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USING TARGETED RADIOTHERAPY IN HIGHLY REFRACTORY MULTIPLE MYELOMA: IOPOFOSINE I 131

SNMMI JUNE 26, 2023

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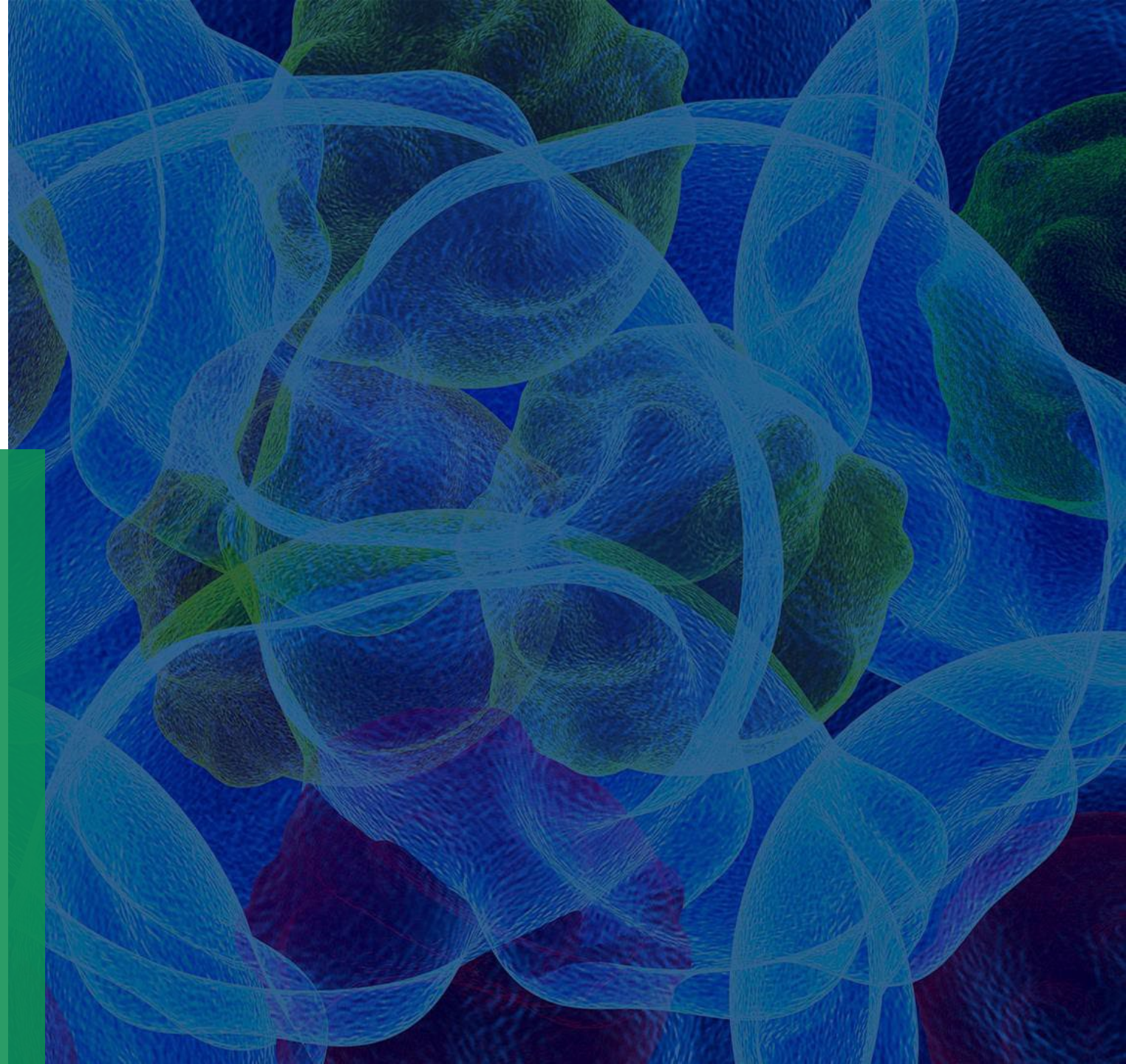
SESSION TITLE: HEMATOLOGIC MALIGNANCIES
ABSTRACT # P1243

