

## APPENDIX 2

### Charter and responsibilities of the Data Monitoring and Safety Committee

A Data Monitoring and Safety Committee (DMSC) has been established, and its lead by Clinical Study Center at Thomayer University Hospital, Prague. The DMSC is an independent organ from the study investigators. During the period of recruitment to the study, interim analyses will be supplied, in strict confidence, to the DMSC. In the light of these interim analyses, the DMSC will advise the study steering committee (SSC) if, in its view, the active intervention has been proven, beyond reasonable doubt, to be different from the placebo in some or all patients

Based on the reports of DMSC, the Study steering committee (SSC) can then decide whether or not to modify recruitment to the study and its oncoming course. Unless this happens, however, the SSC, will remain ignorant of the interim results.

The frequency of interim analyses will depend on the judgement of the Chair of the DMSC, in consultation with the SSC. However, we anticipate that there might be two to three interim analyses and one final analysis.

The Chair of DSMC is Mr. Jiri Skopek, M.D., Ph.D. who is available on request at [jiri.skopek1@ftn.cz](mailto:jiri.skopek1@ftn.cz)

### Premature termination of the study

An interim analysis is performed when 50% of patients have already got to Visit 5 (where primary outcome is evaluated.) The interim analysis is performed by a member of the study's statistical unit who is blinded for the allocation of the active study mixture. The statistician will report to the DMSC. The DMSC will have unblinded Access to all data and discuss the interim-analysis results with the SSC. The SSC decides on continuation or termination of the study and will report to the central Ethics committee. The study will be ended if the frequency of severe adverse events crosses the 5% line. Severe adverse event is defined as that one requiring hospitalisation.