CLR 131 Demonstrates High Rate of Activity in a Phase 1, Dose Escalation Study in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

Longcor J1, Ailawadhi S2, Oliver K3, Callander NS3, Stiff P4

1Cellectar Biosciences; 2Mayo Clinic Florida; 3 University of Wisconsin Carbone Cancer Center; 4 Loyola University Cardinal Bernardin Cancer Center

BACKGROUND

CLR 131 is a novel targeted radionuclide therapy that exploits the selective uptake and retention of phospholipid ethers by tumor cells. Based on preclinical and clinical experience and the radiosensitivity of MM, CLR 131 is being examined in a RRMM Phase 1 open-label, dose escalation trial (NCT02278315). Escalating single doses of CLR 131 from 12.5-31.25 mCi/m² were evaluated, along with fractionated doses 31.25-40 mCi/m².

STUDY DESIGN

Open label, dose escalation (minimally modified 3+3 scheme) Phase 1 trial.
- Primary objective: determine safety and tolerability of CLR 131 as single or fractionated dose.
- Secondary objectives:
  - Determine the recommended Phase 2 dose (RP2D) and schedule
  - Determine therapeutic activity in RRMM

Key eligibility criteria:
- Progressive RRMM
- At least one previous exposure to PI and IMiD drugs.
- Prior ASCT and external beam radiation therapy are allowed.
- No limit to the number of prior therapies.

In this cohort, 37.5 mCi/m² CLR 131 fractionated as 2, 30 min IV infusions (18.75 mCi/m² each) on day 1 and 7 (±1 day) with dose (40 mg) PO weekly x12 weeks. Dose-limiting toxicities (DLTs) are assessed through day 85 post-infusion.

TEAEs Grade 3/4 (>25% of patients)

<table>
<thead>
<tr>
<th>SOC</th>
<th>Preferred Term</th>
<th>Grade ≥ 3 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Anaemia</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Neutropenia</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Thrombocytopenia</td>
<td>4 (100)</td>
</tr>
</tbody>
</table>

RESULTS

Data on 4 subjects enrolled to cohort 6 (37.5 mCi/m² fractionated CLR 131) is presented here. Five subjects were enrolled, but 1 subject received only 1 of 2 doses due to disease progression. Median age for cohort 6 was 66 years (range 59-83) and included 2 males and 2 females. The majority of subjects (3/4) were high risk by cytogenetics, median bone marrow plasma cell involvement was 25% (range 10-60%). Number of prior therapies averaged 4 (range 3-6). 50% of subjects had prior ASCT and none had prior radiation therapy. One subject was dual class refractory, 1 was quad-refractory and 2 were penta-refractory, including being refractory to daratumumab.

The overall response rate for cohort 6 was 50% - 2 subjects achieved a partial response (PR), the other 2 subjects achieved a minimal response (MR). One subject with a PR experienced a 61% reduction in κ FLC and the other a 68% reduction in λ FLC; 1 subject with an MR had a 39.1% reduction and the other a 48% reduction in m-protein.

CONCLUSIONS

- CLR 131 well tolerated at 37.5 mCi/m² fractionated dose
- CLR131 provides targeted systemic delivery of radiation to the tumor cells, including in the bone marrow
- 50% response rate and 100% disease control
- Good response in high risk patients
- CLR 131 has activity in chemotherapy-refractory MM, and in this setting radiation has a role for effectively controlling local disease
- This dose of CLR 131 is being further evaluated in a larger population in a Phase 2 trial.