

THE RHEUMATOID DISEASE FOUNDATION

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March 12, 1985

JOHN R. A. SIMOONS, Ph.D.
President

Robert A. Turner, M.D.
Professor of Medicine
Chief, Section on Rheumatology
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Winston-Salem, N.C. 27103

Dear Bob:

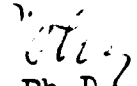
Re: Double-Blind Placebo Controlled Study of Clotrimazole.

Thank you for meeting with us on March 4th., to review the progress of our Clinical trial initiated on October 1, 1984. We kindly acknowledge the receipt of your letter of March 7, 1985 and the estimated budget for the proposed open label extension study with Clotrimazole in about 50 patients. From copies of my letter to Dr. Spiekermann of Miles Pharmaceuticals and Mr. Robert Linkous of the Food and Drug Administration dated March 11, 1985 you can see that we try to obtain their approval and information as requested in your letter.

During our tour with Ms. Sirohman we also visited the section of Sue Crater where patients information of the study are stored. A brief review indicated that one patient had "Flu-like" symptoms and another had complained of "burning sensation during urination". These two symptoms were probably fortuitously reported by the two patients and would have been missed if not reported. From our extensive experience with the use of anti-protozoal drugs in rheumatoid arthritis we know that these symptoms are part of the Herxheimer reaction of which we tried to alert you. During our meeting with you it was obvious that you had not noticed these symptoms in these patients and this is very unfortunate.

I mentioned during the meeting that Dr. de Keijser of the Medical Centrum in Alkmaar, Holland is also conducting a double-blind study in 100 patients with Metronidazole tablets. Dr. de Keijser has used Metronidazole and Tinidazole in about 200 patients during the last two years and is quite familiar with the Herxheimer reaction in patients with rheumatoid arthritis during the treatment. I will be visiting with Dr. de Keijser in September 1985 to review the data. The protocol and other data are unfortunately written in Dutch and I have translated his letter and the form which the patients must complete with the list of symptoms which I kindly refer to your attention. We hope that you would implement some of these warnings into the instructions to your staff and patients in order to collect this valuable information for the study. Thank you for your support.

Yours truly,


John R. A. Simoons, Ph.D.

THE RHEUMATOID DISEASE FOUNDATION IS A PROJECT OF
THE ROGER WYBURN-MASON & JACK M. BLOUNT FOUNDATION
FOR THE ERADICATION OF RHEUMATOID DISEASE

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