PHASE 1B TRIAL OF CAMSIRUBICIN, A NOVEL DOXORUBICIN ANALOG, WITH CONCOMITANT PEGFILGRASTIM IN SUBJECTS WITH ADVANCED SOFT TISSUE SARCOMA TO IDENTIFY A NEW MTD/RP2D

Monopar Therapeutics

Victoria S. Chua, MD[1]; Erlinda Gordon, MD[1]; Sant Chawla, MD[1]; Lee D. Cranmer, MD, PhD[2]; Aidan Kelly[3]; Holli Carlson[3]; Patrice Rioux, MD[3]; Pierre Jordaan, MD[3]; Chandler Robinson, MD, MBA, MS[3]

[1]Sarcoma Oncology Research Center, Santa Monica, CA, [2]University of Washington/Fred Hutchinson Cancer Center, Seattle, WA, and [3]Monopar Therapeutics, Inc. Wilmette, IL.

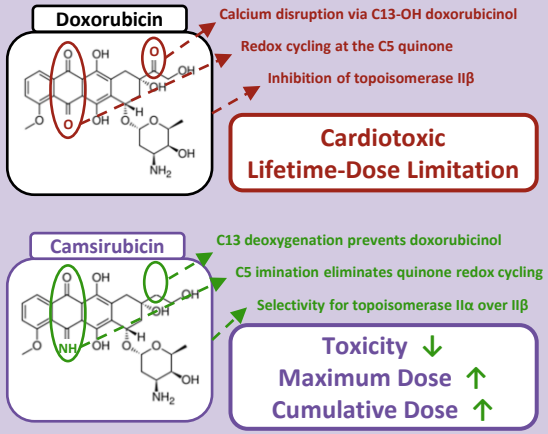
BACKGROUND AND PRIOR PHASE 2 STUDY

Background

Doxorubicin: Vital, but Toxic

Doxorubicin (Dox) is one of the most widely used cancer therapies, administered to > 1.2 million patients annually. It is FDA-approved for 14 different cancers, including first-line monotherapy for advanced soft-tissue sarcoma (ASTS). However, its risk of irreversible, life-threatening cardiotoxicity stops its use once a lifetime cumulative dose is reached in ~4-6 months.

Mechanisms of doxorubicin cardiotoxicity are understood to cover 3 different pathways.



Camsirubicin: Engineered to Avoid Cardiotoxicity

In response to Dox's limitations, Camsirubicin HCl, a novel doxorubicin analogue, was created via chemical modification to mitigate cardiotoxicity while retaining antitumor activity.

Increasing Maximum Tolerated Dose (MTD) via Pegfilgrastim

The prior Phase 1 dose-escalating trial suggested a Phase 2 dose of 265 mg/m^2 due to concerns of acute neutropenia. By administering pegfilgrastim with camsirubicin to address neutropenia, our Phase 1b study in ASTS patients seeks to determine a higher MTD for future studies.

Prior Phase 2 Study (NCT02267083)

38% 6-month progression-free survival; Dox achieves 25-45% in ASTS patients

20 Maximum # of cycles received with camsirubicin; Dox max is 6-8 cycles

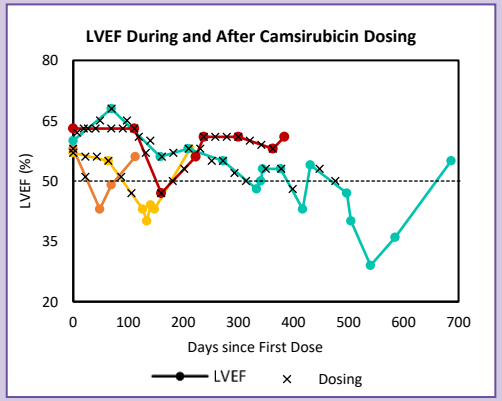
Left Ventricular Ejection Fraction Measurements with Camsirubicin Treatment

N = 22		Screening	Final Visit
LVEF (%)	Mean	61.8	58.4
	Median	61.0	60.0

Average LVEF showed **no significant change vs baseline.**

- Patients received up to 20 cycles and up to a cumulative dose of 5,300 mg/m^2
- No patient experienced irreversible cardiotoxicity
  - 4 patients had LVEF decreases >10% from baseline
  - Changes were **transient** and **returned to normal** during study treatment or prior to final safety visit (see figure below)

Transient, Reversible Decreases in LVEF



ONGOING CAMSIRUBICIN PHASE 1B

Study Design, Status, & Demographics

The trial is a Phase 1b open-label, dose-escalation, **3+3 design.** 2 dose-limiting toxicities at 1 dose level determines the maximum tolerated dose (1 level lower).

