A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Oral RPC1063 as Induction and Maintenance Therapy for Moderate to Severe Ulcerative Colitis

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Induction PeriodPrimary:Demonstrate the efficacy of RPC1063 versus placebo on induction of clinical remission.Secondary:* Demonstrate the efficacy of RPC1063 versus placebo on induction of clinical response* Demonstrate the efficacy of RPC1063...

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

Summary

ID

NL-OMON47446

Source
ToetsingOnline

Brief title
Receptos RPC01-3101

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic inflammation of the mucous membrane of the large intestine, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Celgene International II Sarl (CIS II)
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Oral RPC1063, Ulcerative Colitis

Outcome measures

Primary outcome

Complete Mayo score: the sum of the Rectal Bleeding subscore, Stool Frequency subscore, Physician

Global Assessment subscore, and the Endoscopy subscore. Each subscore has a range of 0-3 points and

the complete Mayo score has a range of 0-12 points

Partial Mayo score: the sum of the Rectal Bleeding subscore, Stool Frequency subscore, and the

Physician Global Assessment subscore. The partial Mayo score has a range of 0-9 points

9-point Mayo score: the sum of the Rectal Bleeding subscore, Stool Frequency subscore, and the

Endoscopy subscore. The 9-point Mayo score has a range of 0-9 points

Clinical Remission

Definition 1: Complete Mayo score of * 2 points with no individual subscore of > 1 point

Definition 2: Rectal Bleeding subscore = 0 and Stool Frequency subscore * 1 (and a decrease of

* 1 point from the Baseline Stool Frequency subscore) and Endoscopy subscore * 1

Clinical Response

Definition 1: A reduction from Baseline in the Complete Mayo score of * 3

points and * 30%, and a

reduction from Baseline in the Rectal Bleeding subscore of * 1 point or an

absolute Rectal Bleeding

subscore of * 1 point

Definition 2: A reduction from Baseline in the 9-point Mayo score of * 2 points

and * 35%, and a

reduction from Baseline in the Rectal Bleeding subscore of * 1 point or an

absolute Rectal Bleeding

subscore of * 1 point

Durable Remission: Clinical remission at Week 10 and at 52 weeks in all

patients who entered the

Maintenance Period

Corticosteroid-free Remission: Clinical remission at 52 weeks while off

corticosteroids for *12 weeks

Endoscopic Improvement: Endoscopy subscore of * 1 point

Mucosal Healing: Endoscopy subscore of * 1 point and a Geboes index score < 3.0

Histologic Remission: Geboes index score < 3.0

Disease relapse: has occurred when all of the following criteria are met:

* An increase in UC disease activity as defined by an increase in partial Mayo

score of *2 points

compared to the Week 10 partial Mayo score with an absolute partial Mayo score

*4 points

* An endoscopic subscore of *2 points

* Exclusion of other causes of an increase in disease activity unrelated to

underlying UC

(e.g., infections, change in medication)

Induction Period, Cohort 1 (Efficacy of RPC1063 vs Placebo):

For statistical analysis purposes, clinical remission and clinical response

will be calculated using Definition

1 for all regulatory regions except the US FDA. For US regulatory purposes,

Definition 2 will be used to

calculate clinical remission and clinical response. All patients will

contribute to each calculation regardless

of enrollment region.

Primary Efficacy Endpoint:

* The proportion of patients in clinical remission at Week 10

Induction Period, Cohort 2

Cohort 2 is open label; therefore no formal analysis of efficacy endpoints will

be conducted. All efficacy

endpoints listed above will be summarized and described without hypothesis

testing.

Maintenance Period:

For statistical analysis purposes, clinical remission and clinical response

will be calculated using Definition

1 for all regulatory regions except the US FDA. For US regulatory purposes,

Definition 2 will be used to

calculate clinical remission and clinical response. All patients will

contribute to each calculation regardless

of enrollment region.

Primary Efficacy Endpoint:

* The proportion of patients in clinical remission at 52 weeks

Safety:

The incidence, severity, and relationship of treatment-emergent adverse events

(TEAEs), serious AEs

(SAEs), TEAEs leading to discontinuation of investigational drug, and TEAEs of

special interest. Clinically

meaningful changes from Baseline on clinical laboratory measures, vital signs,

ECGs, pulmonary function

tests, physical examinations, and optical coherence tomography.

Secondary outcome

Key Secondary Efficacy Endpoints:*

The proportion of patients with a clinical response at Week 10

* The proportion of patients with endoscopic improvement at Week 10

* The proportion of patients with mucosal healing at Week 10

Other Efficacy Endpoints:

* Change in Mayo score from Baseline to Week 10

* Proportion of patients with histologic remission at Week 10

* Proportion of patients with clinical response, remission, or endoscopic

improvement at Week 10

in patients who previously received anti-TNF therapy

* Change in the SF-36 and the EQ-5D from baseline to Week 10

* Health resource utilization at Week 10

* Work productivity at Week 10

Key Secondary Efficacy Endpoints:

* The proportion of patients with a clinical response at 52 weeks

* The proportion of patients with endoscopic improvement at 52 weeks

* The proportion of patients with durable clinical remission

* The proportion of patients in clinical remission at 52 weeks in the subset of

patients who were

in remission at Week 10

* The proportion of patients with corticosteroid-free remission

* The proportion of patients with mucosal healing at 52 weeks

Other Efficacy Endpoints:

* Change in Mayo score from Maintenance Baseline (just prior to entry into the

Maintenance Period)

to 52 weeks

* The proportion of patients with histologic remission at 52 weeks

* The proportion of patients with clinical response, remission, or endoscopic

improvement at

52 weeks in patients who previously received anti-TNF therapy

* The proportion of patients in remission at 52 weeks while off corticosteroids

for any length of time

* Change in the SF-36 and the EQ-5D from Maintenance Baseline (just prior to

entry into the

Maintenance Period) to 52 weeks

* Health resource utilization at Weeks 30 and 42, and at 52 weeks

* Work productivity at Week 30 and at 52 weeks

Study description

Background summary

RPC1063 is a small molecule compound that potently activates the sphingosine-1-phosphate 1 receptor (S1P1R) and the S1P 5 receptor (S1P5R) receptor, although it is more
selective towards S1P1R over S1P5R. In vitro, RPC1063 has little activity on the other
sphingosine-1-phosphate (S1P) receptors, showing greater than 20,000-fold selectivity over
S1P 2R, 3R, or 4R. The RPC1063 metabolites, RP101075 and RP101442, show a similar
potency and selectivity profile to RPC1063. RPC1063 and metabolites were also shown to
be selective for binding to the S1P1R and S1P5R relative to a G protein-coupled receptors
enriched panel of 55 non-target receptors in vitro.

RPC1063 has been studied in two Phase 1 studies completed (RPCS-001 and RPC01-102) in
healthy volunteers, the latter was a thorough QT study that showed RPC1063 at

therapeutic
(1 mg) and supratherapeutic (2 mg) doses did not prolong the QTc interval.
A Phase 2/3 randomized, double-blind, controlled trial (RPC01-201, RADIANCE) in patients with relapsing multiple sclerosis (RMS) is ongoing, with positive efficacy and safety
results reported from the 24-week, Phase 2 portion of the trial in June 2014. The Phase 3
portion of the trial is still enrolling and expected to complete in 2017. The induction phase of
a Phase 2 trial in adult patients with moderate to severe UC (RPC01-202) was completed in
October 2014. At the conclusion of the induction phase, the proportion of patients achieving
clinical response and clinical remission with RPC1063 1 mg was greater than placebo and
the difference was both clinically meaningful and statistically significant. In addition, all
secondary endpoints at the conclusion of the induction phase, including clinical response,
change in the Mayo score, and mucosal improvement on endoscopy, were also positive and
statistically significant for the RPC1063 1 mg dose. The maintenance phase of this trial is
expected to be completed in 2015.

Study objective

Induction Period

Primary:
Demonstrate the efficacy of RPC1063 versus placebo on induction of clinical remission.

Secondary:
* Demonstrate the efficacy of RPC1063 versus placebo on induction of clinical response
* Demonstrate the efficacy of RPC1063 versus placebo on achieving endoscopic improvement
* Demonstrate the efficacy of RPC1063 versus placebo on achieving histologic remission
* Demonstrate the safety and tolerability of RPC1063 induction therapy

Maintenance Period

Primary:
To demonstrate the efficacy of RPC1063 versus placebo maintenance therapy on clinical remission.

Secondary:
* Demonstrate the efficacy of RPC1063 versus placebo in maintaining clinical response
* Demonstrate the efficacy of RPC1063 versus placebo on achieving endoscopic improvement
* Demonstrate the efficacy of RPC1063 versus placebo on durability of clinical remission
* Demonstrate the efficacy of RPC1063 versus placebo on maintaining clinical remission among
patients who achieved remission during induction therapy
* Demonstrate the efficacy of RPC1063 versus placebo, in achieving corticosteroid-free remission
among patients receiving corticosteroids at entry into the Maintenance Period
* Demonstrate the safety and tolerability of RPC1063 maintenance therapy

Study design

Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial

Induction Period:
Cohort 1: On Induction Day 1, patients will be randomly assigned in a 2:1 ratio to:
RPC1063: Taken by mouth, starting with a 7-day dose titration regimen of RPC1063 at 0.25 mg/day on
Days 1 to 4 and RPC1063 at 0.5 mg/day on Days 5 to 7, followed by 1 mg once daily (a single 1.0 mg
capsule starting Day 8) x 9 weeks, or
Matching placebo: Taken by mouth once daily x 10 weeks with matching dose titration Days 1 to 7
Cohort 2: All patients take RPC1063 by mouth, starting with a 7-day dose titration regimen of RPC1063
at 0.25 mg/day on Days 1 to 4 and RPC1063 at 0.5 mg/day on Days 5 to 7, followed by 1 mg once daily
(a single 1.0 mg capsule starting Day 8) x 9 weeks.

Maintenance Period:
On Maintenance Day 1, patients with clinical response to RPC1063 during the Induction Period will be
randomly assigned in a 1:1 ratio to:
RPC1063 taken by mouth (a single 1.0 mg capsule) once daily × 42 weeks, or
Matching placebo taken by mouth (a single capsule) once daily × 42 weeks
Patients with a response to placebo during the Induction Period will continue to receive placebo taken by
mouth once daily x 42 weeks. Patients who have disease relapse during the Maintenance Period will be
given the option to enroll in an open-label extension trial.

Intervention

The trial is composed of 2 periods: Induction and Maintenance. Patients will be entered into the trial in
2 separate cohorts through the Induction Period and those patients in clinical response at the end of the
Induction Period will proceed through to the Maintenance Period. Patients who participate in this trial may
also qualify to participate in an optional Open-Label Extension trial.

Induction Period:
The 10-week Induction Period is composed of 2 cohorts:
* Cohort 1: Approximately 495 patients will be randomized in a 2:1 ratio to receive either RPC1063
1 mg or placebo once daily in a double-blind fashion, stratified by corticosteroid use at screening
(yes or no) and prior anti-TNF use (yes or no)
* Cohort 2: Approximately 405 patients will receive open-label RPC1063 1 mg once daily
Patient eligibility for the Induction Period will be determined during a 5-week Screening Period.
The trial will include both patients that have received anti-TNF therapy and those that have not. The
proportion of patients who have previously received anti-TNF therapy will be limited to *30% in Cohort 1.
All patients will initiate investigational drug via a 7-day dose titration regimen starting with RPC1063
0.25 mg or matching placebo (matching placebo for Cohort 1 only) on Days 1 to 4 and RPC1063 0.5 mg
once daily or matching placebo on Days 5 to 7. On Day 8, patients will receive the final dose level
(1 mg once daily or matching placebo) for 9 weeks.
Patients from either Cohort who are determined to be in clinical response at the end of the Induction Period
(Week 10) may enter the Maintenance Period, while patients not showing a clinical response may enter an
optional Open-Label Extension trial.

Maintenance Period:
It is anticipated that at least 400 patients who complete the Induction Period (both Cohort 1 and Cohort 2)
will be in clinical response at Week 10 and will be eligible to enter the randomized, double-blind, placebocontrolled
Maintenance Period. Patients in clinical response at Week 10 of the Induction Period who
received RPC1063 during Induction will be randomized to receive either RPC1063

1 mg or matching
placebo in a 1:1 ratio. Patients in clinical response at Week 10 of the Induction Period who were randomized
to placebo (Cohort 1) will continue to receive placebo in the Maintenance Period in a double-blind manner.
The randomization in the Maintenance Period will be stratified by clinical remission status at Week 10
(yes or no) and corticosteroids use at Week 10 (yes or no). Patients will be evaluated for disease
activity/efficacy at Week 42 of the Maintenance Period (52 weeks of treatment).

Optional Open-Label Extension Trial:
Patients who complete the Induction Period and are non-responders at Week 10, and those that complete the
Maintenance Period or experience disease relapse during the Maintenance Period, will have the option to
enter a separate Open-Label Extension trial (submitted under NL54683.029.15).

Study burden and risks

The following side effects were considered as related, probably related or possibly related to the study drug. All of these events were mild or moderate in severity. No severe side effects occurred.
Common (frequent) seen in both patients with UC and Multiple Sclerosis (MS)* expected to occur in at least 1 of 100 persons but less than 10 of 100 persons (* 1% to < 10%):
* Increased level of alanine aminotransferase (a liver enzyme that might suggest the existence of other medical problems): 6 patients
* Increased level of aspartate aminotransferase (also a liver enzyme that might suggest the existence of other medical problems): 4 patients
* Orthostatic hypotension (low blood pressure): 4 patients
* Insomnia (trouble to fall asleep and/or staying asleep): 4 patients
Uncommon (infrequent) * expected to occur in at least 1 of 1000 persons but less than 10 of 1000 persons (* 0.1% to < 1%):
* Weight loss: 2 patients
* Vitreous detachment (The jelly in the eye peels away from the retina. Symptoms may include sudden onset of floaters (an impression like flying insects), bright flashes of light, and blurred vision): 2 patients
* Nausea (feeling sick): 2 patients
* Back pain: 2 patients
* Asthma (sore and swollen, sensitive airways): 2 patients
* Increased gamma-glutamyltransferase (an enzyme that may indicate malfunction of the liver and bile): 2 patients

In addition, macular degeneration, which is often diagnosed in patients with MS as part of their disease, has been seen only in MS (3 patients). Macular degeneration, when severe, can decrease your ability to see objects clearly.

There were no severe cases reported among these patients.
As for all new drugs, there may also be side effects and discomforts that are not yet known, which include UC getting worse or even death.

Side effects of procedures and assessments
The following side effects of the procedures/assessments might occur during participation in the study:
Blood draw: During this study, blood will be taken to perform a variety of tests. This may cause discomfort, pain, bruising, swelling, blood clot formation, and very rarely infection at the site where the skin is punctured by the needle. Patients may also experience dizziness, nausea or fainting during the blood draw.
To reduce the number of punctures of blood vessels, a catheter may be inserted into the vein of the arm of the patient and will remain in place until after completion of the pharmacokinetic sample collection. If a catheter is used, it may cause discomfort, redness or bruising around the insertion site. In rare cases, the insertion site may become infected.
Tuberculosis skin test: The test may cause mild itching or discomfort at the injection site.
Electrocardiogram (ECG): The patches that the study staff will stick to the chest and other areas of the body to monitor the heart may irritate the skin and cause itching and redness. The study staff might need to shave body hair so that they can stick the pads to the skin. The shaving may cause some irritation (depending on the tools and soap used); also, a local allergic reaction could occur. When the sticky patches are removed, it might sting for a few seconds. The test itself is painless.
Pulmonary Function Tests: This could possibly make the patient feel lightheaded. After the first test, a medicine used to open the small airways in the lungs (bronchodilator) will be used and the test repeated to check for any changes. Side effects are rare and short-lived and may include cough, trembling and fast heartbeat.
Optical coherence tomography (OCT): During the OCT examination, patients might experience some discomfort related to dilated pupils.
Colonoscopy or sigmoidoscopy with colonic biopsy: The study doctor or study staff will perform a procedure to look inside the colon to take a sample of the colon tissue. In rare cases this will result in problems, such as bleeding.
Side effects from the sedation or anesthesia given for the procedure may also occur.
Chest X-ray: The chest x-ray at screening exposes the body to radiation;

Risk of receiving placebo instead of active drug during the study: Some people in the study will get placebo instead of the study drug. Taking placebo is the same as not taking anything for UC and the UC may get worse.

There is a risk of loss of confidentiality of the personal information that is used in this study. However, the data collected cannot be traced back to the patient.

Harm to the unborn child
For women:
Currently we are not fully aware of the effects of the study drug on unborn babies, or pregnant or breastfeeding women. If the patient is pregnant, or may become pregnant, treatment with the study drug may lead to new, previously unknown, side effects that we currently do not know about and this may involve risks to the patient or the unborn baby. Because of this, women who are not surgically sterilized and can have children will be asked to take a pregnancy test at the start of the study and at each study visit. the patient must be using an effective form of birth control before they start the study drug and while taking part in the study.

Any treatment with a new substance may lead to the occurrence of new, previously unknown side effects/adverse events, which are currently unforeseeable.
We do not know if the study drug will affect sperm or semen so patients should not father a child during this study or for 30 days after treatment. If the patient is not vasectomized and the partner might become pregnant, the patient must use effective, reliable forms of birth control during the study and for 30 days afterwards.

Positive Phase 2 results on remission rates during the Induction Period of protocol RPC01-202 suggest that RPC1063 has the potential to be a clinically-meaningful addition to the therapeutic armamentarium for the treatment of moderate to severe UC.

Contacts

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CH
Scientific
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Couvet 2108
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male or female patients aged 18 to 75 years (at screening), inclusive
2. Have had UC diagnosed at least 3 months prior to first investigational drug administration. The diagnosis should be confirmed by clinical and endoscopic evidence and corroborated by a histopathology report (note: endoscopy and histopathology may be performed at Screening if no prior report is readily available).
3. Evidence of UC extending * 15 cm from the anal verge as determined by Baseline endoscopy (flexible sigmoidoscopy or colonoscopy)
4. Have active UC defined as Mayo score of 6 to 12 inclusive, with endoscopic subscore of * 2, a rectal bleeding score of * 1, and a stool frequency score * 1
5. Must be currently receiving treatment with at least 1 of the following therapies and must continue on these therapies during Induction:
* - Oral aminosalicylates at a therapeutic dose for their disease (eg, mesalamine, sulfasalazine, olsalazine, balsalazide), with the dose stable for at least 3 weeks, prior to Screening endoscopy
* - Prednisone (doses * 20 mg per day) or equivalent receiving a stable dose for at least 2 weeks prior to Screening endoscopy
* - Budesonide MMX therapy receiving a stable dose for at least 2 weeks prior to screening endoscopy.
6. Have undergone colonoscopy (or are willing to undergo colonoscopy during Screening):
- within the past 2 years, to screen for dysplasia (unless otherwise recommended by local and national guidelines) if the patient has had left-sided colitis of > 12 years duration or total / extensive colitis of > 8 years duration
- within the past 5 years, to screen for polyps if the patient age is > 45 years
7. If oral aminosalicylates or corticosteroids have been recently discontinued, they must have been stopped for at least 2 weeks prior to the endoscopy used for Baseline Mayo Score
8. Female patients of childbearing potential:
Must agree to practice a highly effective method of contraception throughout the trial until completion of the 75- day safety follow-up visit. Highly effective methods of contraception are

those that alone or in
combination result in a failure rate of a Pearl index of less than 1% per year when used consistently and correctly. Acceptable methods of birth control in the trial are the following:
-combined hormonal (oestrogen and progestogen containing) contraception, which may be oral, intravaginal, or transdermal
-progestogen-only hormonal contraception associated with inhibition of ovulation, which may be oral, injectable, or implantable
-placement of an intrauterine device (IUD)
-placement of an intrauterine hormone-releasing system (IUS)
-bilateral tubal occlusion
-vasectomised partner
-sexual abstinence;Male patients:
Must agree to use a latex condom during sexual contact with women of childbearing potential while participating in the study until completion of the 75-day safety follow-up visit.;All patients:
Periodic abstinence (calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhoea method are not acceptable methods of contraception.
Female condom and male condom should not be used together.
9. Must provide written informed consent and have the ability to be compliant with the schedule of protocol assessments
10. Patients must have documentation of positive Varicella zoster virus IgG antibody status or complete Varicella zoster virus vaccination at least 30 days prior to randomization

