ASX Announcement

Webinar transcript and presentation update

19 June 2020 – is pleased to release a copy of the transcript from this week's webinar (announced 16 June 2020) on the results of the investigator initiated Phase II clinical trial of bisantrene, for relapsed or refractory Acute Myleoid Leukaemia (AML), conducted by Israel's Sheba Medical Centre.

During the session, Race's Executive Chairman, Dr John Cullity covered trial highlights; Clinical Advisory Board Chair, Professor Borje Andersson spoke in depth about the trial and Dr Daniel Tillett discussed other advancements under the Company's 5-path strategy for the development of bisantrene.

Executive Chairman, Dr John Cullity commented, "We were humbled by the strong level of engagement from shareholders and investors on our data release call this week. Our thanks go to all those who were able to attend.

"Through the Phase II data announced this week, bisantrene's potential has been underscored. While the full size, scope, timing and plan is yet to be finalised, a follow-up AML study, combining bisantrene with other anti-leukaemic drugs is currently in advanced planning. We look forward to sharing more detail with the market once the details have been finalised."

The attached transcript has been annotated to improve clarity on certain aspects regarding the trial results and future activities. In line with this, an updated presentation will be lodged separately to this announcement, including corrections to relevant slides.

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About Race Oncology (RAC: ASX)

Race Oncology (RAC) is a drug development biotech with a Phase II/III cancer drug called Bisantrene. RAC has compelling clinical data for Bisantrene in acute myeloid leukaemia (AML) as well as breast and ovarian cancer. RAC is pursuing an exciting '5-Path' clinical development strategy that involves parallel US and Australian clinical trials in AML, breast and ovarian with clinical trials to begin in 2020.

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Transcript: investor briefing webinar

Date: **17 June 2020**

Time: **10:30 am AEST**

Title: **Race Oncology Phase II Bisantrene AML Trial webinar**

Start of transcript

Dr John Cullity: Good morning everyone. This is John Cullity. I'm Executive Chairman of Race Oncology. We'll just wait for everyone to get situated and then get started. Welcome to the call.

Okay, let's get on the way. Well, it's a pleasure to welcome you to this investor briefing, as we provide further detail and context regarding the data from the phase two clinical study[1] that was announced to the Australian market yesterday.

As borne out in the ASX announcement, impressively analysis of the phase two trial of bisantrene for relapsed or refractory acute myeloid leukaemia shows an objective clinical response of 40% of patients.

Now one of the 10 patients that were treated in this protocol, one patient achieved a complete remission, and three patients achieved a partial remission. A clinical response rate that is broadly comparable to historical bisantrene trials.

Bisantrene had marked activity in four out of four patients with the difficult to treat extramedullary - or outside of the bone marrow - form of acute myeloid leukaemia.

We wish to bear out that bisantrene was well tolerated with no unexpected serious toxicities. And by way of contextual remark, R/R, or relapsed remitting AML represents a significant therapeutic challenge with still no clearly established standard of care.

Now in this morning's session, we'll start with Borje Anderson, Professor of Medicine in the department of stem cell transplantation at MD Anderson Cancer Centre in Houston, Texas. And we're thrilled that Borje is the chair of the Race clinical advisory board.

Borje will take us through the clinical data as released yesterday, and then provide comments regarding follow on studies that we have planned in myeloid leukaemia.

Then I will hand over to my colleague Dr Daniel Tillett, who is our Chief Scientific Officer. Daniel will provide additional commentary regarding our planned protocols in Measurable Residual Disease and also look to our activities in solid tumour oncology.

[1] *"Bisantrene for Relapsed / Refractory AML"* (NCT03820908) was designed and conducted by Israel's Sheba Medical Centre as an investigator initiated trial. Race provided bisantrene drug product and a financial grant to Sheba.

Now, if people want to ask questions, then please click on the Q&A button which will find on your toolbar. We'll be collating questions during the session and go through as many as possible at the end. So with that, let me hand it over to you, Borje to start proceedings.

Professor Borje Andersson: So, bisantrene is a very active anticancer drug and was tested by Lederle the primary patent holder, in almost 2,000 patients in the 1980s and early 90s. It was brought all the way to regulatory approval in Europe, in France, but by the time Lederle was to start marketing bisantrene, Lederle was bought up by another company that was uninterested in oncology at the time and bought Lederle because of its portfolio of antibiotics. So, the bisantrene, in spite of its documented high activity, both in AML and in solid tumours was mothballed.

And since then, bisantrene was rediscovered and formed the basis for Race Oncology, in 2015. The first clinical trial of which I'm going to talk about now was a small trial as you know, 10 patients, so it would be a question, why would we want to do a trial with only 10 patients? Well, let's look first at a general overview of the situation in AML.

The typical scenario is that patients with AML undergo fairly intensive chemotherapy to get into a complete remission (CR). Those patients who are in complete remission are typically considered candidates for a stem cell transplant with curative intent. And two things can happen - either they are cured, or the stem cell transplant serves as a consolidation of the remission and patients relapse later on. Unfortunately, the latter is a fairly common occurrence.

