#903

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

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BACKGROUND

CLR 131 is a novel targeted radiotherapeutic 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 mC/m^2 were evaluated, along with fractionated doses 31.25-40 mCi/m^2.

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/m^2 CLR 131 fractionated as 2, 30 min IV infusions (18.75 mCi/m^2 each) on day 1 and 7 (± 1 day) with lose dose (40 mg) dex PO weekly x12 weeks.

Dose-limiting toxicities (DLTs) are assessed through day 85 post-infusion.

DEMOGRAPHICS

Demographics (n = 4)			
Median (range) age, y	72.5 (59-83)	Renal function (CrCl), n (%)	
Age ≥ 75, n (%)	2 (50)	≥ 60 mL/min	2 (50)
		< 60 mL/min	2 (50)
ISS staging, n (%)		ECOG score, n (%)	
I	2 (50)	0	3 (75)
II	2 (50)	1	1 (25)
III	0	2	0
Median (range) time since diagnosis, y	3.7 (1.1-5.4)	High risk cytogenetics, n (%)	2 (50)
Del p53, n (%)	1 (25)	T (14; 16), n (%)	1 (25)
		T (14; 20), n (%)	1 (25)
Refractory, n (%)			
quad-refractory	1 (25)	REV	4 (100)
penta-refractory	2 (50)	POM	2 (50)
		DARA	2 (50)
		CARF	1 (25)
		BORT	1 (25)
		IXAZ	1 (25)

Prior Therapies

Prior therapies (n = 4)	
Median (range) number of prior therapies	4 (4-6)
Prior chemotherapy, n (%)	
Alkylating agents	4 (100)
Anthracyclines	0
Prior ASCT, n (%)	2 (50)
> 3 lines of prior therapy, n (%)	4 (100)
Prior IMiD, n (%)	
LEN	4 (100)
POM	2 (50)
THAL	0
Prior PI, n (%)	
BORT	3 (75)
CARF	1 (25)
IXAZ	2 (50)
Prior DARA, n (%)	2 (50)

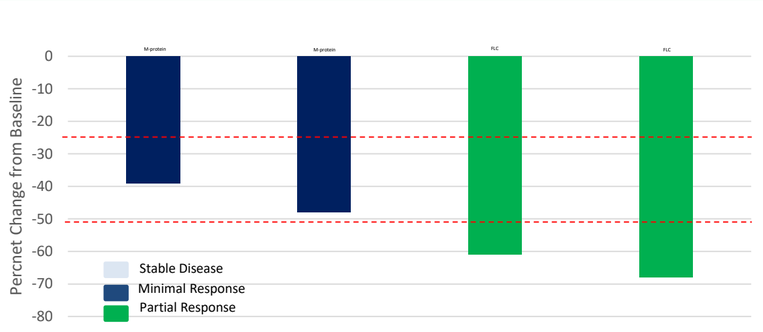
TEAEs Grade 3/4 (>25% of patients)

SOC	Preferred Term	Grade ≥ 3 n (%)
Blood and lymphatic system disorders	Anaemia	2 (50)
Blood and lymphatic system disorders	Neutropenia	2 (50)
Blood and lymphatic system disorders	Thrombocytopenia	4 (100)

Patient Safety

- No unexpected Adverse Events (AEs)
- Most common AEs Grade 1 and 2
- No DLTs observed at this dose

Best Percent Change from Baseline



RESULTS

Data on 4 subjects enrolled to cohort 6 (37.5 mCi/m^2 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. Both subjects with a PR and 1 subject with an MR were high risk by cytogenetics. CLR 131 has been well tolerated. There have been no reported deep vein thrombosis, pulmonary embolisms and no treatment emergent deaths. Grade 3-4 treatment emergent AEs occurring in over 25% of subjects have been neutropenia (50%), anemia (75%) and thrombocytopenia (100%); with an average 2 weeks to recovery from nadir. Fatigue (grade 1-2) and ECG changes (grade 1) have also been noted. Three subjects entered with anemia and 1 also had leukopenia. As no DLTs were seen, dose escalation continues.

CONCLUSIONS

- CLR 131 well tolerated at 37.5 mCi/m^2 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.