# A Phase 2, Randomized, Double-blind, Placebo-controlled Evaluation of the Safety and Efficacy of BMS-986165 with Background Treatment in Subjects with Lupus Nephritis

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Safety: To assess the safety and tolerability of BMS-986165 in LNEfficacy: Efficacy: To evaluate the efficacy of BMS 986165 compared with placebo with regard to proteinuria SecondaryEfficacy - To evaluate the efficacy of BMS-986165 with regard to...

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| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Renal disorders (excl nephropathies) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55520

**Source**
ToetsingOnline

**Brief title**
IM011073

### Condition

- Renal disorders (excl nephropathies)

**Synonym**
Kidney inflammation caused by lupus, LN

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Bristol-Myers Squibb
**Source(s) of monetary or material Support:** Bristol-Myers Squibb International Corporation

## Intervention

**Keyword:** BMS-986165, Lupus Nephritis (LN), Phase 2

## Outcome measures

### Primary outcome

Primary Efficacy Endpoint

• AEs, vital signs, ECGs, and laboratory abnormalities from baseline through

Week 52

• Percentage change from baseline in 24 hour UPCR at Week 24

### Secondary outcome

• PRR at Week 24, defined as >= 50% reduction from baseline in 24-hour UPCR

• CRR at Week 24, defined as both of the following:

* 24-hour UPCR <= 0.75 mg/mg

* eGFR >= 60 mL/min or <= 20% decrease from baseline

• CRR at Week 52

• CRR + successful CS taper to <= 7.5 mg/day at Week 24

• CRR + successful CS taper to <= 7.5 mg/day at Week 52

• PRR at Week 52

# Study description

### Background summary

Lupus nephritis is one of the most serious manifestations of systemic lupus erythematosus (SLE) but the prognosis for patients with LN has not substantially improved since the 1980s.2 BMS-986165 is a novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a
unique mechanism of action distinct from other kinase inhibitors that has shown efficacy in subjects with autoimmune diseases and in murine models of SLE and LN.3-5 This study is designed to assess whether add-on therapy with BMS-986165 might improve renal function in subjects who
do not adequately respond to initial treatment with MMF.

**Study objective**

Safety: To assess the safety and tolerability of BMS-986165 in LN
Efficacy: Efficacy: To evaluate the efficacy of BMS 986165 compared with placebo with regard to proteinuria
Secondary
Efficacy - To evaluate the efficacy of BMS-986165 with regard to measures of renal function and SLE activity

**Study design**

This is a 3-part, multicenter, randomized, double-blind study in which eligible subjects will be assessed for renal response after having received a total of at least 12 weeks (but <= 24 weeks) of treatment with MMF at a target dose of 1.5 to 3.0 g/day. Subjects will receive 12 weeks of target-dose MMF in Part A of the study if they have not been taking target-dose MMF at screening. Subjects who have been taking target-dose MMF for >= 1 day but < 12 weeks at screening will continue to receive target-dose MMF in Part A until they reach 12 weeks of total MMF treatment. Subjects who have been taking target-dose MMF for >= 12 weeks but <= 24 weeks at screening will enter the study at Visit A4 to immediately be assessed for renal response and entry into Part B.

Subjects with an inadequate renal response to MMF may be randomized to blinded study treatment with one of two doses of BMS 986165 or placebo as add-on therapy to MMF in Part B. Inadequate response is defined as < 50% reduction in 24 hour UPCR from the pre-MMF value and a 24 hour UPCR >= 1.0 mg/mg. Randomized subjects will continue taking open-label MMF with or without corticosteroids. Randomization will be stratified by baseline UPCR < 3.0 mg/mg versus >= 3.0 mg/mg and the total cumulative intravenous (IV) corticosteroid (methylprednisolone or parenteral equivalent) dose given in the 16 weeks before randomization (< 250 mg versus >= 250 mg).
Subjects who meet the criteria to continue in Part B but do not meet the randomization criteria may continue in Part B on open-label MMF with or without corticosteroids and will have the same assessments in Part B as randomized subjects. These nonrandomized subjects will exit the study at the end of Part B. Corticosteroids are permitted but not required in this study. Subjects who are

taking corticosteroids will have their dose tapered (if possible) during Part B.

In Part B, all (randomized and nonrandomized) subjects will be evaluated at study visits every 4 weeks through Week 52. At the end of Part B, if the investigator considers it potentially beneficial to continue therapy with study treatment, randomized subjects may continue to receive blinded study treatment in the LTE Period for 52 additional weeks. Subjects will continue to be evaluated every 4 weeks for the first 12 weeks of the LTE Period (through Week 64), then every 10 weeks through Week 104. Subjects randomized to placebo during the initial 52 week Blinded Treatment Period will be rerandomized to blinded BMS-986165 3 mg BID or 6 mg BID during the LTE Period, while subjects initially randomized to BMS 986165 during the 52-week Blinded Treatment Period will continue their Part B assigned dose in the LTE Period.
Optional renal biopsies may be performed at Week 52 and Week 104, as well as at the end of treatment for subjects who discontinue early if discontinuation occurs after Week 24 of Part B. After the last treatment visit (Week 52, Week 104, or early discontinuation), subjects will attend a final end-of-study visit at the end of a 28-day follow-up period.