Alternatively, patients may never even achieve a first remission because the treatment has been ineffective. The leukaemia is too aggressive. These two groups of patients, both those who relapse after a stem cell transplant and those who never made it to a transplant but have active disease because they failed up front, or they got into remission and then failed to maintain that remission, are the type of patients that we have treated in this current trial.

So it's by definition, a group of patients who have “very difficult to treat” disease.

One can ask why would we want to do a bisantrene trial with only bisantrene, since in today's landscape, or in today's climate, we have mainly left single agent trials and embarked on combinations both induce and to maintain remissions when it comes to AML? Well, there are two reasons for why we would elect to do a single agent trial.

The first one is that the historical data were based around single agent bisantrene. And secondly, the treatment traditions have changed. We're today treating patients with combination chemotherapy, and in addition to that, they are more heavily pretreated. Certainly, supportive care has changed over 30 years. And all these factors influence the patient population, such that they may or may not behave the same way as they did in reference to bisantrene 30 years ago.

It was therefore elected by Race[2] to first perform a small single agent trial, to see if we could first get a similar readout on response in very heavily pretreated relapsed refractory AML patients who had already failed multiple prior therapies, and secondly, would we see a similar side effect spectrum,

[2] *“Bisantrene for Relapsed / Refractory AML”* (NCT03820908) was designed and conducted by Israel's Sheba Medical Centre as an investigator initiated trial. Race provided bisantrene drug product and a financial grant to Sheba.

when we use the newly reformulated bisantrene[3] which may or may not be totally equivalent to what was done, what was used over 30 years ago?

In this trial, the investigators used the protocol that had been established 30 years ago, though, which consisted of 250 milligrams, per metre square, given once a day for seven days, in 10 patients. These 10 patients were evaluated both for safety and efficacy, and we see, somewhat to our surprise, but also very gratifyingly that they got an overall response rate of 40%, like Dr. Cullity, just referred to.

We can also summarise the study by saying that it had a favourable safety and tolerance profile, very similar to what was recorded in the historical data.

That pretty much summarises the study. So unless you want to continue with me, you can turn off the computer now. No, I'm just kidding!

So, the study design was that of a Phase II, basically because everyone got the same dose, the dose that had been used in the historical trials. It was single arm, single centre. This study was performed at the Chaim Sheba Medical Centre, the biggest leading and most advanced medical centre in Israel, in Tel Aviv, and it was performed by professor Arnon Nagler, a well recognised international authority in haematology leukaemia treatment and stem cell transplantation.

So, the inclusion criteria included patients with relapsed and/or refractory AML. They needed to be adults, meaning aged 18 and older; have good performance status and what we call adequate heart function with a left ventricular ejection fraction or more than 40%. My comment here is that normal cardiac ejection fraction is counted as 50% and up to about 70%. So this study accepted patients that were a little bit lower than normal, but we have to remember also that these 10 patients likely have received a lot of previous anthracycline therapy, which is cardiotoxic and may have lowered their ejection fraction.) Additionally of course, patients must exercise adequate birth control if potentially fertile and sexually active - that is a standing criteria for inclusion.

Exclusion criteria included active lung disease or poor lung function overall; normal diffusing capacity for carbon monoxide is in the high 90% range and the classical criteria actually, for most clinical studies we expect the patients to have a diffusing capacity of more than 50%; but this study accepted patients with a diffusing capacity as low as 30%, but no lower. Symptomatic heart failure: more than grade two in the New York Heart Association's grading criteria was an exclusion criterion. High bilirubin as a sign of impending liver failure was an exclusion criterion, simply because anthracene and similar drugs are metabolised in the liver. Therefore also transaminase levels that were more than three times the upper normal limit were considered exclusion criteria. Further, poor kidney function, since a fraction, or probably about 20 to 30% of bisantrene could go out through the urine and would also be there as a limiting criterion for tolerance if the kidneys have shut down and, finally, active central nervous system involvement with leukaemia were exclusion criteria. But we're coming back to that because there were two patients who were made exceptions and accepted into the trial, even with active CNS disease.

Since patients could come to this trial if relapsing after a stem cell transplant, if they had complicating problems of the transplant such as serious Graft Versus Host Disease, that would also be an exclusion

[3] The bisantrene formulation remains as it was during the original trials, however Race did manufacture new drug product for the trial.

criterion. So overall, the entry criteria were very liberal, allowing for patients to be entering the study with advanced disease, borderline heart function, and borderline kidney, lung and liver function, based on these criteria.

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Clarification:

This section has been modified to align with the trial criterion as published with clinicaltrials.gov.

Original statement:

The primary endpoint of the trial was a composite of complete remission and complete remission with incomplete hematologic recovery.

Secondary endpoints defined from the time of study entry to death were survival or overall survival; duration of remission if there was one; complete partial or complete with incomplete hematologic recovery, and incidence and severity of adverse events.

Updated statement

The primary endpoint of the trial was a composite of overall survival and leukemia-free survival.

Secondary endpoints included remission duration, type, incidence, and severity of adverse events (AEs), and mutational analyses on patient bone marrow samples to evaluate for possible associations between somatic mutations and clinical response patterns.

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Transcript resumes:

Prof Borje Andersson: the study of gene mutational analyses, were added since different gene mutations are known to influence the likelihood of responding to this type of chemotherapy.

As I said before, bisantrene was given at 250 milligrams per metre square, once a day, for seven days as a two hour infusion.

And we assess the patients for safety - the acute safety, meaning they were followed for both signs of allergic reactions in conjunction with the infusion of the bisantrene and physical exam, prior to and following the infusions. Clinical lab testing before and daily during and following the infusions, serial EKGs; and all adverse events were evaluated as according to the standardised criteria published by the US NCI. And all patients received one course of bisantrene.

I want to comment there that there was a provision for giving a second course with an attenuated dose in patients who achieved complete remission, only. And we'll come back to that in a little bit.

Response was assessed as disappearance of blast cells in the bone marrow and in blood. In comparison with a pre-treatment evaluation, including both bone marrow and blood counts. And responses were evaluated according to the International Working Group for Acute Leukaemia, from their 2003 published criteria. And all ten patients that completed were assessed there. Disease mutations were evaluated with next generation sequencing. But unfortunately, we only had samples from bone marrow, in seven patients from before the treatment that had enough cells to allow for a complete

sequencing, so when the final report / manuscript will be published, there will only be data from seven patients when it comes to the mutation sequencing.

So, if we look at the patients, the median age was 43, with a range from 22 to 80. There was six male and four female patients. They all had good performance status. 9 of 10 had the performance status of zero in the ECOG grading system, meaning 100% performance. And one was slightly lower, but still very good performance status at 80 to 90%. Three patients had antecedent haematological disorder, meaning myelodysplastic syndrome or equivalent, prior to developing AML. These patients are more difficult to get into remission than your average patient. And four of the 10 had extramedullary disease, a fairly uncommon occurrence but for unclear reasons, there was by chance a selection of patients with extramedullary disease in this small cohort. And the average prior therapy were three, ranging from one and up to four previous lines of therapy, prior to coming into this treatment programme. Seven patients were relapsing after prior allogeneic stem cell transplant.

When it comes to the cytogenetic risk factors, these were patients with intermediate or advanced risk, meaning that they were high risk for not responding at all. And when it comes to the ELN risk category, same thing: two were considered favourable only out of 10, the others were intermediate or high risk.

When it comes to the actual gene mutations known to correlate with refractory disease, two of the 10 patients had NPM-1 mutations, the rest were wild type; and we had four of the 10 who were FLT3 positive. Patients with refractory or relapsing AML, with FLT3 positive disease are notoriously very difficult to treat, and you would not expect that anyone in this kind of setting where they have already failed several lines of therapy would respond to anything, unfortunately, unless you have the newest targeted agents for FLT3 mutations involved in the combination that was being offered.

When we're looking at the safety aspect of this study, the most common adverse effects were the haematological side effects, and also mucositis or sores of the mouth, throat and to some extent the gut.

Now, this is to be expected with classic AML therapy. We used to say that you will get worse before you get better, because of the similarity and sensitivity to the anti-leukaemia agents between the leukemic cells and the normal bone marrow cells as well as the rapidly growing cells in the lining of the mouth and throat. So, there was nothing unexpected there.

I do want to comment on the fact that two patients were listed as having had myocardial infarction and it takes a special comment on that and you may wonder, ‘is bisantrene cardiotoxic if two of 10 patients got myocardial infarction?’

Well, they were classified as such. But looking closer at what really happened, the first patient went through three days of bisantrene and showed some elevated cardiac enzymes in routine surveillance testing. The bisantrene was stopped; the patient underwent a complete workup for myocardial infarction. Nothing was found - myocardial infarction was ruled out in other words, and subsequently the bisantrene was reinstituted; the patient completed the full course and had no more suspected cardiac problems during, or following this course in therapy.

The second patient who was listed as having developed myocardial infarction, was actually the patient who had a complete response, and was taken off study a little bit more than three weeks after completing his course of bisantrene, because he had a donor lined up for an allogeneic stem cell

transplant. Normally, you would then take the patient off study which was done, and then he was followed for overall survival only.

Sadly enough, while he was undergoing the conditioning therapy, the high dose chemotherapy for his stem cell transplant, he had an unexplained sudden cardiac arrest from which he could not be resuscitated and the investigator listed this as a myocardial infarction and that his death possibly was related to myocardial infarction, since that was the closest that for this type of event could be found in the CTCAE criteria. We would not classify this as related to bisantrene for the reason that he had already started a new treatment program and sudden rhythm disturbances, possibly causing sudden death, occasionally happens with high dose chemotherapy regimens that are commonly used to prepare patients for allogeneic stem cell transplantation.

