RACE ONCOLOGY

ASX Announcement

Bisantrene Phase 2 AML Trial Data Presented at the 65th American Society of Hematology Annual Conference

- Bisantrene in combination with fludarabine and clofarabine administered over four days induced a clinical response in 6 of 15 (40%) evaluable patients with advanced relapsed or refractory Acute Myeloid Leukaemia, with five patients receiving a potentially curative stem cell transplant
- The bisantrene combination was found to be safe and well-tolerated without clinically relevant cardiotoxicity or tumour lysis syndrome
- Poster containing interim trial results was presented at the prestigious American Society of Hematology 65th Annual Meeting and Exposition, 9-12 December 2023

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13 December 2023 – Race Oncology Limited ("Race") is pleased to release a presentation detailing interim clinical results from an ongoing investigator-initiated Phase 2 trial of bisantrene in combination with fludarabine and clofarabine in relapsed or refractory Acute Myeloid Leukaemia (R/R AML) patients.

The trial is running at the Sheba Medical Centre, Israel, under the supervision of key opinion leader Professor Arnon Nagler. Results of this trial were presented at the prestigious American Society of Hematology (ASH) 65th Annual Conference held in San Diego (USA) on the 9-12th December 2023. This presentation follows the release of the abstract to ASX on 6 November 2023.

The oral poster presentation entitled *"Bisantrene in combination with Fludarabine and Clofarabine as Salvage Therapy for Adult Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML) – An Open-label, Phase II Study"* describes clinical results from the first 20 patients treated on study since August 2021 (NCT04989335). The poster presentation is attached to this announcement.

-ENDS-

About Race Oncology (ASX: RAC)

Race Oncology (ASX: RAC) is an ASX-listed clinical stage biopharmaceutical company with a dedicated mission to be at the heart of cancer care.

Race's lead asset, bisantrene, is a small molecule chemotherapeutic. Bisantrene has a rich and unique clinical history with demonstrated therapeutic benefits in both adult and paediatric patients, a well characterised safety profile, and compelling clinical data demonstrating an anticancer effect and less cardiotoxicity over certain anthracyclines, such as doxorubicin.

Race is advancing a reformulated bisantrene (RC220) to address the high unmet needs of patients across multiple oncology indications, with a clinical focus on anthracycline combinations, where we hope to deliver cardioprotection and enhanced anti-cancer activity in solid tumours. Race is also exploring RC220 as a low intensity treatment for acute myeloid leukaemia.

Race is investigating the effect of bisantrene on the m^6A RNA pathway, following independent research published by the City of Hope identifying bisantrene as a potent inhibitor of FTO (Fat mass and obesity-associated protein). Dysregulation of the m^6A RNA pathway has been described in numerous peer reviewed studies to be a driver of a diverse range of cancers.

Race Oncology has collaborated with Astex, City of Hope, MD Anderson, Sheba City of Health, UNC School of Medicine, University of Wollongong and University of Newcastle, and is actively exploring partnerships, licence agreements or a commercial merger and acquisition to accelerate access to bisantrene for patients with cancer across the world.

Learn more at www.raceoncology.com.

If you have any questions on this announcement or any past Race Oncology announcements, please go to the Interactive Announcements page in our Investor Hub https://announcements.raceoncology.com

Race encourages all investors to go paperless by registering their details with the Company's share registry, Automic Registry Services, at www.automicgroup.com.au.

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Bisantrene in combination with Fludarabine and Clofarabine as Salvage Therapy for Adult Patients with Relapsed or Refractory Acute Myeloid Leukemia – an Open-Label, Phase II Study

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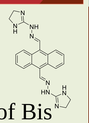
INTRODUCTION



- Bisantrene (Bis), is a topoisomerase-II inhibitor with anthracycline-like activity but lower cardiotoxicity.
- In a previous Phase I study, we demonstrated the activity of Bis monotherapy in patients (pts) with relapsed/primary refractory acute myeloid leukemia (AML) who had received a median of 3 lines of prior therapy, including 7 pts who had relapsed following allogeneic stem cell transplantation (HSCT) (Am J Hematol 106:260-266,2021).
- In an *in vitro* study, Bis was found to synergize with the cytotoxic purine nucleoside analogs clofarabine (Clo) and fludarabine (Flu) (J Clin Exp Oncol. 10:4, 2021).
- With this background, we conducted a Phase II study combining Bis with Clo and Flu as salvage treatment in pts with relapsed/refractory AML (NCT04989335).

METHODS

-This was a Phase II open-label single-center study with 2 stages: (1) a dose escalation stage using a 3+3 design to assess safety and tolerability and provide the recommended phase 2 dose (4 vs 5 days) of infusion (i.v.) combination in up to 12 pts and 2) an expansion phase in up to 17 pts (using a Simon 2-stage design) to assess primary efficacy and confirm the safety of the Bis/Clo/Flu combination treatment in pts with relapsed/primary refractory AML.
- Treatment was administered daily for 4 days in the following sequence: Flu (10 mg/m^2) i.v. over 1 hour (h), followed by a 1-h infusion of Clo (30 mg/m^2), and then a 2-h infusion of Bis at 250 mg/m^2, with a 1-hour break between agents.
- The primary endpoint was overall response rate (ORR), defined as the combined proportion of patients with either complete remission (CR), or complete remission with incomplete blood count recovery (CRi), or partial response.
- Efficacy was assessed by bone marrow (BM) examination between 21 – 30 days post-therapy.
- Safety included treatment-emergent adverse events (TEAEs), all-cause mortality, and cardiac monitoring with ECG and troponins. -
- Toxicity was assessed according to Common Terminology Criteria for Adverse Events (CTCAE *v5.0*). Interim analysis was performed after the first 12 pts.

