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PeNSAMI Phase 2: a multicenter Italian trial of home-based palliative care for people with severe multiple sclerosis and their carers

Submission date 26/04/2014	**Recruitment status** No longer recruiting	☒ Prospectively registered
		☒ Protocol
Registration date 19/06/2014	**Overall study status** Completed	☐ Statistical analysis plan
		☒ Results
Last Edited 25/01/2021	**Condition category** Nervous System Diseases	☐ Individual participant data

Plain English summary of protocol

Background and study aims

There is very limited proof that palliative care in people with severe multiple sclerosis (MS) is beneficial. In the initial phase of the study, we identified care needs by asking people with severe MS, their carers, and health professionals from a range of MS-related disciplines. We identified the following needs: Managing everyday life (symptoms, personal care/hygiene, activities of daily living, outdoor mobility/transport); psychosocial aspects (relationships /communication, leisure/holidays, psychological wellbeing/social role); and organizational aspects (information, access to services, co-ordination of services, competent professionals). Based on a literature review and our qualitative findings, we devised the study intervention. In the present phase, our home-based palliative care program (study intervention) will be compared with standard care in people with severe MS and their carers.

Who can participate?

Adults with primary or secondary progressive MS with two or more unmet care needs from those identified in the initial phase of the study.

What does the study involve?

Participants are randomly allocated to one of two groups: either home palliative care integrated with standard care, or standard care alone. At each of the three participating centers, there will be a specially trained palliative care team (PCT) consisting of four professionals (physician, nurse, psychologist, and social worker). At first visit the PCT makes a comprehensive assessment of the patient-carer dyad. The treatment plan is agreed on, discussed with the doctor, and delivered (the intervention is not intended to replace existing services). At subsequent visits (≥ 2 home visits per month in the first trimester, as needed thereafter) the PCT checks the way the programme is delivered and reviews/modifies it as necessary. Participants assigned to the control group will receive the three examiner visits and the monthly telephone interviews, but not the PCT visits (see the Interventions field). At the end of follow-up, control group dyads are offered the home palliative care program. We will ask the participants how they felt about the intervention.

What are the possible benefits and risks of participating?
We do not expect negative effects due to participation in this study. However, we will carefully monitor any unplanned hospitalizations, emergency ward visits, and deaths over the 6-month period.

Where is the study run from?
Three Italian MS centres:
1. Foundation IRCCS Neurological Institute 'Carlo Besta', Milan (lead centre)
2. Foundation IRCCS, S. Lucia Rehabilitation Hospital, Rome
3. University Hospital Policlinico Vittorio Emanuele, Catania

When is the study starting and how long is it expected to run for?
Recruitment started in January 2015 and is expected to end by June 2015.

Who is funding the study?
The Italian MS Foundation (Fondazione Italiana Sclerosi Multipla) (FISM), Italy.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Protocol serial number
2014/S/1

Study information

Scientific Title

The Palliative Network for Severely Affected Adults with Multiple Sclerosis in Italy (PeNSAMI) Phase 2: a multicentre, phase II/III, single-blind, randomized controlled trial of home-based palliative care vs standard care for people with severe multiple sclerosis and their carers, and nested qualitative study

Acronym
PeNSAMI Phase 2

Study objectives
The aims of the study are to determine whether the home-based palliative care intervention:
1. Is likely to improve the health-related quality of life (HRQoL) of MS patients and their symptoms (primary study outcomes), reduce their dependence, hospitalizations, anxiety, and depression
2. Is likely to improve HRQoL of MS patients' carers, reduce their anxiety, depression, and caregiving burden
3. Is acceptable to MS patients, their carers and health professionals
4. Is feasible in terms of participation (recruitment rates and reasons of exclusion), procedures (time taken to deliver the intervention, deviations from protocol and non-completed interventions, incorporation with standard care, consistency of functional implementation and blinding), and resources (direct and indirect tangible costs).

Our project will provide evidence to tailor home palliative care services to the requirements of people with severe MS and their families and to support treatment decisions in advanced disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Institutional Review Board (IRB) of the Foundation IRCCS Neurological Institute 'Carlo Besta'; ref. 6/2014

Study design
Multicentre phase II/III single-blind randomised controlled trial and nested qualitative study

Primary study design
Interventional

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Multiple Sclerosis (MS)

Interventions
Study Intervention:
At each center there will be a specially trained palliative care team (PCT) consisting of four professionals (physician, nurse, psychologist, and social worker). At first visit the PCT makes a comprehensive assessment of the patient-carer dyad. Information on the study outcomes (assessed before randomization, and after 3 and 6 months by a blind examiner, and monthly by

an independent professional) will be available to the PCT via a web-based information gathering system. The treatment plan is agreed on, discussed with the caring physician, and activated by involvement of pertinent services available in the area: the intervention is not intended to replace existing services but to complement, collaborate with, and enhance them, minimizing duplication of effort. At subsequent visits (≥ 2 home visits per month in the first trimester, as needed thereafter) the PCT verifies program implementation and reviews/modifies it as necessary.

Qualitative study - We will undertake a qualitative study, nested in the PeNSAMI trial, aiming to scrutinize the experience of participants to the home palliative care intervention. The qualitative study consists of two parts: (a) individual, semistructured interviews (ISIs) with MS patients and carers who received the study intervention. To cover a range of experiences, participants will be selected from those with highest and lowest effect on the primary outcomes (SEIQoL-DW and POS-S-MS) at 3 and 6 months (purposeful sampling). A minimum of 12 dyads will be included, the total number depending on the achievement of data saturation. (b) focus group meetings (FGMs) of the caring physician of MS patients who received the study intervention.

Control Intervention:
Patient-carer dyads assigned to control (usual care) receive the three blind examiner visits and the monthly telephone interviews, but not the PCT visits. At the end of follow-up, control group dyads are offered the home palliative care program.

Statistical Methods
Between-group proportions will be compared by chi-square or Fisher's exact test. Continuous data will be summarized using count, mean, median, standard deviation, min and max. Between-group comparisons will be done using either the two-sided unpaired t-test or the Wilcoxon two-sided two-sample test for non-normal data. Normality assumption will be tested with the Shapiro-Wilk normality test. Correlations will be computed using Spearman's or Pearson's coefficients. Longitudinal changes as well as absolute scores for SEIQoL-DW index and POS-S-MS at baseline, 12 and 24 weeks will be analyzed using linear mixed-model analysis for longitudinal data (Diggle 2002; Verbeke 2000). Univariate and stratified analyses will be done on all clinically relevant covariables not included as a stratification factor in the randomization process (i.e., EDSS score at baseline, presence of severe cognitive compromise and center). All tests will be two-tailed, and values of $p < 0.05$ will be considered significant. The main analysis of the two primary outcomes will include all randomized patients (intention-to-treat, ITT): multiple imputation of missing values will be performed using the Rubin's approach. A per-protocol analysis will be also performed (to be considered as a secondary analysis only).

Sample Size Calculation
The sample size was based on previous data for SEIQoL-DW [Veronese 2010] and POS-S-MS [Edmonds 2010]; for both outcomes we considered changes at 3 months compared to baseline.

SEIQoL-DW: a sample size of 21 patients assigned to home palliative care (study intervention) and 11 assigned to standard care (control) has a power of 80% to detect an assumed mean change of score of 12.1 (standard deviation (SD) 12.8) in the home palliative care group compared to a change of -7.4 (SD 19.3) (null hypothesis) in the standard care group, at alpha level 0.05 using a two-sided, two-sample t test. Assuming 20% dropout, 25 patients are required in the home palliative care group and 13 in the standard care group (total sample size 38).