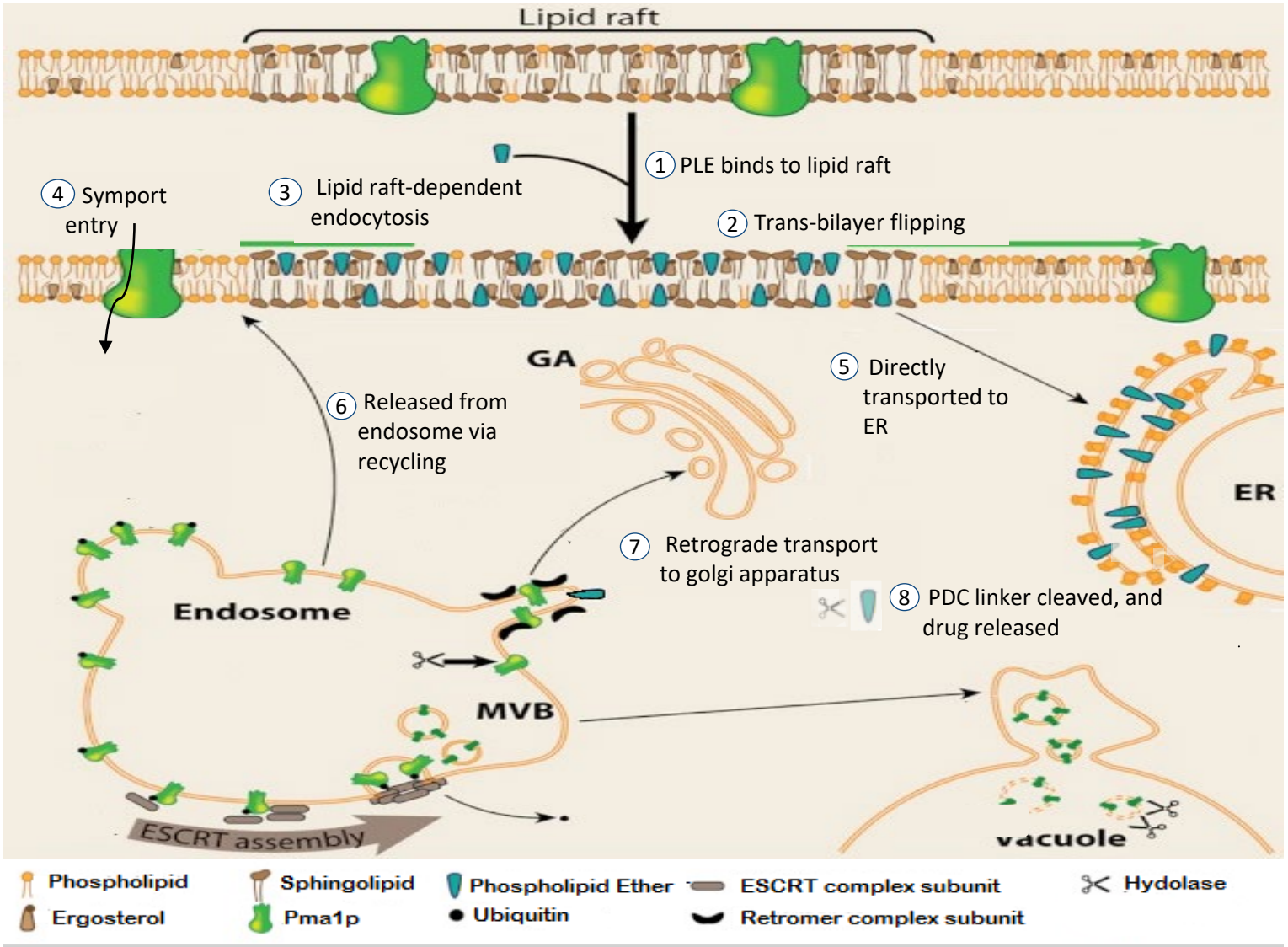


Disclosures

- **J. Longcor:** Cellectar Biosciences employee
- N. Callander: Employee University of Wisconsin Madison; Research funding from Cellectar Biosciences
- K. Oliver: Cellectar Biosciences employee
- S. Ailawadhi: Employee Mayo Clinic, Jacksonville, FL; Research funding from Cellectar Biosciences
- Ongoing study: Presentation contains preliminary data that are partially monitored and validated

