A Phase 2, Multicenter, Randomized, Parallel-Arm, Placebo-Controlled Study of LY3074828 in Subjects with Active Crohn*s Disease (Serenity)

Published: 08-12-2016
Last updated: 12-04-2024

Primary objective: To test the hypothesis that treatment with LY3074828 is superior to placebo in the proportion of subjects with endoscopic response at Week 12, defined as 50% reduction from baseline in SES-CD ScoreSecondary objective: • To…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON49704

Source
ToetsingOnline

Brief title
SERENITY (I6T-MC-AMAG)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohns disease

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly

Source(s) of monetary or material Support: the pharmaceutical industry

Intervention

Keyword: Crohn□s disease, Efficacy, LY3074828, Safety

Outcome measures

Primary outcome

Proportion of subjects achieving endoscopic response at Week 12

Secondary outcome

• AEs and discontinuation rates; mean change vital signs; laboratory values

• Proportion of subjects achieving endoscopic response at Week 52

• Proportion of subjects achieving endoscopic remission at Week 12

• Proportion of subjects achieving endoscopic remission at Week 52

• Proportion of subjects achieving PRO remission at Week 12

• Proportion of subjects achieving PRO remission at Week 52

• The mean change from baseline for PGRS score, PGRC score, IBDQ score,

FACIT-Fatigue, and SF-36 at Weeks 12 and 52

• Clearance and volume of distribution

Study description

Background summary

LY3074828 is being developed for the treatment of autoimmune diseases where the IL-23 pathway is thought to have a significant pathogenic role. LY3074828 neutralizes IL-23 activity by binding the p19 subunit.
Treatment of autoimmune/inflammatory diseases with IL-23 targeted therapy is being pursued by several companies. The first such biologic to demonstrate clinical benefit in autoimmune disease was ustekinumab, which is a Food and Drug Administration (FDA)-approved monoclonal antibody for the treatment of psoriasis and psoriatic arthritis (Stelara® prescribing information 2014).

Ustekinumab has recently demonstrated clinical activity in Phase 3 trials for the treatment of Crohn*s disease (Toussirot et al. 2013; Sanborn et al. 2008; Sandborn et al 2012; Simon et al. 2016). Ustekinumab binds the common p40 subunit of IL-12 and IL-23; therefore, it targets both cytokines, rather than IL-23 specifically. Blockade of the IL-12 pathway may prevent Th1 cell-induced interferon blockade of Th17 cell development, thus potentially limiting the clinical activity of p40 targeting antibodies. Experimental studies suggest that blocking the IL-23/Th17/IL-17 immune axis alone is sufficient to treat autoimmune inflammation (Monteleone et al. 2009). Agents specifically targeting the IL-23 p19 subunit have demonstrated clinical activity in psoriasis (including LY3074828 in Study AMAA) and Crohn*s disease (Sofen et al. 2014; Kopp et al. 2015; Krueger et al. 2015). IL-23 p19-specific antibodies have also demonstrated clinical activity in Crohn*s disease (Sands et al. 2015; Feagan et al. 2016). The IL-23/Th17 pathway is believed to have a significant role in this disease (Gheita et al. 2014; Globig et al. 2014; El-Bassat et al. 2015).
Eli Lilly and Company (hereafter Lilly) has one completed study (AMAA) and 2 ongoing studies (AMAD and AMAC). The most updated information about these studies can be found in the Investigator*s Brochure (IB).

Study objective

Primary objective: To test the hypothesis that treatment with LY3074828 is superior to placebo in the proportion of subjects with endoscopic response at Week 12, defined as 50% reduction from baseline in SES-CD Score
Secondary objective:
• To evaluate the safety and tolerability of treatment with LY3074828
• To evaluate the effect of LY3074828 on the proportion of subjects with endoscopic response at Week 52, defined as 50% reduction from baseline in SES-CD score
• To evaluate the efficacy of treatment with LY3074828 as superior to placebo in endoscopic
remission (defined as an SES-CD score of <4 ilealcolonic or <2 for isolated ileal disease, and no subscore >1) at Week 12
• To evaluate the effect of LY3074828 on the proportion of subjects with endoscopic remission (defined as an SES-CD score of <4 ileal-colonic or <2 for isolated ileal disease, and no subscore >1) at Week 52
• To evaluate the efficacy of treatment with LY3074828 as superior to placebo in PRO remission (defined as SF <=2.5 and AP <=1) at Week 12
• To evaluate the effect of LY3074828 on the proportion of subjects with PRO remission (defined as SF <=2.5 and AP <=1) at Week 52
• To evaluate the effect of LY3074828 on health outcomes/quality of life measures (including: PGRS score, PGRC score, IBDQ score, SF-36 score, and FACIT-Fatigue) at Weeks 12 and 52
• To characterize the PK of LY3074828

Study design

Study AMAG is a multicenter, randomized, parallel-arm, placebo-controlled trial in which approximately 180 subjects will be randomized.

Intervention

Period 1 (Weeks 0 to 12): A 12-week dosing period is designed to evaluate the efficacy and safety of LY3074828 administered intravenously (IV) at Weeks 0, 4, 8. At baseline, subjects will be randomized with a 2:1:1:2 allocation across the 4 treatment arms (LY3074828, and placebo) and stratified on the basis of previous
exposure to biologic therapy for treatment of Crohn*s disease.

Period 2 (Weeks 12 to 52): In Period 2, all subjects will continue dosing and be randomized evenly to continue baseline treatment assignment or subcutaneous (SC) LY3074828 every 4 weeks (Q4W)*except for all subjects in the placebo group, and subjects in the LY3074828 treatment groups who have not had any improvement in SES-CD score from baseline at Week 12 (determined by the central reader), who will receive intravenous (IV) LY3074828 Q4W.

