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VIRAX review

VIR201 CLINICAL DATA GAINS INTERNATIONAL RECOGNITION

The positive results of Virax's landmark clinical trial, identifying VIR201 as a leader in a new generation of treatment for HIV, were well received by researchers at a recent pre-eminent international conference on HIV/AIDS in San Francisco.

On Wednesday February 11, Professor David Cooper AO, Director of the Australian National Centre in HIV Epidemiology and Clinical Research (NCHECR), presented the results of clinical testing of the potential HIV treatment vaccine VIR201 to medical and scientific research peers at the prestigious 11th Conference on Retroviruses and Opportunistic Infections in San Francisco.

In his presentation Professor Cooper explained the extent to which VIR201 controlled patients' HIV level or viral load, when compared to placebo.

"On the clinical evidence now available, VIR201 is one of the most promising treatment vaccines currently under development and further trials are warranted," said Professor Cooper. "Twenty weeks after a booster injection, patients on VIR201 had a lower HIV level, compared to the participants who received placebo."

"Controlling the level of virus is fundamental for the management of HIV. If we are able to keep the viral load low, patients will not develop AIDS and can live long and relatively healthy, normal lives," he said.

Although current treatments, known as Highly Active Anti-Retroviral Therapy (HAART), have been successful in maintaining low viral load and prolonging the lives of many HIV positive people around the world, an alternative like VIR201 is needed, as there are inherent and growing problems with HAART.

The trial results indicate that VIR201 has the potential to change the future management of HIV.

"Together with Virax, we are looking to progress VIR201's development with a larger Phase II trial," said Professor Cooper.

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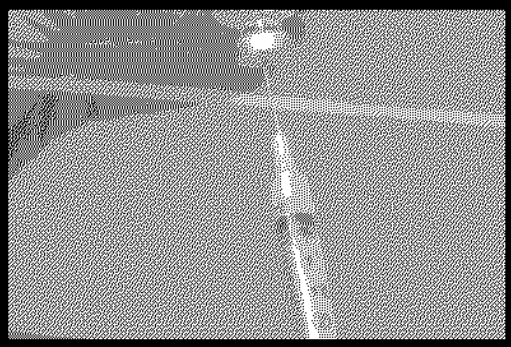
VIR201 CLINICAL TRIAL EXPLAINED

Treatment Vaccines and VIR201

VIR201 is a treatment vaccine that harnesses the power of the body's own immune system, rather than fight the virus itself, like current anti-viral drugs. VIR201 stimulates the immune system to produce a specific response to the HIV virus.

VIR201 is a recombinant pox virus with co-expression properties, which set it apart from most other treatment vaccines under development. By expression of two genes together it is designed to stimulate an immune response to fight disease and target this immune response towards the HIV virus.



The Data

The primary endpoint for the second part of the study was time weighted mean change (±sd) from participants' baseline plasma viral load (pVL).

Baseline plasma viral load (pVL) refers to the level of virus in the blood at the beginning of the study which was generally undetectable.

Viruses spread by reproducing themselves inside cells in the body. Viral load is a measurement of the number of copies of the virus per millilitre of blood. This is expressed in terms of logs which means 10 to the power of.

Analysis showed the change from baseline pVL was 0.96 (0.91)$\log_{10}$ copies/ml for patients receiving VIR201 compared to 1.80 (0.72)$\log_{10}$ for those on placebo. This is a 0.8 log reduction in pVL for VIR201 compared with placebo.

In other words, the viral load of patients on VIR201 rose on average by nine copies of the virus. While untreated patients had an increase of 63 copies of the virus, or about six times greater.

Thus VIR201 appeared to control replication of HIV better than placebo.

While this difference is striking, it cannot yet claim to be statistically significant. The study involved too few patients to expect to reach this gold standard in scientific analysis.

Experts agree that further development and the collection of more data is necessary for this product that is showing a great deal of promise.

The Trial Design

The VIR201 Phase I/IIa clinical trial was a multi-centre, randomised, double-blind, placebo-controlled trial involving 35 patients.

The drug's safety and its ability to control the level of virus in the blood (viral load) were measured.

Three doses of the treatment, given at weeks 0, 4 and 12, were shown to be safe for patients whose viral load was controlled by highly active anti-retroviral therapy (HAART). No adverse side-effects were found.

Twelve months after their commencement in the safety study, participants were given the opportunity to participate in an extension study. Of the 35 involved in the initial trial, 25 agreed to continue and received a booster (4th dose), before stopping their anti-retroviral therapy, which had previously kept their viral load at an undetectable level. Viral load was measured almost every week for 20 weeks.

