

## SYNOPSIS 07-REV

### Evaluation of Lenalidomide as Maintenance Therapy after Allogeneic Hematopoietic Stem Cell Transplantation for High Risk Multiple Myeloma

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**Study Design:** This is a multi-institution, non-randomized, open label, Phase IIa prospective trial to evaluate the safety and tolerability of maintenance lenalidomide after allogeneic hematopoietic stem cell transplantation (HCT).

**Primary Objective:** To determine tolerability and safety profile of a maximum of 12 cycles or 12 months from first dose (which ever comes first) of lenalidomide maintenance therapy post allogeneic hematopoietic cell transplantation for high risk multiple myeloma

**Secondary Objectives:** To estimate the incidences of  $\geq$ grade 3 adverse events, graft failure, infections, treatment-related mortality (TRM) and incidence and severity of acute and chronic GVHD after initiation of lenalidomide. To measure the overall response and best response rates to lenalidomide maintenance therapy following allogeneic HCT. To determine time to disease progression and overall survival after lenalidomide.

**Eligibility Criteria:** Patients age 18 to 70 years with chemosensitive, high risk multiple myeloma who underwent an allogeneic HCT with reduced intensity conditioning (Flu/Mel, Flu/BU, Flu/TBI  $\pm$  cyclophosphamide), GVHD prophylaxis of a calcineurin inhibitor in combination with; methotrexate, micophenolate mofetil (MMF) or sirolimus, no active grades III-IV GVHD, with ANC  $\geq$  1,500/ $\mu$ L and platelets  $\geq$  75,000/ $\mu$ L, Hemoglobin  $>$ 8.0g/dL, creatinine clearance  $>$  50ml/min (creatinine  $\leq$  2.5 mg/dL), total bilirubin  $\leq$  2.0 mg/dL and serum transaminases  $<$  3x upper limit of normal will be eligible to initiate lenalidomide.

**Treatment Description:** Lenalidomide maintenance therapy will start within 60 to 90 days after allogeneic HCT at a starting dose of 10mg PO once daily. Dose escalation and de-escalation are performed depending on tolerability of lenalidomide. The dose range is 5mg every other day and 5 to 25 mg daily from days 1-21 followed by 7 days of rest for 12 cycles (each cycle 28 days).

**Accrual:** The sample size for this study is 30 patients. The accrual period will be 2 years.

**Study Duration:**

Patients will be followed from initiation of lenalidomide maintenance therapy to 30 days after completion of 12 cycles of therapy or 12 months from first dose of study drug (which ever comes first); or discontinuation of therapy.

## Outline of Treatment Plan

### Allogeneic HCT for High Risk Multiple Myeloma:

- Allogeneic HCT as primary therapy or after failed autologous HCT or other therapies ;
- Therapy-sensitive MM (at time of staging pre allogeneic HCT) defined as at least a partial response to immediate pretransplant therapy. (International Uniform Criteria)
- High risk as defined:
  - Del(13), Hypodiploidy, t(4;14), t(14;16) or del(17p)
  - Plasmablastic morphology (> 2%)
  - Elevated  $\beta_2$ -microglobulin ( $\geq 5.5$  mg/L)

**Reduced Intensity Conditioning Regimens:** With one of the following regimens:

- Fludarabine (Flu)/ Melphalan ( $\leq 140$  mg/m<sup>2</sup>),
- Flu /Total Body Irradiation (TBI)  $\pm$  cyclophosphamide (TBI dose < 500 cGy single dose, or < 800 cGy fractionated dose)
- Flu/ Busulfan ( $\leq 8$ mg/kg)

and

### GVHD Prophylaxis:

Calcineurin inhibitors in combination with methotrexate, mycophenolate mofetil (MMF) or sirolimus.

### Eligibility Assessment:

- Age 18 to 70 years
- ANC  $\geq 1,500/\mu\text{L}$  AND platelets  $\geq 75,000/\mu\text{L}$
- No active acute GVHD except Stage I/II skin/ Stage I upper GI (see 2.3.1-16)
- Creatinine clearance  $>50$ ml/min and Cr  $\leq 2.5$  mg/dL
- Hgb  $>8.0$  g/dL
- Total bilirubins  $<2.0$ mg/dL, serum transaminases  $<3$ x ULN
- 50% donor chimerism

### Study Enrollment

### Day 60 to 90 post HCT:

- Initiate Lenalidomide at 10mg.
- Dose given daily for days 1 through 21, followed by 7 days of rest in each 28 day cycle

### Scheduled Evaluations for Toxicity Response:

Done weekly for cycles 1-4 then monthly cycles 5-12 and then 28 days after completion of the 12th cycle of therapy or 12 months from first dose of study drug (which ever comes first) or discontinuation of therapy.