

## **Supplementary Material 5**

### **Data Management and Monitoring**

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### **D.4.1 Data Monitoring Committee**

An independent Data Monitoring Committee (DMC) was appointed, the terms of reference of which were governed by a signed DMC charter. It consisted of an independent chairperson, an independent expert clinician and an independent statistician and was convened to undertake independent review. The purpose of this committee was to monitor efficacy and safety endpoints. Only the independent DMC members and the unblinded statistician had access to unblinded trial data. The committee met three times during the trial (once annually).

Data analyses was supplied in confidence to an independent DMC, who advised on whether the accumulated data from the trial, together with the results from other relevant research, justified the continuation of recruitment of further patients. The DMC operated in accordance with a trial specific charter based upon the template created by the Damocles Group.

### **D.4.2 Trial Steering Committee**

A TSC was established to provide overall supervision of the trial, the terms of reference of which were governed by a signed TSC charter. The TSC included representation for both the funders and sponsor of the trial, whilst providing advice through its independent chairperson. The TSC consisted of an independent chairperson, members of the TMG, CRCTU Trial Management Team Leader, and selected PIs. Other members/observers were invited upon request. The committee met three times during the trial.

### **D.4.3 Trial Monitoring**

Monitoring of trial conduct and data collected was performed by a combination of central

review and on-site monitoring visits to ensure that the trial was conducted in accordance with GCP, the protocol and clinical trial regulations.

Independent on-site monitoring was carried out following an initial site-specific risk assessment and as documented in the BUTEO Quality Management Plan (QMP). Any major problems identified during monitoring were reported to the TMG and the TSC and the relevant regulatory bodies.