A Randomized, Controlled, Open-Label, Rater-Blinded, Phase 3b Study of the Efficacy, Safety, and Tolerability of 6-Week Extended Interval Dosing (EID) of Natalizumab (BG00002) in Subjects With Relapsing-Remitting Multiple Sclerosis witching From Treatment With 4-Week Natalizumab Standard Interval Dosing (SID) in Relation to Continued SID Treatment - Followed by an Open-Label Crossover Extension Study Comprising Subcutaneous and Intravenous Natalizumab Administration

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Part 1: The primary objective of this study is to evaluate the efficacy of natalizumab extended interval dosing (EID) in subjects who have previously been treated with natalizumab standard interval dosing (SID) for at least 12 months, in relation to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON54587

Source
ToetsingOnline

Brief title
Biogen 101MS329 (Nova)

Condition

- Neuromuscular disorders

Synonym
damage central nervous system, multiple-sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Biogen
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: relapsing-remitting Multiple Sclerose, Standard Interval Dosing

Outcome measures

Primary outcome

Part 1: Number of New or Newly Enlarging T2 Hyperintense Lesions at Week 72

Part 2: Percentage of Participants Indicating a Preference for Natalizumab SC

Administration at the End of Part 2

Secondary outcome

Part 1:

•Time to First Relapse as Adjudicated by an Independent Neurology Evaluation

Committee (INEC)

•Number of new Gadolinium (Gd) Enhancing and new T1 Hypointense Lesions at

Weeks 24, 48 and 72

•Annualized Relapse Rate at Weeks 72

•Number of New or Newly Enlarging T2 Hyperintense Lesions at Weeks 24 and 48

•Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

•Time to Expanded Disability Status Scale (EDSS) worsening

Part 2:

• Total Score on Treatment Satisfaction Questionnaire for Medication (TSQM)

• Mean Time for Drug Preparation and Administration

• Number of Participants with Treatment Emergent AEs (TEAEs)

• Percentage of Participants With Anti-Natalizumab Antibodies

• Number of New or Newly Enlarging T2 Hyperintense Lesions

• Time to First Relapse

• Annualized Relapse Rate

• Change in Expanded Disability Status Scale (EDSS) Score

• Number of New Gadolinium (Gd) Enhancing Lesions

• Number of New T1 Hypointense Lesions

• Percentage of Brain Volume Change

• Change in Cortical and Thalamic Brain Region Volume

• Trough Serum Concentration of Natalizumab (Ctrough)

• Part 2: Trough α4 Integrin Saturation

Study description

Background summary

Natalizumab is a recombinant humanized anti-α4 integrin antibody, derived from a monoclonal antibody (mAb) [AN100226m] raised against human α4 integrin. The murine mAb (AN100226m) was humanized by complementarity-determining region grafting of the hypervariable region of the gene encoding AN100226m onto a human immunoglobulin G4 framework, producing the humanized immunoglobulin G4/kappa antibody, natalizumab.

Study objective

Part 1: The primary objective of this study is to evaluate the efficacy of natalizumab extended interval dosing (EID) in subjects who have previously been treated with natalizumab standard interval dosing (SID) for at least 12 months, in relation to continued SID treatment.

Part 2: The primary objective is to evaluate participant preference for subcutaneous (SC) versus intravenous (IV) route of natalizumab administration.

Study design

Part 1 is a prospective, randomized, interventional, controlled, open-label, rater-blinded study of IV natalizumab administered under SID and EID.

Part 2 is an OLE study of natalizumab EID delivered by SC and IV administration in a randomized crossover design that is available to all qualified subjects who have completed Part 1. New subjects who did not participate in Part 1 but meet Part 1 enrollment criteria and satisfy the requirements for enrollment in Part 2 are also eligible.

Intervention

Part 1
SID group: approximately 240 subjects will receive natalizumab as a 300 mg IV infusion Q4W (28 [-2/+5] days).
EID group: approximately 240 subjects will receive natalizumab as a 300 mg IV infusion Q6W (42 [-2/+5] days).