**Intervention**

Subjects who are eligible to continue in Part B of the study will continue open-label MMF with or without corticosteroids. Subjects who also meet the randomization criteria will be randomized in a double-blind manner to add-on therapy with one of the following:
• 3 mg BMS 986165 twice daily (BID)
• 6 mg BMS 986165 BID
• Placebo BID
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**Study burden and risks**

BMS-986165

VERY COMMON - May affect more than 1 in 10 people (>10%)
• Headache

COMMON - May affect up to 1 in 10 people (1-10%)
• Mouth/Throat/Stomach/intestine: cold sore, canker sore, toothache, throat inflammation, sore throat, stomach or intestine inflammation, nausea, vomiting, stomach pain, diarrhea, indigestion or heartburn
• Nose: stuffy nose, common cold or flu-like feeling
• Skin: rash, acne, itching, hives, skin infection
• Nervous system: dizziness, sleepiness
• Muscles/joints: joint pain, back pain
• Kidneys/bladder: urinary infection

• Changes in the blood: increase in muscle enzyme in the blood
• Other: allergic reaction

Mycophenolate mofetil (MMF)
The most common side effects seen with mycophenolate mofetil are:
• diarrhea
• vomiting
• pain
• stomach area pain
• swelling of the lower legs, ankles and feet
• high blood pressure

Serious side effect seen with mycophenolate mofetil are:
• Low blood cell counts including:
• white blood cells, especially neutrophils (neutrophils fight against bacterial infections)
• red blood cells (red blood cells carry oxygen to your body tissues)
• platelets (platelets help with blood clotting)
Stomach and intestinal bleeding can happen in people who take high doses of mycophenolate mofetil. Taking mycophenolate mofetil can increase the risk of getting certain cancers such as lymphoma, and other cancers, especially skin cancer.

In some patients who have immunosuppression, mycophenolate mofetil may cause an infection of the brain, called PML that may cause death. Immunosuppression is the partial or complete suppression of the immune response of a person.

An overview of the risks and discomforts can be found in the ICF in Appendix D.

# Contacts

**Public**
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE
**Scientific**
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

1) Signed Written Informed Consent
a. Willing to participate in the study and have the ability to give informed consent
b. Willing and able to complete all study-specific procedures and visits
2) SLE Disease Characteristics
a. Meets the SLICC criteria for SLE (see APPENDIX 5)
b. Renal biopsy confirming a histologic diagnosis of active LN ISN/RPS Classes III (A or A/C), IV-S (A or A/C), or IV-G (A or A/C); or Class V (in combination with Class III or IV) (see APPENDIX 12):
i. N/A per Revised Protocol 10
ii. N/A per Revised Protocol 10
iii. If a biopsy was done within <= 6 months before screening, sites/laboratories have the option of providing at least one of the following samples: Renal fresh biopsy; renal historical biopsy (Formalin Fixed Paraffin Embedded block); renal archival slides; or digital image slides (refer to the Arkana laboratory manual for further details)
iv. If a biopsy has not been done within 6 months before screening and the subject meets all other eligibility criteria, a biopsy will be performed as part of the study
c. N/A per Revised Protocol 10
d. UPCR >= 1.5 mg/mg (for subjects with biopsies taken <= 6 months prior to screening) or UPCR >= 1 mg/mg (for subjects with biopsies taken <= 3 months prior to screening) assessed with a 24-hour urine specimen
3) Medications for SLE/Concomitant Medications
a. N/A per Revised Protocol 10
b. If subjects are taking an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), or antimalarial drug, the dose must be stable for at least 4 weeks before randomization into Part B, with no

anticipated changes in dosage in Part B
c. Required discontinuation periods for other immunomodulatory drugs or biologic drugs must be met as outlined in APPENDIX 7. If a specific drug is not listed, consult the PRA medical monitor for guidance; usual discontinuation periods are 4 weeks or 5 half lives, whichever is longer
d. It is allowed but not required for prospective subjects to have been taking MMF for <= 24 weeks at the time of screening. The suggested target dose is 1.5 to 2.0 g/day (maximum 3.0 g/day) unless limited by toxicity or intolerance (refer to Section 6.1 for further details regarding individual target dose)
4) Age and Reproductive Status
a. Men and women aged 18 (or local age of majority) to 75 years inclusive at the time of screening
b. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of beta-human chorionic gonadotropin) at screening, within 24 hours before the first dose of MMF in Part A, and before the first dose of blinded study treatment in Part B.
c. Women must not be breastfeeding
d. The contraception requirements for MMF are stricter than those for BMS 986165; therefore the requirements for MMF (see APPENDIX 4) must be followed throughout study participation and for a period of time after the final dose of MMF or blinded study treatment as follows:
i. WOCBP:
a. Per the MMF prescribing information, subjects taking MMF must use acceptable contraception (see options in APPENDIX 4) throughout the study and continue for at least 6 weeks after the final dose of MMF
b. Subjects must be counseled that MMF may reduce the effectiveness of oral contraceptives, and use of additional barrier contraceptive methods is required
ii. Men who are sexually active with WOCBP:
a. Subjects must inform any and all partners of their participation in the study and the need to use contraception during the man*s study participation and for at least 90 days after his last dose of MMF
b. Per the MMF prescribing information, male subjects taking MMF must continue to use effective contraception and should not donate sperm for at least 90 days after the final dose of MMF

### Exclusion criteria

See Synopsis enclosed

## Study design

## Design

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| 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

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|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 6 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | BMS-986165 |
| Generic name: | BMS-986165 |
| Product type: | Medicine |
| Brand name: | CellCept |
| Generic name: | MYCOPHENOLATE MOFETIL |
| Registration: | Yes - NL intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 16-04-2019 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 11-11-2019 |
| Application type: | First submission |

| | |
|---|---|
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 28-11-2019 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 08-01-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 28-01-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 22-04-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 15-10-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 18-11-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 06-03-2021 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO | |

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|---|---|
| Date: | 07-04-2021 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

# 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 | EUCTR2018-004142-42-NL |
| ClinicalTrials.gov | NCT03943147 |
| CCMO | NL69457.068.19 |