# Inhibitor Working Party

## Membership

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|---|---|
| P Collins | Chairman |
| D Hart | Secretary |
| E Chalmers | |
| C Hay | |
| R Liesner | |
| B Palmer | |
| S Rangarajan | |
| K Talks | |
| M Williams | |

The working party reformed in March 2011

There have been two face to face meetings this year and two teleconferences.

## Activities

### Revision of UKHCDO Inhibitor guidelines

Revised guidelines for the diagnosis and treatment of inhibitors in congenital haemophilia A and B have been developed through UKHCDO and the BCSH Thrombosis and Haemostasis Task Force. The guidelines have been published in the British Journal of Haematology (Brit J Haematol 160:153-170, 2013).

Guidelines on acquired coagulation factor inhibitors been developed through the same process and have been published (Brit J Haematol 162:758-73, 2013).

### National immune tolerance induction protocol

A protocol for first line ITI for minimally treated severe patients has been developed by the working party in collaboration with the paediatric working party and this has been ratified by the advisory committee. This protocol is based on the recently published inhibitor guidelines. All centres in the inhibitor and paediatric working parties have agreed to use the protocol and to report their outcomes prospectively. The protocol has been submitted to the English Clinical Reference Group and, if adopted, all first line ITI in the UK will follow the protocol and outcomes will be reported.

## Analysis of data held by NHD

### Inhibitor surveillance in previously treated patients

The UK undertook a national procurement exercised which led to a substantial number of patients changing factor VIII concentrate. This was done on the assumption that if patients

change from one factor VIII concentrate to another the risk of inhibitor formation would be low. Given the available data at the time this was a reasonable assumption but close surveillance has been undertaken around the time of the switching to ensure that if any unexpected inhibitors had occurred these would identified early.

All centres have been asked to submit information on all inhibitor tests taken both before and after the new contract came into effect so that the effect of switching can be followed closely. It is important that both negative and positive inhibitor tests were reported in patients who did and did not switch product to ensure that any observed changes were not due to increased test frequency. It is recommended that all patients who switch products should have an inhibitor test done both before a switch and twice in the 6 months after a switch. The results do not suggest any increase in inhibitor formation related to switching although, even with the large number of patients available for UKHCDO to analyse, the study is underpowered.

## Inhibitor rates associated with brands of recombinant factor VIII

A recent study has suggested that the risk of a PUP developing an inhibitor varies with the brand of recombinant factor VIII (NEJM 368:231-9, 2013). It is important that this finding is investigated in other cohorts of patients. The NHD has identified all PUPs first treated between 2000 and 2011 and is investigating the rate of inhibitor development associated with each product in the first 2 years of treatment. Centres have been asked to clarify important data points and to ensure that the cohort investigated is appropriate. The data are being analysed.

This exercise is being extended so that a multivariate analysis can be performed to include the main known risk factors for inhibitor development (mutation, family history, ethnicity and intensive treatment). The results will be an important contribution to patient safety.

### Translational immunological projects

Collaboration with studies investigating the immunology of inhibitor formation are being considered.

### Future of the working party

The 3 year term of the working party ends in March 2014. UKHCDO will need to decide whether to reform the working party at that time.

Dr Peter Collins
Chairman, Inhibitor Working Party
September 2013