starpharma

SHAREHOLDER Update

DECEMBER 2013

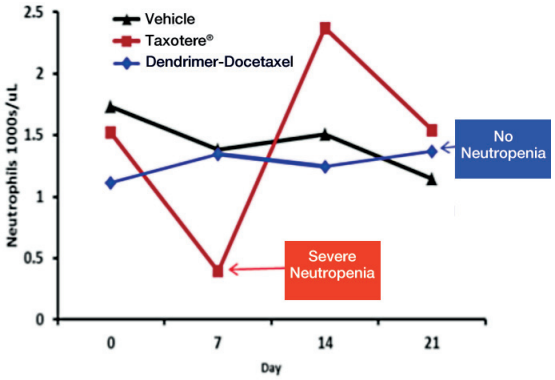
IN THIS ISSUE

›› Dendrimer-Docetaxel to enter human clinical trials

Starpharma's internal drug delivery program is approaching a major milestone and entering human clinical trials with its dendrimer-reformulated version of Docetaxel.

A Phase 1 clinical trial of Dendrimer-Docetaxel – an enhanced version of the off-patent blockbuster anti-cancer drug docetaxel (Taxotere®) – is due to begin early in the New Year. The move into the clinic follows the successful results of a number of pre-clinical studies. Docetaxel, which is now generic, has reported annual sales of US$3.1 billion.

The latest of these studies compared Dendrimer-Docetaxel to Taxotere® and demonstrated that Starpharma's Dendrimer-Docetaxel did not cause neutropenia (reduced circulating neutrophil numbers) and other important bone marrow-related toxicities (refer below). Severe neutropenia occurs in more than 75% of patients treated with Taxotere®.



Dendrimer-Docetaxel treated rats were also free from thrombocytopenia (low platelets) which, along with neutropenia, was observed in Taxotere® treated animals. Bone marrow toxicities are the most important dose-limiting side effects of Taxotere®. Taxotere® carries a FDA "black box" warning (refer right) in its Product Information regarding toxicities including neutropenia, contraindications and management requirements for certain patients.

Another toxicity-reducing benefit attributed to Dendrimer-Docetaxel is the removal of the detergent – Polysorbate 80 – from its formulation. Dendrimer-Docetaxel has markedly improved solubility making the Dendrimer-Docetaxel formulation water soluble so it is free of detergent (Polysorbate 80). Drugs containing Polysorbate 80 (eg. Taxotere® and other docetaxel formulations) can trigger hypersensitivity reactions, or fatal anaphylaxis, in patients and this is also noted in the "black box" warning for all docetaxel formulations including Polysorbate 80.

"The results from the Dendrimer-Docetaxel clinical trial will not only validate this product but add value to Starpharma's entire drug delivery portfolio."

Dr Jackie Fairley, CEO

WARNING: TOXIC DEATHS, HEPATOTOXICITY, NEUTROPENIA, HYPERSENSITIVITY REACTIONS, and FLUID RETENTION

Treatment-related mortality increases with abnormal liver function, at higher doses, and in patients with NSCLC and prior platinum-based therapy receiving TAXOTERE at 100 mg/m2 Should not be given if bilirubin > ULN, or if AST and/or ALT > 1.5 × ULN concomitant with alkaline phosphatase > 2.5 × ULN. LFT elevations increase risk of severe or life-threatening complications. Obtain LFTs before each treatment cycle

Should not be given if neutrophil counts are < 1500 cells/mm3. Obtain frequent blood counts to monitor for neutropenia

Severe hypersensitivity, including very rare fatal anaphylaxis, has been reported in patients who received dexamethasone premedication. Severe reactions require immediate discontinuation of TAXOTERE and administration of appropriate therapy

Contraindicated if history of severe hypersensitivity reactions to TAXOTERE or to drugs formulated with polysorbate 80

Severe fluid retention may occur despite dexamethasone

›› continued on page 2

DRUG DELIVERY

Dendrimer-Docetaxel to enter human clinical trials

(continued from page 1)

Apart from these reduced toxicities, earlier pre-clinical studies of Starpharma's Dendrimer-Docetaxel have also demonstrated its significantly superior anti-cancer effectiveness – across a range of important cancer types including breast, prostate, lung and ovarian cancer – compared to Taxotere®.

Starpharma's dendrimers have also shown broad applicability to the delivery of drugs outside of oncology. It is estimated that dendrimers are applicable to more than 50% of leading pharmaceuticals – this includes small molecule drug, proteins (including insulin) and biologics such as antibodies.

	Product Benefits	Dendrimer-Docetaxel	Dendrimer-Enhanced Oxaliplatin
Therapeutic Performance	Enhanced Pharmacokinetics	✓Plasma half life >60x Taxotere®	✓Plasma half life >50x Eloxatin®
	Enhanced Efficacy	✓Enhanced efficacy in various Tumor models	✓Enhanced efficacy in platinum-insensitive colon model
	Tumor Targeting	✓Tumor accumulation 40x cf. Taxotere®	✓Expect enhanced accumulation in tumor
	Improved Side Effect profile	✓Protection against neutropenia (DLT) ✓No Polysorbate 80 (avoiding anaphylaxis and steriod pre-treatment)	✓Protection against Peripheral Neuropathy (DLT) ✓Protection against Neutropenia
Commercial Performance	Extended Patent Life	✓Filings to 2032	✓Filings to 2034
	Accelerated development	✓	✓
	Robust, scalable manufacturing; stable	✓	✓
	Competitive advantages	✓	✓
	Elevated ROI	✓	✓
	Lower Technical and Financial Risk	✓	✓

VIVAGEL®

VivaGel® Phase 3 trial for prevention of recurrent BV

Starpharma's lead women's health product VivaGel® will soon progress to pivotal Phase 3 clinical trials to confirm its ability to prevent recurrence of bacterial vaginosis (R-BV) infection.

This trial will build on the positive results of a Phase 2 efficacy study earlier this year, which demonstrated both reduced overall risk of R-BV in patients using 1% VivaGel® and delayed time to first recurrence, compared with placebo.

"Positive Phase 2 data was observed in April this year. We are now progressing VivaGel® to a phase 3 trial for a prevention of R-BV indication, and our preparations for this pivotal trial program are well advanced," said Starpharma chief executive Dr Jackie Fairley.

Preparations for the Phase 3 studies including designing the trial with regulatory input, as well as selection of trial sites and appointment of a leading global Contract Research Organisation.

Existing treatments for BV are considered suboptimal. They do not offer a long term solution and are associated with high rates of recurrence, unpleasant side-effects, and high levels of bacterial resistance. There are currently no approved products to prevent R-BV, so VivaGel® has the potential to be a 1st in class therapeutic for prevention of R-BV.

BV is the most common cause of vaginal infection worldwide and BV prevalence is known to vary by country and population group. A recent review of almost 1,700 BV research papers, identified BV prevalence approaching 60% of women in some African nations. In the US, overall BV prevalence was 29.2% and highest among non-Hispanic blacks (51.4%) followed by Hispanics (31.9%) then non-Hispanic whites (23.2%). In the UK, overall BV prevalence was 10.9%.

VIVAGEL®

›› VivaGel®-coated condom: Consumer feedback

Ansell has partnered with Starpharma to validate a process of coating an Ansell condom with unique VivaGel®. This ground breaking technology has been shown in lab trials to deactivate many viruses that cause STI's. The dendrimer technology perfected by Starpharma over many years is supported by millions of dollars of clinical trials, and Ansell is fortunate enough to be the partner to help bring the resulting condom product to market. Regulatory review processes are already underway for this product with plans to commercialise this world-leading Condom technology in the near future.

2013 Ansell Annual Report

The VivaGel®-coated condom is currently undergoing regulatory review and significant prelaunch activities have already been completed including consumer research, product positioning, packaging design and manufacturing validation.

Consumer feedback on the VivaGel®-coated condom collected via formal market research this year shows positive feedback and demand. The international research demonstrated very positive results in terms of product relevance and benefits to consumers. 86% of participants rated the VivaGel®-coated condom as "very interesting" with >90% saying they would buy it.

Actual consumer comments included:
"I would buy this product right now";
"I think this product is amazing…This product is very special and interesting"; and
"I have rated this product 5/5 as this is a major breakthrough in the condom market and for world health…"

Starpharma has licensed commercial rights to Ansell and Okamoto for the VivaGel®-coated condom.

DRUG DELIVERY

›› Impressive results for Dendrimer-Enhanced Oxaliplatin

Starpharma has recently released impressive pre-clinical results showing the superior performance of Dendrimer Enhanced Oxaliplatin (DEO) compared to oxaliplatin alone (Eloxatin®), a leading bowel cancer drug.

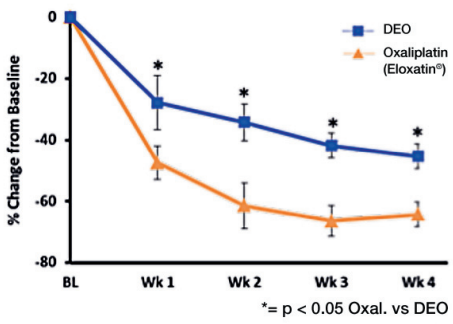
The dendrimer-enhanced version of the drug has been shown, in animal models, to have:

- improved anti-tumour efficacy
- reduced toxicity for bone marrow, and
- reduced toxicity for the nervous system (neurotoxicity).

The neurotoxicity improvement is particularly important as this effect is Eloxatin®'s major dose-limiting toxicity and the cause of its most debilitating side-effects. Around 85-95% of patients who undergo Eloxatin® therapy will suffer irreversible nerve damage to the hands and feet (peripheral neuropathy). The drug also triggers a short-term heightened sensitivity to cold around the time of treatment (see case study).

Starpharma's novel, proprietary DEO showed significantly reduced neurotoxicity in validated animal models for both peripheral neuropathy and cold sensitivity. In fact, DEO showed a significant reduction in both neurotoxicities even when DEO was used at twice the dose of oxaliplatin.