Part 2
All subjects enrolled in Part 2 will receive natalizumab as a 300 mg IV infusion Q6W (42 [-2/+5] days) for a period of 36 weeks. Subjects will then be randomized 1:1 by Part 1 treatment group (SID, EID, new subjects) to receive natalizumab 300 mg SC Q6W for 24 weeks followed by 300 mg IV Q6W for 24 weeks or the same 48-week crossover in reverse order.

Study burden and risks

After more than 10 years of postmarketing experience, natalizumab continues to demonstrate a high level of efficacy with a well-characterized safety profile and a significant beneficial impact on the quality of life in patients with RRMS. In pivotal clinical studies, natalizumab demonstrated a 67% reduction in annualized relapse rate and a 42% reduction in the risk of disability progression over 2 years. Since the marketing of natalizumab, publications from multiple independent groups, as well as publications from the Sponsor, have further demonstrated the clinical effectiveness of natalizumab when used in patients with MS with high disease activity despite treatment with first-line therapies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

For Part 1: • Ability of the participant to understand the purpose and risks of

the study and provide signed and dated informed consent and authorization to use confidential health information in accordance with national and local participant privacy regulations. • Aged 18 to 60 years old, inclusive, at the time of informed consent • Diagnosis of relapsing remitting multiple sclerosis (RRMS) according to the McDonald criteria. • Treatment with natalizumab as disease-modifying monotherapy for RRMS that is consistent with the approved dosing for a minimum of 12 months prior to randomization. The participant must have received at least 11 doses of natalizumab in the 12 months prior to randomization with no missed doses in the 3 months prior to randomization. • Expanded Disability Status Scale (EDSS) <=5.5 at screening. • No relapses in the last 12 months prior to randomization, as determined by the enrolling Investigator For Part 2: • Ability of the participants to understand the purpose and risks of the study and provide signed and dated informed consent for Part 2 and authorization to use confidential health information in accordance with national and local participant privacy regulations. • Completed Part 1 Week 72 visit while remaining on their randomized treatment assignment of SID or EID. • The inclusion and exclusion criteria for new participants who did not participate in Part 1 of the study are the same as those for participants who did participate in Part 1.

Exclusion criteria

For Part 1:
• Primary and secondary progressive multiple sclerosis (MS).
• MRI positive for Gd-enhancing lesions at screening.
• Participants for whom MRI is contraindicated (e.g., have a contraindicated pacemaker or other contraindicated implanted metal device, have suffered, or are at risk for, side effects from Gd, or have claustrophobia that cannot be medically managed).
• History of any clinically significant (as determined by the Investigator) cardiac, endocrinologic, hematologic, hepatic, immunologic, metabolic (including diabetes), urologic, pulmonary, neurologic (except for RRMS), dermatologic, psychiatric, renal, or other major disease that would preclude participation in a clinical study, in the opinion of the Investigator.
• Presence of anti-natalizumab antibodies at screening.

For Part 2:
• Participants treated with natalizumab EID was reverted to natalizumab SID by choice or as rescue treatment in Part 1.
• Participant received treatment with any MS disease-modifying therapy other than natalizumab in Part 1 or in the period between Part 1 and Part 2.
• History of human immunodeficiency virus or history of other immunodeficient conditions.
• Current enrollment or a plan to enroll in any interventional clinical study in which an investigational treatment or approved therapy for investigational

use is administered within 30 days (or 5 half-lives of the agent, whichever is longer) prior to the Baseline Visit or at any time during this study.
• Inability to comply with study requirements.
• Other unspecified reasons that, in the opinion of the Investigator or Biogen, make the participant unsuitable for enrollment.

The inclusion and exclusion criteria for new participants who did not participate in Part 1 of the study are the same as those for participants who did participate in Part 1.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2019
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AN100226, BG00002
Generic name:	TYSABRI
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-11-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-03-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-05-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	27-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-02-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-02-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2018-002145-11-NL
CCMO	NL67716.100.18