Interoffice correspondence

TRAVENOL

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date: January 27, 1983

from: A. Cameron

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J. O'Sullivan
G. Rolland - TIS

subject: HYLAND THERAPEUTICS - MEETING TO DISCUSS REGULATORY ISSUES - JANUARY 19, 1983, LONDON

DISTRIBUTION: C. Chard
C. Kernahan
M. Lee - Glenoaks
J. Van Calster - TIS
J. M. Noel - Lessines

A meeting was held to discuss several Hyland Therapeutic Products (regulatory and clinical trial aspects). The main topics were the U.K. Autoplex Trial, U.K. Hemofil-T Study and the prospects for a trial with IVGG-Native.

1. AUTOPLEX

M. Lee opened the meeting by mentioning Hyland Management concerns over the U.K. Autoplex Trial which has been called "a study failure because of lack of bleeds". C. Chard discussed the U.K. Regulatory response.

Enough product has been sequestered in the USA to replace all product currently held at trial centres. However this will not be issued until the short dated stocks, already issued, have been sold.

As the product expires at the end of March 1983 considerable discount will have to be given to encourage a rapid sale.

Problems associated with product liability were discussed. C. Chard stated that reissue of hospital held product could be acceptable if an assurance was given by a professional person that controlled storage conditions had been met.

TIS management are insistent that the product stays in the U.K. and will not be exported for re-sale.

Extension of Shelf Life

W. Thomas has stated that extension of shelf life over the current 18 months is not feasible due to potentially increased thrombogenicity and instability of F.E.C.U.'s.

C. Kernahan discussed the possibilities of marketing this quantity of Autoplex - approximately 140,000 F.E.C.U., which represents 50% of the current UK market. The marketing plan suggested was a list of centres to be approached.

Initially:
1. Sales in Ireland (esp. Belfast) - non-incremental

2. Approach known Feiba users (sales at low unit cost) - incremental sales.

Finally:
3. Approach St. Thomas's Hospital, London for sales of Autoplex for use in elective surgery.

Actions

M. Lee to discuss pricing with H. Termeer and labelling with M. Rodell.

C. Chard to discuss stability data and possible reworking with W. Thomas.

The need to register Autoplex in the U.K. was discussed. Currently the product is registered in W. Germany, Holland, Switzerland and Italy and in the second phase of registration in Spain. Scandinavia is probably the major area where lack of U.K. registration would affect product licensing. Lack of UK registration would mean that absolutely no advertising or promotion of any sort could take place and long term sales would be jeopardised by necessity for prescription release only.

Sample Numbers

M. Lee discussed the numbers of trial bleeds required. Initially 40 bleeds were to be enough to demonstrate equivalence of AHF with Autoplex. However to detect an advantage in one treatment the following bleed numbers are required:-

1. To detect a 15% difference in treatments - 120 bleeds

2. To detect a 25% difference in treatments - 60 bleeds

C. Kernahan is to write a memo on the dangers to marketing prospects of abandoning the trial and cancelling the March meeting.

A. Cameron mentioned the possibility of widening the protocol limits to include a wider range of bleed types, but M. Lee mentioned that following discussion in the USA over the second Autoplex Trial, the U.K. bleed criteria should be adhered to.

2. HEMOFIL-T

The UK trial at St. Thomas's Hospital was discussed. Dr. G Savidge is very keen to have product immediately as he has had to treat 3 of his 5 initial virgin haemophiliacs with non-treated product and

so now has only 2 patients left in the trial. It has therefore been decided to supply product on a Prescription Release basis until full Clinical Trial Exemption approval has been received.

C. Kernahan is to deal with all billing and sending arrangements. J. Van Calster is to discuss the consultancy agreement of Dr. G. Savidge with Dr. G. Rolland.

Target dates for completion of stages of the CTX is as follows:-

1. A. Cameron - January 28, 1983
2. C. Chard - February 2, 1983
3. Dr. G. Rolland - February 9, 1983
4. Dr. G. Savidge - February 16, 1983

Concern over potential competitors such as Cutter (Chimp Study Completed?) and Immuno (Marketing Plans?) was voiced. Very little information on these competitors appears to be available at present.

3. IVGG-NATIVE

For registration in the U.K. demonstration of efficacy in a controlled clinical trial will be required. This would involve a large and expensive trial. Before any decision is made on IVGG-NATIVE registration in the U.K. a business decision will have to be made on the cost v return of such a project.

M. Lee mentioned a trial proposed for the USA involving a controlled double blind study of IVGG against placebo in 100 cancer patients. (M. Lee to send C. Chard details of the US IVGG studies).

It is then proposed to cost a UK IVGG-Native study - action A. Cameron and C. Chard after an estimation of the size of the UK market by C. Kernahan.

Regards,

GRO-C

A. Cameron