A 48 weeks, phase II, randomized, double-blind, placebo-controlled, proof of concept and dose finding study of three different dose regimens of BI 655066 administered subcutaneously in patients with ankylosing spondylitis.

Published: 03-01-2014
Last updated: 24-04-2024

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

Summary

ID

NL-OMON40442

Source
ToetsingOnline

Brief title
BI 1311.8

Condition

- Autoimmune disorders

Synonym
Ankylosing spondylitis

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim BV

Intervention

Keyword: Ankylosing Spondylitis, BI 655066, Monoclonal antibody, 'Proof of concept'

Outcome measures

Primary outcome

Primary efficacy endpoint:

* ASAS 40 response at Week 12

Secondary outcome

Key secondary endpoint is:

* Change in ASDAS score at Week 12 as compared to baseline

Secondary efficacy endpoints are:

* ASAS 5/6 response at Week 12

* ASAS partial remission criteria at Week 12

* ASAS 20 response at Week 12

* ASAS 40 response at Week 24 (EOT)

* Change in BASDAI score at Week 12 as compared to baseline

Study description

Background summary

Ankylosing spondylitis, previously known as Bechterew's disease (or syndrome)

and Marie-Strümpell disease, is a chronic inflammatory disease of the axial skeleton (e.g. skeleton of the spine) with variable involvement of peripheral joints and some nonarticular structures. It is a form of spondyloarthritis, a chronic, inflammatory arthritis where immune mechanisms are thought to have a key role. It mainly affects joints in the spine and the sacroiliac joint in the pelvis, and can cause eventual fusion of the spine.

BI 655066 belongs to a class of drugs known as humanized monoclonal antibodies. A monoclonal antibody is a protein made in the laboratory that can bind to substances in the body. BI 655066 works by binding to a protein called IL-23 p19. In simple words, it works by neutralizing a protein called IL-23-p19 involved in the development of ankylosing spondylitis.

Study objective

The overall purpose of the trial is to assess clinical efficacy and safety of three different doses of BI 655066 administered by multiple subcutaneous injections in adult patients with defined ankylosing spondylitis. We will also explore its pharmacokinetics (PK, which shows how your body absorbs, breaks down, and removes the study drug in the blood) and pharmacodynamics (PD, which shows how the study drug is reacting with the target molecule - IL23 p19).

Study design

Wordwide, the study will be conducted at about 50 centers with about 160 patients. In the Netherlands, about 8 patients will participate to the study. The total treatment duration will be 24 weeks. During this period, the study drug or placebo will be administered to you 4 times at the study center: at Day 1, Week 8, Week 16 and Week 24. You will have 1 out of 4 chances to receive placebo and 3 out of 4 chances to receive an active BI 655066 treatment (equal chances for each of the three active treatment regimens).

Intervention

A total of approximately 160 AS patients will be randomized 1:1:1:1 into four intervention arms. There will be 3 active arms, corresponding to different dose regimens (D1, 2 and 3), and one placebo arm.
* Arm 1 (D1): 18 mg BI 655066 administered s.c. at Day 1, followed by placebo to BI 655066 every 8 weeks (i.e. at Week 8, 16 and 24), up to a total duration of 24 weeks (n~40 patients)
* Arm 2 (D2): 90 mg BI 655066 administered s.c. at every 8 weeks (i.e at Day 1, Week 8, 16 and 24), up to a total duration of 24 weeks (n~40 patients)
* Arm 3 (D3): 180 mg BI 655066 administered s.c. at every 8 weeks (i.e at Day 1, Week 8, 16 and 24), up to a total duration of 24 weeks (n~40 patients)
* Arm 4: placebo to BI 655066, administered s.c. at every 8 weeks (i.e at Day

1, Week 8, 16 and 24), up to a total duration of 24 weeks (n~40 patients)

