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International Pharmaceuticals

DATE: January 20, 1994  
TO: Dr. E. Giller - Groton  
FROM: Roger Lane, M.D.  
SUBJECT: USE OF ZOLOFT IN IMPULSIVE/AGGRESSIVE BEHAVIOUR

Thank you for your memorandum to Mr. W. Heessels which he has passed to me for comment. I agree this is an interesting area with a great deal of evidence to suggest utility for the SSRIs. I have received numerous requests for studies in many of the areas you mention from aggressive behaviour in mentally handicapped children to aggressive behavioural disturbances in demented elderly patients. However, research in these areas, if it is not precluded by methodological differences, is a very difficult "sell" within the company due to the problems Prozac has encountered. Marketing (especially Roerig) are very aware that a patient on ZOLOFT involved in an incident of mass homicide could severely affect the image and commercial success of ZOLOFT. Patients with borderline personality disorder, psychopathic traits, aggressive impulse control disorders, etc. may be the very group who are likely to generate such an incident. Any proposal to study these patients is likely to be vetoed, therefore.

I do not think fluoxetine are "out of the woods" as regards their association with violence/suicidality. The recent meta-analysis of controlled clinical trials (Beasley et al, BMJ 303: 685-692, 1991) was initially followed by favorable comment but skeptical voices remain. A recent re-analysis of the data from this study using Monte-Carlo simulations demonstrates the conclusions of the Beasley paper to be invalid as this original meta-analysis had low power (Liwan PoA. Pharmacoepidemiology and Drug Safety 2: 78-84, 1994).

However, some of the disorders you mention, such as pathological gambling, belong to the group of OCD spectrum disorders. I am very interested in sponsoring small open studies in several OCD spectrum disorders (e.g. pathological gambling, trichotillomania, body-dysmorphic disorder, etc.). We are currently sponsoring an open study in pedophilia. This would support our work in OCD and expand the market beyond pure OCD. Would this be a way forward to involve investigators/experts such as, Linnolia and Coccaro?

Please do not hesitate to discuss these issues with me further.

Kind regards,

*Roger Lane*  
Roger Lane

RL:ela

- cc: W. Heessels
- I. Henry
- C. Truchan
- R. Wiseman

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