RESULTS

- 20 pts were enrolled from August 2021. The median age was 48 (19-69) years and 55% were male.
- 15 pts had *de novo* AML and 5 had secondary AML, 11 pts were in relapse, while 9 had primary refractory disease.
- Median lines of therapy were 4 (range 3-9); 12 with ≤ 4 and 8 >4.
- All pts were refractory to the last line of therapy. 15 pts (75%) were in relapse post HSCT. 5 pts (25%) had active extramedullary disease (EMD, 1 with CNS involvement).
- Median bone marrow blasts pre-Bis/Clo/Flu treatment was 50%.
- Cytogenetics were normal in 10 pts (50%), 5 had a complex karyotype, 2 MLL rearrangements, 1 t8;21 and 2 pts had other chromosomal abnormalities.
- The maximum tolerated dose of the Bis/Clo/Flu combination was 4 days of infusion, informed by grade 3 liver toxicity in 2 pts and 1 pt that died from sepsis in the first stage of the study.
- 10 pts developed liver toxicity with elevated liver enzymes and bilirubin in 9 of them (grade 1-4 pts; grade 2-3 pts and grade 3-3 pts).
- Liver toxicity was transient and resolved in all pts. Two pts had treatment interruption due to liver toxicity. 4 pts had grade I renal toxicity, 7 had mild fluid retention, and 18 developed neutropenic fever, of which 10 pts had verified bacteremia.
- Five pts had pneumonia, 4 invasive fungal infections, and 2 sepsis (1/2 died). 1 additional pt died from cerebral venous sinus thrombosis.
- Overall, 5 pts could not be evaluated for response due to death.
- Clinically-relevant cardiac toxicity was not observed in any of the pts and there were no ECG changes. Transient grade 1 elevation of troponin levels were observed in 4 pts.
- Six pts responded (CR-5, PR-1), including 3 with EMD, and lasted up to 3 months.
- Five pts underwent HSCT 1-3 months post-Bis/Clo/Flu with reduced /intermediate intensity conditioning (4/5 pts had 2nd and 1/5 pts had 1st allo-HSCT, respectively).
- Stem cell donors were haploidentical -2, matched unrelated -2, and matched sibling -1, respectively. Three pts died: 1 from graft versus host disease, the second from relapse within 4 months post-transplant, and the third from sepsis 2 years post-HSCT. Two of the transplanted pts are in complete remission.

Table 1. Patients' characteristics

Characteristics	Number
Total N of patients	20
Gender	
Female	11
Male	9
Median age	48 (19-69) years
Secondary AML	5
Post Ca of breast Tx	1
Post MDS	3
Post MF	1
Cytogenetics	
Normal Karyotype	10
Complex Karyotype	5
MLL Rearrangement	2
Other	3
Molecular mutations	6
JAK2	1
FLT3 ITD	3
FLT3 TKD	1
NPM1	1
Extra-medullary disease (EMD) at Start Tx	5
Isolated EMD relapse	1
BM and EMD	4
CNS involvement	1
Median Lines of Tx before Bis/Clo/Flu Tx	4 (3-9)
Primary refractory disease	9/20
Relapsed refractory disease	11/20
Previous HSCT	15/20

Table 2. Toxicity after Bis-based Tx

Adverse events	Number
Tumour lysis syndrome (TLS) pts	0
Liver Toxicity pts	10
Elevated Liver enzymes	10
Elevated Bilirubin	9
Median bilirubin level mg/dl	1.25 (0.8-11.5)
Resolution liver toxicity days after Tx	9.5 (3-25)
Creatinine elevation pts	4 (mild)
Heart Failure pts	0
ECG changes pts	0
Troponin elevation pts	4 (transient)
Fluid retention pts	7
Infectious pts	
Neutropenic fever	18
Bacteremia	10
Septic shock	2
Pneumonia	5
Invasive fungal	3
Mucourmucosis	1
GvHD exacerbation	No
Other toxicity pts	
CVA/Sinus Vein thrombosis	1

Table 3. Response and outcomes

Characteristics	Number
ORR	6 (30%)
CR	5 (25%)
PR	1 (5%)
PD	8 (40%)
Death post-dosing, prior to response assessment	5 (25%)
Post Bis/Clo/Flu Tx	
Additional salvage Allo-HSCT	0
	5
1st allo-SCT	1
2nd alloSCT	4
DLI	1
Median Time of response days	112 (55-620)
Pts outcomes	
Death	17
Alive	3 (2/3 pts after allo-HSCT in CR; 1/3 has PD)
Causes of death (N=17 pts)	
Relapse/Progression	14
Non Relapse Mortality	3
Early death post-dosing, prior to response assessment	5* 4/5 infections , 1/5 from CVA and Superior Vein Thrombosis

**1/5 was considered possibly related to study therapy by the investigator*

CONCLUSIONS

-In this Phase II study in a very advanced group of relapsed refractory AML pts resistant to multiple previous lines of chemotherapy, including transplantation, and with a median of 50% blasts at study initiation, Bis/Clo/Flu combination therapy was found to be safe and well tolerated without cardiac toxicity or tumor lysis syndrome.
- The maximum tolerated duration of Bis/Clo/Flu administration was 4 days due to rapidly reversible liver toxicity, and transaminitis.
- As expected in this highly pretreated population, the infection rates were high.
- Six of the 15 evaluable pts (40%) responded, enabling an HSCT in 5 of them.
- These rather impressive results in such a heavily pretreated population support further studies of Bisantrene-based combinations.

Disclosures: AN-research grant (7256-20-smc) and travel grant from Race Oncology Ltd; BA--consulting for Race Oncology Ltd