BEL114674: A 2 year study of efficacy and safety of intravenous belimumab versus placebo in subjects with idiopathic membranous nephropathy

Published: 19-10-2012
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Primary: efficacy of belimumab for the treatment of IMN.Secondary: safety and tolerability, PK, PD, quality of life, benefit of earlier treatment initiation.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON37265

Source
ToetsingOnline

Brief title
BEL114674

Condition

- Nephropathies

Synonym
IMN; idiopathic membranous nephropathy

Research involving
Human

Sponsors and support

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

Intervention

Keyword: belimumab, idiopathic, membranous, nephropathy

Outcome measures

Primary outcome

Incidence of remission at week 104.

Secondary outcome

Key: Incidence of progression of IMN/failure to respond, eGFR <15mL/min/1.73m2,

dialysis or transplantation, adverse events.

Study description

Background summary

Idiopathic membranous nephropathy (IMN) is an autoimmune disease associated with auto-antibody generation and elevated BLyS levels and is responsive to B-cell depleting therapies.
Belimumab is a monoclonal antibody that binds soluble B lymphocyte stimulator (BLyS), is used to treat Systemic Lupus Erythematosus and is being developed for treatment of IMN. Existing therapies have significant toxicities and relapses occur, leading to the need for safer, effective therapies.
Reduction of B-cells through BLyS neutralisation using belimumab, which has already been shown to reduce auto-antibodies and have clinical efficacy in SLE, is expected to be an effective therapy. The safety profile of belimumab, which has already been demonstrated, suggests that treatment with belimumab should overcome the adverse events (AE) previously encountered with other immunosuppressive therapies and fulfill a high unmet need.
The primary purpose of this study is to evaluate the use of belimumab compared to placebo for the treatment of IMN with nephrotic syndrome, when added to supportive therapy (excludes immunosuppressants) as well as the effect of initiating therapy earlier than would be recommended with more toxic immunosuppressive agents.

Study objective

Primary: efficacy of belimumab for the treatment of IMN.
Secondary: safety and tolerability, PK, PD, quality of life, benefit of earlier

treatment initiation.

Study design

Multi-center, Randomized Parallel Group, Placebo-Controlled Double-Blind phase II Trial.
Randomisation (1:1) to
• Belimumab 10 mg/kg infusion
• Placebo infusion
In addition to supportive treatment with MTD ACE or AT inhibitor (unless contra-indicated) +/- statins, diuretics, salt restriction).
Preparation by unblended pharmacist.
Dosing day 1, 14, 28 and every 4 weeks thereafter.
Treatment duration 104 weeks (27 infusions in total).
Possibility to increase dosing frequency to every 2 weeks.
Early termination study treatment in case of progressive deterioration in renal function attributable to IMN or worsening proteinuria or reduction in serum albumin and provision of rescue immunosuppressive treatment (with continuation of study follow-up).
Long term outcome data from subjects beyond two year trial end is planned to be collected on at least an annual basis and entered into a membranous nephropathy registry database.
Approx. 100 patients.
Interim-analyses, see protocol page 45.
IDMC, see protocol page 91.

Intervention

Treatment with belimumab or placebo.

Study burden and risks

Risk: adverse events of study treatment.
Burden: Study visits screening, day 1, 14, 28, thereafter every 4 weeks until week 104.
Belimumab infusions or placebo every 2 weeks (3 times) and thereafter every 4 weeks. Duration at least 1 h.
Blood draws every visit, 7-20 ml/occasion.
Urine collection every visit.
ECG at screening.
6 min walk test: screening, day 1, every 24 weeks and end of treatment.
Questionnaires 6 times in 104 weeks.
Diary co-morbidity, signs and symptoms co-medication, entire study period.
Optional pharmacogenetic research (10 ml blood)
After end of study: at least annually: collection of outcome data.

Contacts

Public
GlaxoSmithKline BV

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline BV

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Subjects between 18 and 75 years of age (inclusive) with active IMN (confirmed with biopsy in last 3 y; biopsy should be available for independent evaluation) and proteinuria >400 mg/mmol. See protocol page 30 for details.
• Capable of giving IC.
• Females of childbearing potential: adequate method of contraception. See protocol page 39-40 for details.

Exclusion criteria

• Non-Idiopathic MN or other condition affecting the kidney. See protocol page 40 for details.
• Patients known to be negative for anti-PLA2R autoantibody.

• Severely reduced or deteriorating kidney function (eGFR< 40mL/min/1.73m2). See protocol page 40 for details.
• Uncontrolled hypertension (>150/90).
• Defined prior therapies. See protocol page 41-42 for details.
• Pregnancy or breastfeeding

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:	Will not start
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Benlysta
Generic name:	belimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	19-10-2012
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-02-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2011□000242□38-NL
CCMO	NL42295.091.12
Other	www.gsk-clinicalstudyregister.com; registratienummer n.n.b.