: Number of patients with overall hematologic response and 2-year vital organ (heart or kidney) deterioration and mortality rate <li data-bbox="639 1446 1382 1474">» Enrollment: Approximately 250 patients worldwide; Open for enrollment <p data-bbox="662 1488 1057 1516">https://clinicaltrials.gov/ct2/show/NCT01659658</p>

For more information, please visit <https://www.clinicaltrials.gov/>.

1 Palumbo A, Anderson K. Multiple Myeloma. *New England Journal of Medicine*. 2011;364:1046-60.

2 Mateos MV, San Miguel JF. How should we treat newly diagnosed multiple myeloma patients? *Hematology Am Soc Hematol Educ Program*. 2013;2013:488-495.

3 Palumbo A, Gay F, Cavallo F et al. Continuous Therapy Versus Fixed Duration of Therapy in Patients With Newly Diagnosed Multiple Myeloma. *Journal of Clinical Oncology*. 2015;60:2466

4 American Society of Clinical Oncology. Multiple Myeloma: Treatment Options. <http://www.cancer.net/cancer-types/multiple-myeloma/treatment-options>. Updated June, 2015. Accessed February 25, 2016.

5 US National Institutes of Health Clinical Trials Registry. A phase 3 study comparing oral ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with relapsed and/or refractory multiple myeloma. <https://clinicaltrials.gov/ct2/show/NCT01564537>. Updated August 4, 2015. Accessed September 1, 2015.

6 US National Institutes of Health Clinical Trials Registry. IXAZOMIB plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with newly diagnosed multiple myeloma. <https://clinicaltrials.gov/ct2/show/NCT01850524>. Updated February 23, 2015. Accessed September 1, 2015.

7 US National Institutes of Health Clinical Trials Registry. A study of oral ixazomib citrate (MLN9708) maintenance therapy in patients with multiple myeloma following autologous stem cell transplant. <https://clinicaltrials.gov/ct2/show/NCT02181413>. Updated March 31, 2015. Accessed September 1, 2015.

8 US National Institutes of Health Clinical Trials Registry. A study of oral ixazomib maintenance therapy in patients with newly diagnosed multiple myeloma not treated with stem cell transplantation. <https://clinicaltrials.gov/ct2/show/NCT02312258>. Updated July 26, 2015. Accessed September 1, 2015.

9 US National Institutes of Health Clinical Trials Registry. Study of dexamethasone plus ixazomib or physicians choice of treatment in relapsed or refractory systemic light chain (AL) amyloidosis. <https://clinicaltrials.gov/ct2/show/NCT01659658>. Updated February 24, 2015. Accessed September 1, 2015.