The rest of the side effects in the safety table are what would have been expected as well, with diarrhoea, vomiting, skin rash, and mouth sores with bleeding, secondary to low platelets. But, nothing unusual in this clinical setting.

So, on the gratifying side, one patient achieved a complete remission. And I want to comment on that one because it was said in the outset that patients who achieved the complete remission were eligible to receive a consolidation course with attenuated dose of three days of bisantrene, at 250 milligrams, per metre square, per day.

However, from a medical point of view, a patient who has achieved a complete remission, who is eligible for a stem cell transplant and when the donor is available, this patient will not be subjected to a consolidation course when the transplant team is ready to take over - this patient will be funnelled right over to the transplant team. He will be taken off study and start the pre transplant conditioning regimen as soon as deemed appropriate.

All other patients were to undergo one course of bisantrene only - that was a stipulation of the protocol.

And then if we look at the other responders - or the rest of the responders, interestingly enough, the patient who had the complete remission, had extensive involvement of skin, relapsing in the skin as solid tumours. This is difficult to treat, but he achieved the complete remission. And as I said, he was bridged to an allogeneic stem cell transplant.

Then we had one patient who had relapsed with solid tumours in the form of chloromas in her breast, skin and lymph nodes. She achieved a partial remission, based on assessment with PET scans before and after treatment, so that one could get a very good assessment of overall disease response.

There were also two patients who were allowed to enter the treatment with active disease with CNS involvement: one with eye involvement and one with leptomeningeal or central nervous system involvement, both of them achieved a partial remission.

Based on what we have seen, we feel that in today's climate, in today's patient population and with the change in supportive care and concomitant medications, we have established that bisantrene is safe; the adverse event or side effect profile did not significantly change from what was reported 30 years ago, and the dose of 250 milligrams per metre square, daily for seven days, remains effective against relapsed / refractory AML in a similar range to what was reported in various studies in the literature more than three decades ago.

And, it is also telling us that we should use bisantrene to re-enter the AML therapy landscape again today.

So when we say enter the landscape of AML therapy today, we can ask, how and where do we go with bisantrene?

Well, that's actually not something that we have taken lightly upon. I will touch upon that in a very general way by saying that, based on preclinical studies that have been performed in model systems under the leadership of Dr. Ben Valdez at the MD Anderson Cancer Centre, who has been collaborating together with Race Oncology under a sponsored research agreement, we developed an algorithm for how we can hopefully, optimally combine bisantrene with another class of agents, commonly referred to as nucleoside analogues and we will enter that into a clinical study to be performed and open within the next four to six months, hopefully to be performed again at the Chaim Sheba Medical Centre under Professor Nagler in Tel Aviv[4], based on the very positive experience we have working with him and his world class investigative team. This study will be performed in similar patients, relapse patients with AML and it will be performed in adults only.

And secondly that we are preparing for, and entering the paediatric AML arena with a study that also is comprised of a combination of nucleoside analogues and bisantrene, where we will have early data already from the adult study to support the paediatric study, and we have also further developments that are to be explored, but I will now turn over the chair for presentation to Dr. Daniel Tillett.

Thank you very much for your attention.

Dr Daniel Tillett: Thank you, Borje.

So I'd like to talk about the other activities that form part of the five pathway strategy of Race Oncology. The first one remains with AML. But in a different indication, which is, what we've termed the MRD opportunity. And so what's been observed is, in patients that are fit enough to go through the induction chemotherapeutic pathway, about 25% of those patients have a small amount of residual cancer remaining in their bone marrow after treatment. So they're in clinical remission or complete remission, but they still have a small amount of cancer left inside their body.

And if you study those patients using very sensitive techniques that can detect very low levels of cancer, you can identify two population groups: those that you can measure the small level of cancer, and those that you can't. And the outcome for that is very, very different.

The two year survival, if you have a small amount of cancer left, is less than 25%. If you have (this is after bone marrow transplant, or stem cell transplant) if you don't have any residual cancer left, or at least measurable residual, you have an 80% survival rate. It’s a massive difference in the outcome for the patient. Obviously, if you're a patient that’s in CR, you would like to be MRD negative, before you get a stem cell transplant, your likelihood of survival is very good - close to 80%.

[4] The size, scope, timing, drug combinations and full strategy for the follow-up trial are in planning, however have not yet been fully finalised, so this statement is subject to change. Race will update the market in line with its disclosure obligations when material decisions are made on this, and other clinical programs.

If you happen to be MRD positive, at the moment your likelihood of survival is quite low, and there is nothing available clinically, to change that status.

So if you're MRD positive, the doctors can tell you you've got a high chance of relapsing and dying, but they can't really offer you any extra treatment.

So bisantrene has the potential to convert patients who are MRD positive into MRD negative.

And so we have looked at the overview, this is very similar to the slide that Borje presented previously. And you can see there that the idea is after induction chemotherapy, those patients that are MRD positive would receive a course of bisantrene as a single agent treatment. And the idea would be the outcome there would be to try and convert those to MRD negative before they get passed into a stem cell transplant, with the hope of increasing the probability of a cure.

