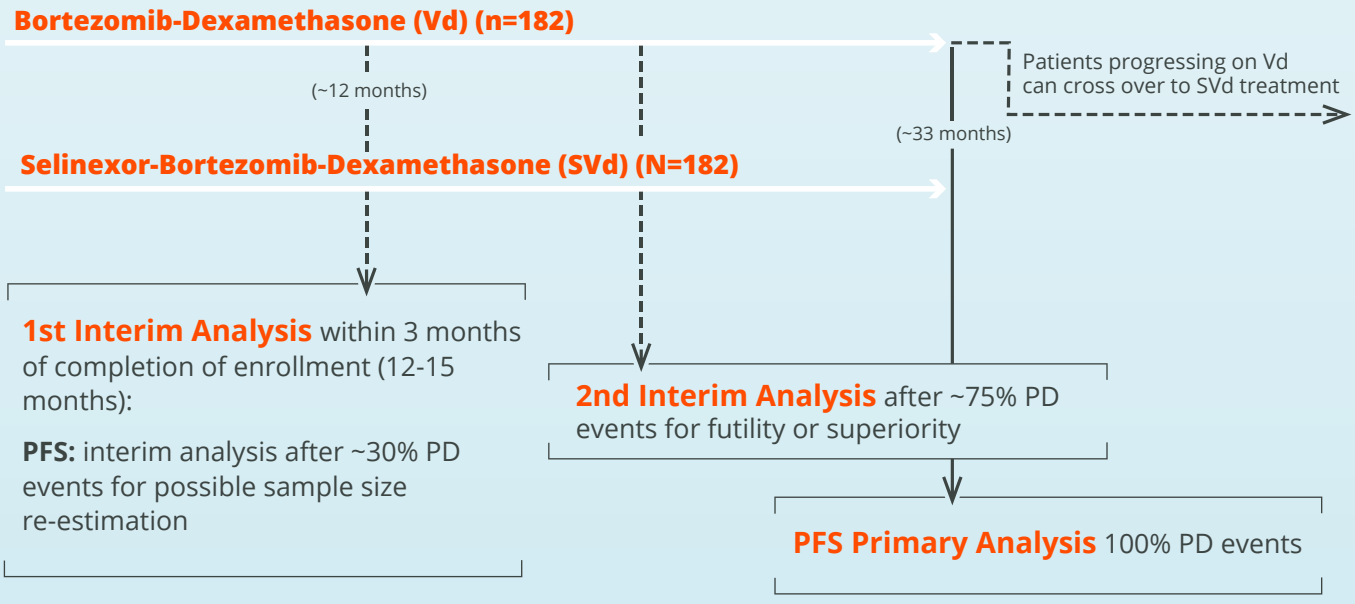
The BOSTON Trial

A Phase 3 Randomized, Controlled, Open-label Study of Selinexor, Bortezomib, and Dexamethasone (SVd) versus Bortezomib and Dexamethasone (Vd) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

Overall Study with Crossover Design: This open-label study will compare the efficacy and assess the safety of oral selinexor plus bortezomib (Velcade® or generic equivalent once weekly) plus low-dose dexamethasone (SVd) versus bortezomib (twice weekly) plus low-dose dexamethasone (Vd) in patients with RRMM who have received 1 to 3 prior anti-multiple myeloma regimens.

STUDY OVERVIEW



- ~360 patients with 1-3 prior lines of therapy
- Both bortezomib-exposed and bortezomib-naïve pts allowed
- SVd Arm: weekly subcutaneous bortezomib dosing QW 4/5 weeks throughout
- Vd Arm: bortezomib subcutaneous BIW 2/3 weeks x 8 cycles then QW 4/5 weeks
- For Vd arm, crossover to SVd permitted at confirmed objective progression
- Interim PFS analysis after 75% of the PFS events
- Global trial

Karyopharm Therapeutics

To learn more contact: **BOSTON@karyopharm.com**

Now Enrolling

CLINICAL TRIAL FACT SHEET

clinicaltrials.gov Identifier: NCT03110562

A Phase 3 Randomized, Controlled, Open-Label Study of Selinexor, Bortezomib (Velcade®), and Dexamethasone (SVd) Versus Bortezomib and Dexamethasone (Vd) in Patients with Relapsed or Refractory Multiple Myeloma (The "BOSTON" Trial)

Trial Description: The BOSTON trial will compare selinexor + Velcade + low-dose dexamethasone (SVd) to Velcade + low-dose dexamethasone (Vd). Approximately 364 myeloma patients who have been treated with 1 to 3 prior anti-myeloma regimens and have disease that has progressed during or within 60 days after prior treatment will be randomly assigned by a computer to receive either SVd or Vd. Trial participants will know whether they are receiving SVd or Vd.

Patients in the Vd arm of the study whose disease progression is confirmed by an independent review committee may cross over to receive SVd treatment.

Selinexor is a novel, first-in-class, orally administered "**S**elective **I**nhibitor of **N**ucelar **E**xport" (SINE™) compound. Selinexor blocks the ability of cancer cells to export tumor suppressor proteins from their cell nuclei. This restores the tumor suppressor proteins' ability to detect cancerous DNA changes and induce cancer cell death. Selinexor also reduces levels of key proteins that promote cancer cell growth.

The most common side effects of selinexor include nausea, fatigue, weight loss, vomiting, diarrhea, and low blood cell counts.

Trial Objectives: To compare the effectiveness and safety of SVd versus Vd, and to compare the health-related quality of life of patients receiving each regimen.

