Dutch Multiple sclerosis study (DMSS)

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON22564

Source
NTR

Brief title
Not applicable

Health condition

Multiple sclerosis

Sponsors and support

Primary sponsor: Nationaal MS Fonds Industrieweg 130C 3044 AT Rotterdam 010 – 591 98 39 info@nationaalmsfonds.nl Curavista bv Markt 9 4931 BR Geertruidenberg Tel: 0162 520 964 info@curavista.nl MS4 Research Institute Dr. Peter Joseph (Sjef) Jongen Ubbergseweg 34 6522 KJ Nijmegen The Netherlands
Source(s) of monetary or material Support: See sponsors

Intervention

Outcome measures

Primary outcome

The primary study outcomes are disabilities (MSIP-Disability) and disability perceptions (MSIP-Disability perception)

Secondary outcome

Disabilities as reported by an MS-specialized nurse (EDSS), health-related quality of life (MSQoL-54), and disease-modifying treatment utilization and persistence are the secondary outcomes of the study. Due to miscommunication, the two outcome measures; the Modified Fatigue Impact Scale-5 items (MFIS-5) and the Leeds Multiple Sclerosis Quality of Life (LMSQoL) reported in the initial study protocol were not included in the current study.

Study description

Background summary

MS is a chronic disease of the central nervous system, in which immune-mediated inflammation or degeneration leads to loss of myelin and axons. In most patients disease course is initially characterized by relapses and remissions: relapsing remitting MS (RRMS). After the first relapse patients are diagnosed as Clinically Isolated Syndrome (CIS) suggestive of MS. In CIS and RRMS immune activity and inflammation are the major pathophysiological processes, which may be positively influenced by disease-modifying treatment (DMT). In most patients with RRMS the disease course changes into secondary progression (SP), a phase that is characterized by slow increase of disability and disappearance of relapses. In about 10-15% of MS patients symptoms start and develop slowly without relapses (primary progression, PP). In PPMS and SPMS the continuous slow increase in disability is thought to result from degenerative processes, that are not modified by DMT.
Data on the long-term changes in disability in patients with MS or CIS are fragmented. Prospective studies on long-term disability were performed in the Australia, USA, Canada, France and Italy. These studies were often limited to certain regions or to patients treated in academic centers. As a result, the findings cannot easily be generalized to patients in the Netherlands. Information on the patient-reported long-term disability in MS and CIS patients in the Netherlands is lacking. Likewise, prospective data on the long-term changes in disability perception and HR-QoL are limited, and virtually absent for patients in the Netherlands.
Data on the patient-reported long-term disability (Multiple Sclerosis Impact Scale) and quality of life (Multiple Sclerosis Quality of Life-54) in patients with MS or CIS in the Netherlands will significantly contribute to better understand the risk of Dutch patients a to develop major levels of disability. In addition, the Expanded Disability Status Scale (EDSS) will be used to measure disability from a clinical point of view. In RRMS, SPMS and CIS patients data on long-term disability and self-reported adherence to DMT will enable to study relations between disease modifying treatment (DMT) and the risk to reach major levels of disability. In PPMS patients information on the long-term disability will provide essential data on the natural course of progressive MS in the Netherlands and are a reference for future treatments

Study objective

1. Disability & Quality of life (descriptive nature, primary analyses)

Change in patient-reported outcome variables in overall group (MS diagnosis) and subgroups

(CIS, RRMS, SPMS, PPMS) from baseline to 8-year follow-up

• Change in disabilities [MSIP], corrected for demographic and disease characteristics
1. H0: Disabilities [MSIP] remain constant over time between baseline and last follow-up
Ha: Disabilities [MSIP] change over time between baseline and last follow-up
And/or
2. H0: Disabilities [MSIP] remain constant from study enrolment and follow-up time depending on data
Ha: Disabilities [MSIP] change from study enrolment and follow-up time depending on data

• Change in disability perceptions [MSIP], corrected for demographic and disease characteristics
1. H0: Disability perceptions [MSIP] remain constant over time between baseline and last follow-up
Ha: Disability perceptions [MSIP] change over time between baseline and last follow-up
And/or
2. H0: Disability perceptions [MSIP] remain constant from study enrolment and follow-up time depending on data
Ha: Disability perceptions [MSIP] change from study enrolment study enrolment and follow-up time depending on data

• Change in mental HRQoL [MSQoL-54], corrected for demographic and disease characteristics
1. H0: Mental HRQoL [MSQoL-54] remains constant over time between baseline and last follow-up
Ha: Mental HRQoL [MSQoL-54] changes (if mean change in score =/> MCID) over time between baseline and last follow-up
And/or
2. H0: Mental HRQoL [MSQoL-54] remains constant from study enrolment and follow-up time depending on data
Ha: Mental HRQoL [MSQoL-54] changes (if mean change in score =/> MCID) from study enrolment and follow-up time depending on data from baseline to MX