This is a secondary separate use of bisantrene that's separate to the salvage approaches, the combination type treatment - and it allows a market that is potentially a much larger market and also less competitive market. So there's a lot of treatments, a lot of treatments out there chasing the salvage pathways, combinations, but there are less in MRD. So it's got a lot of potential. Of course, at this stage, we have to actually do the studies to identify whether this holds out, but there's a lot of potential if we're to do so.

So the idea of this would be to do a Phase II trial. The aim is to run it in the USA or potentially somewhere else, for example, Israel, in partnership with a leading cancer centre, so you would have transplant eligible MRD positive patients that are in CR, and you also have the potential there for expanding that into a paediatric study as well.

The study design is very similar to the trial that has just been completed in Israel. Seven days, 250 milligrams/m^2, in approximately 28 MRD positive patients. The endpoint's really basically MRD status, post bisantrene treatment. You would know that within 30 days of treatment, and then also overall survival or leukaemia-free survival, post transplant. That would tell you that when you're actually making a difference to the overall survival the patients.

The advantage of this is that we have a large amount of historical data for bisantrene which can be incorporated into a New Drug Application or registration. And this is under a particular pathway, called the 505 v2 pathway. And what that allows you is you can effectively establish a large amount of safety by using the historical data, provided you treat in the same manner as in the historical trials.

And so we were able to leverage the value of the data that we have, from the historical trials into accelerating the process, the potential of approval for bisantrene. Now, of course, this requires that it actually does make a difference, that you can convert MRD positive patients to MRD negative and you also need to show that it improves overall survival. But it does allow the goal of getting to approval in a faster pathway which has a lot of value to the shareholders of Race.

One of the other major focuses for bisantrene is breast cancer. There was a large amount of work in fact, by patient number, more work done on breast cancer, than on AML. And a large phase three trial was run in the USA, where it was discovered that bisantrene, despite being given in the wrong dose, and the wrong administration pathway showed that it was as effective as doxorubicin, (which is one of these anthracyclines) in overall survival, and progression free survival.

On top of that, the side effects seen in the patient were considerably less.

For example, 24% of the patients given doxorubicin experienced heart failure in the trial, where only 4% of the patients who were administered bisantrene, suffered heart failure. That is a very significant difference in side effect profile for the patients. And today, doctors would be very interested to use a drug that had much lower cardiotoxic side effects.

Of course, breast cancer, like AML has moved on in the last 30 years. And the idea of using a single agent in breast cancer is a very old idea and no one does that anymore. So much like what Borje and his collaborators have done with AML - working out which combinations of existing drugs work best with bisantrene in preclinical studies, we're undertaking this with the University of Newcastle to work out which combinations of breast cancer drugs work best in combination with bisantrene.

And once we have that data we'll be in a position to be able to go into a proof of concept trial, a Phase I/II type trial; limited number of patients, a relatively cheap trial to undertake, but the ability to show that bisantrene has value, it still has value in breast cancer. And of course breast cancer is a very large market with over 2 million cases of breast cancer every year. And there is there is a strong clinical need for anthracycline type drugs with lower cardio toxicity.

In this case, the intention here is not to show improvements, but just to show equivalency. If it has the same level of efficacy as doxorubicin, but without the damage to the heart, then that becomes a provable target, a provable drug. And the aim would be that doctors over time would shift from using a dangerous drug like doxorubicin to a less dangerous drug like bisantrene.

The final pathway which we are pursuing is in the ovarian cancer market.

So ovarian cancer is probably the opposite of breast cancer. Breast cancer's diagnosed often very early and the patient has a long life expectancy these days after diagnosis.

Ovarian cancer's often diagnosed very late after it's metastasized around the patient. And there is very little that we can still do for ovarian cancer. It's still a death sentence for many, many women.

Bisantrene in in the historical trials showed some efficacy, and we be we believe it's worthwhile pursuing whether bisantrene today can be something that could still work with ovarian cancer, which is certainly a great need.

A lot of the historical trials for ovarian cancer were done at sub optimal doses. They didn't use any combinations as they currently do. And the way they were dosed, the patients was also suboptimal.

It's a much larger cancer market than AML. Once again, it's about 200,000 cases a year. And this also opens up the ability to attract partners that are interested in this particular indication. So obviously, different companies have different, even oncology companies, have different markets they're interested in targeting. By having a drug like bisantrene which is so broad in application, you have the ability of attracting different partners for progression of bisantrene through the clinical trial process.

And with that, I will pass it back to John, who's just got up and run away!

Dr John Cullity: I just had to plug my laptop in. So unexpected break!

A lot of excellent questions have come into us and I'm looking forward to fielding those with Daniel and Borje as well. Let me just toggle over and look at them now.

Borje, first a few for you. Let's start with this one. Is the old formulation used in the 80s known? And if so, how close is the formulation that we're currently applying to the old one. How do we go compare apples to apples here?