Period 3 (Weeks 52 to 104): All subjects having clinical benefit will continue on study in Period 3 and receive SC LY3074828 Q4W open-label. Clinical benefit is defined as having an endoscopic response (50% reduction from baseline in SES-CD score), or a 25% reduction from baseline in SES-CD score, combined with a 40% reduction from baseline in stool frequency (SF) or abdominal pain (AP) score.

Follow-Up: At Week 104, subjects will stop treatment and be followed for safety for an additional 16 weeks.

Study burden and risks

The study medicine may have side effects and other undesirable effects.
Very common effects (happening in more than 1 in 10 patients) reported after giving LY3074828 that could have been related to the patient*s disease(s), other medications taken by the patient, LY3074828, or a combination of some or all of these factors are summarized below:
• common cold
• headache

You can find more details about possible side effects in Appendix D of the subject information form.

Contacts

Public
Eli Lilly

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US
Scientific
Eli Lilly

Lilly Corporate Center DC1526
Indianapolis, Indiana 46285
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects will be eligible for the study only if they meet all of the following criteria within the screening period, which is <=28 days prior to the start of study treatment, unless specifically defined:
Type of Subject and Disease Characteristics
• have had a diagnosis of Crohn*s disease for >=3 months before baseline
• have active Crohn*s disease as defined absolute SF >=4 (loose and waterystools defined as Bristol Stool Scale Category 6 or 7) and/or AP >=2 at baseline
• have a SES-CD score >=7 (centrally read) for subjects with ileal-colonic or >=4 for subjects with isolated ileal disease within 14 days before the first dose ofstudy treatment
Prior IBD Treatment
• must have received prior treatment for Crohn*s disease (according to the criteria below): have received treatment with >=1 biologic agents (such as TNF antagonists, vedolizumab,

experimental biologic Crohn*s disease therapeutics) with or without documented history of failure to respond to or tolerate suchtreatment:
o The treatment must have been discontinued according to the followingtimeline:
* anti-TNF therapy at least 8 weeks before baseline
* vedolizumab treatment at least 12 weeks before baseline
* experimental biologic Crohn*s disease therapy at least 8 weeks beforebaseline.
• may be receiving a therapeutic dosage of the following drugs:
• Oral 5-aminosalicylic (ASA) compounds: if the prescribed dose has been stablefor at least 3 weeks before screening colonoscopy or stopped treatment at least 3 weeks prior to screening colonoscopy.
• Oral corticosteroids must be at a prednisone-equivalent dose of <=20 mg/day, or <=9 mg/day of budesonide, and have been at a stable dose for at least 3 weeks prior to the screening colonoscopy. If stopping oral corticosteroid treatment prior to baseline, they must be stopped at least 3 weeks prior to screening colonoscopy.
• AZA, 6-MP, or methotrexate (MTX): if the prescribed dose has been stable for at least 4 weeks before screening endoscopy. Subjects who have discontinued therapy with AZA, 6-MP, or MTX must have stopped the medication at least 4 weeks prior to screening endoscopy to be considered eligible for enrollment.
• Crohn*s disease-specific antibiotics: if the prescribed dose has been stable 4 weeks prior to baseline or stopped treatment at least 3 weeks prior to screening endoscopy.;A complete list of inclusion criteria can be found in the protocol (section 6.1)

Exclusion criteria

Subjects will be excluded from study enrollment if they meet any of the following criteria within the screening period, which is <=28 days prior to the start of study treatment, unless specifically defined:
Study Disease Conditions or Treatments
• have complications of Crohn*s disease such as strictures, stenoses, or any other manifestation for which surgery might be indicated or could confoundthe evaluation of efficacy
• diagnosis of conditions affecting the digestive tract, such as UC, indeterminate colitis, fistulizing disease, abdominal or perianal abscess, adenomatous colonic polyps not excised, colonic mucosal dysplasia, and short bowelsyndrome
• have had any kind of bowel resection, diversion, or placement of a stoma within 6 months or any other intra-abdominal surgery within 3 months prior toscreening
• have received any of the following for treatment of Crohn*s disease:
• 6-thioguanine (6-TG), cyclosporine, tacrolimus, sirolimus, pentoxifylline, or mycophenolate mofetil within 8 weeks prior to baseline
• corticosteroid enemas, IV corticosteroids, corticosteroid suppositories, or topical treatment within 3 weeks prior to screening colonoscopy
• rectal 5-ASA within 3 weeks prior to screening colonoscopy
• have used apheresis (for example, Adacolumn apheresis) <=2 weeks prior to screening.
• have previous exposure to any biologic therapy targeting IL-23 p19 eitherlicensed or investigational, or prior exposure to ustekinumab

• have received natalizumab or agents that deplete B or T cells (for example, rituximab, alemtuzumab, or visilizumab) within 12 months of screening, or, if after receiving these agents, evidence is available at screening of persistentdepletion of the targeted lymphocyte population
• have been treated with any investigational drug for Crohn*s disease within8 weeks prior to baseline or 5 half-lives of the drug (whichever is longer), OR
with interferon therapy within 8 weeks before baseline;A complete list of exclusion criteria can be found in the protocol (section 6.2)

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:	Recruiting
Start date (anticipated):	03-07-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	LY3074828

Ethics review

Approved WMO Date:	08-12-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	12-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2020
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	EUCTR2016-002204-84-NL
ClinicalTrials.gov	NCT02891226
CCMO	NL59632.018.16