PledPharma

Data from the POP study support further development of Aladote® as a new treatment option for reducing liver damage due to paracetamol overdose

Stockholm, March 26, 2019. PledPharma AB (publ) today announces further data from the Proof of Principle (POP) study. Patients in need of additional NAC infusions after the planned 12 hrs of NAC infusion were 50% for the NAC-alone group and 11% for the NAC+Aladote® group.

The scientific rationale as well as clinical results from the completed POP study indicate that Aladote® in combination with N-acetylcysteine (NAC) has the potential to reduce liver damage in the specified patient population. Results in summary:

- Aladote® is safe and tolerable in patients treated with NAC for paracetamol overdose
- Aladote® may reduce liver toxicity after paracetamol overdose
- Biomarkers for hepatic liver injury:
  - All patients with NAC alone had an increase in both K18 isoforms which is consistent with liver cell death.
  - K18 (Patients with decreased levels from baseline to 20hrs: n (%)): NAC alone: 0 (0%); NAC+Aladote: 6 (33%)
  - CCK18 (Patients with decreased levels from baseline to 20hrs: n (%)): NAC alone: 0 (0%); NAC+Aladote: 7 (39%)
  - miR-122 (Patients with decreased levels from baseline to 20hrs: n (%)): NAC alone: 2 (33%); NAC+Aladote: 11 (61%)
- Patients in need of additional NAC infusions after the planned 12 hrs NAC infusion, n (%): NAC alone: 3 (50%); NAC+Aladote: 2 (11%)

PledPharma intends to conduct regulatory interactions to determine the next step in development of Aladote®.

Dr James Dear, principal investigator, will be presenting the results at PledPharma's capital markets day. Dr Dear, an internationally leading paracetamol toxicity expert, was the Principal Investigator for the POP study, conducted at the Royal Infirmary of Edinburgh and the Queen's Medical Research Institute, University of Edinburgh.

"We are very pleased to see indications of clinical relevance through the reduced need for continued NAC in patients treated with Aladote®. This has the potential to reduce hospital stay in this patient population. With these encouraging results and the recent orphan drug designation for Aladote® we are committed to continue the development of Aladote®." says Nicklas Westerholm, CEO PledPharma AB.

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About Aladote®

Aladote® is a "first-in-class" drug candidate with the potential to prevent the development of acute liver failure caused by paracetamol overdose. Aladote® has shown good efficacy in relevant preclinical models, even in the time-window when N-acetylcysteine (NAC) treatment is no longer is effective. A proof of principle study in patients with paracetamol poisoning has been successfully completed.

Paracetamol is the most used drug in the world for the treatment of fever and pain, but also one of the most overdosed drugs – intentional or unintentional. Paracetamol overdose is also one of the most common method in intentional suicide attempts. When excessive amounts of paracetamol are broken down in the liver, the harmful metabolite NAPQI is formed, which can cause acute liver failure. The current standard of care for paracetamol poisoning (NAC) is effective if the patient seeks medical care within 8 hours of ingestion. However, NAC is substantially less effective if started more than 8 hours after overdose.

About Biomarkers

Keratin-18 (K18)

In paracetamol overdose, the full-length variant of K18 (FLK18) is released by necrotic cell death. A shorter, caspase cleaved form of K18 (CCK18) is released following cell apoptosis (programmed cell death). Both forms of K18, measured in the first serum sample at presentation at the hospital after paracetamol overdose, correlate with peak ALT activity during the hospital stay. Full length K18 distinguished patients with and without acute liver injury at an early time where ALT activity was still normal. This is consistent with necrosis being more prominent than apoptosis in the pathophysiology of paracetamol-induced acute liver injury.

References: JW Dear et al. Lancet Gastroenterol Hepatol 2018; 3: 104–13; ADB Vliegenthart et al. Br J Clin Pharmacol. 2015; 80: 351–362.

microRNA-122 (miR-122)

miR-122 is a biomarker specific for liver injury and fully conserved (translational) across in vitro models, in vivo models and humans. MiR-122 is an early marker for acute liver injury which predicts a rise in ALT activity following paracetamol overdose. When miR-122 was measured at hospital presentation after a paracetamol overdose in patients requiring subsequent NAC therapy the circulating miR-122 concentration correlated significantly with peak hospital stay ALT activity. MiR-122 was significantly higher in those patients who developed subsequent acute liver injury. miR-122 can accurately separate patients with and without acute liver injury at an early time when ALT activity was still normal. This is consistent with miR-122 having enhanced sensitivity and

specificity in this context of use.

References: JW Dear et al. Lancet Gastroenterol Hepatol 2018; 3: 104–13; ADB Vliegenthart et al. Br J Clin Pharmacol. 2015; 80: 351–362.

About Us

PledPharma is an innovative, unique and integrated pharmaceutical drug development company, focusing on improving treatments for diseases with substantial unmet medical need. The company's most advanced project PledOx® is being developed to reduce nerve damage associated with chemotherapy. A global phase III program is ongoing. The drug candidate Aladote® is being developed to reduce the risk of acute liver injury associated with acetaminophen poisoning. A proof of principle study has been successfully completed and will serve as the basis for the continued development. PledPharma (STO: PLED) is listed on Nasdaq First North. Erik Penser Bank is the company's Certified Adviser (tel +46 8 463 83 00, certifiedadviser@penser.se). For more information, see http://www.pledpharma.com/

Attachments

Data from the POP study support further development of Aladote® as a new treatment option for reducing liver damage due to paracetamol overdose