Prof Borje Andersson: so we're still comparing apples to apples, John because even if the formulation is slightly different, the active drug component is bisantrene and that is what is important. The formulation is just like a carrier that stabilises the drug and prevents it from crystallising when it is being administered into the patient. So the active component is no different now than it was 30 years ago.

What we were concerned about prior to starting the first clinical trial was not so much that the bisantrene had changed, but more so, that we were targeting a patient population that has been treated differently. And therefore, the leukaemia's ability to respond to bisantrene could, to some extent have changed. And also when different drugs and drug combinations have been used in patients and different concomitant medications have been used, that can affect the side effect spectrum of a drugs, even if you think that you know the side effect spectrum.

We have seen that in other instances with drugs that have been introduced and are being used to treat leukaemia patients now, before they come to allogeneic transplantation. And we see in certain groups of patients, we have to be very careful because we have identified newer drugs that will be inducing problems that are not obvious until you give the new chemotherapy agents, prior to stem cell transplant in stem cell transplantation. Then you realise too late that we have a major problem.

Dr John Cullity: Borje, a couple here while we're on the theme of toxicity, one question has come through. Are there any safety data from Lederle that are available to Race? (Perhaps could speak to the drug master file.) And was QT interval prolonged in any of the ECGs that were taken during the study - perhaps alluding to the cardiotox profiles?

Prof Borje Andersson: we have not yet seen the aggregate ECGs so I cannot comment on whether we had QT prolongations, unfortunately.

And the answer to the first part of the question, do we have access to the master file? Yes, we have access, we have been allowed access through the NCI to the majority of the master file data for bisantrene as it was filed previously with the NCI.

Dr John Cullity: thanks, Borje, and for those who are not familiar with it on the ECG, the QT is the last section of the ECG, the excitation relaxation, and it's often associated with arrythmia, so it's just something that doctors look to. Okay, staying with that Borje, going back to the levels of cardiotoxicity that were picked up in the bisantrene file we inherited from Lederle, would you say that these levels

of cardiotoxicity that we're identifying here, quite low levels, are consistent with what's been observed in the past?

Prof Borje Andersson: well, it's easy to say yes. However, please remember that we have only treated 10 patients. We have not seen anything in those 10 patients that would make us overly worried.

However, when we go forward, we will follow each and every patient in both the upcoming adult study and in the paediatric study as well as in the MRD studies, with very close cardiac monitoring. We will set the baseline with an echocardiogram. We will follow patients with daily high sensitivity troponins, before, during and following the administration of the course of bisantrene-based therapy, and we will repeat echocardiograms at one and two months post treatment to make sure that we don't see any change in the heart contractility function, which would be a hallmark of the type of cardiotoxicity that you expect to see from both anthracyclines and potentially also with the anthracenes, aka bisantrene, but hopefully to a much lower extent.

Dr John Cullity: Borje, just one here that's asking you to put your hat on as a stem cell transplant expert: due to the exclusion of higher levels of Graft Versus Host Disease patients from the study, wouldn't the potential number of patients and accordingly the target markets / target population that might be addressed, be considered considerably lowered?

Prof Borje Andersson: well, the potential patient population, you can say that it would be lower if you exclude any kind of patient sub population. But please remember that the patients who were excluded, were those who would have active grade three or four Graft Versus Host Disease.

Now, let's take a look at a typical scenario after stem cell transplant, grades three to four, and in today's very effective and well managed transplant programmes, you will expect that you have at most, 10% of the patients developing grade three or four, or rather grade three and four combined. So it would be one in 10. And out of those, the likelihood that the patients would have time to relapse and make it out from the transplant programme and be subjected to salvage chemotherapy of a conventional type with bisantrene, or other agents is very low.

So, from a practical standpoint, I would say that excluding patients with active grade 3-4 Graft Versus Host Disease would not really impact the volume of patients that would be subjected to salvage chemotherapy after they relapse, because they would already have died from progressive Graft Versus Host Disease before they can come to an alternative treatment situation. It is sad but it's a fact.

Dr John Cullity: It's multi-layered.

Just one more for you, Borje and then Daniel a few to come your direction. So, one of the viewers today has said according to clinicaltrials.gov, the stated primary objective for the trial is overall survival, combined with leukaemia free survival. Borje, would you comment on that?

Prof Borje Andersson: Well, it's still very early and we cannot comment very much on overall survival for the whole group, but we can comment on leukaemia-free survival for the one who developed a complete remission, and as I said, he came off study and was routed to an allogeneic stem cell transplant, he sadly died because he suffered a cardiac arrest in the middle of his pre-transplant, high dose chemotherapy regimen. At that time he was still in a complete remission. Would that have been a lasting remission with a stem cell transplant? It's possible. Unfortunately, we would not have been able to attribute a long lasting remission or a cure to the bisantrene; we should remember that part of our (medical) goal was to bridge patients so that they could have their disease stabilised and qualify for a stem cell transplant. So that goal was reached in him. But other things, sadly took a different turn of events, later on.