Background: Phospholipid Ether (PLE) Cancer Targeting Platform

Mechanism of Entry and Intracellular Transport



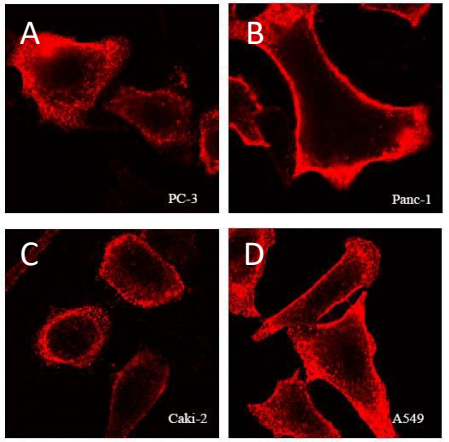
- Tumor cells have different metabolic needs
  - Increased need for phospholipids and fatty acids
- Unlike normal tissue, tumor cells cannot endogenously produce enough lipids to satisfy needs
- In order to satisfy need for lipids, increase and stabilize lipid rafts to bind and internalize lipids
- Lipid rafts also act as signalling hubs; coalesce tyrosine kinase receptors, GPCRs, etc
- PLEs target, bind and enter tumor cells via lipid rafts

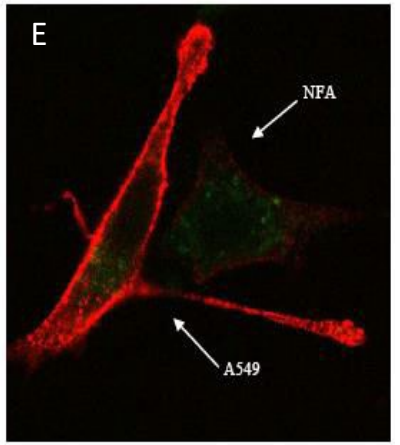
PDCs Exploit Key Metabolic Pathway

In vitro & *In vivo* Validation

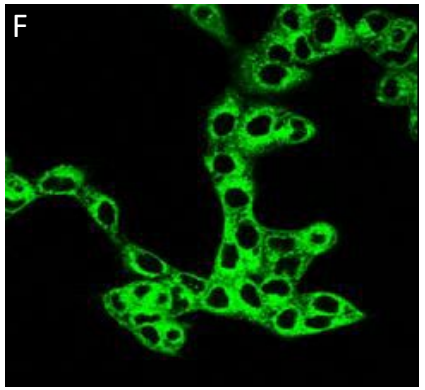
PLEs Provide Novel Method to Target Cancer More Uniformly

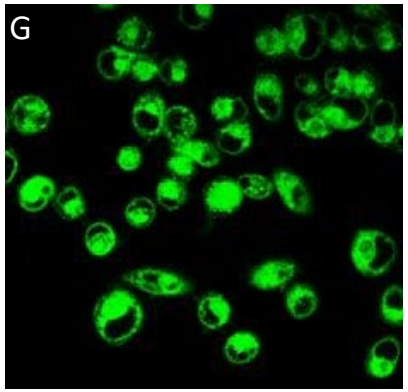
- Lipid rafts are present on nearly all tumor types (A-E)
- PLE molecules are being utilized to deliver fluorescent and cytotoxic molecules to tumors (F-H)
- PLEs show preferential uptake in broad range of tumor cells with near uniform uptake (F & G)
- Iopofosine I 131 is a targeted radiotherapeutic composed of ^{131}I covalently bound to a PLE
- Preclinical studies demonstrate that the PLEs provide delivery of the I-131 to a wide range of tumors, metastases and stem-like cancer cells (I)

