RACE ONCOLOGY

ASX Announcement

Bisantrene Shows Broad Anti-cancer Activity in 143 Human Cancer Cell Lines

- Bisantrene shows potent anti-cancer activity when screened on a diverse panel of blood and solid organ tumour cells
- When used at low drug concentrations, bisantrene improved the cancer cell killing efficacy of the widely used anti-cancer drug doxorubicin ($p<0.0001$)
- Data further supports the potential clinical use of bisantrene in combination with doxorubicin

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21 September 2023 – Race Oncology Limited ("Race") is pleased to share results from recent preclinical work performed under contract at Oncolines (Netherlands). In these studies, bisantrene was screened for anti-cancer activity in a broad panel of 143 human cancer cell lines, representing 15 distinct cancer types, alone and in combination with doxorubicin, an anthracycline chemotherapeutic that is one of the most widely used anti-cancer drugs.

Race has previously announced that bisantrene improves the cell killing activity of doxorubicin and cyclophosphamide in breast cancer cells (ASX Announcement: 9 March 2021) and protects mouse hearts from anthracycline-induced cardiac damage in an established model (ASX Announcement: 30 June 2022).

In this preclinical study, bisantrene was found to be highly active as a single agent against 113 of 143 tumour cell lines, representing a broad cross-section of the most common haematological (blood / liquid) and solid organ cancers. Combining bisantrene at clinically relevant concentrations with doxorubicin was found to significantly enhance cancer cell killing in the majority of cells.

Executive Director, Dr Pete Smith commented: *"Due to its history, plus a wealth of published pre-clinical and clinical data, bisantrene has long been known to be an active anti-cancer drug. What is interesting from these recent studies is the remarkable breadth of its activity, where bisantrene was shown to kill a wide range of cancer cells, representing tumours from many human tissues. The strength of bisantrene's performance with doxorubicin, a standard of care chemotherapy drug, is particularly exciting as it informs our clinical development plans and bolsters confidence that combining other cancer drugs with bisantrene will produce positive results for patients. We look forward to formally releasing this comprehensive set of cell screening data in upcoming peer-reviewed publications."*

Study Highlights

Bisantrene shows potent cell-killing activity against a diverse range of human cancers

Bisantrene, when tested in 143 cancer cell lines covering more than 15 different major cancer types, was found to kill more than 79% of the cancer cell lines at a concentration below 500 nM (Figure 1). Previous studies have shown that doses of bisantrene that are well tolerated by patients achieve drug concentrations above 3,000 nM in the blood[1], highlighting the clinical relevance of this potent *in vitro* tumour cell killing activity. In historical clinical trials where bisantrene was used as a single agent, it demonstrated anti-cancer activity in patients with breast cancer[2], acute myeloid leukaemia (AML), other leukaemias[3] and ovarian cancer[4].

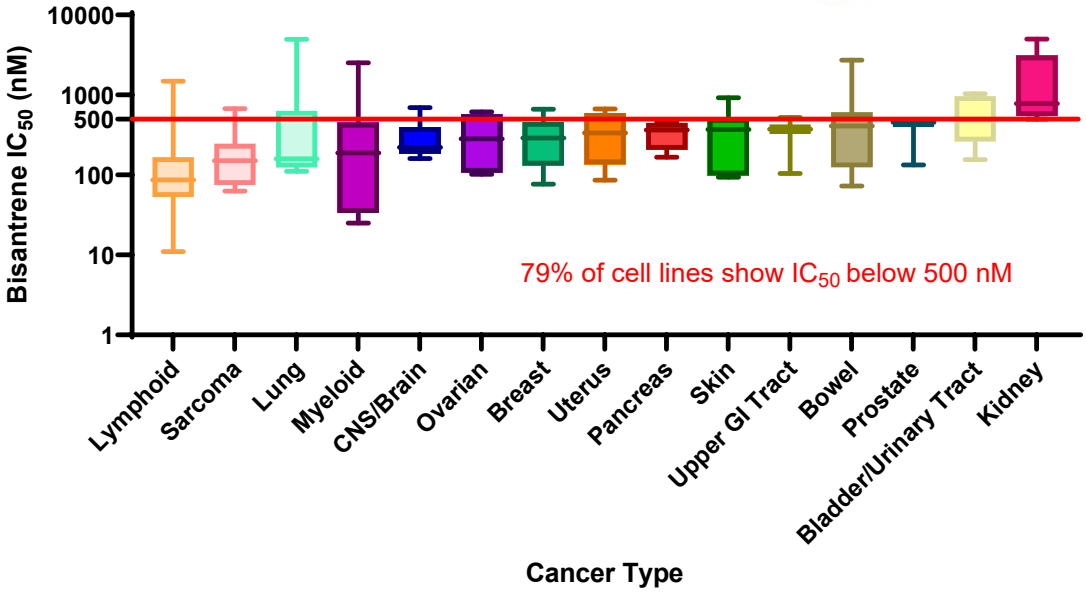

Figure 1. Bisantrene shows broad anti-cancer activity. The half-maximal inhibitory concentration (IC_{50}) was determined for bisantrene against 143 cancer cell lines derived from diverse human tumour types. Boxes show the 25%-75% range, with the line within each box representing the median IC_{50} value. The upper and lower edges of the box represent the 75th and 25th percentiles, respectively. Whiskers show the minimum and maximum IC_{50} values observed for each cancer cell type.