When it came to the survival of the three patients with partial remission, it's too early yet to say how long the partial remissions were lasting. We don't yet have those data. And as far as overall survival of the entire patient population goes, it is also a little bit early to say how long the last few patients will live, but patients who do not respond to any salvage chemotherapy program will on average, as a group, not have a survival that is much different from patients who are completely untreated. In the historical data from the late 1940s and 1950s, the first papers that were published on Acute Myeloid Leukaemia in the late 1940s and early 1950s tell us that the average survival from diagnosis was in the order of 9 to 12 weeks without modern chemotherapy. So one can probably deduce that patients who went into our trial and did not respond at all bisantrene, and who had not responded to previous chemotherapy have overall a very poor prognosis.

Dr John Cullity: we would also add that it's important that those of you reviewing these data recognise that these patients receive but one cycle of therapy: seven days of bisantrene. There was no consolidation with second and third cycles, as we typically see in clinical practice. So we were detecting signal here from this series, and we were putting that signal through to you with these data. Borje, would you build out on that comment?

Prof. Borje Andersson: Yes, it's common practice to give more than one cycle of therapy if patients show a response, and preferably at least a partial remission, then you often give a second cycle and some of these partial remissions can be expected to convert into a complete remission.

The design of this protocol only made the provision for giving, as I alluded to from the beginning, an attenuated course of consolidation if you had first achieved the complete remission, but not in patients who had less than a complete remission. From a company perspective, one of the goals of the study was to detect activity and confirm that there was no excessive toxicity with our current bisantrene formulation in today's patient population, and we feel that that has been accomplished.

Dr John Cullity: thanks Borje. Just looking at the clock - we're now past 11:00am AEST. We will be extending for another 15 minutes to go through some additional questions.

Daniel, one for you here: is Race actively seeking to encourage more investigator initiated protocols of bisantrene, either in single agent or in combination, Daniel Tillett?

Dr Daniel Tillett: not actively, but if we're approached, if an investigator that approaches us and says, 'I would like to run an investigator initiated trial', and we thought that what they are intending to do made clinical sense, then we would be open to that. And I think that's something that investors could look forward to seeing when these results are released. There will be interest from clinicians in bisantrene, and I think that the opportunity of that is very real. But going forward in the future, we intend to have company sponsored trials which are heading towards registration, rather than these sorts of initial type studies. So we've moved on from that as a focus of the company.

Dr John Cullity: thanks, Daniel. So here's a question that I'm going to split between the two of you. Can you please clarify the timing and locations for pathway two, which is paediatric AML. And Borje, that goes through to you. And then Daniel, the question says, also for pathway three, which is for MRD.

So perhaps, Borje could you lead off? I know that you've convened the clinical advisory board recently with relation to paediatric AML, could you give people a bit of an update on that one?

Prof Borje Andersson: yes, we reviewed the plans for the upcoming clinical trials. And the recommendation of the Clinical Advisory Board was to first do the adult study, hopefully also this one can be carried in Israel at the Chaim Sheba Medical Center in Tel Aviv by Professor Nagler's group. Secondly, we will embark on the paediatric trial, which will be using a very similar combination - basically the same combination as in the adult trial, and where we will be supported by early data from the adult trial, even though it's a different target patient population, that of children with relapsed AML.

The main reason for the paediatric trial is that we have an orphan drug designation and we have the provision for getting a paediatric indication voucher from the US FDA. We are currently discussing whether we could[5] potentially be in a good situation to get additional funding to support that trial, in the US as a multicenter study in the US from the Texas Cancer Prevention Research Institute, where we are planning to submit the grant application in the late fall of this year.

Dr John Cullity: thanks, Borje. And, Daniel, over to you for some comments on MRD. Again, can you clarify timing and locations for taking the MRD programme forward?

Dr Daniel Tillett: the intention of the MRD trial is to run it as a single site in the US, but at the same time, we have to be flexible, given the situation with COVID in the US, which can potentially make things difficult. And so there is potential to run that trial either in Australia, or to run it in Israel

[5] At all times, Race is exploring options for acquiring non-dilutive capital. Ability to submit for this grant relies upon reopening of this grant procedure by the Texas government after the COVID19 situation calms down.

potentially, as well. There's no particular reason it has to be run in the US, particularly the first initial phase of that trial, to try and generate proof of principle that this will actually work.

But if you're intending to go for registration, you'll need do to at least to at least two sites. The FDA doesn't approve a drug, no matter how well it's worked for an indication, based off a single site. So there will need to be multiple sites, but at least one of those sites will be within the US.

Dr John Cullity: right, I'll just clean up a couple here - the first is now that we have these results, what activity and potential news flow like can we expect over the next six months, well, I've written some hand notes here and I'll just read them through to you.

The first is that from this primary protocol that we've reported out on this week, we will be publishing[6] these data in a peer reviewed journal, and as that goes through to that journal as accepted for publication, we will update the market.