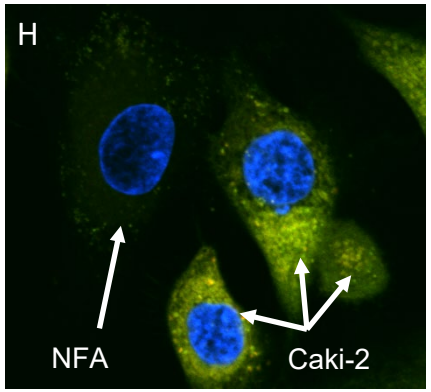




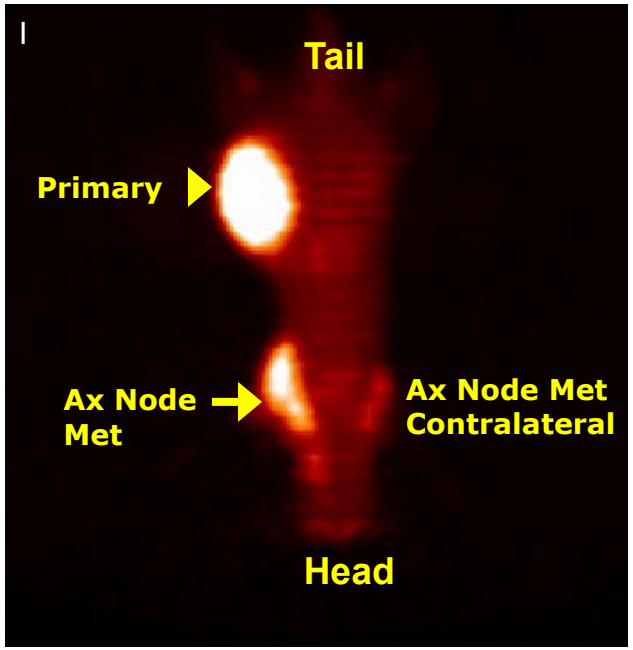
A, B, C, D, E demonstrates presence of lipid rafts on various tumors . A=prostate; B=pancreatic; C=renal; D=lung; E is co-culture of lung tumor and normal fibroblasts and treated or 24 hours. Staining is with cholera toxin B.







F, G and H show in vitro uptake of fluorescently labeled PLE. F=colorectal; G=glioma; H is co-culture



I shows iopofosine I 131 targeting in metastatic xenograft model

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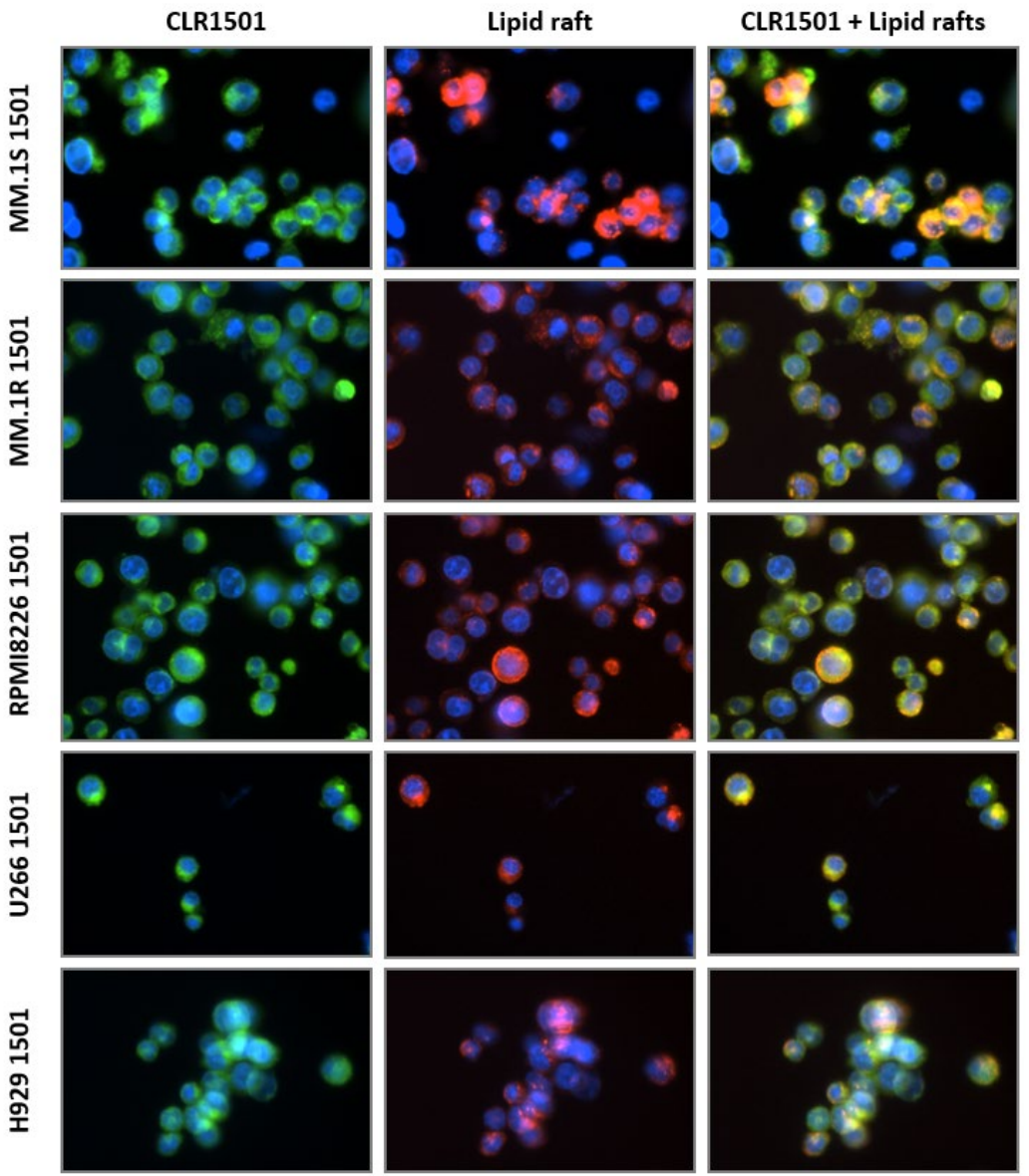
Rationale for Iopofosine I 131 in MM