• Change in physical HRQoL [MSQoL-54], corrected for demographic and disease characteristics
1. H0: Physical HRQoL [MSQoL-54] remains constant over time between baseline and last follow-up
Ha: Physical HRQoL [MSQoL-54] changes (if mean change in score =/> MCID) over time between baseline and last follow-up
And/or
2. H0: Physical HRQoL [MSQoL-54] remains constant from study enrolment and follow-up time depending on data
Ha: Physical HRQoL [MSQoL-54] changes (if mean change in score =/> MCID) from study enrolment and follow-up time depending on data from baseline to MX

2. Disability & Quality of life (secondary analyses)

• Intra-individual HRQoL change in overall groups and subgroups

1. H0: Intra-individual change in HRQoL from baseline to last follow-up in subgroup 1a is equal to intra-individual change in HRQoL in subgroup 1b (e.g. male vs. female)
Ha: Intra-individual change in HRQoL from baseline to last follow-up in subgroup 1a is not equal to intra-individual change in HRQoL in subgroup 1b (e.g. male vs.
female)
H0: There is no interaction of subgroups on the within-subject change in HRQoL over multiple follow-up measurements between baseline and last-follow-up.
Ha: There is an interaction of subgroups on the within-subject change in HRQoL over multiple follow-up measurements between baseline and last-follow-up.

Specify subgroups (subgroup 1a vs. 1b (vs. 1c))
Sex: male vs. female: not equal
Duration disease: longer vs. shorter: not equal
Type MS: CIS, RRMS, SPMS, PPMS: not equal
Age: subgroups based on literature (e.g. MS Base)/ median
Degree of disabilities (each domain of MSIP): low vs. moderate vs. high, median: not equal
Degree of HRQoL: low vs. moderate vs. high: not equal
Treatment center: generic vs. specialized: not equal
Treatment center: South NL vs. North NL: not equal
Specialist education: year of education: not equal
Type DMD: first-line vs. second-line: not equal
Or
2. H0: mean HRQoL in subgroup 1a is equal to mean HRQoL in subgroup 1b at M0, M24, M48, M72, M96
Ha: mean HRQoL in subgroup 1a is not equal to mean HRQoL in subgroup 1b at M0, M24, M48, M72, M96

Specify subgroups (subgroup 1a vs. 1b (vs. 1c))
Sex: male vs. female: not equal
Duration disease: longer vs. shorter: not equal
Type MS: CIS, RRMS, SPMS, PPMS: not equal
Age: subgroups based on literature (e.g. MS Base)/ median
Degree of disabilities (each domain of MSIP): low vs. moderate vs. high, median: not equal
Degree of HRQoL: low vs. moderate vs. high: not equal
Treatment center: generic vs. specialized: not equal
Treatment center: South NL vs. North NL: not equal
Specialist education: year of education: not equal
Type DMD: first-line vs. second-line: not equal

• Comparison of HRQoL of study sample with Dutch population and/or other chronic diseases
1. H0: HRQoL is equal in patients with MS at study enrolment and the general Dutch population/ other chronic disease (incl. MS Base)
2. Ha: HRQoL is not equal in patients with MS and the general Dutch population other chronic disease (incl. MS Base) at study enrolmentH0: HRQoL is equal in patients
with MS at X months at study enrolment and the general Dutch population/ other chronic disease (incl. MS Base)
Ha: HRQoL is not equal in patients with MS at X months at study enrolment and the general

Dutch population other chronic disease (incl. MS Base)

Association between disease variables:
• Change in disabilities and change in disability perceptions
1. H0: Long-term increase in disabilities is not correlated with an increase in disability perceptions
Ha: Long-term increase in disabilities is correlated with long-term increase in disabilities perceptions (‘response shift’ due to adaptation to situation)

• Change in disabilities and change in HRQoL
1. H0: Long-term increase in disabilities is not correlated with long-term decrease in quality of life
Ha: Long-term increase in disabilities is correlated with the long-term decrease in quality of life (‘response shift’ due to adaptation to situation).
2. Increase in disabilities (perceptions) is preceded by decrease in quality of life
Descriptive: differences in QoL preceding the decrease in disabilities (perceptions)

• Increase in disabilities and relapses
1 H0: There is no association between number of relapses (Annualized Relapse Rate) and increase in disabilities.
Ha: There is an association between number of relapses (Annualized Relapse Rate) and increase in disabilities.
Lineaire regression: an extra relapse (onafhankelijke variabele), contributes to the increase in disabilities (dependent variabele)

• Change in assessment adherence and change in disabilities (perceptions)
1. H0: There is no association between early discontinuation of assessment and an increase in disabilities (perceptions) in the year before discontinuation
Ha: There is an association between early discontinuation of assessment and an increase in disabilities (perceptions) in the year before discontinuation

• Change in assessment adherence and change in HRQOL
2. H0: There is no association between early discontinuation of assessment and an increase in physical HRQoL in the year before discontinuation
Ha: There is an association between early discontinuation of assessment and an increase in physical HRQoL in the year before discontinuation
3. H0: There is no association between early discontinuation of assessment and an increase in mental HRQoL) in the year before discontinuation
Ha: There is an association between early discontinuation of assessment and an increase in mental HRQoL in the year before discontinuation

3. Trends in treatment utilization, persistence and effectiveness (descriptive and change over time, primary analyses)

Trends in treatment utilization
• Trends in the prescription of first-line and second-line DMDs
o Time between diagnosis and prescription first-line DMD, prescription second-line DMD
o Time between first-line and second-line DMDs: differences between subgroups based on

gender, EDSS, relapses
Descriptive: mean (SD)
• Prescription trends follow Dutch guidelines
Qualitative discussion

Effectiveness of first-line and second-line DMDs (RRMS and SPMS patients)
Descriptive:
• Frequencies on first-line DMD
o Number of relapses: Mean (SD)
o Disabilities and disability perceptions: Mean (SD)
o Mental and physical HRQoL: Mean (SD)
• Frequencies on second-line DMD
o Number of relapses: mean (SD)
o Disabilities and disability perceptions: Mean (SD)
o Mental and physical HRQoL: Mean (SD)

• Adherence (discontinuation) to DMD treatment and change in disabilities
1. H0:Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of disabilities compared to non-persistent (<2yrs) patients
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of disabilities compared to non-persistent (<2yrs) patients
2. H0:Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of less mental HRQoL compared to non-persistent (<2yrs) patients
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of less mental HRQoL compared to non-persistent (<2yrs) patients
3. H0:Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of less physical HRQoL compared to non-persistent (<2yrs) patients
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of less physical HRQoL compared to non-persistent (<2yrs) patients
4. H0: There is no association between patients with stable disease over study period and treatment persistence
Ha: There is an association between patients with stable disease over study period and treatment persistence
5. H0: There is no relationship between patients with highdisease activity and treatment persistence
Ha: There is a positive relationship between patients with high disease activity and treatment persistence

4. Trends in treatment utilization, persistence and effectiveness (secondary analysis)

• Time-to-first DMD and conversion to SPMS/ change in disabilities

1. Relationship between time-to-first DMD, and increase in disabilities.
H0: there is no association between time-to-first DMD and increase in disabilities
Ha: there is an association between time-to-first DMD and increase in disabilities

2. Relationship between DMD duration-disease duration ratio, and increase in disabilities.
H0: there is no association between DMD duration-disease duration ratio and increase in

disabilities
Ha: there is an association between DMD duration-disease duration ratio and increase in disabilities

3. Negative relationship between time-to-first DMD and conversion to SPMS/ reaching clinical milestone of EDSS 4.0 and EDSS 6.
H0: there is no association between time-to-first DMD and conversion to SPMS
Ha: there is an association between time-to-first DMD and conversion to SPMS
H0: there is no association between time-to-first DMD and reaching clinical milestone of EDSS 4.0/ EDSS 6.0
Ha: there is a an association between time-to-first DMD and reaching clinical milestone of EDSS 4.0/ EDSS 6.0

Study design

At baseline the Multiple Sclerosis Impact Profile (MSIP), Multiple Sclerosis Quality of Life-54 items (MSQoL-54), Relapse Self-Report, and Medication and Adherence Inventory were completed by means of an online questionnaire, and the EDSS score was assessed by phone. At follow-up the MSIP, MSQoL-54 and Relapse Self-Report, are completed every 6 months. Monthly completion of Medication and Adherence Inventory is optional. The EDSS score was assessed in 2016, at variable follow-up time points. In 2021, EDSS score will be assessed again, this means for each patient at a different follow up.

Intervention

Care as usual

Contacts

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Eligibility criteria

Inclusion criteria

1) Diagnosis of MS or Clinically Isolated Syndrome (CIS)
2) Willing and able to comply with the study protocol
3) Having access to the internet
4) Have given informed consent

Exclusion criteria

Not defined

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2011
Enrollment:	500
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Plan description

xx

Ethics review

Positive opinion

Date:	27-05-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9520
Other	METC: Medical Ethical Assessment Research Patients and Test Subjects (METOPP), Tilburg, The Netherlands : Registration number; M397; issue of an investigation not subject to the WMO, dated 1 March 2011

Study results