

To:

cc:

Kenneth C Kwong/AM/LLY@Lilly

Charles M Beasley Jr/AM/LLY@Lilly, Jeffrey T Ramsey/AM/LLY@Lilly, Anna Thornton/AM/LLY@Lilly

Subject: Re: Resending of revised file on hyperglycemia

Yes, time to onset is extremely interesting and very important in planning our study. If the phenomenon is really caused by olanzapine (and it clearly may not be) and it is do to an effect on insulin production or release, the we would expect this to be something happening relatively rapidly. If it is do to an effect on the insulin receptor, it might be immediate or delayed by some weeks. An interference with the receptor through direct interaction with the receptor would be relatively immediate. Indirect influence on the receptor, perhaps, by interference with receptor synthesis or acceleration of receptor catabolism would be delayed in onset. In any event, I'm going to get MJB to describe distributions of time to onset overall, by the 3 prfesentation types and within the 3 presentation types by hx diabetes, risk factors, no risk factors when I get back.

Charles





To:

Charles M Beasley Jr/AM/LLY@Lilly

cc:

Anna Thornton/AM/LLY@Lilly

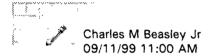
Subject: Re: Resending of revised file on hyperglycemia

Aside from time of onset analysis, I think analysis of outcome after discontinuation of olanzapine or other suspected drug might be informative.

One would not expect a true type I be reversible. Type II can, in principle, be reversible if someone has hyperglycemia from obesity and lose sufficient weight later to regain normal insulin sensitivity. A rapid (within a couple week) normalization of glycemic control (without diabetic drug) upon cessation of suspected drug would suggest a drug reaction. I think it might be worthwhile to ask MJ to categorize reports by dechallenge findings.

Given the importance of this issue, I think it warrants analyzing the data in all different angles.

## Charles M Beasley Jr



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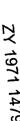
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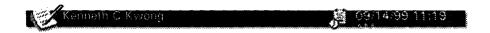
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Charles





To: Charles M Beasley Jr/AM/LLY@Lilly cc: Anna Thornton/AM/LLY@Lilly

Subject: Analysis of time of onset of the diagnosis of hyperglycemia

Based on the information that MJ had tabulated. Attached please find my findings:



Time of onset in pts without history of diabetes.R



Anna Thornton/AM/LLY@Lilly

Matt Kuntz/AM/LLY@Lilly

Subject: Requested case summaries -- Germany and glucose

Hello Anna!

Here are the requested case summaries for you (DE\_980600095 and EWC980400445).





case.rtf

case.rtf

Enjoy!

Winnie