We're also seeking to submit an abstract to the American Society of Haematology will ASH and as the number of you would know, that meeting takes place in December of each year.

Turning then to the rational combinations that we'll be taking into the follow on study through Professor Nagler, internally we call that Nagler 2, where we'll be identifying the one plus one equals three (if I can put it that way), combinatorial efficacy of bisantrene, plus complimentary chemotherapeutic agents; this builds from Professor Andersson's work at MD Anderson with in silico analyses and that manuscript will go for publication during the second half of the year and we will release a related update to the market.

And then as the Nagler 2 protocol is finalised, and we're now actively working towards that, we will update the market when that has been accepted by the IRB at the Sheba Medical Centre.

Furthermore, I'm pleased to advise that we'll be developing a number of video updates for the market, where Borje, Daniel and myself, plus others will be appearing, including I should add Professor Jaap-Jan Boelens who is professor of paediatric haematology oncology at MD Anderson Cancer Centre in New York. Daniel will be looking to interview thought leaders in MRD. And we'll be drawing Borje out further on aspects of the follow-on protocol.

So hopefully that addresses your question there.

And then a final one: do these results change the priorities and in the 5-paths for Race? No they purely consolidate them. We see here that we have four tenths of distinct efficacy in the relapsed / refractory AML setting. So naturally enough, we're going to be building on that and carrying that forward with some expectation. Also moving into the paediatric programme, which as Borje identified gives us a rich shot at that priority review voucher, which a number of you would know has a tradable value of approximately 90 to 100 million US dollars, so we'll be pursuing that to benefit those children and also to benefit shareholders.

[6] Data will be published by the investigators, in this case, Professor Arnon Nagler and his team at Sheba Medical Centre. Race does not have a co-authorship role on this paper.

So I believe that there might have been one or two other questions that have come through, excuse me, whilst I toggle through to my email here and try and pull those up for you. And with that, we'll conclude the session here.

Borje, here's one for you. Will we be looking to do a trial for AML in an AML setting, prior to a patient going into the relapsed / refractory stage? How do you respond?

Prof Borje Andersson: if we will be looking for a trial, for patients before they relapse?

Dr John Cullity: yes, this is the earliest stage management. Perhaps I think the questioner was asking, would we see for example, that we could move into first line, second line, induction chemotherapy. Perhaps pipping daunorubicin in seven + three.

Prof Borje Andersson: yes, absolutely. There are two questions really coming up, one of them is when you already are in remission, but you have detectable disease, but before you have an overt clinical relapse, can we consolidate and deepen that remission and get rid of the detectable disease? Which is just what Daniel was talking about in the MRD situation.

These patients who are in a high-risk remission, they will have a clinical relapse soon, but from a psychological point of view, just looking at the bone marrow; looking at the cells and the blood counts, they are in remission. But with more sophisticated analysis, they have detectable disease. So that's one scenario.

The other scenario comes to newly diagnosed, not yet treated patients. I believe personally that it will be a - excuse me for using the word - a no brainer.

But if we can show that we have very effective induction therapy, and we can continue to document that bisantrene is highly effective and has very little cardiotoxicity, then we don't really need to tell clinicians that here is a better alternative. It's going to be a medical field-driven change. The treating physicians would want to have a non-cardiotoxic alternative, they will favour that.

Because today, when you talk about seven + three or FLAG-IDA, or any one of these combinations that are used to induce remissions, both in paediatrics and adults, people don't really talk about the fact that you keep track of the daunorubicin and adriamycin and doxorubicin. And in adriamycin equivalence, once you once you reach 300 milligrams per metre square, patients don't get any more. Clinicians would rather see the patients if they relapse. They will give them a second line - meaningless effective therapy - to prevent heart failure to develop, because it's an unspoken rule that it's less bad to die from the leukaemia than it is to die from a medically induced complication of treating the leukaemia.

And be that as it may, once we have established and gotten bisantrene approved, people will look to that as a better alternative and they will replace daunorubicin and Adriamycin and they will replace the anthracyclines with a non-cardiotoxic anthracene. In other words, bisantrene, in these combinations.

Dr John Cullity: I think I think actually what we might do is we might leave it there due to the constraints of time, but what a great way to wrap up the session today to really bear out one of the core points of difference of the bisantrene programme: achieving efficiency, whilst preserving cardiac function, and with that, providing clinicians with an active choice, we trust, in prospect, downstream of a kinder anthracycline-like product. We don't say an anthracycline itself, because ours is an anthracene – a variant, but preserving that fundamental efficacy.

We're looking to bear that out in our clinical study programmes over the next months.

So we're going to wrap it up for this morning. I want to thank Borje. I want to thank Daniel for their excellent commentary, and for informing you, our viewers.

Thank you for participating. We look forward to keeping you updated with those matters that I referred to earlier on our manuscripts and our future clinical study protocols.

So let's wrap it up there. I want to wish you all a great day. We will look forward to speaking with you again soon.

Thanks and goodbye.

- ENDS -