Analysis showed that the viral load of patients on VIR201 only rose slightly. While patients on the placebo had a far more distinct rise in their viral load.

In fact patients on VIR201 had a viral load that was approximately 6.3 times lower than those on placebo.

GROWING POTENTIAL OF IMMUNE BASED THERAPIES

editorial

Evidence is now growing on the validity of immune based therapies or immunotherapeutics as a revolutionary approach to the management and treatment of a range of serious illnesses. Virax's recent success with VIR201, together with the positive indications in the Transgene clinical trials (outlined below), provides significant data to support further development in this medical field.

Simultaneously, while the legitimacy of immunotherapeutics increases, questions have been raised in some quarters about pursuing preventative vaccines for HIV at this point in medical science's understanding of the HIV disease model. However undeniable the need for a prophylactic to protect individuals and so stop the spread of this deadly virus, a major problem lies in the current inability to find indicators which would demonstrate if vaccinated people are likely to be successfully protected.

The same difficulty does not apply with therapeutics, like VIR201 and the other products in Virax's pipeline. Measures can be taken to assess the success of these treatments, as we have found in the most recent stage of the HIV clinical trial. At this stage in the development of these drugs, we are also gaining valuable insight into the human immune system.

Thus an increasing body of opinion is turning towards immunotherapeutics as a solution to the HIV/AIDS crisis. Not only do we believe that treatments like VIR201 can control those infected with this virus, but there is the potential for this type of product to lead us to the discovery of a prophylactic vaccine. By taking what we learn in the development of therapeutics, we may also reveal the key for preventative medicines.

The road ahead for those working in immunotherapeutics is certainly an exciting one.

Dr David Beames, CEO

MORE POSITIVE RESULTS FOR CO-X-GENE™ TECHNOLOGY IN FRANCE

French biotechnology company Transgene, recently announced positive interim results from the Phase II clinical trials of its cancer treatment MVA-Muc1-IL2, which uses Virax's Co-X-Gene™ technology platform.

According to a Transgene statement released on February 9, 2004, this multi-facetted ongoing clinical trial has to date produced data that confirms the potential of this immunotherapeutic as an innovative and safe treatment for a variety of cancers.

Significantly Transgene's cancer treatment has been shown to be safe and well tolerated by clinical trial participants at a variety of doses and in combination with several other therapies. Establishing drug safety is crucial for ongoing development of all products, which use Co-X-Gene™ technology.

MVA-Muc1-IL2 is currently being targeted as a treatment for lung, prostate and kidney cancer. This product development is not in direct competition with any products in Virax's pipeline. The stage of prostate cancer MVA-Muc1-IL2 is targeting differs from the application of the cancer therapy Virax is currently developing in conjunction with the Royal Adelaide Hospital.

In Transgene's lung cancer trial the treatment is already showing an encouraging tumour response rate when used in conjunction with chemotherapy. Tumour response rate is the primary end point or goal of this trial.

Similarly Transgene has reported a highly significant decrease in PSA (prostate specific antigen) progression rate in its prostate cancer trial, which is considered a measure of the success of the vaccine.

Several patients in the kidney cancer trial have stable disease and further data is expected in third quarter of 2004.

"Not only does this international data provide further evidence of the potential of products based on Co-X-Gene™ technology, it also strengthens the position of immunotherapeutics which adds value to Virax's cause," said Virax CEO Dr David Beames.

"Many medical scientists have hypothesized about the potential of immunotherapeutics for some time," said Dr Beames.

"We hope that this data and the recent results with Virax's own VIR201 will inspire growing confidence in the wider biopharmaceutical community, in this therapeutic approach."

Transgene's trials are continuing.

Virax holds the patent for Co-X-Gene™ and any products developed using this technology will require a license before they are commercially released.

VIR201— A MEDICAL BREAKTHROUGH ?

Is this a medical breakthrough?
VIR201 is dramatically different to any of the current drugs available. Many groups around the world have been trying to identify an alternative to the current anti-viral therapies. This is the first clinical evidence that this approach could work and potentially revolutionize the management of HIV.

How is VIR201 so different to other drugs on the market?
VIR201 is an immunotherapeutic or immune based therapy, which is a different concept to other drugs on the market. Instead of trying to kill or directly attack the virus, it is designed to harness the power of the body's own immune system to fight disease.

How does this compare to other HIV drugs under development around the world?
This is the first treatment vaccine in the world to show an ability to block the progression of HIV. No other treatments under development in this area have achieved this kind of positive result. Virax and the NCHECR are thus leading the way.

