Reviewer's report

Title: Membrane Sealant Poloxamer P188 Protects Against Isoproterenol Induced Cardiomyopathy in Dystrophin Deficient Mice

Version: 1 Date: 31 January 2011

Reviewer: DeWayne Townsend

Reviewer's report:

Summary:
This paper describes an important study examining the chronic effects of the tri-block polymer Poloxamer 188. Utilizing the mdx mouse model of Duchenne muscular dystrophy challenged with a low dose of the beta-adrenergic receptor agonist to exacerbate the cardiac disease. These mice were then treated with an intermittent daily dosing protocol with intra peritoneal administered P188. After two and four weeks of isoproterenol infusions cardiac function was assessed by echocardiography.

This study addresses an important question regarding the ability of Poloxamer 188 to effectively protect the dystrophin deficient heart during stress. However, I do have several significant concerns that are outlined below:

Major Compulsory Revisions:

The method section fails to describe how the blood pressure measurements were assessed. Without having this information it is impossible to judge the reliability of these measurements.

I question the extensive use of non-parametric statistics for data that should be normally distributed. Which test of normality was used? It is a bit surprising that 3 points would be sufficient to determine if data was normally distributed or not. Furthermore, it is not clear why a given parameter should be non-Gaussian at 2 weeks, but normally distributed at 4 weeks. Help me understand why this is the best analysis.

There are also changes observed in heart rate and LVID(d), how is P188 affecting these parameters?

The number of animals seems to vary throughout the experimental protocol, please explain the origins of this variability. Did animals die during the protocol? Were analyses discarded? If so, what was the basis for exclusion?

When in relation to your echocardiography studies was the daily dose of P188 administered? Were the serum levels of P188 following IP injection measured? What are the author’s estimation regarding the amount of time that mice had therapeutic (#>100 micromolar) with this dosing protocol.

Given P188’s known effects on blood rheology, the potential for changes in aortic
velocity is not surprising, but these data are inconsistent between the 2 week and 4 week time points. Please discuss how this finding may explain the increases systolic function (i.e. does blood just leave the ventricle easier?).

Minor Essential Revisions:
The data demonstrating improved systolic function with P188 is difficult to extract from the tables as presented. Please utilize a figure to summarize these central findings.

Osmotic pumps generally require a day or two of incubation before they reach the documented flow rate. Please include any pre-implantation procedures. These are important for defining when the infusion actually begins.

Please confirm that untreated mice also received daily IP injections of saline.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I am listed on a patent (7,846,426) that relates the use of Poloxamer 188 in the treatment of heart disease. However, I have no financial stake in the publication of the current paper.