Interview – AM-Pharma heads back to the clinic with kidney contender

Amy Brown

Having completed a return trip to the drawing board with its lead asset and raised a further €12.2m ($15.8m), AM-Pharma is heading back to the clinic. By the end of the year the Dutch inflammatory specialist hopes to have a trial under way that it believes will be the largest study ever run with a therapeutic in acute kidney injury.

Its project, recAP, is recombinant human alkaline phosphatase; a bovine form successfully completed phase II studies in 2012 but regulators advised that a recombinant would be a better way forward. Erik van den Berg, AM-Pharma’s chief executive, tells EP Vantage that should the encouraging results be repeated a partner will likely be sought, and says interested parties are already keeping a close eye on progress.

Acute kidney injury (AKI) develops very quickly and is caused in many cases by sepsis. Various studies suggest that anywhere from a third to almost half of AKI cases result from this condition, and this is the population that AM-Pharma has chosen to target.

“We have already done two trials in this setting with our bovine product and observed a beneficial effect,” Mr van den Berg says. “They were small studies – 36 patients each – but they were very positively received within the clinical community.”

The most recent study, conducted specifically in sepsis patients with AKI, generated a statistically significant improvement in kidney function, a measure that will also form the primary endpoint of the next, 290-patient trial. AM-Pharma has also shown that alkaline phosphatase works extremely quickly; responses were seen on systemic and local markers of inflammation within hours of administration.

Alkaline phosphatase is found throughout the body but particularly on barrier organs like the kidney. It is an anti-inflammatory molecule and has a beneficial effect in AKI because it essentially neutralises the harmful immune-stimulating compounds that are the ultimate cause of the organ damage.

Hard outcomes

The aim of the proof-of-concept study is to repeat results of the previous trials with the new recombinant product. However, the real hope for reCAP is that preservation of kidney function will help prevent the longer-term health implications of AKI.

“We know that episodes of AKI, the duration of AKI and its severity, are all associated with hard clinical outcomes like mortality, progression to end-stage renal disease or [worsening] chronic kidney disease,” Mr van den Berg says.

“In our previous study with alkaline phosphatase within four days patients recovered their normal kidney function. Patients in the placebo arm had impaired kidney function through the 28 days that we followed them.”

Given the lack of options in this space AM-Pharma is unlikely to need to establish longer-term benefits for recAP to win approval, Mr van den Berg says; demonstrating a recovery in kidney function should be enough.

An adaptive trial design will be used. The first stage will see three dosages tested against placebo, with the most effective dose progressing to the second stage. Final results are expected in mid-2016.

Appropriate path

The decision to run a much larger trial than originally intended prompted the fundraising announced last week. The company raised €29m in 2011 and still has cash left over from that; together with the new funds this will allow the AKI study to be completed and an oral formulation, designed to treat ulcerative colitis, moved into the clinic hopefully next year.
The company’s existing investors, which include AbbVie and BB Biotech, were joined by Gilde Healthcare, which led the new round. The presence of AbbVie is notable: the US group is a rare player in this space with a compound called ABT-719 and is no doubt keeping an eye on its investment’s progress.

“There are already interested parties,” Mr van den Berg says, adding that finding a partner – if the trial succeeds – would be the “appropriate” way forward.

There are no therapeutic options available to treat AKI and sepsis remains a huge unmet need, largely because this is a very tough area of medicine. The approval in the US of a diagnostic for the condition has highlighted this further (NephroCheck approval could pit Astute’s backer against its partner, September 9, 2014).

However, the sizeable study that AM-Pharma has planned, and which will run in both the US and Europe, should paint an informative picture of the potential of alkaline phosphatase.

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