How safe is VIR201?
So far the studies have shown that VIR201 is very safe and doesn't have any side-effects apart from the small discomfort of an injection. This is in contrast to existing HIV therapies which have several side-effects.

Is the VIR201 a cure for HIV?
It is too early to determine exactly how this drug will be used. It could be used in conjunction with existing treatments or prove to work completely independently. Longer-term studies will be needed before any understanding on VIR201's power to manage or eventually cure HIV.
At this stage it is being targeted towards the management of the HIV virus to prevent progression to AIDS.

Could VIR201 reduce the spread of HIV?
By keeping viral loads low, VIR201 has the potential to reduce the spread of HIV. This virus is more likely to be passed on from an infected person if their level of virus is high. This is particularly relevant in developing countries. However, safe sex remains the best solution to reducing the spread of HIV and is encouraged.

THE PATH FORWARD

How significant are these results for Virax?
These are the most significant results in Virax's history. This data is an important validation of VIR201 and Virax's Co-X-Gene™ technology platform.

How does Virax intend to progress the drug's development?
Virax and the NCHECR are currently looking at a number of avenues for further clinical trials. The protocols or structure to these trials is yet to be determined.

What does this mean for Virax's Co-X-Gene™ technology?
Virax believes that these results are a further validation of its faith in Co-X-Gene™ technology and vindicate the decision to expand the pipeline of products using this technology into other therapeutic areas, namely prostate cancer and hepatitis B.

How much will it cost for the next trial?
Until future trial protocols are confirmed it is difficult to accurately estimate how much the ongoing development of this drug will cost. However it is likely that the ongoing development program will be in excess of the Phase I trial expenses of $4 million.

How will this be funded?
We are seeking funding from possible partners or granting bodies.

How will this impact on Virax's other development programs?
Besides the obvious scientific validation this data provides, it has no direct bearing on the progress of Virax's development programs in prostate cancer and hepatitis B. This pipeline is moving forward and these results further justify the ongoing work in this area.

SCIENTIFIC CLARIFICATIONS

What is an immunotherapeutic or treatment vaccine?
Immunotherapeutics work in a similar way to preventative vaccinations, which are given to stop people, particularly children, contracting serious illnesses. However, treatment vaccines are given to already infected people, to direct the body's recovery.
The body's immune system normally overcomes most viruses given time.
Unfortunately with conditions like HIV/AIDS, cancer and some hepatitis the immune system does not respond. Immunotherapeutics are designed to change this. These treatments channel the immune system to fight the disease.

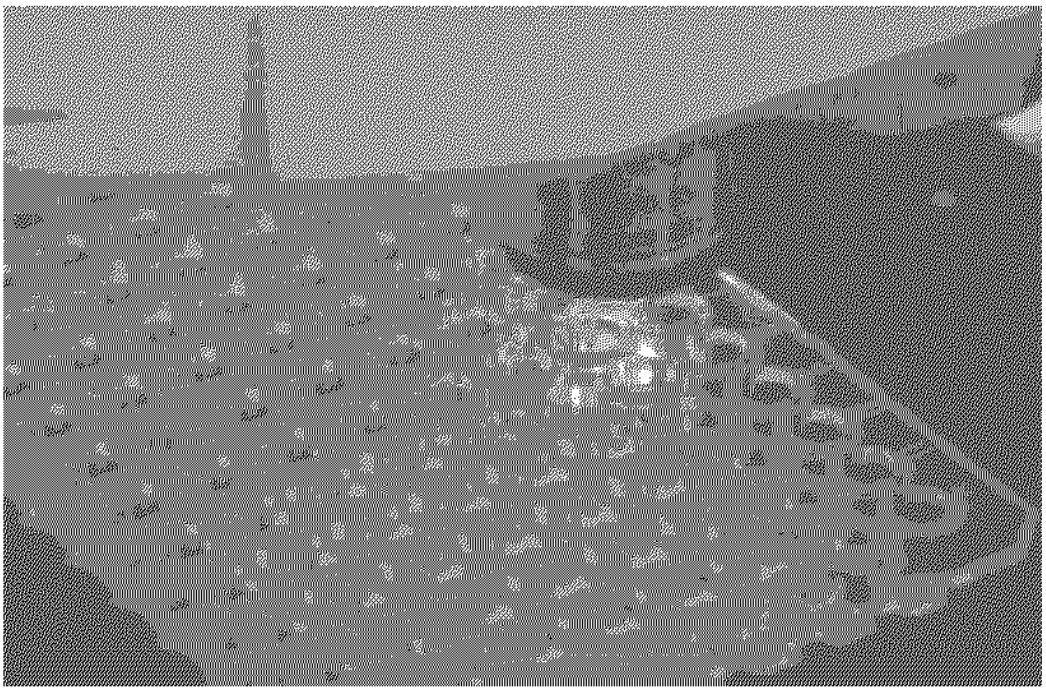
Why is it referred to as a treatment vaccine, when in previous communications it has been called an immune based therapy?
This latest announcement relates to the presentation of data in the highly precise context of one of the most respected HIV related conferences in the world. Internationally accepted terminology for this form of treatment is "treatment vaccine", "therapeutic immunization" and "immunotherapeutic". In the past Virax has referred to its products as immune-based therapies to simplify the language and avoid any confusion between this type of drug that treats disease and prophylactic vaccines that prevent people catching disease.

