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Study to investigate the combination of methylprednisolone and interferon-beta in the treatment of multiple sclerosis

Submission date
24/04/2009

Recruitment status
No longer recruiting

Registration date
24/04/2009

Overall study status
Completed

Last Edited
30/06/2009

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Nordic trial of methylprednisolone as add-on therapy to interferon-beta for the treatment of relapsing-remitting multiple sclerosis: a randomised, double-blind, placebo-controlled, parallel-group, multicentre trial

Acronym
NORMIMS

Study objectives
Interferon-beta (IFN-beta) is the approved standard therapy in relapsing-remitting multiple sclerosis (MS). The effect of IFN-beta in relapsing-remitting MS is primarily directed against the Th1-driven inflammatory demyelinating attack. IFN-beta may interfere with cell trafficking by decreasing the expression of adhesion molecules and inhibit matrix metalloproteinases; reduce the expression of major histocompatibility complex (MHC) II molecules on antigen presenting cells; inhibit pro-inflammatory cytokines and induce anti-inflammatory cytokines. However, the effect of IFN-beta on clinical disease activity is only moderate and many patients have only a partial treatment response.

The possible beneficial effect of intravenous methylprednisolone in delaying the onset of MS after optic neuritis has been suggested to be due to its anti-inflammatory and/or immune regulatory activity. Since IFN-beta also has such biological and immunological properties it seems justified to investigate the potential effect of the combination of methylprednisolone and IFN-beta in patients with relapsing-remitting MS. Further methylprednisolone might have a positive effect on the occurrence of side effects to IFN-beta treatment and might reduce the occurrence of neutralising antibodies against IFN-beta. Adjuvant intermittent treatment with methylprednisolone is easy to administer, well tolerated and relatively inexpensive. The objective of the study is to compare the effect of methylprednisolone given at 4-week intervals with the effect of placebo in patients treated with IFN-beta-1a who during therapy have shown clinical activity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Scientific Ethics Committee of Copenhagen approved on the 23rd May 2003 (ref: KF 02-012 /03)
2. Danish Regulatory Authorities (Danish Medicinal Agency) approved on the 30th May 2003 (ref: 2612-2236)

Study design
Randomised double-blind placebo-controlled parallel-group multicentre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsing-remitting multiple sclerosis

Interventions

Methylprednisolone 100 mg tablets or identically appearing placebo tablets. Dose and administration: 2 tablets after the morning meal on 5 consecutive days at 4-week intervals for at least 96 weeks (extension to 144 weeks possible).

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Methylprednisolone, interferon-beta

Primary outcome(s)
The mean number of documented relapses per patient per year at 96 weeks. A documented relapse was defined as the appearance of a new or worsening of old neurological symptoms or signs, in the absence of fever, persisting for more than 48 hours and causing objective changes on neurological examination and preceded by a period of more than 30 days with a stable or improving condition. Changes in bowel and bladder or cerebral functions should not have been solely responsible for a relapse.

Key secondary outcome(s))
1. The mean number of documented relapses per patient per year at 48 weeks
2. The occurrence of neutralising antibodies at 96 weeks
3. Changes in the Multiple Sclerosis Functional Composite (MSFC) score
4. The time to a permanent increase in disability of 1.0 point as measured by the Extended Disability Status Score (EDSS) and confirmed at 2 consecutive visits with an interval of 24 weeks
5. The number of active lesions (new or enlarging lesions) on T2 weighted magnetic resonance imaging (MRI)

Completion date
10/12/2007

Eligibility

Key inclusion criteria
1. Males and females between the age of 18 and 55 years (both included)
2. Has multiple sclerosis according to the McDonald criteria and suffers from clinically definite relapsing-remitting MS according to the Poser criteria
3. Has a disability equivalent to Expanded Disability Status Scale (EDSS) of 5.5 or less
4. Has been on treatment with IFN-beta-1a (Rebif®) for at least 1 year and has received IFN-beta-1a (Rebif®) 44 µg three times weekly for at least 1 month
5. Has shown clinical activity defined as at least one relapse during the previous 12 months and thereby is classified as a patient with partial treatment response. A historical relapse may be accepted as qualifying as judged by the treating physician.
6. Is prepared to and considered able to follow the protocol during the whole study period and to attend the planned visits
7. Female of childbearing potential must use adequate contraceptive methods and must have negative pregnancy test results
8. Has given written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Has received treatment with lymphoid irradiation, mitoxantrone, cyclophosphamide, or long-term systemic glucocorticoids
2. Has received treatment with azathioprine, cyclosporine, glatiramer acetate, or other immunosuppressive agents or intravenous immunoglobulin within 6 months prior to inclusion in the study
3. Has changed IFN-beta preparation or dose within 3 months of inclusion in the study
4. Has received treatment with systemic glucocorticoids (relapse treatment) or adrenocorticotropic hormone (ACTH) within 8 weeks prior to inclusion in the study
5. Has experienced a relapse within one month prior to the inclusion in the study
6. Has converted to secondary progressive MS
7. Has a history of peptic ulcer or present symptoms of dyspepsia
8. Has suffered from major depression or any other psychiatric disorder that would preclude safe participation in the study
9. Has diabetes mellitus
10. Has alcohol or drug abuse
11. Has cardiac insufficiency, cardiomyopathy, significant cardiac dysrhythmia, unstable or advanced ischaemic heart disease (New York Heart Association [NYHA] Functional Classification III or IV), or malignant hypertension
12. Has renal insufficiency
13. Has aspartate aminotransferase (ASAT) greater than 2.5 x normal upper limit
14. Has leucopenia less than 2500 leucocytes per microlitre or thrombocytopenia less than 100,000 thrombocytes per microlitre
15. Has any medical illness requiring treatment with systemic corticosteroids
16. Has any systemic disease, which can influence his/her safety and compliance, or the evaluation of the disability
17. Has formerly shown severe reactions against corticosteroids
18. Is pregnant or breast-feeding
19. Has epilepsy not under control by anti-epileptic drug (AED)

Date of first enrolment
25/08/2003

Date of final enrolment
10/12/2007

Locations

Countries of recruitment
Denmark

Finland

Norway

Sweden

Study participating centre
Danish Multiple Sclerosis Research Center
Copenhagen
Denmark
DK-2100

Sponsor information

Organisation
Danish Multiple Sclerosis Research Center (Denmark)

ROR
https://ror.org/04anq5q02

Funder(s)

Funder type
Industry

Funder Name
Merck Serono (Denmark) - non-conditional grant; investigator-initiated and investigator-driven study

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2009		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes