#1652

CLR 131 (Iopofosine I-131) Treatment in Triple Class Refractory and Beyond Multiple Myeloma Patients: Preliminary Efficacy and Safety Results from the Phase 2 CLOVER-1 Trial

Sikander Ailawadhi, MD[1], Patrick Stiff, MD[2], Emad Ibrahim, MBBCh, MD[3], Damian J. Green, MD[4], Brea Lipe, MD[5], Elizabeth H. Cull, MD[6], Natalie S. Callander, MD[7], John Friend, MD[8], Jarrod Longcor[8]* and Kate Oliver, BS[8]*

[1]Division of Hematology, Mayo Clinic, Jacksonville, FL, [2]Loyola University Medical Center, Cardinal Bernardin Cancer Center, Maywood, IL, [3]Redlands Community Hospital, Redlands, CA, [4]Fred Hutchinson Cancer Research Center, Seattle, WA, [5]Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, [6]Cancer Institute, Prisma Health, Piedmont, SC7, [7]University of Wisconsin, Madison, WI, [8]Cellectar Biosciences, Florham Park, NJ

BACKGROUND

Phospholipid ethers (PLE) provide a novel mechanism to target tumor cells. Tumor cells contain increased amounts of lipid rafts in their cell membranes, which are thought to enhance signaling and resist apoptosis. Phospholipid drug conjugates (PDC) are specifically designed to have high affinity for lipid rafts which upon binding results in trans-membrane inversion with the ability to deliver an attached therapeutic directly to the cytosol. Iopofosine I-131 (formerly identified as CLR 131) is a novel PDC delivering I-131 as a targeted tumor cell radiotherapy. Iopofosine I-131 is being examined in relapsed or refractory multiple myeloma (RRMM) patients through an open-label, Phase 2 trial, CLOVER-1 (NCT02952508).

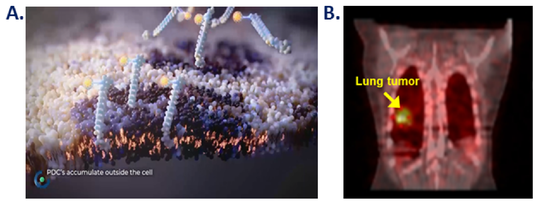


Figure 1: A. Schematic showing iopofosine I-131 binding to lipid raft B. NSCLC SPECT scan showing iopofosine I-131 uptake.

STUDY OVERVIEW

Primary objective:
To determine the safety and efficacy of iopofosine I-131 in heavily pretreated multiple myeloma patients.

Eligibility criteria for MM patients include:
Progression or relapsed disease that is refractory[1] to at least 1 proteasome inhibitor and 1 immunomodulatory agent unless intolerable/ineligible to receive such agents with no upper limit to the number of prior lines of therapy.

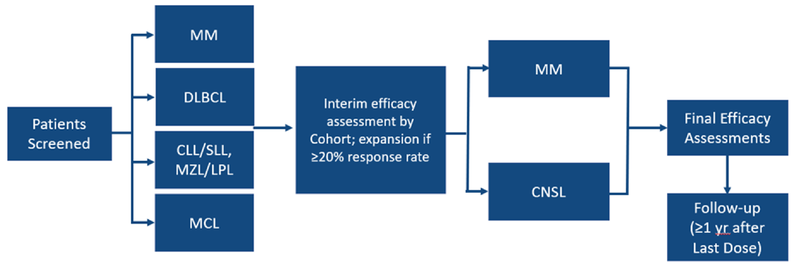
Administration:
Iopofosine I-131 is administered in up to 4 IV infusions (15-20 min) over 3 months, with doses given over 2 cycles on Day 1 and 15 of each cycle, along with dexamethasone 40 mg weekly (20 mg in patients > 75), for up to 12 weeks.

Additional information about the CLOVER-1 study can be found at https://clinicaltrials.gov/ct2/show/NCT02952508

[1]Refractory is defined as no response to treatment (response is defined as partial response or better) OR progressive disease while on therapy OR progressive disease ≤ 90 days post end of prior therapy OR initiation of new therapy within 90 days of last therapy.

CLOVER-1 Phase 2 Study Design

Figure 2: CLOVER-1 is a two-part, non-randomized open-label, multi-center study evaluating the effects of iopofosine I-131 in patients with B-cell malignancies who have failed standard of care treatment for their underlying malignancy. Part A of the study is a phase 2, dose finding clinical study evaluating iopofosine I-131 in patients with B-cell malignancies including MM and various NHL subsets primarily; WM, DLBCL, CLL, MZL and MCL. The primary efficacy endpoint is clinical benefit rate. Secondary endpoints include ORR, PFS, OS, among others.