Study Design

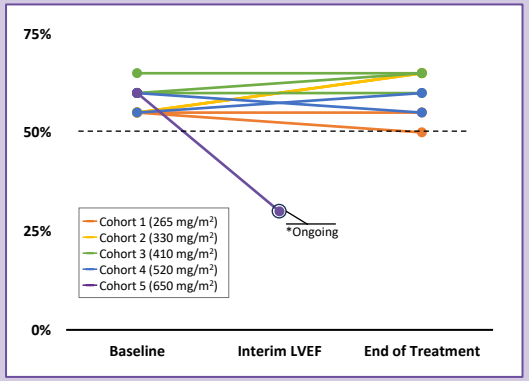
Screening *(28 days)* → Intervention Period *(6 cycles of 21 days, with extension up to 16 cycles)* → EoT Safety Visit *(with 1-Yr Long-Term Follow-Up)*

Trial is ongoing and is in the 5th cohort. No dose-limiting toxicity observed within the protocol-specified first cycle.

Demographics	N=14
Median Age in years [min, max]	52.5 [26, 81]
Sex (Female, Male)	9, 5
ECOG Score (0, 1)	1, 13
Tumor at Baseline (Localized, Locally Advanced, Metastatic)	1, 6, 7

Safety: LVEF Trends

LVEF Trends across Dose-Escalating Cohorts[1,2]



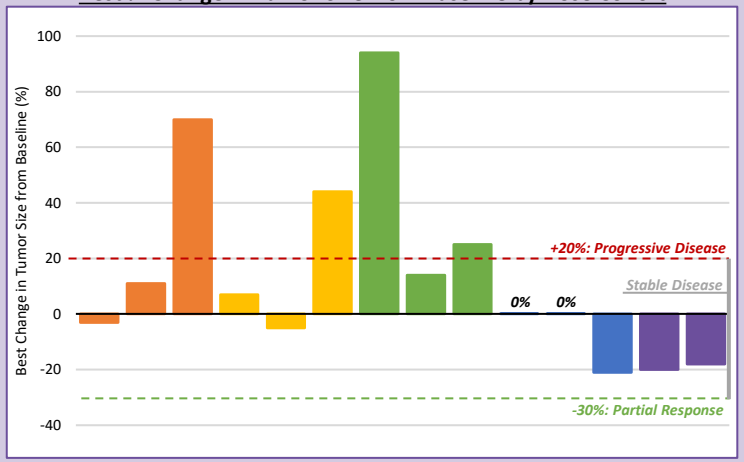
* Patient with ongoing LVEF decrease is being monitored for progression/recovery. Patient is medically complex, with one kidney, BMI of 42.5, and maternal history of heart failure

[1]Contains interim data, additional data pending entry in electronic database

[2]Three patients excluded from this graph: 1 patient died before their end of treatment visit due to COVID-19; 1 patient died from a sepsis-related event (not drug-related); 1 patient has had no LVEF decrease but is pending data entry

Clinical Outcomes: Disease Status

Best % Change in Tumor Size from Baseline by Dose Cohort



Patient	1.1	1.2	1.3	2.1	2.2	2.3	3.1	3.2	3.3	4.1	4.2	4.3	5.1	5.2
Dose cohort (mg/m^2)	265	265	265	330	330	330	410	410	410	520	520	520	650	650
Response	SD	SD	PD	SD	SD	PD	PD	*SD[3]*	PD	SD	SD	SD	SD	SD

[3] Patient's scan occurred 2 days early for protocol defined criteria of SD, but did not progress at this scan

SD = stable disease, PD = progressive disease

Conclusions & Next Steps

CLINICAL OUTCOMES

- Majority of patients have had stable disease after treatment with camsirubicin, including 5/5 of the most recent patients
- 1 underwent surgical resection after a 21% reduction in tumor
- 3 most recent patients have averaged ~20% reduction in tumor size at last study scan

SAFETY

No dose-limiting toxicity, as defined in the protocol, observed to date. A medically complex patient in the highest dose cohort has LVEF decrease that is being thoroughly monitored.

DOSE ESCALATION

Presently in 650 mg/m^2 dose cohort, which is **2.5X the prior Phase 2 dose.** MTD/RP2D has not been reached.

Citations: