

Trial record **1 of 1** for: C16011[Previous Study](#) | [Return to List](#) | [Next Study](#)**Study of Dexamethasone Plus MLN9708 or Physician's Choice of Treatment in Relapsed or Refractory Systemic Light Chain (AL) Amyloidosis****This study is currently recruiting participants.***Verified March 2013 by Millennium Pharmaceuticals, Inc.***Sponsor:**

Millennium Pharmaceuticals, Inc.

Information provided by (Responsible Party):

Millennium Pharmaceuticals, Inc.

ClinicalTrials.gov Identifier:

NCT01659658

First received: August 2, 2012

Last updated: March 11, 2013

Last verified: March 2013

[History of Changes](#)[Full Text View](#)[Tabular View](#)[No Study Results Posted](#)[Disclaimer](#)[How to Read a Study Record](#)**▶ Purpose**

This is a phase 3, randomized, controlled, open-label, multicenter study of the oral formulation of dexamethasone plus MLN9708 compared with treatment chosen by the investigator from a prespecified list of regimens available in clinical practice. Treatment options will include: dexamethasone alone, dexamethasone plus an alkylating agent (melphalan or cyclophosphamide), or dexamethasone plus an immunomodulatory drug (IMiD, thalidomide or lenalidomide) in patients with relapsed or refractory AL amyloidosis. Crossover to the investigational treatment arm is not permitted during participation in this study.

Condition	Intervention	Phase
Relapsed or Refractory Systemic Light Chain Amyloidosis	Drug: MLN9708 Drug: Dexamethasone Drug: Melphalan Drug: Cyclophosphamide Drug: Thalidomide Drug: Lenalidomide	Phase 3

Study Type: **Interventional**Study Design: Allocation: **Randomized**Endpoint Classification: **Safety/Efficacy Study**Intervention Model: **Parallel Assignment**Masking: **Open Label**Primary Purpose: **Treatment**

Official Title: **A Phase 3, Randomized, Controlled, Open-label, Multicenter, Safety and Efficacy Study of Dexamethasone Plus MLN9708 or Physician's Choice of Treatment Administered to Patients With Relapsed or Refractory Systemic Light Chain (AL) Amyloidosis**

Resource links provided by NLM:MedlinePlus related topics: [Amyloidosis](#)

Drug Information available for: [Dexamethasone](#) [Cyclophosphamide](#) [Thalidomide](#) [Melphalan](#) [Dexamethasone acetate](#)
[Dexamethasone Sodium Phosphate](#) [Melphalan hydrochloride](#) [Lenalidomide](#)

[U.S. FDA Resources](#)**Further study details as provided by Millennium Pharmaceuticals, Inc.:****Primary Outcome Measures:**

- Number of patients with overall hematologic response [Time Frame: Assessed every 4 weeks (median length of the endpoint assessment period is projected to be approximately 36 months)] [Designated as safety issue: No]
Complete response, very good partial response and partial response
- 2-year vital organ deterioration and mortality rate [Time Frame: Monthly for up to 2 years or until death] [Designated as safety issue: No]
Rate of hospitalization for congestive heart failure or progression to end stage renal disease or death at 2 years

Secondary Outcome Measures:

- Number of patients with complete hematologic response [Time Frame: Assessed every 4 weeks (median length of the endpoint assessment period is projected to be approximately 36 months)] [Designated as safety issue: No]
Overall complete hematologic response
- Overall survival [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from randomization to the date of death
- Progression free survival [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from date of randomization to the date of first documentation of disease progression or death, whichever occurs first
- Hematologic disease progression free survival [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from the date of randomization to the date of first documented hematologic disease progression or death, whichever occurs first
- Time to vital organ deterioration and mortality rate [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from date of randomization to the first date of either death or hospitalization for congestive heart failure or progression to endstage renal disease
- Number of patients with cardiac and/or kidney response [Time Frame: Every 3 cycles until disease progression]
[Designated as safety issue: No]
Overall organ response rate
- Vital organ progression free survival [Time Frame: Every 3 cycles until disease progression] [Designated as safety issue: No]
Time from the date of randomization to the date of first documentation of progression of vital organ, or death, whichever occurs first
- Duration of hematologic response [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from the date of first documentation of hematologic response to the date of first documented hematologic disease progression
- Number of adverse events [Time Frame: Monthly up to 5 years] [Designated as safety issue: Yes]
Adverse events, serious adverse events, assessment of clinical laboratory values from the date of signing of the informed consent form through 30 days after the last dose of study drug.
- Time to treatment failure [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from date of randomization to the date of first documented treatment failure
- Time to subsequent anticancer treatment [Time Frame: Monthly up to 5 years] [Designated as safety issue: No]
Time from date of randomization to the start date of subsequent anticancer treatment
- Results of Quality of Life Assessment [Time Frame: At screening; Cycle 1, Day 1; Cycle 2, Day 1; Cycle 3, Day 1; Day 1 of every 3 cycles until disease progression] [Designated as safety issue: No]
- Number of medical encounters patient experiences [Time Frame: At screening; Cycle 1, Day 1; Cycle 2, Day 1; Cycle 3, Day 1; Day 1 of every 3 cycles until disease progression] [Designated as safety issue: No]
Number of admissions to an inpatient and outpatient setting for any reason (including length of stay, inpatient, outpatient, reason, number of missing days from work or other activities by patient or care-giver and EQ-5D scores questionnaire data
- Time to reach plasma concentration [Time Frame: Cycle 1, Days 1 and 14; Cycle 2, Days 1 and 14; Cycles 3-10, Day 1]
[Designated as safety issue: No]
Pharmacokinetics
- Investigate the association of clinical outcomes and polymorphic genes [Time Frame: At screening] [Designated as safety issue: No]
Analysis of relevant signaling pathway genes in whole blood samples

Estimated Enrollment: 248
 Study Start Date: December 2012
 Estimated Study Completion Date: August 2018
 Estimated Primary Completion Date: May 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
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<p>Experimental: MLN9708 plus Dexamethasone</p> <p>Patients will receive MLN9708 (4.0 mg) orally (PO) on Days 1, 8, and 15 plus dexamethasone 20 mg/day PO weekly on Days 1, 8, 15, and 22 of each 28-day cycle; dexamethasone may be increased up to 40 mg/day after 4 weeks, if tolerated. Patients may continue to receive treatment until PD or unacceptable toxicity, whichever comes first.</p>	<p>Drug: MLN9708 Drug: Dexamethasone</p>
<p>Active Comparator: Physician's Choice</p> <p>Patients will receive one of the following treatment options as selected by the physician:</p> <ul style="list-style-type: none"> • Dexamethasone: 20 mg/day orally (PO) on Days 1-4, 9-12 & 17- 20 of each 28-day cycle • Dexamethasone + melphalan: Dexamethasone 20 mg/day PO on Days 1-4 of each 28-day; plus melphalan 0.22 mg/kg PO on Days 1-4 every 28 days. • Dexamethasone + cyclophosphamide: Dexamethasone 20 mg/day PO weekly on Days 1, 8, 15 & 22 of each 28-day cycle; plus cyclophosphamide 500 mg PO Days 1, 8 & 15 every 28 days. • Dexamethasone + thalidomide: Dexamethasone 20 mg/day PO weekly Days 1, 8, 15 & 22 of each 28-day cycle; plus thalidomide total dose up to 200 mg/day PO • Dexamethasone + lenalidomide: Dexamethasone 20 mg/day PO weekly on Days 1, 8, 15 & 22 of each 28-day cycle; plus lenalidomide 15 mg/day for 21 days every 28 days. <p>In all treatments dexamethasone may be increased up to 40 mg/day after 4 weeks, if the lower dose is tolerated without any > Grade 2 dexamethasone-related toxicities.</p>	<p>Drug: Dexamethasone Drug: Melphalan Drug: Cyclophosphamide Drug: Thalidomide Drug: Lenalidomide</p>

► Eligibility

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

Criteria

Inclusion Criteria:

- Male or female patients 18 years or older
- Biopsy-proven AL amyloidosis with relapsed or refractory disease despite 1 or 2 prior therapies. Patients may be proteasome inhibitor-exposed or naive, but cannot be refractory to proteasome inhibitor therapy
- Disease requiring further treatment
- Measurable disease as defined by serum differential free light chain concentration (dFLC)
- Objective and measurable major organ involvement (ie, cardiac or renal) as defined by the standard International Society of Amyloidosis (ISA) criteria.
- Eastern Cooperative Oncology Group (ECOG) performance status of less than or equal to 2
- Meet the clinical laboratories criteria as specified in the protocol
- Female patients who are post menopausal, surgically sterile, or agree to practice 2 effective methods of contraception through 90 days after the last dose of study treatment or agree to practice true abstinence; must also adhere to the guidelines of any treatment specific pregnancy prevention program
- Male patients who agree to practice effective barrier contraception through 90 days after the last dose of study treatment or agree to practice true abstinence AND must adhere to the guidelines of any treatment specific pregnancy prevention program
- Voluntary written consent

Exclusion Criteria:

- Amyloidosis due to mutations of the transthyretin gene or presence of other non-AL amyloidosis
- Female patients who are lactating, breastfeeding or pregnant
- Evidence of current uncontrolled cardiovascular conditions as specified in study protocol
- Clinically overt multiple myeloma as specified in study protocol
- Inability to swallow medication, inability or unwillingness to comply with the drug administration requirements, or gastrointestinal (GI) procedure that could interfere with the oral absorption or tolerance of treatment
- Requirement for other concomitant chemotherapy, immunotherapy, radiotherapy, or any ancillary therapy considered to be investigational or which would be considered as a treatment of AL amyloidosis. However, patients may be on chronic steroids (maximum dose 20 mg/day prednisone or equivalent if they are being given for disorders other than amyloidosis
- Comorbid systemic illnesses or other severe concurrent disease which, in the judgment of the investigator, would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of safety and toxicity of the prescribed regimens
- Ongoing or active infection, known HIV positive, active hepatitis B or C infection
- Psychiatric illness/social situations that would limit compliance with study requirements
- Known allergy to any of the study medications, their analogues or excipients
- Systemic treatment with strong inhibitors of CYP1A2, strong inhibitors of CYP3A, or strong CYP3A inducers, or use of Ginkgo biloba or St. John's wort within 14 days before the first dose of study treatment
- Diagnosed or treated for another malignancy within 5 years before study enrollment or previously diagnosed with another malignancy and have any evidence of residual disease. Patients with nonmelanoma skin cancer or carcinoma in situ of any type are not excluded if they have

undergone complete resection

▶ Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01659658

Contacts

Contact: For an updated listing of recruitment sites contact: Millennium Medical and Drug Information Center 1-877-674-3784 medical@mlnm.com

+ Show 19 Study Locations

Sponsors and Collaborators

Millennium Pharmaceuticals, Inc.

Investigators

Study Director: Medical Monitor Millennium Pharmaceuticals, Inc.

▶ More Information

No publications provided

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 ClinicalTrials.gov Identifier: [NCT01659658](#) [History of Changes](#)
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 Study First Received: August 2, 2012
 Last Updated: March 11, 2013
 Health Authority: United States: Food and Drug Administration
 European Union: European Medicines Agency

Keywords provided by Millennium Pharmaceuticals, Inc.:

MLN9708
 Amyloidosis
 Light Chain

Additional relevant MeSH terms:

Amyloidosis	Antirheumatic Agents
Proteostasis Deficiencies	Therapeutic Uses
Metabolic Diseases	Antineoplastic Agents, Alkylating
Cyclophosphamide	Alkylating Agents
Melphalan	Molecular Mechanisms of Pharmacological Action
Thalidomide	Antineoplastic Agents
Lenalidomide	Myeloablative Agonists
Dexamethasone	Anti-Inflammatory Agents
Dexamethasone acetate	Antiemetics
Dexamethasone 21-phosphate	Autonomic Agents
BB 1101	Peripheral Nervous System Agents
Immunosuppressive Agents	Central Nervous System Agents
Immunologic Factors	Gastrointestinal Agents
Physiological Effects of Drugs	Glucocorticoids
Pharmacologic Actions	Hormones

ClinicalTrials.gov processed this record on April 01, 2013