Study burden and risks

During all visits, pregnancy test will be done (if applicable), routine lab tests will be taken, including PK samples.
On day 1, week 8, week 16 and week 24, BI 655066 will be administered.
ADA sampling will be done at visit 2 (randomisation), week 8, 12, 16, 24 and during the follow-up period.
ASAS response will be determined at week 2, 8, 12, 24 and during the follow-up period.
MRI was performed at visit 2 (randomisation) and week 24 (EOT).
X-ray of the spine will be performed during the screening period.
ECG will be made at every visit during the treatment period.
Vital signs will be measured at all visits.
Questionnaires will be completed by the patients during all visits (except week 1) and the swollen and tender joints will be counted.
Diaries will be completed from randomisation to end of treatment.
At visit 2 (randomisation), farmacogenomic samples will be taken. For the farmacogenomic samples a seperate consent will be given.
Visits will last for 2-4 hours.
For details in the flow chart, please refer to pages 7-11 of the protocol.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male and female patients
2. Age * 18 years and * 70 years at screening
3. Definite AS based on the modified New York criteria (1984)
4. Documented disease duration * 3 months at screening
5. Active disease at screening, defined as:
a. BASDAI score (0-10) * 4, AND
b. Spinal pain level assessed by patient on NRS (0-10) * 4 (2nd question from BASDAI will be used here)
6. Have either a documented inadequate response for axial symptoms to 30 days of optimal daily doses of at least two non-steroidal anti-inflammatory drugs (NSAIDs), or documented intolerance to NSAIDs.
7. Female patients must meet at least one of the following criteria from screening visit up to End of Observation visit in the current trial:
- using adequate contraception, e.g. any of the following methods plus condom: implants, injectables, combined oral contraceptives, intrauterine device (IUD)
- sexually abstinent
- have a vasectomised sexual partner (vasectomy at least 1 year prior to enrolment)
- surgically sterilised (including hysterectomy)
- postmenopausal defined as at least 1 year of spontaneous amenorrhea (in questionable cases a blood sample with simultaneous levels of follicle stimulating hormone (FSH) above 40 U/L and estradiol below 30 ng/L is confirmatory)
8. Patients (males or females) receiving background MTX or Leflunomide therapy who are following the national regulatory guidelines regarding contraception.
9. Signed and dated written informed consent prior to admission to the study in accordance with GCP and local legislation.

Exclusion criteria

1. Radiographic evidence of total ankylosis of the spine at screening or before (spinal X-Ray examinations at screening visit/ during screening period are not mandatory - see footnote 12 from Flow-Chart 1).

2. Patient previously treated with any biological immunomodulating agent for AS, either licensed or experimental.
3. Previous or current participation in a clinical trial testing an investigational drug for AS within 12 weeks prior to randomization (any biological immunomodulating agents are excluded).
4. Usage of any investigational drug within 30 days prior to randomization or the planned use of an investigational drug during the course of the actual study.
5. Active uveitis or inflammatory bowel disease at screening.
6. Diagnosed psoriatic arthritis at screening, satisfying the modified New York criteria.
7. Patients who had received intraarticular injection(s) with corticosteroids within 4 weeks prior to screening visit.
8. Patients who must or wish to continue the intake of restricted medications (cf. Section 4.2.2.1) or any drug considered likely to interfere with the safe conduct of the study.
9. Major surgery performed within 8 weeks prior to screening or planned within 12 months after screening (e.g. hip replacement).
10. Chronic or relevant acute infections including HIV, viral hepatitis and tuberculosis (positive tests for HIV, HBV/HCV or positive QuantiFERON Gold testing at screening will be exclusionary).
11. Any documented active or suspected malignancy or history of malignancy within 5 years prior to screening, except appropriately treated basal cell carcinoma of the skin or in situ carcinoma of uterine cervix.
12. Evidence of current or previous clinically significant disease, medical condition other than AS, finding of the medical examination (including vital signs and ECG), or laboratory value at the screening visit outside the reference range that is of clinical relevance, that in the opinion of the Investigator, would compromise the safety of the patient or the quality of the data. This criterion provides an opportunity for the investigator to exclude patients based on clinical judgment, even if other eligibility criteria are satisfied.
13. History of allergy/hypersensitivity to a systemically administered biologic agent or its excipients.
14. History of alcohol abuse within last 12 months (intake of more than 30 g/day).
15. History of drug abuse within last 12 months or positive drug screen at screening.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	unknown
Generic name:	unknown

Ethics review

Approved WMO Date:	03-01-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2013-003666-13-NL
ClinicalTrials.gov	NCT02047110
CCMO	NL46662.018.13