Background

Thalidomide and its immunomodulatory derivatives (IMiDs) such as lenalidomide have shown great promise as a treatment option for multiple myeloma (MM) patients. However, Dexamethasone at a very high dose is often chosen as an effective treatment option for refractory (R/R) MM patients. Dexamethasone reduces anti-angiogenic effects as thalidomide but modestly improves anti-tumor and immunomodulatory activities. Recent data has shown promising tolerability to be effective in combination with lenalidomide, even for patients refractory to lenalidomide and bortezomib.

Other data shows that progressive trilocal disease (PLD) is effective in combination with lenalidomide.

Finally, our recent trial has shown that the efficacy and tolerability of regimens combining bortezomib and lenalidomide is feasible in relapsed MM (R/R-MM) patients. These data directly point to the preferential condition of combination therapy with Dexamethasone and PLD using a modified dosing schedule as a potentially effective treatment option for R/R-MM patients.

Purpose

We investigated the safety and efficacy of the combination of pomalidomide with dexamethasone and PLD using a modified dosing schedule for patients with progressive myeloma.

Design

Phase 1/2 multi-center, open-label, single-arm study

Pharmacokinetics: 12 patients

Phase 1: Eligible Patients

Phase 1/2 multi-center, open-label, single-arm study

Phase 2: Eligible Patients

Eligible Patients

Phase 1/2 multi-center, open-label, single-arm study

a modified dosing schedule as a potentially effective treatment option for R/R-MM patients

Finally, our recent trial has shown that the efficacy and tolerability of regimens combining bortezomib and lenalidomide is feasible in relapsed MM (R/R-MM) patients.

Table 1. Dosing Regimes By Phase & Cohort

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>End</td>
<td>D1</td>
<td>D2-D21</td>
</tr>
<tr>
<td>Cohort 1</td>
<td>7 mg</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>11 mg</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>15 mg</td>
<td>0</td>
<td>48</td>
</tr>
</tbody>
</table>

MTD & AEs

MTD was determined as the maximum administered dose (MAD) with no more than 1 class-limiting toxicity. (DLT defined in the following occurring during Cycle 1: G4 neutropenia or thrombocytopenia leading to treatment delay >7 days, fever, severe organ toxicity, fever, severe organ toxicity, death, or severe non-hematological toxicity (except infection).)

Dose Modifications

Early data from this Phase 1/2 trial suggests that the combination of pomalidomide, Dexamethasone and PLD is feasible and is associated with a manageable toxicity profile, thus indicating a need to evaluate its potential as the standard therapy in patients progressing on R/R-MM therapies.