[1]Previously open cohorts closed to recruitment include CLL/SLL, MZL, MCL, DLBCL
[2]Additional cohort of LPL/WM has been expanded to pivotal Phase 2b (CLOVER-WaM)

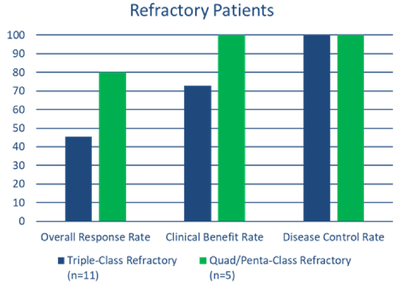
RESULTS

Table 1: Patient demographics

Criteria	Patients with Total Body Dose ≥60mCi (n=11)
Median Age (Min-Max)	72 (34-77)
Male (%)	100
Median Prior Regimens (Min-Max)	7.2 (3-17)
Number of patients with prior ASCT	8
Mean Total Body Dose (range)	75.4mCi (59.7-118.7)
Patient Class Refractory Category	
Triple-class refractory (n)	7
Quad/Penta-class refractory (n)	4
Patient Categorized as High Risk at Diagnosis	
High Risk Cytogenetics [n/N] (%)	4/11 (36.4)
High Risk FISH* [n/N] (%)	5/10* (50)

*FISH results not available for 1 patient

Figure 3: Patient Response



PATIENT RESPONSE

Figure 4: Maximum Reduction of Marker of Response in Patients Treated with Iopofosine I-131

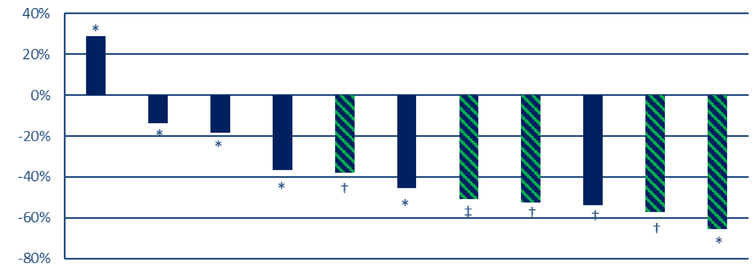


Figure 4: The maximum reduction in serum M protein (*), FLC Kappa/Lambda (†), or lesion size (‡) from baseline for refractory multiple myeloma patients treated with iopofosine I-131.

ADVERSE EVENTS

The primary treatment emergent AEs in patients with MM included cytopenias (87.5%), in line with prior experience with iopofosine I-131. The most commonly observed cytopenias included Grade 3 or 4 thrombocytopenia (62.5%), anemia (62.5%), neutropenia (62.5%) and decreased white blood cell count (50%). There were no infusion-related reactions or AEs.

CONCLUSIONS

- Initial results for iopofosine I-131 show efficacy with a promising ORR of 45.5% and a CBR or 72.7% in heavily pretreated triple class refractory multiple myeloma patients.
- Iopofosine I-131 showed its highest efficacy in patients that were quad/penta drug refractory with ORR of 80%, highlighting its potential as a later line therapy.
- Iopofosine I-131 is a novel cancer radiotherapeutic that may provide benefit to patients that are refractory/unresponsive to traditional MM therapies.
- CLOVER-1 is actively enrolling MM patients that are at least triple class refractory across the United States.

Funding and Disclosures

This research was funded by Cellectar Biosciences (Florham Park, NJ) and SBIR grant HHSN261201500071C. Disclosures: Ailawadhi: AbbVie: Consultancy; Pharmacyclics: Consultancy, Research Funding; Ascentage: Research Funding; Cellectar: Research Funding; GSK: Consultancy, Research Funding; Genentech: Consultancy; BMS: Consultancy, Research Funding; Karyopharm: Consultancy; Sanofi: Consultancy; Medimmune: Research Funding; Janssen: Consultancy, Research Funding; Amgen: Consultancy, Research Funding; Xencor: Research Funding; Takeda: Consultancy; Beigene: Consultancy. Stiff: CRISPR: Consultancy; Gamida-Cell, Atara, Amgen, Incyte, Takeda, Macrogenetics, Eisai: Research Funding; Cellectar: Research Funding. Green: Seagen Inc.: Research Funding; bristol myers squibb: Membership on an entity's Board of Directors or advisory committees, Patents & Royalties, Research Funding; Cellectar Biosciences: Research Funding; GSK: Membership on an entity's Board of Directors or advisory committees; Janssen Biotech: Membership on an entity's Board of Directors or advisory committees, Research Funding; Juno Therapeutics: Patents & Royalties, Research Funding; Legend Biotech: Consultancy; Neoleukin Therapeutics: Membership on an entity's Board of Directors or advisory committees; Seattle Genetics: Membership on an entity's Board of Directors or advisory committees, Research Funding; SpringWorks Therapeutics: Research Funding. Lipe: Seagen Inc.: Research Funding; BMS: Consultancy, Research Funding; Janssen: Consultancy, Research Funding; sanofi: Consultancy; GlaxoSmithKline: Consultancy; amgen: Research Funding; Cellectar: Research Funding; Karyopharm: Research Funding; Harpoon: Research Funding. Cull: Aptevo: Research Funding. Friend: Cellectar: Former Employment. Longcor: Cellectar: Current Employment. Oliver: Cellectar: Current Employment.