What is "randomized, double-blind, placebo controlled"?
Randomized, double-blind placebo-controlled studies are the gold standard for clinical trials. Randomized refers to the fact that the trial participants are randomly placed into a group to receive either drug or placebo. Double-blind refers to the fact that neither the patient nor the medical staff treating them know which injections are being given. Independent parties store the code that identifies the group the patient is in. Placebo-controlled refers to the fact that one group in the study received a placebo or a "blank".

What is meant by "control replication of HIV"?
Viruses spread through the body by reproducing themselves inside infected cells. The level of virus in a patient's body is a measurement of how many copies of the virus are found in their blood. To stop the progression of HIV into AIDS, this reproduction or replication must be controlled.

What is statistical significance?
Statistical significance is the standard test used in science to determine the strength of data. It is often described in terms of probability or p values. To be statistically significant p values need to be low, preferably equal to or less than 0.05. Such results are very difficult to achieve in small sample sizes. Thus statistical significance was not expected in this study, which only had 25 participants in the final stage.

How valid are these results if they lacked statistical significance?
These clinical results are considered to be extremely relevant in the world of HIV management. There was a clear distinction between the blood test results of patients on VIR201 compared to the results of patients on placebo and for a drug at this stage of development that is a valid claim. Furthermore, despite the small number involved in the trial some of the measures came close to statistical significance.



NEED FOR NEXT GENERATION HIV TREATMENT

Dr Cassy Workman

"Anti-retroviral therapy is tough," said Dr Cassy Workman, Darlinghurst General Practitioner and a key co-investigator in the VIR201 clinical trial.

- Existing drugs impact significantly on the patients' quality of life,
- Several tablets must be taken without fail once or twice a day, every day.
- A lapse in this strict drug routine can lead to the development of resistance to the therapy
- Toxicity problems associated with these drugs also mean that current therapies do not offer a long term solution or cure,

"VIR201 is looking very promising and offers hope for people living with HIV/AIDS around the world," said Dr Workman.

Given that no obvious side-effects have emerged in the NCHECR's trials to date and the therapy consists of a straightforward injection, a treatment vaccine like VIR201 is an attractive candidate for further development.

VIR201—IN THE MEDIA SPOTLIGHT

Recent developments with Virax's HIV therapy VIR201 gained significant local media attention when the results were presented in San Francisco by Professor David Cooper from the National Centre for HIV Epidemiology and Clinical Research (NCHECR)

The story of this breakthrough in the future management of HIV gained positive national coverage in all forms of media.

National and daily metropolitan newspapers gave good coverage news of this world first by Virax and the NCHECR.

The Australian ran the headline "Aussie vaccine blocks out HIV" while the Courier Mail claimed "Virax thrives on HIV test results". "Virax unblocked" lead a piece in the Daily Telegraph and the West Australian wrote "Virax just the tonic as index finds form."

Eleven TV news broadcasts also ran the story, with over 30 pieces on radio around the country. As was anticipated most of the electronic media did not directly acknowledge Virax's role in this project. Television, in particular, rarely mention drug company names, however the product was clearly identified as VIR201 in some broadcasts.

HEPATITIS B PRECLINICAL MILESTONE

In December 2003 Virax moved into the preclinical phase of work on its proposed hepatitis B treatment.

This innovative hepatitis B drug uses the patented Co-X-Gene™ technology platform, and like other therapeutic products in the Virax portfolio, seeks to treat the disease rather than prevent it.

In the development of this latest product, Virax is collaborating with internationally renowned hepatitis expert, Alfred Prince MD, who heads the Virology Laboratory at the Lindsley F Kimball Research Institute at the prestigious New York Blood Centre, USA.

