Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

EAA171 - Optimizing Prolonged Treatment In Myeloma Using MRD Assessment (OPTIMUM)

Eligibility criteria

Step 0 Pre-Registration

1. Patient must be ≥ 18 years of age
2. Patient must be previously diagnosed with multiple myeloma (MM) and be on lenalidomide maintenance with ≥ 10mg daily dose (≥5 mg for patients with creatinine clearance 30-60 mL/min) for at least 10 months and no more than 15 months after an early autologous stem cell transplantation (SCT ≤ 12 months of diagnosis). Patient must not be off lenalidomide maintenance therapy for more than 30 days prior to start of treatment on Step 1 of this protocol.
3. Patient must be able to undergo a diagnostic bone marrow aspirate following pre-registration to Step 0.
    a. NOTE: A bone marrow aspirate specimen must be submitted to Mayo Clinic Hematology Laboratory for central assessment of Minimal Residual Disease (MRD) status to confirm patient's eligibility for Step 1 randomization. Mayo Clinic will forward results to the submitting institution within three (3) business days of receipt of the bone marrow specimen.
4. Patient must have an ECOG performance status 0, 1, or 2.
5. Patient must not have primary refractory or progressive disease on a proteasome inhibitor-based regimen during induction therapy prior to stem cell transplant.
6. Patient must not be on other concurrent chemotherapy, or any ancillary therapy considered investigational.
    a. NOTE: Bisphosphonates are considered to be supportive care rather than therapy and are allowed while on protocol treatment.
7. Patient must not have uncontrolled psychiatric illness or social situations that would limit compliance with study requirements.
8. Patient must not have another malignancy requiring treatment or have received treatment within 2 years before pre-registration or previously diagnosed with another malignancy and have any evidence of residual disease. Patients with non-melanoma skin cancer or carcinoma in situ of any type are not excluded if they have undergone complete resection.
9. Patient must have been able to maintain at least 10 mg dose of lenalidomide without growth factor support (at least 5 mg for patients with creatinine clearance 30-60 mL/min).
10. Patient must not have known gastrointestinal (GI) disease or GI procedure that could interfere with the oral absorption or tolerance of ixazomib or lenalidomide including difficulty swallowing
11. Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.
12. Patient must not have known hepatitis B surface antigen-positive status or known or suspected active hepatitis C infection, but testing specifically for the trial is not required.

Step 1 Randomization

1. Patient must meet all eligibility criteria in Section 3.1 at the time of Step 1 randomization.
2. Patient must not be off lenalidomide maintenance therapy for more than 30 days prior to start of treatment on Step 1 of this protocol.
3. Patient must have evidence of residual disease by central MRD testing or by presence of monoclonal protein in serum or urine.
4. Patient must have SPEP, UPEP, and serum FLC performed ≤ 28 days prior to randomization. Serum M-protein by SPEP _____ (g/dL) Date of Test: _____
5. Urine M-protein light chain excretion by UPEP_____ (mg/24hr) Date of Test: _____
    a. NOTE: UPEP (on a 24-hour collection) is required, no substitute method is acceptable. Urine must be followed monthly if the baseline urine M-spike is ≥ 200 mg/24 hr. Please note that if both serum and urine M-components are present, both must be followed in order to evaluate response

    Serum Free Light Chain
    Kappa FLC _____ (mg/dL) or _____ (mg/L);
    Lambda FLC _____ (mg/dL) or _____ (mg/L);
    Kappa/lambda ratio _____ Date of Test: _____
6. Patient must have the following laboratory levels obtained ≤ 14 days prior to randomization:
    a. Hemoglobin ≥ 8 g/dL Hemoglobin:_____ Date:_____
    b. Un-transfused platelet count ≥ 75,000 cells/mm3 Platelet:_____ Date:_____
    c. Absolute neutrophil count (ANC) ≥ 1000 cells/mm3 ANC:_____ Date:_____
    d. Calculated creatinine clearance ≥ 30 mL/min Creatinine clearance:_____ Date:_____
    e. Total bilirubin ≤ 1.5 times the upper limit of normal (ULN) Total bilirubin:_____ ULN:_____ Date:_____
    f. SGPT (ALT) and SGOT (AST) ≤ 3 times the upper limit of normal (ULN) SGPT (ALT):_____ ULN:_____ Date:_____ SGOT (AST):_____ ULN:_____ Date:_____
7. Patient must not have Grade 2 or higher peripheral neuropathy or grade 1 peripheral neuropathy with pain per CTCAE.
8. Patient must not have uncontrolled intercurrent illness.
9. Patient must not have Grade 2 or higher diarrhea per CTCAE in the absence of antidiarrheals.
10. Patient must not have been on systemic treatment, within 14 days before the first dose of ixazomib, with strong CYP3A inducers (such as rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of St. John's wort.
11. Patient must agree to register into the mandatory Revlimid REMS® program and be willing and able to comply with the requirements of Revlimid REMS®. Refer to Section 8.2.8 of the protocol for more information on the Revlimid REMS® Program.
12. Patient must not be pregnant due to potential harm to the fetus from ixazomib and lenalidomide. All patients of childbearing potential must have a blood test or urine study with a sensitivity of at least 25 mIU/mL within 10-14 days prior to the first dose of lenalidomide and again within 24 hours prior to the first dose of lenalidomide. Patients of childbearing potential must also agree to ongoing pregnancy testing while on treatment. A patient of childbearing potential is defined as anyone, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy, or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding

24 consecutive months). Please see Appendix VI: Risks of Fetal Exposure, Pregnancy Testing Guidelines and Acceptable Birth Control Methods.
Patient of childbearing potential (Y/N)? _____
Date of blood test or urine study: _____
Result (positive/negative): _____

13. Patients of childbearing potential must either abstain from sexual intercourse for the duration of their participation in the study or agree to use TWO acceptable methods of birth control, one highly effective method and one additional effective method AT THE SAME TIME for 1) at least 28 days before starting study treatment; 2) while participating in the study; 3) during dose interruptions; and 4) for at least 90 days after the last dose of protocol treatment. Patients must also agree to not breastfeed during this same time period. Men must agree to either abstain from sexual intercourse for the duration of their participation in the study or use a latex condom during sexual contact with a partner of childbearing potential while participating in the study and for 90 days after the last dose of protocol treatment even if they have had a successful vasectomy. Patients must also agree to abstain from donating sperm while on study treatment and for 28 days after the last dose of protocol treatment even if they have had a successful vasectomy. All patients must agree to abstain from donating blood during study participation and for at least 28 days after the last dose of protocol treatment.

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