- MM cells show high concentration of lipid rafts (primary patient and cell lines)
- Uptake confirmed with a fluorescent analog of iopofosine I 131
- Iopofosine has been dosed in over 170 patients to date
  - Phase 1 and Phase 2 studies
  - Hematologic and solid tumor
- Here we provide initial data on the efficacy and safety of iopofosine in relapsed or refractory multiple myeloma patients including patients with progressive disease post CAR-T therapy



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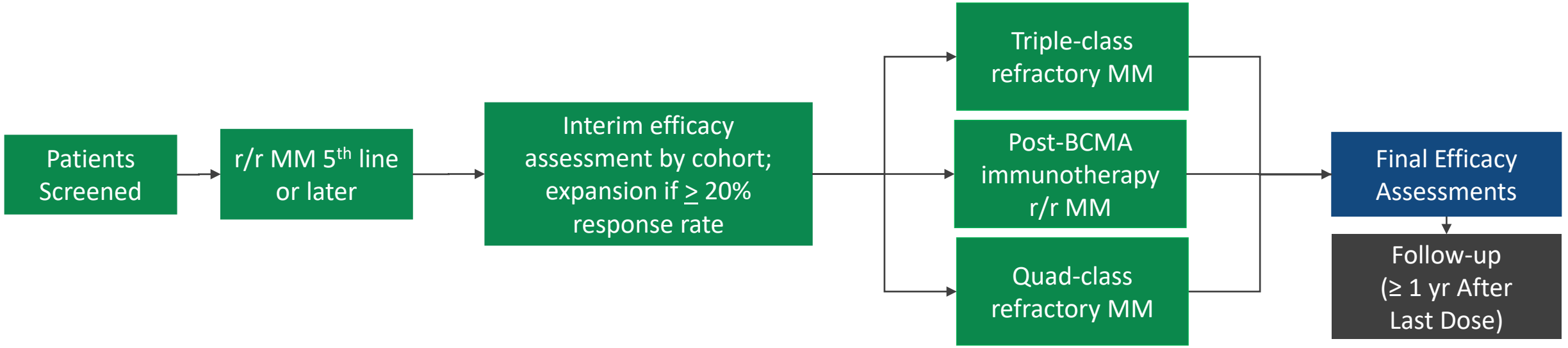
CLR 131: r/r Multiple Myeloma (MM) Phase 2 Study Overview



- Dose finding study evaluating either <60 or >60 mCi Total Administered Dose (TAD)
  - Dosed in 1 or 2 cycles each composed of 2 doses (cycle 1 = day 1 and 14; cycle 2 = day 57 and 71)
  - Each dose is 15 mCi/m^2 requiring approximately 20 mins to infuse
- Primary endpoint is Overall Response Rate (ORR) as determined by IMWG criteria
- Initial major eligibility requirements for MM patients
  - Relapsed or refractory to at least 5 prior lines of treatment
  - ECOG 0 – 2: expected survival no less than 6 months
  - Treatment with CLR 131 would not exceed life-time maximum exposure to radiation
- Modified to be even more refractory: triple-class/quad-class/post-BCMA immunotherapy

Iopofosine I 131 Multiple Myeloma Patient Characteristics

Characteristic	
Median Age (range)	68 (34 – 85)
Male – no. (%)	44 (61)
Median Time Since Diagnosis (range) - yrs	5 (1 – 22)
Median Bone Marrow Involvement (range) - %	46 (5 – 92)
ECOG performance-status score - no. (%)	
0	29 (40)
1	39 (54)
2	4 (6)
High Risk cytogenetics – no. (%)	26 (36)
Median Prior Lines (range)	5 (2 – 17)
Progression on last therapy – no. (%)	63 (88)
Previous Therapies: Exposed/Refractory	
Immunomodulator Drug	53/37
Proteasome Inhibitor	53/32
Anti-CD38 antibody	30/25
BCMA Therapy	7/3

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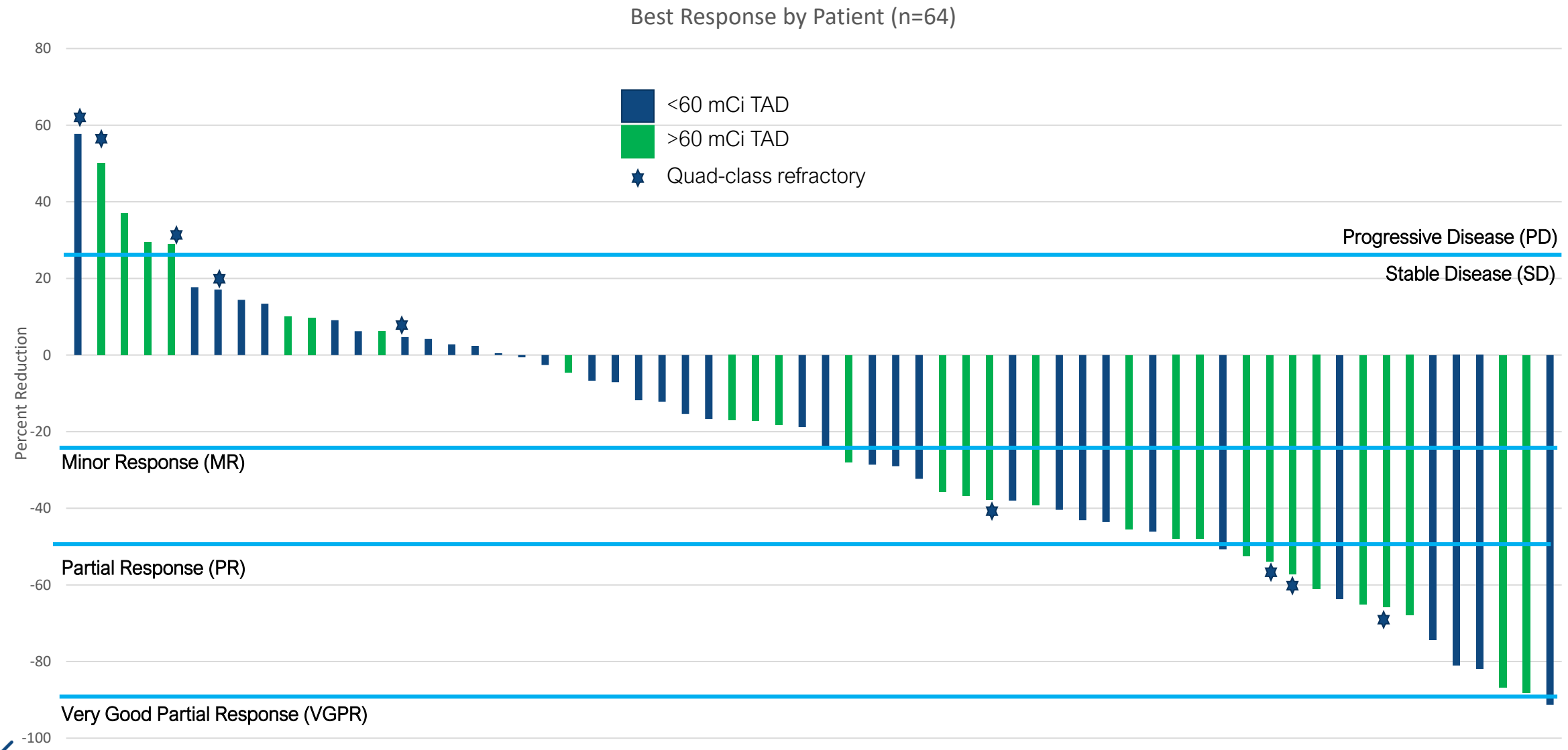
Waterfall Plot of All Multiple Myeloma Patients

(Best Response per IMWG Criteria)



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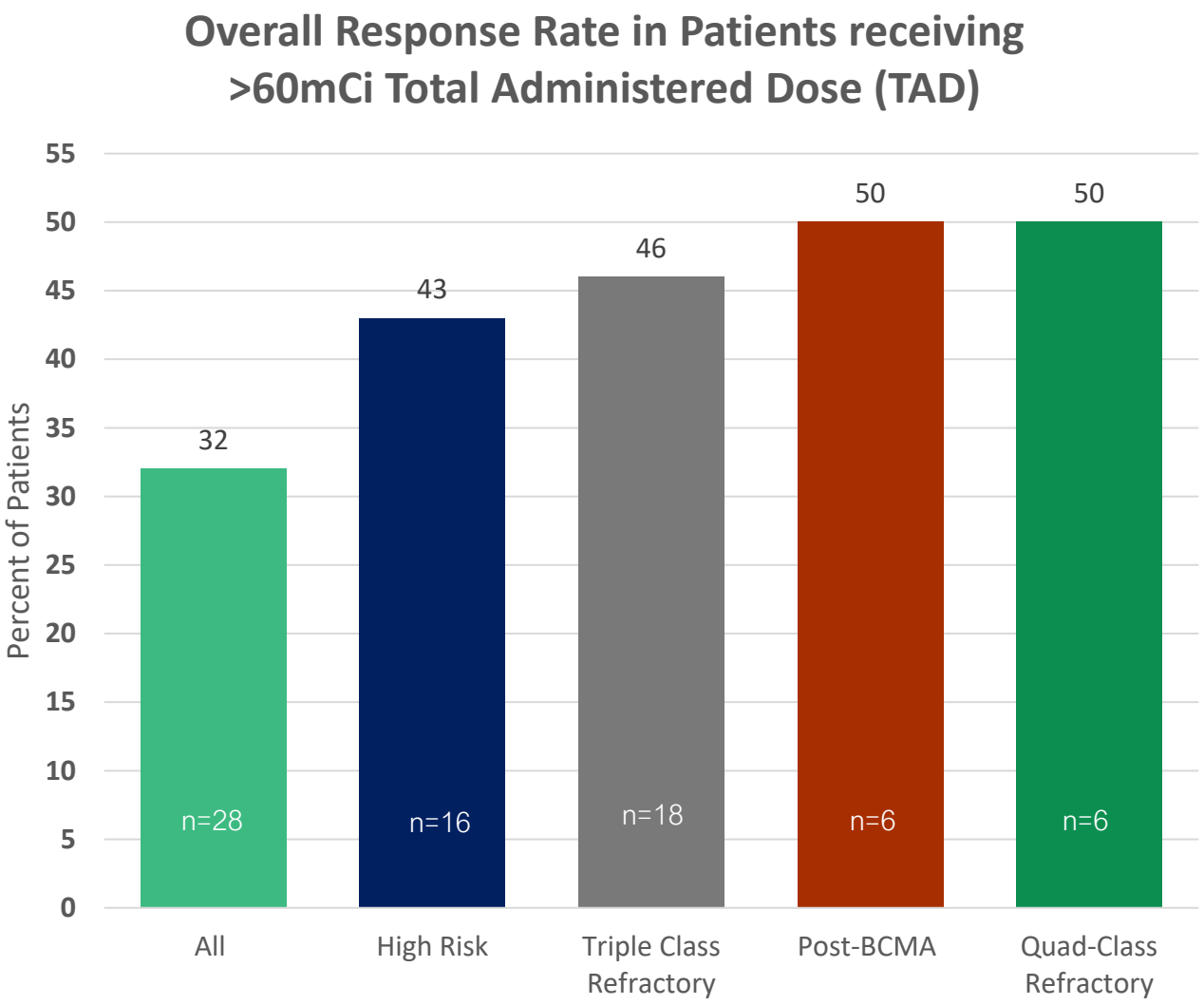
Evaluation of Patients at Target Dose