Mechanical Hypersensitivity as measured by the von Frey method



Following treatment with DEO or oxaliplatin, mice were assessed to check for treatment-related neuropathy. The DEO treated mice had a statistically significant reduction in peripheral neuropathy seen by a lower change from baseline in the von Frey test (refer above) and a lower cold sensitivity as measured by the Cold Plate test, when compared to mice treated with oxaliplatin.

Starpharma has also released the results of a separate pre-clinical study which demonstrated improved tumour-inhibiting effectiveness in a colon cancer model and a reduction in bone marrow toxicity.

"These findings are very significant because this condition is a serious clinical problem and the dendrimer version of oxaliplatin clearly shows a reduced level of neurotoxicity. We are unaware of any other examples of this effect reported for other oxaliplatin formulations in the literature."

Professor Susan Dorsey
Director, Center for Pain Studies,
University of Maryland

"The reduction in neurotoxicity alone would represent a significant commercial and clinical advantage for DEO but when considered alongside the earlier improvements in efficacy and reduced bone marrow toxicity, this finding demonstrates that Starpharma's dendrimer technology can deliver a considerable overall enhancement to this blockbuster drug," said Starpharma CEO Dr Jackie Fairley.

Oxaliplatin, sold as Eloxatin® by Sanofi, is primarily used to treat colon and colorectal cancer and the drug achieved sales of approximately US$2B in 2012.

OXALIPLATIN CASE STUDY

Sydney man Ben Bravery commenced a regime of chemo-therapy called FOLFOX4 which includes oxaliplatin after he was diagnosed with stage 3 colorectal cancer in 2011, when he was 28 years old.

Mr Bravery's cancer was surgically removed prior to chemotherapy and has not returned, however he has an ongoing reminder of the toxicity of his treatment.

"I'm reminded on a daily basis of the chemotherapy I had," said Mr Bravery, now aged 31.

"I still have nerve damage in my fingers and feet, and this is something I'll probably have to live with for the rest of my life. The nerve damage in my feet is such that I have to check them regularly for damage – because I won't feel small cuts or abrasions, and that means they could go on to get infected if I'm not careful."

Mr Bravery also described the short-term heightened sensitivity to cold as like "drinking shattered glass" if he consumed anything that was not warm during the week after an infusion of oxaliplatin.

"It was a very uncomfortable and sharp feeling and can be really painful," he said.

"With me, it gradually worsened during chemotherapy whereby I couldn't drink beverages at room temperature, everything had to be heated up or it would upset my mouth and throat.

"I went through chemo in spring and summer, but still had to wear gloves and shoes to keep my hands and feet warm because they were so sensitive to the cold. While touching or walking on cold surfaces wasn't that painful at the time, the more you trigger this during chemo the worse the side-effect becomes."

Mr Bravery said he would welcome a form of oxaliplatin that had a reduced side-effect profile as "chemotherapy is already very tough".

"Anything that reduces the side-effects is a good thing. Starpharma's lab results are really promising and may go on to improve the lives of people having treatment for colorectal cancer in the future."

APPOINTMENT

Starpharma appoints Rob Thomas to the Board

Rob Thomas has been appointed to the Board of Directors as a non-executive director and will assume the role of Chairman in 2014 with the retirement of Peter Bartels, which is part of a deliberate succession plan and board renewal.

Mr Thomas has a strong background in banking and is a non executive director on a number of listed healthcare companies in Australia and the United States. He has more than 35 years' experience in the securities industry with Potter Partners (now UBS), County Natwest and Citigroup. He is currently Chairman of TAL Limited (formerly Tower Australia Limited), Gragher Capital Securities and the NSW State Library. Mr Thomas also has extensive relevant experience in healthcare, including as the immediate past Chairman of Heartware International.

AGROCHEMICALS

Progress continues in agrochemical activities

Starpharma continues its agrochemical activities with agreements now signed with the majority of the top 10 agro-chemical companies, the most recent being with Isagro for a partnership in fungicides. This builds on our previously announced agreements this year with Gowan and Makteshim Agan.

Under the agreement, Isagro will test Starpharma's Priostar® dendrimer technology with a number of its fungicides to assess potential performance gains over existing formulations. Isagro is an agrochemical company with global sales of approximately €150 million and 620 employees.

In addition, Starpharma is developing its own complete formulations of selected generic actives with enhanced characteristics. A number of programs including glyphosate are underway with additional glyphosate field trials ongoing.

Dendrimers enhance existing agrochemicals and create patentable formulations by improving formulation characteristics such as solubility and stability which lead to improved biological performance. New formulations using Priostar® dendrimers create superior agrochemical formulations with a strong patent position lifting the barrier to entry for competing products and hence raising the commercial value of the agrochemical.

ISAGRO

SPL TV – a new communication channel

Starpharma has created a new communication channel, called "Starpharma TV", for shareholders and prospective investors.

The first instalment is focused on Dendrimer-Docetaxel and its move into Phase 1 clinical trials. Subsequent editions will examine the Company's other programs and key developments within the R&D portfolio.

To watch, go online to www.starpharma.com/news-room or check under the "news" tab on the website.

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