Comparing the Combination of Selinexor-Daratumumab-Velcade-Dexamethasone (Dara-SVD) With the Usual Treatment (Dara-RVD) for High-Risk Newly Diagnosed Multiple Myeloma

Status: RECRUITING

Eligibility Criteria

Age:

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Presence of newly diagnosed (dx) multiple myeloma (MM) as defined by standard International Myeloma working group (IMWG). * Presence of high risk cytogenetics using fluorescent in situ hybridization (FISH) \[del(17p), t(4;14), t(14;16), t(14;20), chromosome 1 abnormalities, MYC translocation, tetrasomies, complex karyotype, high lactate dehydrogenase (LDH), or extramedullary MM. * Patients are allowed to have received one cycle of bortezomib-based doublet or triplet therapy. For instance, if a newly diagnosed patient with MM is in need of urgent therapy, they may be enrolled after having received one cycle of bortezomib, cyclophosphamide, dexamethasone. * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (Karnofsky ≥ 60%). * Absolute neutrophil count ≥ 1,000/mcL (\> 500 if bone marrow \[BM\] clonal plasma cell involvement greater than 50%). * Platelets ≥ 100,000/mcL (\> 50,000 if BM clonal plasma cell involvement greater than 50%). * Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (with the exception of patients with Gilbert's syndrome who have a high baseline bilirubin). * Aspartate aminotransferase (AST)(serum glutamic oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT)(serum glutamate pyruvate transaminase \[SGPT\]) ≤ 3 × institutional ULN. * Glomerular filtration rate (GFR) ≥ 30 mL/min. * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. * For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. * Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load. * Patients with treated brain involvement are eligible if follow-up brain imaging performed within 10 days after central nervous system (CNS)-directed therapy shows no. * Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. * Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better. * The effects of selinexor (KPT-330) on the developing human fetus are unknown. For this reason and because selective nuclear export inhibitors as well as other therapeutic agents used in this trial are known to be teratogenic, women of child-bearing potential and men with partners of women of childbearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men (with partners of women of childbearing potential) treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 4 months after completion of study treatment administration. Adequate contraception should continue for 7 months for females and for 4 months for males after completion of the study treatment. * Female of childbearing potential (FCBP) must have a negative pregnancy test during screening. They must either commit to continue abstinence from heterosexual intercourse or begin TWO acceptable methods of birth control, one highly effective method and one additional effective method AT THE SAME TIME, at least 4 weeks before therapy, while taking lenalidomide, during dose interruptions, and for 7 months after study treatment. If menstrual cycles are irregular, the pregnancy testing should occur every 2 weeks. Pregnancy testing and counseling should be performed if a patient misses her period or if there is any abnormality in her menstrual bleeding. Lenalidomide treatment must be discontinued during this evaluation. * Men who are sexually active with FCBP must agree to use a latex or synthetic condom while taking lenalidomide, during dose interruptions and for up to 4 weeks after discontinuing lenalidomide, even if they have undergone a successful vasectomy. Male patients taking lenalidomide must abstain from donating blood, semen, or sperm during study participation and for at least 4 weeks after discontinuation from lenalidomide. * Patients who are randomized to receive lenalidomide need to register into the mandatory Risk Evaluation and Mitigation Strategies (REMS) program and be willing and able to comply with the requirements of REMS. * Ability to understand and the willingness to sign a written informed consent document. Legally authorized representatives may sign and give informed consent on behalf of study participants.

Exclusion Criteria:

* Patients who are in urgent need for MM therapy (such as in the setting of acute kidney injury, or high disease burden concerning for impending organ failure) may begin study treatment immediately after receiving one cycle of bortezomib combination (e.g. bortezomib-dexamethasone or cyclophosphamide-bortezomib-dexamethasone) or one course of pulse dose dexamethasone 20-40mg once daily for four days. No washout period is required. * Patients who have not recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities \> grade 1) with the exception of alopecia. * Patients who are receiving any other investigational agents. * History of allergic reactions attributed to compounds of similar chemical or biologic composition to selinexor (KPT-330) or other agents used in study. * Concomitant medications: Supportive care therapies such as bone directed therapies (zoledronic acid, denosumab), intravenous immunoglobulin therapy (IVIG) and anti-viral agents are allowed and recommended as per standard of care (SOC). Strong CYP3A4 inhibitors and strong CYP3A4 inducers are prohibited, due to their respective increase or decrease in bortezomib exposure. If strong CYP3A4 inhibitors cannot be avoided, then patients will be monitored for signs of bortezomib toxicity and a dose reduction of bortezomib will be considered. * Patients with uncontrolled intercurrent illness or any other significant condition(s) that would make participation in this protocol unreasonably hazardous. * Pregnant women are excluded because this study involves an investigational drug that may cause genotoxic, teratogenic, and mutagenic effects on the developing fetus and newborn and drugs that have known genotoxic, teratogenic, or abortifacient effect. * Because there is potential risk for adverse events in nursing infants secondary to treatment of the mother with the drugs used in this study, breastfeeding is not allowed during treatment for all drugs and for 2 months after last dose of bortezomib and 1 week after the last dose of selinexor.

Conditions & Interventions

Interventions:

PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, DRUG: Bortezomib, PROCEDURE: Computed Tomography, DRUG: Daratumumab and Recombinant Human Hyaluronidase, DRUG: Dexamethasone, DRUG: Lenalidomide, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Positron Emission Tomography, DRUG: Selinexor

Conditions:

Multiple Myeloma

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

Phase: PHASE2

IRB Number:
System ID: NCT06169215

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