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MINUTES

OF THE

ANNUAL MEETING OF THE SCOTLAND AND NORTHERN IRELAND HAEMOPHILIA DIRECTORS, SNBTS DIRECTORS AND SCOTTISH OFFICE DEPARTMENT OF HEALTH

Held on 22nd May 1997
at
SNBTS Protein Fractionation Centre (2pm to 4.20pm)

PRESENT:	Sir David Carter (Chair)	Dr P Cachia	Mr P Taylor
	Dr A Keel	Dr E Chalmers	Professor I M Franklin
	Mr M Palmer	Dr E E Mayne	Dr P Foster
	Mr I Snedden	Dr A Thomas	Dr R J Perry
	Dr A Mairs	Dr T Taylor	Miss S J Pelly (Minutes)
	Dr C A Ludlam	Dr I D Walker	Dr S J Urbaniak
	Professor G D O Lowe	Dr H Watson	
APOLOGIES:	Mr A Macmillan Douglas	Dr C V Prowse	Dr T Ferguson
	Dr W M McClelland	Dr G Galea	Mr J Blythe
	Dr D B L McClelland	Dr R Green	Mrs M M Tunstall

1. INTRODUCTION

Sir David Carter opened the meeting and thanked the group for the invitation to attend and chair the meeting.

Apologies were noted from those listed above

2. MINUTES OF THE PREVIOUS MEETING (6th JUNE 1996)

These were accepted as a correct record. Professor Lowe wished it to be noted that the meeting on recombinant factor VIII had actually been held on 16th April 1997 at Harrogate.

3. MATTERS ARISING

There were no matters arising

4. COAGULATION FACTOR WORKING PARTY (SCOTLAND AND NORTHERN IRELAND) 9th ANNUAL REPORT

4.1 9th Annual Report

Dr Ludlam reported that there had been 8 meetings, and he welcomed Mr Macmillan Douglas and Professor Franklin who had joined the group during the past year.

The safety of coagulation factors remains a primary concern and the Haemophilia Directors are supportive of SNBTS in the production of double virus inactivated products. They were also pleased to note that the MSBT were promoting the use of virus inactivated plasma.

Liberate® was now licensed and widely used in Scotland and Northern Ireland and plans were underway to trial the new double virus inactivated product Liberate® HT. The continuous infusion trial of Liberate® was still ongoing although recruitment was slow but, in response to Sir David Carter's inquiry, Dr Ludlam confirmed that the Haemophilia Directors were keen to promote continuous infusion of Factor VIII. Professor Franklin asked about the possibility of extending the trial outside Scotland. Dr Ludlam said that there would be no objection in principle, but as Liberate® was not widely available outside Scotland it would be unlikely that patients would be receiving it and it was best to keep them on a single product.

Dr Ludlam expressed concern that HTDEFIX was now licensed for 'acquired coagulopathies' which could include patients with liver disease where there is an increased risk of possible thrombotic side effects. A warning is included in the Summary of Product Characteristics to this effect.

The Haemophilia Directors were pleased that SNBTS had been able to overcome the problem with HIPFIX and were hoping to restart the trial in the near future with a view to being in a position to offer it to all patients with Haemophilia B in early 1998.

Dr Ludlam outlined the planned trial strategy and Sir David Carter asked whether this was not a very cautious approach, was there any particular reason to expect a higher rate of inhibitors in the modified product.

The Haemophilia Directors felt that previous experience with Factor VIII had led them to be cautious and the suggested approach could benefit long term recruitment of patients onto the study. In response to Ian Snedden's question, Dr Ludlam confirmed that the incidence of inhibitors to Factor IX in Scotland was consistently zero, but rising in the UK.

Professor Lowe pointed out that recent experience with Factor VIII had demonstrated that even minor changes could affect the antigenicity of the product, but suggested that the proposed approach to the clinical trial could be deliberated by the Safety Committee as part of their remit. Dr Perry welcomed this suggestion as he felt it was important to look at ways of telescoping the process.

Dr Ludlam acknowledged the enthusiasm of everyone who had attended the meetings of the Working Party over the past year.

4.2 Appendix on Product Usage

Miss Pelly commented briefly on her paper confirming that total Factor VIII usage had increased by 2.09% over the last year compared with an increase of 16.9% in the previous year. Recombinant Factor VIII accounted for 29.07% of this total.

Sir David Carter inquired what the predicted figures for recombinant usage were based on. Dr Ludlam informed him that these had been based on use for treatment of virally naive patients first, and then extending its use as funding allowed. However, it was the treatment of choice and the Haemophilia Directors would like to put all patients on recombinant as soon as possible if funding became available.

In response to Mr Snedden's question concerning inhibitors to recombinant Factor VIII, Dr Ludlam summarised the experimental evidence which suggests it is no more antigenic than plasma derived Factor VIII. He informed the group that Canada have completely switched to recombinant Factor VIII.

Dr Perry stated that the SNBTS was supportive of a mixed economy and felt that the double virus inactivated plasma product would be a useful one in the medium term future. Mr Snedden remarked that the uptake of recombinant was moving ahead faster in Scotland than in England and Dr Ludlam agreed that the Haemophilia Directors were pleased to have avoided the patchy uptake that had arisen south of the Border.

4.3 Update on SNBTS Product Range

Dr Perry spoke briefly on his report, confirming that SNBTS are strong advocates of terminal heat treatment as a secure virus inactivation procedure.

It is intended to submit a Product Licence application for Fibrin Sealant at the end of 1997 and an increase in product uptake is envisaged once a Licence has been granted. Professor Lowe pointed out that once the Liberate® HT trial was ongoing it would not be possible to recruit the same patients for both this and the Fibrin Sealant trial.

SNBTS are the only UK manufacturer of a double virus inactivated Human Fibrinogen Concentrate which could be used to replace cryoprecipitate. The product would be undergoing clinical trial in the near future and there was the possibility of supplying it UK wide.

SNBTS Thrombin is the subject of a trial in bleeding peptic ulcers.

Dr Keel clarified that the MSBT were recommending only that 20% of FFP should be replaced by Virus Inactivated Plasma (VIP). VIP was not an ideal product in every situation and the increased cost had to be weighed against the benefit in safety.

5. PUBLISHED UK GUIDELINES ON RECOMMENDED PRODUCTS

Dr Ludlam made 3 points concerning the Guidelines:

- They replaced the 1992 Guidelines
- They were evidence based
- They covered numerous other issues apart from recombinant Factor VIII

He informed the meeting that the Guidelines had been viewed favourably in Europe and adopted with minor amendments in Australia.

6. ARRANGEMENTS FOR PROVISION OF FACTOR IX AND RECOMBINANT FACTOR VIII IN SCOTLAND

6.1 Factor IX

Dr Cachia summarised the current position regarding Factor IX. Since the suspension of the HIPFIX trial all patients had been receiving commercial products and it was undesirable that they should be subjected to further unnecessary changes of product. Now there is a timetable for reintroduction of HIPFIX three issues arise:

- Interim arrangements for supply of product. The Haemophilia Directors feel strongly that patients should remain on one product.
- What arrangements will be made for patients who decline to enter the HIPFIX trial.
- Recombinant Factor IX is likely to be licensed in late 1997 and the Haemophilia Directors would hope for its introduction on the same basis as recombinant Factor VIII, with support from the SODoH.

Sir David Carter accepted the desirability of patients remaining on one product but said this may not be possible to achieve, and the next 6 months might be difficult. He noted the willingness of the Haemophilia Directors to endeavour to re-enter their patients on the HIPFIX trial. He was not in a position at this time to answer positively on the question of recombinant Factor IX and Ministerial approval would have to be sought.

Professor Franklin stated that both HIPFIX and Liberate were important products for SNBTS and the goal was to get HIPFIX licensed. SNBTS need a good estimate on demand for these products and information on how the plasma products are likely to be phased out if that is what is going to happen.

In response to Dr Perry's question on whether the Haemophilia Directors would prescribe HIPFIX if it were licensed, Dr Mayne replied that it was a good product, but because of the problem patients may be reticent and the uptake might only be 10-20%.

Mr Snedden reaffirmed the current position concerning funding for Factor IX. In Scotland the SNBTS are centrally funded to provide Factor IX free of charge to users and any move away from this would constitute a major change. There is no separate budget for provision of Factor IX but funding had been made available for purchase of Replenine in recognition that there was a moral obligation to provide a substitute product during the problem with HIPFIX. If the Haemophilia Directors wish money to be devolved to purchasers for provision of recombinant Factor IX then this is a separate issue.

Professor Lowe made the point that provision must be made for any patients who do not wish to re-enter the trial. Dr Cachia asked whether the interim funding could be used to purchase the product the patient was currently receiving rather than Replenine. Sir David Carter agreed to consider this, but did not believe it would be possible to resolve the issue this afternoon. He also agreed to take back to the Department the suggestion that the Haemophilia Directors be reimbursed the equivalent cost of Replenine for Mononine already in stock.

Dr Ludlam enquired whether he should write to the Scottish Office requesting funding for recombinant Factor IX. Sir David Carter felt it would be beneficial to raise this issue at an early stage but could not promise an early response. Dr Ludlam expressed the Haemophilia Directors' appreciation of everything Sir David had done.

6.2 Recombinant Factor VIII

The Haemophilia Directors were pleased the SODoH had endorsed the use of recombinant Factor VIII but expressed their concerns over the position once funding was devolved to Health Boards. Dr Cachia asked whether the funding would be ring fenced to ensure its use for purchase of recombinant Factor VIII in subsequent years. Sir David Carter explained that during the transition from central to devolved funding, the money would be ring fenced for one year only to underline the necessity for funding in this area. It would be the responsibility of the purchasers who had haemophiliacs in their area to persuade their colleagues regarding a national purchasing consortium.

7. SAFETY COMMITTEE

Professor Franklin informed the group that invitations to participate had been issued to the proposed members of the Safety Committee on Factor VIII and Factor IX. Dr Brian Colvin had intimated that he would be prepared to act as Chairman and Dr Frank Hill had also provisionally accepted. Dr Martin Vessey was unable to accept and no reply had yet been received from the other three approached. Professor Franklin apprised the group of the proposal to modify the group slightly for other products.

Mr Snedden informed the group that the issue of indemnity for the Safety Committee members had been resolved. SNBTS expressed their appreciation to him and Mr Palmer for their input on this.

8. REVIEW OF HAEMOPHILIA CARE IN SCOTLAND

Professor Lowe outlined the review of Haemophilia Care that had been performed between 1980 and 1994 supported by a generous grant from the SODoH. The results will be presented at the ISTH meeting in Florence in June in 4 papers as follows:

- Demographics
- Treatment
- Muscular and skeletal function
- A crystal ball for the future

9. UK TRIAL COMPARING ION EXCHANGE AND MONOCLONAL PRODUCTS IN HIV SEROPOSITIVE PATIENTS

This study had shown no significant difference between the 2 products although the rate of HIV progression on either type of product was somewhat greater than previously reported. The results of the study will be presented at the ISTH meeting in Florence in June.

10. AOCB

Dr Ludlam thanked Sir David Carter for his time, energy and inspiration and invited him to attend and Chair the meeting again next year.

11. DATE OF NEXT MEETING

May 1998. Date to be confirmed.