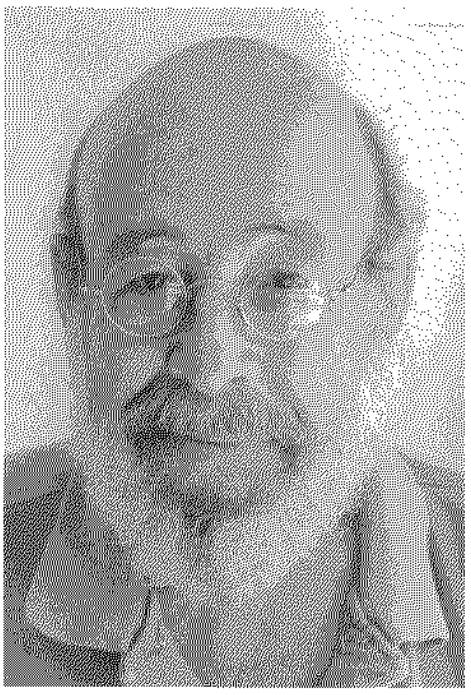
"We have always been impressed by Virax's Co-X-Gene™ technology," said Dr Prince. "This is largely what attracted us to the collaboration."

"We were therefore pleased to hear of Virax's early successes recently with its HIV therapy. This is most encouraging news for our joint hepatitis B program," he said.

The World Health Organisation estimates that there are over 350 million people worldwide and 1.25 million in the United States suffering from chronic hepatitis B. Current therapies have a tendency to become ineffective as the virus develops resistance to the treatments.

"Virax's immune-based therapeutic approach offers a positive alternative," said Virax CEO Dr David Beames.

"Starting pre-clinical work on the hepatitis B program is another important milestone for our expanding product pipeline, said Dr Beames.



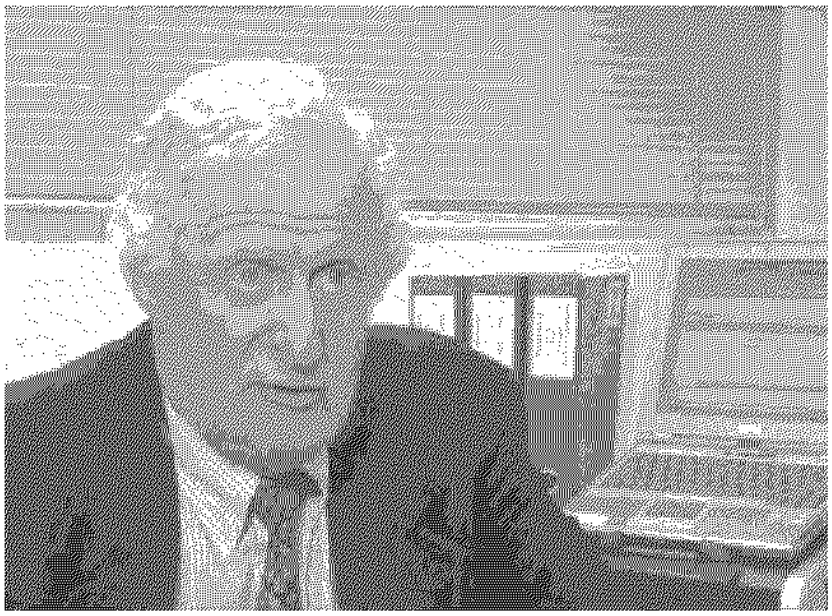
Dr Fred Prince

"Our Co-X-Gene™ technology is looking very promising and we are capitalizing upon this by progressing the pipeline of different therapies."

"We have always been impressed by Virax's Co-X-Gene™ technology. This [VIR201 result] is most encouraging news for our joint hepatitis B program," said Alfred M Prince, New York Blood Center.

EXPERT RESPONDS AFTER VIR201 RESULTS

Professor Ian Gust



Professor Ian Gust
Ex-officio, Chairperson, International AIDS Vaccine Initiative (IAVI) Scientific Advisory Committee.

What is the situation with the AID virus today?
The latest estimates are that in the two decades that AIDS has been sweeping the world, some 75 million people have been infected. About 14 thousand new infections occur every day and about 30 million people have already died from the disease.

Is AIDS still a serious problem?
As far as the public health community is concerned it still remains just about the number one public health issue at the moment.

Why do the trial results provide hope in the HIV crisis?
It's always been a kind of an alchemist's dream to develop an immunization that would eradicate either chronic viral infection or cancer and this data that's just been generated recently is of particular interest in this respect.

Why have these results attracted international attention?
What science has been looking for a long time are some other methods that could be used alone or in conjunction with anti viral chemotherapy and one of the most popular approaches has been therapeutic immunization. The data we're hearing about at the moment is the first glimpse of the possibility that therapeutic immunization may be possible.

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