NCI National Clinical Trials Network

EAA241

ECOG-ACRIN cancer research group

Please Enroll Your Eligible Patients!

For Patients with Newly Diagnosed Multiple Myeloma

EAA241 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase II Trial Comparing Daratumumab-Bortezomib-Dexamethasone vs Cyclophosphamide-Bortezomib-Dexamethasone in Newly Diagnosed Multiple Myeloma with Light Chain Cast Nephropathy (LCCN)

Patient Population

See protocol Section 3 for complete eligibility criteria

- Age ≥ 18 years, ECOG PS 0-2 (or 3, if attributable to pathological fractures and/or cancer-related bone pain), adequate lab values
- Newly diagnosed with multiple myeloma (MM) ≤ 90 days prior to randomization, with original MM diagnosis meeting BOTH of these IMWG criteria:
  - ◊ Bone marrow plasmacytosis with ≥ 10% plasma cells/ sheets of plasma cells or biopsy-proven plasmacyto-ma
  - ◊ ≥ 1 myeloma-defining events per criterion 3.1.3.2 (smoldering myeloma and MGUS not eligible)
- Newly diagnosed (≤ 90 days) light chain cast neuropathy (LCCN) per criterion 3.1.4
- Must have new onset of renal failure (≤ 90 days), and one of the following criteria:
  - ◊ Any serum creatinine with eGFR < 40 mL/ min/1.73m² (calculated with MDRD formula)
  - ◊ Serum creatinine > 2 mg/dL (with eGFR < 50 mL/ min/1.73m²)
  - ◊ On dialysis (with eGFR < 50 mL/min/1.73m²)
- May have received up to one cycle of myeloma-targeting therapy (including cyclophosphamide, bortezomib and/or dexamethasone) ≤ 30 days prior to randomization (no washout period required)
- May have received plasma exchange to treat LCCN ≤ 30 days prior to randomization
- No prior or current exposure to anti-CD38 monoclonal antibodies; no prior or current focal RT ≤ 14 days prior to randomization, except palliative RT per criterion 3.1.10
- Patients with history of respiratory disease within the past 2 years are eligible per criterion 3.1.17 (current uncon-trolled asthma of any classification is not eligible)
- Patients with known history or current symptoms of cardi-ac disease, or history of treatment with cardiotoxic agents, must be NYHA Class II or better
- No grade 3 or 4 peripheral neuropathy, AL amyloidosis (amyloid light chain or primary amyloidosis), plasma cell leukemia, or CNS involvement

Treatment Plan

See protocol Section 5 for complete treatment details

Cycle = 28 days

For patients on dialysis, if treatment day coincides with dialysis day, protocol treatment should be administered after dialysis is completed. If a patient receives myeloma -targeting therapy prior to randomization, they will still receive all 4 cycles of treatment on EAA241

Arm A: Cyclophosphamide-Bortezomib-Dex

- Cyclophosphamide 300 mg/m² PO or IV (dose may be rounded to available oral capsule or tablet size)
  - ◊ Days 1, 8, 15, and 22 for Cycles 1-4
- Bortezomib 1.5 mg/m² SQ
  - ◊ Days 1, 8, 15, and 22 for Cycles 1-4
- Dexamethasone 40 mg PO or IV
  - ◊ Days 1-4, 8, 15, and 22 for Cycle 1
  - ◊ Days 1, 8, 15, and 22 for Cycles 2-4

Arm B: Daratumumab-Bortezomib-Dex

- See Section 5.1.2 for pre– and post-medications
- Daratumumab-hyaluronidase 1800 mg/30,000 units SQ (do not administer via IV)
  - ◊ Days 1, 8, 15, and 22 for Cycles 1 and 2
  - ◊ Days 1 and 15 for Cycle 3 and 4
- Bortezomib 1.5 mg/m² SQ (do not administer in same injection site as daratumumab-hyaluronidase)
  - ◊ Days 1, 8, 15, and 22 for Cycles 1-4
- Dexamethasone 40 mg PO or IV (administer be-fore bortezomib and daratumumab-hyaluronidase)
  - ◊ Days 1-4, 8, 15, and 22 for Cycle 1
  - ◊ Days 1, 8, 15, and 22 for Cycles 2-4

After 4 cycles of protocol treatment, any/all further treatment (including transplant) is at investigator discre-tion. Patients with disease response of partial response or better, per IMWG myeloma response definitions, may proceed to ASCT if eligible

Study Chair:
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Study Co-Chair:
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Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

v.06/25/25

EA241

Schema

Key Eligibility:

- Newly diagnosed (within the last 90 days) light chain cast nephropathy (LCCN) defined as patients with >1g/dl proteinuria with <10% albuminuria, and/or an involved serum FLC concentration >150mg/dL
- New onset of renal failure (within the last 90 days) defined as either any serum creatinine with an eGFR[1] of < 40 ml/min/ 1.73 m^2 or a serum creatinine > 2 mg/dL and/or are on dialysis.
- No prior exposure to or currently be on any anti-CD38 monoclonal antibodies
- Patients with newly diagnosed myeloma per IMWG guidelines
- Adult patients (≥ 18 years old)
- ECOG Performance Status 0-2

Stratification Factor:

- Severity of Renal Impairment: severe (eGFR[1] ≤ 29 mL/min/ 1.73 m^2 or if patient requires hemodialysis) vs non-severe (eGFR[1] > 29 mL/min/1.73 m^2)

RANDOMIZATION

Arm A
Cyclophosphamide-Bortezomib-Dexamethasone for 4 cycles[2,3]

Arm B
Daratumumab-Bortezomib-Dexamethasone for 4 cycles[2,3]

Randomization = 1:1
N = 74

1. eGFR to be calculated with the Modification of Diet Renal Disease (MDRD) formula. See Section 3.1.5 for additional details.
2. Please refer to Section 5.1 for details regarding dosing.
3. Patients will be evaluated after 4 cycles of protocol therapy, at which time any and all further treatment – including transplant – is at the investigator's discretion.
   NOTE: Patients who have achieved a disease response per IMWG myeloma response definitions (see Section 6.2) of partial response (PR) or better may elect to proceed to ASCT if eligible.