Trial Design: Participants in the SVd arm of the study will receive:

- 100 mg selinexor orally (as a tablet) once weekly on days 1, 8, 15, 22, and 29 of each 35-day cycle
- Velcade subcutaneously (as a shot) at a dose of 1.3 mg per square meter of body mass on days 1, 8, 15, and 22 of each 35-day cycle
- 20 mg dexamethasone orally the day of, and the day after, each selinexor dose (i.e., on days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle)

Participants in the Vd arm of the study will receive:

- Velcade subcutaneously (as a shot) at a dose of 1.3 mg per square meter of body mass on days 1, 4, 8, and 11 of each 21-day cycle for the first 8 cycles. For all subsequent cycles starting with cycle 9, Velcade will be given on days 1, 8, 15, and 22 of each 35-day cycle.
- 20 mg dexamethasone orally on days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle for the first 8 cycles. For cycles 9 on, dexamethasone will be given on days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle.

For Velcade-related side effects, the dose may be adjusted according to prescribing information guidelines.

If a patient has peripheral neuropathy, Velcade may be given once-weekly rather than twice-weekly during the first 8 cycles.

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International Myeloma Foundation®

International Myeloma Foundation
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(continued)

Duration of Treatment: Patients will receive treatment until their myeloma progresses or until they are unable to tolerate the regimen. Patients may decide not to participate and withdraw their consent at any time, for any reason. Patients will be followed every 3 months after they discontinue treatment until the end of the study, which is when the last patient treated in the study has been followed for 5 years after their last dose.

Other Medications: All patients will receive medications to reduce nausea during the trial. Other medications may be given as needed to help reduce side effects. Patients may continue to take medications that they need to treat pre-existing diseases like diabetes, high blood pressure, etc. Patients will not be able to take any other anti-cancer therapy or any other experimental agents while they are participating in this trial.

Inclusion Criteria: An eligible myeloma patient must be age 18 or older and must have:

- Confirmed myeloma with measurable disease as defined by at least 1 of the following:
  - Serum M-protein of at least 0.5 grams per deciliter (g/dL)
  - Urinary M-protein excretion of at least 200 mg in 24 hours
  - Serum free light chains of at least 100 milligrams per liter (mg/L), provided that the serum free light chain ratio is abnormal
- At least 1 prior anti-myeloma regimen and no more than 3 prior anti-myeloma regimens (induction therapy followed by stem cell transplant and consolidation/maintenance therapy is considered 1 regimen)
- Documented evidence of progressive myeloma on or after a patient's most recent regimen
- Prior treatment with Velcade or another proteasome inhibitor (Kyprolis® or Ninlaro®) is allowed, provided all of the following criteria are met:
  - best response achieved with prior Velcade at any time was at least a partial response
  - response to the last proteasome inhibitor was at least a PR
  - the participant did not discontinue Velcade due to a serious side effect
  - there must have been at least a 6-month proteasome inhibitor-free interval before the patient receives his or her first study treatment
- Any significant side effects to previous treatments must have been resolved by the time the patient receives his or her first study treatment
- Liver and kidney function must be adequate within 28 days before the patient receives his or her first study treatment
- Blood cell levels must be adequate within 7 days before the patient receives his or her first study treatment

Exclusion Criteria: Patients are excluded who are unwilling or unable to comply with the trial protocol, including providing 24-hour urine samples at the required time points.

Female participants may not be pregnant or breastfeeding.

Patients of either sex may not have:

- Previously received selinexor or another similar drug (i.e., XPO1 inhibitor)
- A prior cancer that required treatment, or that has shown evidence of recurrence (except for non-melanoma skin cancer or adequately treated very early-stage cervical cancer) during the 5 years prior to randomization for this study

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(continued)

- Any concurrent medical condition or disease that is likely to interfere with study procedures (such as uncontrolled active high blood pressure, uncontrolled active diabetes, active systemic infection, etc.)
- Active infection requiring antibiotics, antivirals, or antifungals within 1 week before starting study treatment
- Active plasma cell leukemia
- Documented systemic light chain amyloidosis
- Myeloma involving the central nervous system
- POEMS syndrome
- Spinal cord compression
- Neuropathy that interferes with the tasks of daily living, or neuropathy with any pain
- Inability to tolerate dexamethasone or other glucocorticoid (steroid) drugs
- Any anti-cancer therapy within 2 weeks prior to starting study treatment other than glucocorticoids; patients may have localized radiation to a single site at least 1 week before starting study treatment
- Autologous stem cell transplant less than 1 month prior, or allogeneic transplant less than 4 months prior to starting study treatment
- Active graft-versus-host disease at the time that study treatment is started
- Life expectancy of less than 4 months
- Major surgery within 4 weeks prior to starting study treatment
- Active, unstable heart function
- Known active HIV infection
- Known hepatitis A, B, or C infection
- Active gastrointestinal dysfunction interfering with the patient's ability to swallow tablets or interfering with the absorption of study treatments
- Inability to take or tolerate any of the required drugs or supportive treatments used in the trial

Locations Enrolling Patients and Contact Information:

Choosing to participate in a clinical trial is an important personal decision. Talk with your doctor, family members, and friends about deciding to join a study.

To learn more about this study, you or your doctor may contact the study research staff. Please refer to this study by its **clinicaltrials.gov** identifier, **NCT03110562**.

New sites will be opening in the coming weeks and months. Please check current site status on the **clinicaltrials.gov** website using its identifier, **NCT03110562**.

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