Bisantrene significantly improves the cancer cell killing activity of doxorubicin

When cancer cell cultures were treated with mixtures containing clinically achievable concentrations of bisantrene and the widely used, standard of care anti-cancer drug, doxorubicin, greater cell killing activity was seen in 86% of tumour cells, relative to doxorubicin treatment alone (Figure 2). These data suggest that the use of bisantrene in combination with doxorubicin may provide additional anti-cancer benefits in patients receiving doxorubicin-containing therapies and support the clinical use of bisantrene in patients where doxorubicin is indicated.

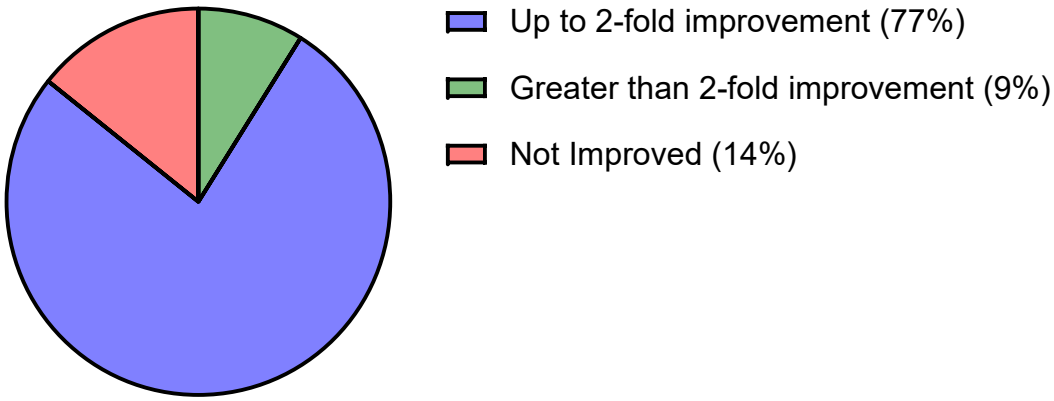

Figure 2. Combining bisantrene with doxorubicin increases cell-killing activity. Proportion of cell lines showing improved (i.e. lower) IC_{50} values when comparing doxorubicin + bisantrene treatments to doxorubicin alone. A significant difference was observed for the median IC_{50} of cells treated with doxorubicin + bisantrene when compared to doxorubicin alone, $p<0.0001$. Statistical analysis was performed using the non-parametric Wilcoxon matched-pairs signed rank test.

Next Steps

- Optimisation of the dosage and drug combinations through additional preclinical studies to identify the best clinical treatment opportunities
- Further preclinical studies to explore the molecular mechanisms responsible for the enhanced cancer cell killing with doxorubicin and other drug combinations
- Publication of the completed data package in a high quality, international, peer-reviewed journal
- Consultation with key opinion leaders to explore clinical studies utilising bisantrene in combination with doxorubicin to improve outcomes for cancer patients.

Q&A

What does this result mean for future clinical trials of bisantrene?

The results of this study suggest that bisantrene may have broad clinical utility across the cancer landscape, especially when used in combination with doxorubicin in its standard of care oncology treatments.

What is the market significance of this discovery?

This discovery expands the potential clinical use of bisantrene as a cardio-protective anti-cancer agent beyond breast cancer and AML. If in future clinical and preclinical studies, bisantrene demonstrates cardioprotective and anti-cancer utility in a broad range of cancers, then its commercial and clinical value will be far greater than if bisantrene is limited to use in only breast cancer and AML. How to best advance this potential commercial opportunity is being actively explored by the Race team and advisors.

References

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About Race Oncology (ASX: RAC)

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

Race's lead asset, bisantrene, is a small molecule anthracene chemotherapeutic. Bisantrene has a unique and rich clinical history with demonstrated therapeutic benefits in both adult and paediatric patients, a well characterised safety profile, and compelling clinical data demonstrating an anti-cancer effect and less cardiotoxicity than other comparable agents.

Race is developing bisantrene to address the high unmet need of patients across multiple oncology indications, with an initial focus on metastatic breast cancer (lead indication) and acute myeloid leukaemia (AML) exploring anti-cancer plus cardio-protection in synergy with known standards of care.

As part of its clinical and preclinical programs, Race is investigating the effect of bisantrene on the m^6A RNA pathway, following independent research 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 is in collaboration with City of Hope, MD Anderson, Sheba City of Health and UNC School of Medicine, 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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