Exclusion criteria

1. Have severe extensive colitis as evidenced by:
* Physician judgment that the patient is likely to require colectomy or ileostomy within 12 weeks of Baseline
* Current or recent (within 3 months) evidence of fulminant colitis, toxic megacolon, or bowel perforation
2. Diagnosis of Crohn*s disease or indeterminate colitis or the presence or history of a fistula consistent with Crohn*s disease or microscopic colitis or radiation colitis or ischemic colitis
3. Have positive stool examination for pathogens (ova and parasites, bacteria) or positive test for toxin producing Clostridium difficile (C. difficile) at Screening. PCR (polymerase chain reaction) examination of the stool for C. difficile may be used to excude false positives. If positive, patients may be treated and retested. Documentation of a negative test result for pathogens (ova and parisites, bacteria) is required within 60 days of Day 1.
4. Pregnancy, lactation, or a positive serum *-human chorionic gonadotropin (*-hCG) measured during Screning
5. Clinically relevant hepatic, neurological, pulmonary, ophthalmological, endocrine, psychiatric, or other major systemic disease making implementation of the protocol or

interpretation of the trial difficult or that would put the patient at risk by participating in the trial
6. Clinically relevant cardiovascular conditions, including history or presence of:
* Recent (within the last 6 months) occurrence of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, Class III/IV heart failure, sick sinus syndrome, or severe untreated sleep apnea
* Prolonged Fridericia's corrected QT interval (QTcF; QTcF > 450 msec for males, > 470 msec for females), or at additional risk for QT interval prolongation (eg, hypokalemia, hypomagnesemia, congenital long-QT syndrome)
* Resting HR < bpm when taking vital signs as part of a physical exam at Screening
7. History of diabetes mellitus type 1, or uncontrolled diabetes mellitus type 2 with glycosylated Hb (HbA1c) > 9% , or diabetic patients with significant comorbid conditions such as retinopathy or nephropathy
8. History of uveitis (within the last year) or macular edema
9. Known active bacterial, viral, fungal, mycobacterial infection, or other infection (including tuberculosis or atypical mycobacterial disease [but excluding fungal infection of nail beds, minor upper respiratory tract infections and minor skin infections]) or any major episode of infection that required hospitalization or treatment with intravenous antibiotics within 30 days of Screening or oral antibiotics within 14 days of Screening
10. History of cancer, including solid tumors and hematological malignancies (except basal cell and in situ squamous cell carcinomas of the skin or uterine cervix that have been excised and resolved) or colonic mucosal dysplasia
11. History of alcohol or drug abuse within 1 year prior to randomization;Exclusions Related to Medications:;12. History of treatment with a biologic agent within 8 weeks or 5 elimination half-lives (whichever is less) of that agent prior to randomization
13. History of treatment with an investigational agent within 5 elimination half-lives of that agent prior to randomization
14. History of treatment with topical rectal 5-aminosalicylic acid or topical rectal steroids within 2 weeks of Screening endoscopy or anti-motility medications (such as diphenoxylate/atropine) during Screening
15. Receipt of a live vaccine or live attenuated vaccine within 4 weeks prior to randomization
16. Planned concurrent treatment with immunosuppressive agents (eg, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate) after randomization. Patients receiving AZA, 6-MP, or methotrexate at Screening must discontinue treatment with these agents prior to randomization
17. Treatment with Class Ia or Class III anti-arrhythmic drugs or treatment with two or more agents in combination known to prolong PR interval
18. Patients who were primary non-responders to 2 or more biologic agents approved for the treatment of UC (eg, anti-TNF agents or vedolizumab);Exclusions Related to Laboratory Results:;19. Serum creatinine * 1.4 mg/dL for females or * 1.6 mg/dL for males
20. Liver function impairment or persisting elevations of AST or ALT * 2 times the ULN, or direct bilirubin * 1.5 times the ULN
21. Platelet count * 100,000/µL

22. Hemoglobin * 8.5 g/dL
23. Neutrophils * 1500 /µL
24. Absolute white blood cell count * 3500 /µL
25. Absolute lymphocyte count * 800/µL
26. ECG showing any clinically significant abnormality
27. Forced expiratory volume at 1 second (FEV1) or forced vital capacity (FVC) < 70% of predicted values at screening

Study design

Design

Study phase:	3
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):	04-08-2016
Enrollment:	33
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ozanimod
Generic name:	RPC1063

Ethics review

Approved WMO

Date:	01-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-01-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	29-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2019
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:	02-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	06-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2020
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	EUCTR2015-000319-41-NL
ClinicalTrials.gov	NCT02435992
CCMO	NL53430.029.15