Subset Analyses



Additional Efficacy-Related Patient Benefits

85.7% disease control

75% of patients experienced tumor volume reduction

Triple class refractory
mPFS = 3.4m

Post-BCMA
mPFS = 3.3m

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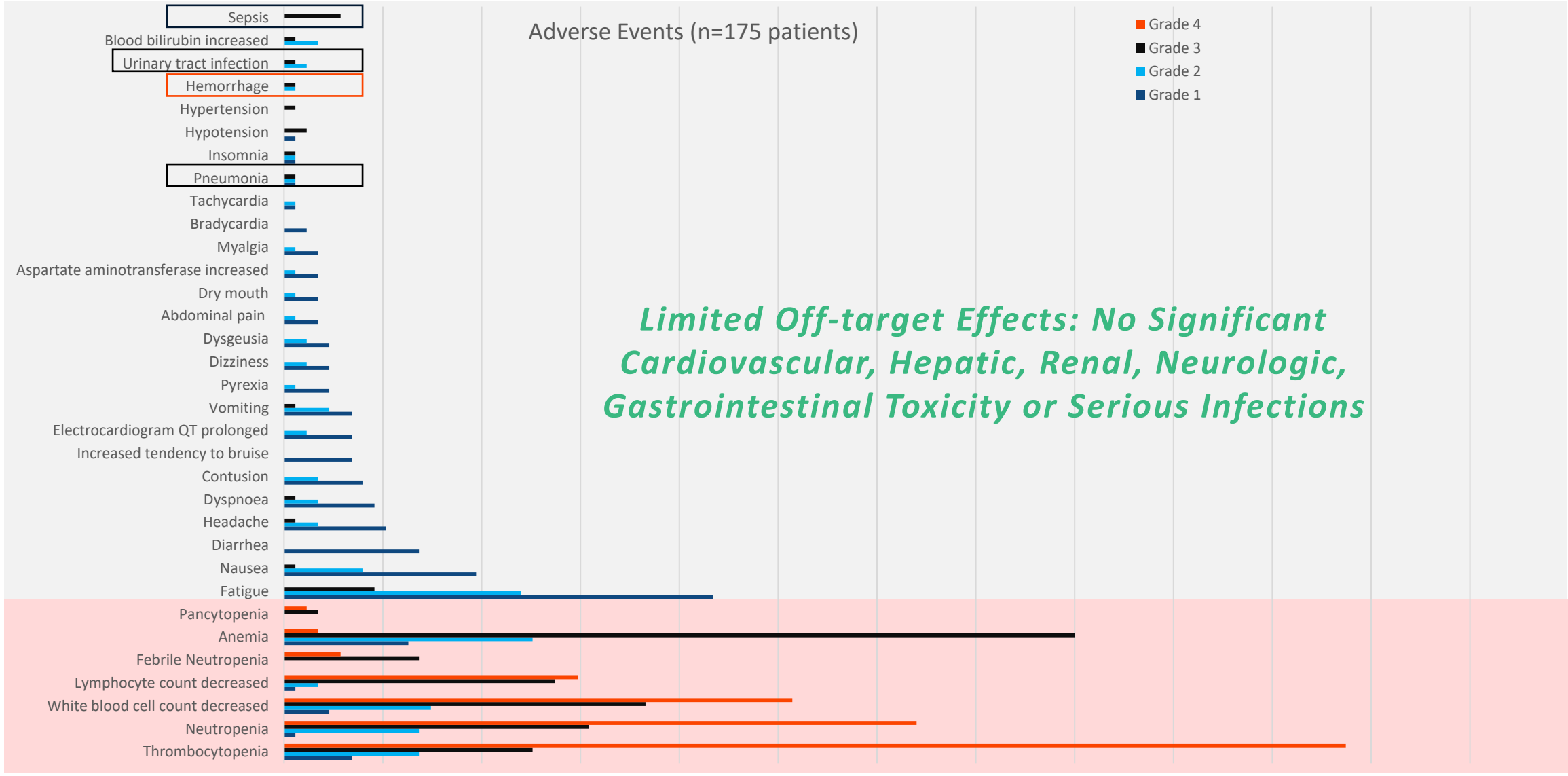
Iopofosine I 131: Well-Tolerated Safety Profile

Predictable and Manageable AE Profile



Limited Off-target Effects: No Significant Cardiovascular, Hepatic, Renal, Neurologic, Gastrointestinal Toxicity or Serious Infections

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Conclusions

- Iopofosine I 131 is shows encouraging response rates and disease control in highly refractory multiple myeloma patients
  - Activity against all kinds of refractory patients
  - Importantly provides potential post-BCMA immunotherapy
- Iopofosine I 131 is well tolerated with cytopenic events being the dominate TEAE reported
  - Cytopenias are predictable
  - Cytopenias are manageable
  - Limited to no off-target effects
- Iopofosine I 131 is currently in a pivotal study in Waldenstrom's macroglobulinemia (rare hematologic cancer) and a Phase 1 in adolescents and young adults with high grade gliomas
  - Based upon this data, potential to expand into additional hematologic cancers
- Future evaluations
  - P53 mutation and impact on response
  - Expand quad-class refractory and post-BCMA immunotherapy cohorts

Acknowledgements

We would like to thank all of the patients, their families and the site staff participating in our clinical trials

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