POS-S-MS: A sample size of 41 (home palliative care) and 21 (standard care) has a power of 85% to detect an assumed mean change of -0.4 (SD 0.5) in the home palliative care group, with a concomitant change of 0.2 (SD 0.8) (null hypothesis) in the standard care group; assuming an alpha level of 0.05 and a two-sided, two-sample t-test. Assuming 20% dropouts 49 patients are required in the home palliative care group and 25 patients in the standard care group (total sample size 74).

It is expected that up to 50% of MS patients have severe cognitive compromise, and will not be able to complete SEIQoL-DW, in these the only primary endpoint will be the POS-S-MS.

We aim to recruit 49 patients in the home palliative care group and 25 patients in the standard care group.

Qualitative analysis plan - We will use Framework analysis, an inductive approach toward content of ISIs and FGMs, as a way of identifying themes and categories of responses (Crabtree 1992; Silverman 1993; Denzin 2000). Analysis of ISI and FGM transcripts will be performed by two researchers in successive steps, each of which represents an increasing level of generalization (McCracken 1988). ISIs will be analyzed sequentially, and the researchers will decide to interrupt the accrual when they consider all the thematic categories sufficiently defined (data saturation). Each FGM report will be submitted to FGM participants for review (respondent validation).

Intervention Type
Other

Phase
Phase II/III

Primary outcome(s)
Patient-related outcomes:
1. SEIQoL-DW - It was developed to assess quality of life from the individual's perspective (O'Boyle 1992). It is an interview-based instrument to assess the level of functioning in, and relative importance of, areas of life nominated by the respondent. The SEIQoL-DW index is obtained from the satisfaction and the weight of each elicited area, and can range from 0 (worst possible score) to 100 (best possible HRQoL score).

2. POS-S-MS - It comprises 18 items plus two open questions, using a 0-4 scale (Sleeman 2012). The psychometric properties of Core-POS (see below) and POS-S-MS have been assessed in patients severely affected by MS confirming that both are acceptable, reliable, and valid in this population (Sleeman 2012). An Italian version of POS-S-MS was devised for this study by the PeNSAMI lead centre. The score is the sum of the scores from each of the first 17 items, and therefore can range from 0 to 68.

Key secondary outcome(s))
Patient-related outcomes:
1. Core-POS - Self-assessed questionnaire on emotional, psychological and spiritual needs and provision of information and support [Hearn 1999; Higginson 2004]. It consists of 10 items, each scored from 0 (best) to 4 (worst). An additional question gives patients the opportunity to list their 'main problems'. The score is the sum of the scores from each of the 10 questions, and therefore can range from 0 to 40.
2. FIM - Care burden scale that consists of 13 physical (based on the Barthel Index) and 5 cognitive items [Hamilton 1987, Stineman 1997]. Each item is scored on the level of assistance required for an individual to perform activities of daily living from 1 (total dependence) to 7 (complete independence). The scale can be administered by a physician, nurse, therapist or lay person. Possible scores range from 18 to 126, with higher scores indicating more independence.

3. HADS - Self-assessed questionnaire consisting of 14 multiple choice (0-3 Likert scale) items probing symptoms of anxiety (7 items) and depression (7 items). HADS anxiety (HADS-A) and depression (HADS-D) scores range from 0 (no symptoms) to 21 (most severe symptoms) [Zigmond 1983].

Carer-related outcomes
1. SF-36 - Widely used self-reported generic measure of HRQoL consisting of 36 items in eight domains (physical function, social function, physical role limitations, emotional role limitations, pain, vitality, mental health, and general health) [Ware 1993, Apolone 1998]. Two composite scores (physical and mental) can be calculated.
2. HADS
3. EQ-5D - Most used generic preference-based measure of HRQoL which produces utility scores anchored at 0 (death) and 1 (perfect health) [Kind 1998; Johnson 1998]. EQ-5D utility scores represent preferences for particular health states. The descriptive system has five dimensions (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression) and three levels (no problems, some problems, extreme problems), which create 243 unique health states [Torrance 1986; Dolan 1997] or can be converted into a single summary index (EQ-5D index) [Rabin 2001] by applying scores from a set of general population preference weights.
4. ZBI - 22-item self-report measure of subjective caregiver burden [Hérbert 2000]. Items are scored on a 5-point Likert scale ranging from 0 (never) to 4 (nearly always present). A total 0 (low burden) to 88 (high burden) score is obtained by summing item responses.

System related outcomes
Recruitment rates, reasons of exclusion, time to deliver and adherence to the intervention, protocol deviations, incorporation with standard care, unplanned hospital admissions, referrals to hospice.

Economic measures
Direct and indirect tangible costs will be assessed by the MS foundation Costs Questionnaire (MSCQ) devised by Italian MS Society. The MSCQ, completed by the dyad assisted by the blind examiner (at baseline) or an independent professional (at follow-up), collects information over the preceding 3 months, and previous month for selected items (i.e., drugs, complementary and alternative medicines, and use of paid care and related services), on health care, rehabilitation and social service use, professionals involved in care/services, personal expenditures, work issues, involvement of other carers, and recourse to informal networks. The patient EQ-5D is part of MSCQ. Information on hospitalizations are also obtained from the administrative records.

All scales are available in Italian except POS-S-MS, which has been translated-adapted from the original English using standard guidelines [Acquadro 2004; Wild 2005] by the team of A Solari.

Safety Measures
We do not expect negative effects due to the participation to the home palliative care program. However, we will carefully monitor:
1. Emergency ward visits that do not result in admission to the hospital
2. Hospitalizations (overnight stay at the hospital or emergency ward for observation and/or treatment)
3. Deaths (any cause)

An Independent Data and Safety Monitoring Committee will monitor serious adverse event reports throughout the trial and, if appropriate, recommend to the Trial Steering Committee to suspend or amend the study protocol.

Completion date
01/11/2016

Eligibility

Key inclusion criteria
Subjects are eligible for recruitment if all of the following criteria are satisfied:
1. Definite MS (Polman 2011)
2. Age ≥18 years
3. Primary or secondary progressive MS course
4. EDSS ≥ 8.0
5. Two or more unmet care needs from those identified in PeNSAMI Phase 1 (see above), or patient choice for comfort care only
6. One or more of the following patient clinical indicators (Thomas 2011):
6.1. Significant complex symptoms and medical complications
6.2. Dysphagia and poor nutritional status
6.3. Communication difficulties
6.4. Cognitive impairment, notably the onset of dementia
7. Presence of a carer (family member, relative, or friend, who is next of kin or is the key decision maker as designated by the [cognitively competent] patient and with whom the patient shares his/her life)
8. Signed informed consent (of both patient and carer)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
1. Hospitalized/institutionalized patients
2. Patients already receiving palliative care
3. Patient-carer dyads living out of the study area

Date of first enrolment
01/01/2015

Date of final enrolment
01/06/2015

Locations

Countries of recruitment
Italy

Study participating centre
Foundation IRCCS Neurological Institute 'Carlo Besta'
Milan
Italy
20133

Study participating centre
Foundation IRCCS, S. Lucia Rehabilitation Hospital
Rome
Italy
-

Study participating centre
University Hospital Policlinico Vittorio Emanuele
Catania
Italy
-

Sponsor information

Organisation
Foundation IRCCS Neurological Institute 'Carlo Besta' (Italy)

ROR
https://ror.org/05rbx8m02

Funder(s)

Funder type
Charity

Funder Name
Fondazione Italiana Sclerosi Multipla

Alternative Name(s)
Italian Multiple Sclerosis Foundation, Italian MS Foundation, FISM

Funding Body Type

Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Italy

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2018		Yes	No
Results article	results	12/07/2018		Yes	No
Results article	cost-effectiveness results	15/01/2021	25/01/2021	Yes	No
Protocol article	protocol	23/04/2015		Yes	No