

The Duchenne community UPPMD had the opportunity to ask some questions to GSK and Prosensa concerning the PRO051 clinical trial.

Sent on Behalf of John Kraus, MD and Giles Campion, MD

Q. How many boys and what ages participated? Were all of the boys ambulatory?

12 boys participated in Study PRO051-02. The age range was 5 – 13 years. One boy was non-ambulatory.

Q. Were all boys on open label at a certain moment and what was the regimen?

After the dose escalation portion of this study was completed, all boys entered an open-label follow up phase and all received PRO051/GSK2402968 6mg/kg once a week.

A. Did you see any serious side effects? Did any of the patients/participants have to stop because of side effects?

No serious adverse events, considered drug related, were observed in Study PO051-02. No patient discontinued from the study. Injection site reaction was the most commonly reported adverse event.

Q. Did any of them complain or refuse to take the injections?

No child refused the weekly injections.

Q. Do you have any data or insight into the potential toxicities of long term systemic delivery?

Small amounts of protein were present in intermittent urine tests during Study PRO051-02 and need to be investigated further. Longer term placebo controlled studies are needed to understand long term systemic delivery of this investigational drug.

Q. What do the results of this trial show in terms of dystrophin expression, changes in blood work (PK)? Was Dystrophin expressed in all boys? Were you able to quantify the amount? Were you able to correlate dystrophin expression to functional improvement? Does Prosensa plan to show or have data to show dystrophin as a surrogate market for clinical benefit?

In the dose escalation part of Study PRO051-02, stable dystrophin was measured in all treatment groups in a dose related manner. These results are compatible with dystrophin levels of approximately 10 – 15%, although the dose escalation portion of this study was not long enough for the drug to have reached steady state. Longer term placebo controlled studies are needed to determine if these dystrophin levels are associated with improved muscle function.

Q. While we understand this was a Phase 1/2 safety/dose escalation trial, do you believe you now know the therapeutic dose?

It is too early to know the therapeutic dose of this investigational drug. Placebo controlled trials and regulatory approval are needed to determine the therapeutic dose.

Q. Did the 6mwt show any significant changes? And if so is this enough to approve the drug? Do we, with the results of this trial in hand, still need placebo controlled trials? And if so why?

Statistical significance was not determined in Study PRO051-02, as the study was small and did not have a control group for comparison. Most, but not all, boys had variable improvement in the 6-Minute Walk Distance measured after 12 weeks at a dose of 6 mg/kg. Larger placebo-controlled studies are needed for regulatory approval.

Q. Will you consult the patient population in an effort to understand what outcomes measures they believe carry the most significance?

The selection of outcome measures for clinical trials is based on discussions with clinical experts and regulatory authorities.

Q. Because the trial included several different mutations wherein skipping exon 51 would restore the frame, did you see variability in terms of expression across mutations?

This study was not large enough to answer this question.

Q. What are your plans for further development of exon skipping as a viable treatment for DMD?

New studies for PRO051/GSK2402968 are planned to start mid-2010, pending regulatory feedback.

Q. Which secondary outcome measures were tested during this trial? Did you look at other biomarkers?

Secondary endpoints from this study will be included in the scientific publication.

Q. Which outcome measures will be used in the next trial(s)?

Study endpoints will be posted on www.clinicaltrials.gov <<http://www.clinicaltrials.gov>> when study plans are completed.

Q. Are you planning to include non-ambulant patients in future trials? Are you able to share that timeline?

It is anticipated that the next series of clinical studies with PRO051/GSK2402968 will include studies for ambulatory and non-ambulatory boys with a mutation correctable by skipping exon 51. These studies are planned to start in mid-2010, pending regulatory feedback. Clinical trial details will be posted on www.clinicaltrials.gov <<http://www.clinicaltrials.gov>> when study plans are completed.

Q. What does the outcome of this trial mean for the next steps in development of AO's to skip other exons?

These results support starting new PRO051/GSK2402968 studies in mid-2010, pending regulatory feedback.

Q. Are you able to provide details with regard to future plans in terms of what exons will follow? At what stage will 44 and 51 need to get to before further exons can be rolled out? What timeline does Prosensa see for getting each further Exon to Market assuming 51 and 44 get passed next trial stages? Will these be run in parallel? What is the plan to get rarer exons to market (community scheme etc)...

Compounds currently in clinical development are being studied in mutations amenable to skipping exon 51 (GSK) and exon 44 (Prosensa). Compounds suitable for targeting other dystrophin mutations are under investigation in the laboratory setting.

Q. Are you considering expanded access programs and/or compassion for individuals who are unable to participate based on the inclusion criteria?

Not at this time.