

Mueller, Karin

From: Stening, Göran K
Sent: Wednesday, January 12, 2005 6:58 AM
To: Daniels, Stephanie; Johansen, Patricia A; McCormack, Eileen; Mullen, Jamie A; Tumas, John A; Timdahl, Kristina; Silva, Luis M (CNS/Seroquel); Mueller, Karin; Souder, Susan
Cc: Carlsson, Anders
Subject: Target dose 600 mg

Dear all,
I enclose some CST analyses related to the discussion of finding evidence to support the need for a target dose of 600 mg.

The first analysis is a simple split of patients in study 43 looking at patients treated with doses of 600 mg and above, compared to patients treated with doses < 600 mg.



Study_43_600.ppt

There is no evidence indicating that the high dose group performs better than the low dose (<600 mg) group, which is the expected outcome because of the flexible dosing regimen in study 43.

For possible marketing purposes in UK, the CST made an exploratory analysis of the outcome in study 43 by censoring data generated on doses >750 mg. We used two models of excluding >750 mg data (Excluding all patients who at some time during treatment reached doses > 750 mg, and the other model keeping all patients but deleting all data generated at doses > 750 mg)



Study 43 750 800
protval vs RI...

This analysis illustrates that the poor responders are titrated up to a maximum dose and that a flexible dosing study is a bad design if we intend to show the benefits of higher doses.

Last but not least we have looked at the effects of dose adjustments in study 43 at different timepoints of the study. The data are interesting, but can hardly be used as evidence of superiority of doses 600 mg or more.



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Sorry that we cannot be of more help.
Hopefully we can generate some good alternative ideas at today's teleconference.

Best regards
Göran

EXHIBIT	18
WIT:	<i>Mueller</i>
DATE:	11/1/07
LINDA ROSSI RIOS	