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**Study protocol on advance care planning in multiple sclerosis (ConCure-SM): Intervention construction and multicenter feasibility trial**

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**ONLINE SUPPLEMENTAL APPENDIX 3 – EXCERPTS FROM THE STUDY PROTOCOL VERSION 1.0**

## 1 PANELS AND CENTERS

### 1.1 Trial Steering Committee (TSC)

The TSC is the executive body for the study. Members are from the Gruppo di Studio di Bioetica e Cure Palliative of the Società Italiana di Neurologia (L De Panfilis, MG Grasso, A Giordano, A Lugaresi, E Pucci, A Solari, S Veronese), from the National ACP programme for New Zealand (L Manson), and from patient associations (M Bruzzone, P Kruger).

### 1.2 Data Safety and Monitoring Committee (DSMC)

The independent DSMC has been established to: (1) oversee the progress of the pilot study and the safety data, and ensure that it is conducted, recorded, and reported in accordance with the protocol, GCP, and the applicable regulatory requirement(s); (2) monitor and supervise the progress of the pilot study, and the safety data. Members are: K Brazil, B Farsides, L Orsi, C Peruselli, and D Oliver (Chair). The DSMC is scheduled to meet (teleconference) before enrollment starts, at the end of the enrollment, and at the end of the follow-up, and depending on the needs of the trial. One week prior to each teleconference, the trial PI will send each DSMC member a report with trial data

(overall and by site) such as recruitment rates, reasons for exclusion, reason for drop out, plus other information if needed. The DSMC should report in writing to the TSC, usually within 3 weeks after the teleconference.

**1.3 Data Management and Analysis Committee (DMAC)**

The DMAC is responsible for data entry, quality assurance, and the statistical analyses. Members are M Farinotti (data manager) and A Giordano. DMAC will be in charge of the data protection to respond to the European and Italian law on privacy and data storage and conservation.

**1.4 Qualitative Analysis Panel (QAP)**

The QAP devised the design, procedures and analysis plan of the qualitative study. QAP members will conduct the personal interviews and the FGMs, and the analysis. Members are: M Cascioli, L De Panfilis, L Ghirotto, K Mattarozzi, and S Veronese.

**8.5 HP Training Panel (HTP)**

The HTP devised the HP training program. HTP members will have responsibility of conducting the residential program, and revise it based on training findings. Members are: M Cascioli, L De Panfilis, K Mattarozzi, E Pucci, M Rimondini, A Solari, and S Veronese.

**1.6 Linguistic validation Panel (LP)**

The LP was appointed to translate and adapt the outcome measures not available in Italian. Members are M Farinotti, A Giordano, A Solari, S Veronese and three independent translators (section 5.3.8).

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**2 ETHICS AND ADMINISTRATIVE CONSIDERATIONS**

**2.1 Ethical Considerations**

This clinical study was designed and shall be implemented and reported in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines for GCP, with applicable local regulations, and with the ethical principles laid down in the Declaration of Helsinki.

**2.2 Ethics Committee Approval**

The protocol, Subject Information Sheet, Informed Consent Form must be reviewed and approved by an appropriately constituted Ethics Committee (EC), as required in chapter 3 of the ICH E6 Guideline. Written EC approval must be obtained by the Sponsor prior to shipment of study agent or subject enrolment.

**2.3 Subject Information and Informed Consent**

Eligible subjects may only be included in the study after providing written (witnessed, where required by law or regulation), EC-approved informed consent, or, if incapable of doing so, after such consent has been provided by a legally acceptable representative of the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. If the subject is capable of doing so, he/she should indicate assent by personally signing and dating the written informed consent document or a separate assent form. Informed consent must be obtained before conducting any study-specific procedures (i.e. all of the procedures described in the protocol). The process of obtaining informed consent should be documented in the subject source documents. No study procedure can be performed before the written informed consent has been provided.

**2.4 Confidentiality**

The investigator must ensure participant anonymity. On database and other documents, participants must not be identified by name but by patient number and initials. The investigator must keep a separate log of participants' codes, names and addresses, and signed informed consent forms, all of which must be kept strictly confidential.

Patient medical information obtained by this study is confidential and may only be disclosed to third parties as permitted by the Informed Consent Form (or separate authorization for use and disclosure of personal health information) signed by the patient, unless permitted or required by law. Medical information may be given to a pwPMS personal physician or other appropriate medical personnel responsible for the pwPMS welfare, for treatment purposes. Data generated by this study must be available for inspection upon request by representatives of the national and local health authorities, monitors, representatives, and collaborators, and the EC for each study site, as appropriate.

**2.5 Protocol Amendments**

Any protocol amendments will be prepared by the PI. Protocol amendments will be submitted to the EC and to regulatory authorities in accordance with local regulatory requirements. Approval must be obtained from the EC and regulatory authorities (as locally required) before implementation of any changes, except for changes necessary to eliminate an immediate hazard to patients or changes that involve logistical or administrative aspects only (e.g. change in monitor or contact information).

**3 STUDY MANAGEMENT AND MONITORING**

**3.1 Source documents**

Source Documents are defined as original documents, data and records. These may include hospital records, medical records / outpatient data, data recorded from automated instruments, etc. Investigators should conserve all the source documents as required in the study protocol for at least two years after the end of the study.

**3.2 Archiving of records**

The investigator is responsible for recording and storing the essential documents of the study, according to what / and for the time required by law and by GCP. The Investigator must maintain adequate and accurate records to enable the conduct of the study to be fully documented, including but not limited to the protocol, protocol amendments, Informed Consent Forms, and documentation of EC and governmental approval.

**3.3 Auditing on site**

In the event that the investigator will be contacted by the Competent Authority in relation to this study, he or she will be required to immediately notify the Sponsor. The investigator must be available to respond to requests and queries by inspectors during the audit process. The investigator must provide the Sponsor copies of all correspondence that may affect the revision of the current study.

**3.4 Use and Publication of Study Results**

The results of the study may be presented during scientific symposia or published in a scientific journal only after review and written approval by the involved parties in full respect of the privacy of the participating subjects.

**3.5 Insurance Policy**

Each of the participating centers has an adequate insurance policy to cover possible damages emerging from this study.