New Study Shows Superior Ability of PledOx to Reduce Chemotherapy Side Effects

Results of a preclinical study, comparing PledOx (calmangafodipir) - with the clinically approved substance mangafodipir, are published in the latest number of Translational Oncology (link to article). The results show that calmangafodipir has a substantial and statistically significantly better protecting effect on blood-forming bone marrow than mangafodipir, when used as an adjunct (complement) to treatment with the chemotherapy drug oxaliplatin. Furthermore, the results of the study show that the risk of brain uptake of potentially harmful manganese is significantly less with PledOx, compared with mangafodipir. Hence, PledOx may result in a more efficacious and less troublesome chemotherapy.

Colorectal cancer is the third most common cancer-related cause of death in the Western world. A standard treatment in this disease is oxaliplatin-based chemotherapy. However, serious side effects in more than half of the patients lead to an intolerable burden and cause dose reductions, delays, or, in worst-case scenarios, complete discontinuation of the therapy. Chemotherapy exerts negative effects on blood-forming bone marrow, which often leads to severe shortage of white blood cells. The Swedish specialty pharmaceutical company PledPharma is developing PledOx as a chemotherapy adjunct to reduce severe and dose-limiting side effects.

The chemotherapy drug oxaliplatin is widely used in colorectal cancer treatment. It is a potent anti-cancer drug but suffers, like many other chemotherapy drugs, from serious side effects. Hence, there is a great medical need for an adjunct drug that can prevent serious side effects of oxaliplatin and other chemotherapy drugs. The new study presented today shows that calmangafodipir is significantly better to protect against serious side effects than mangafodipir, which we evaluated in our first clinical study. Furthermore, calmangafodipir has a better safety profile than mangafodipir. The results are really promising, says Ursula Falkmer, Professor of Oncology at the University Hospital in Aalborg, Denmark, and principal investigator of the first controlled study with mangafodipir (2).

Improved protective effect

The two compounds studied can be used to protect bone marrow blood forming cells against chemotherapy toxicity. Chemotherapy causes toxic effects on blood-forming bone marrow and other normal cells by increasing the oxidative stress (3). Mangafodipir reduces the harmful oxidative stress in healthy cells by mimicking the body’s own enzyme MnSOD. Both mangafodipir and MnSOD are entirely dependent on the metal manganese to exert its cytoprotective effects. In the body a large proportion of manganese is released from mangafodipir and the substance therefore loses a significant portion of its cytoprotective property. Release of manganese may also cause negative
effects if the released manganese is taken up into the brain. In calmangafodipir, which is a further development of mangafodipir, 80% of the manganese has been replaced with calcium, which in the study shows a significantly less manganese release, superior ability to reduce chemotherapy-induced side effects and significantly less manganese uptake into the brain(1).

- We are very pleased with the results of the study. This is a milestone in the development of PledOx, which we hope will contribute to a more effective treatment of many cancer patients in the future, says Jan Olof G. Karlsson, founder of PledPharma and assistant Professor of Pharmacology at the Faculty of medicine at the University of Linköping.

About PledOx

PledOx (calmangafodipir) is a further development of mangafodipir. Mangafodipir is a contrast agent for MRI. The contrast effect is achieved by the released manganese in the body, but the protection of healthy cells against chemotherapy is achieved by manganese still bound to mangafodipir. Already during the development of mangafodipir as a contrast agent, Jan Olof G. Karlsson, together with PledPharma’s two other founders, Per Jynge and Rob Towart, realized that the substance also protected against serious side effects of chemotherapy.

Since then several studies have been conducted which show that mangafodipir protects normal cells against harmful side effects of chemotherapy (1,2,4,5,6,7) without adversely affecting the anticancer effect. On the contrary, it has been shown that mangafodipir enhances the anticancer efficiency (4,6,7).

About the study

In the experimental study, "Superior Therapeutic Index of Calmangafodipir in Comparison to Mangafodipir as a Chemotherapy Adjunct", calmangafodipir and mangafodipir was compared with respect to their bone marrow protection when treated with the cancer drug oxaliplatin. The results showed that, at equivalent doses, calmangafodipir had a significantly better ability to protect from myelosuppressive effect of the oxaliplatin. In addition, the study showed that the uptake of manganese in the brain was significantly lower with calmangafodipir than mangafodipir. The study also showed that calmangafodipir increased the cancer inhibitory activity of oxaliplatin and also has an anticancer activity of its own (1).
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About PledPharma
PledPharma is a Swedish specialty pharma company that develops a new medicine, PledOx™, for prevention of the severe side effects that patients develop as a consequence of chemotherapy of cancer. Many times the treatment cannot be carried out as planned due to severe side effects. The current market for supportive cancer care is some SEK 72 billion. PledOx is a drug within the patent protected substance class PLED, which protects the body’s normal cells against oxidative stress. Oxidative stress is a condition where an overabundance of harmful oxygen molecules (free oxygen radicals) has been formed. We are also evaluating opportunities with PLED substances for other diseases. PledPharma (STO:PLED) is listed on NASDAQ OMX First North. Erik Penser is the Certified Adviser. For further information, please visit www.pledpharma.se

References: