A Phase 1b Study to Evaluate the Efficacy and Safety of JNJ-64251330, a Janus Kinase (JAK) Inhibitor, in Participants with Familial Adenomatous Polyposis

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The purpose of this study is to determine the effect of JNJ-64251330 in participants with Familial Adenomatous Polyposis(FAP) on colorectal polyp burden (sum of the polyp diameters).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52152

Source
ToetsingOnline

Brief title
A Phase 1b Study of JNJ-64251330, a JAK Inhibitor in Participants with FAP

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Familial Adenomatous Polyposis, FAP

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: Janssen-Cilag B.V.

Intervention

Keyword: Familial Adenomatous Polyposis, JAK Inhibitor, JNJ-64251330

Outcome measures

Primary outcome

- Percentage Change from Baseline in Colorectal Polyp Burden for all Polyps at Week 24

- Percentage Change from Baseline in Colorectal Polyp Burden for Polyps >=2 mm at Week 24

Secondary outcome

- Percentage Change in Number of Colon Polyps

- Percentage Change in Number of Rectal Polyps

- Percentage Change in Number of J-pouch Polyps

- Percentage Change in Number of Duodenal Polyps

- Percentage Change in Colon Polyp Burden for all Polyps, Polyps >=2 mm and Polyps >=5 mm

- Percentage Change in Rectal Polyp Burden for all Polyps, Polyps >=2 mm and Polyps >=5 mm

- Percentage Change in J-Pouch Polyp Burden for all Polyps, Polyps >=2 mm and Polyps >=5 mm

- Percentage Change in Duodenal Polyp Burden for all Polyps, Polyps >=2 mm and Polyps >=5 mm

- Change in International Society for Gastrointestinal Hereditary Tumors (InSiGHT) Polyposis Stage (with and Without Colon)

- Change in Spigelman Stage Score

- Number of Participants with Adverse Events (AEs)

- Number of Participants with AEs by Severity

- Plasma Concentration of JNJ-64251330 Over Time

- Tissue Concentration of JNJ-64251330 Over Time

- Levels of JAK/STAT Pathway Signaling Effector Proteins including pSTAT-3

Relative to Baseline Levels in Colorectal Polyps

Study description

Background summary

Familial adenomatous polyposis (FAP) is the most common polyposis syndrome. It is an autosomal dominant inherited disorder characterized by the early onset of hundreds to thousands of adenomatous polyps throughout the colon. JNJ-64251330 (lorpucitinib) is an oral, small molecule, potent pan-janus kinase (JAK) inhibitor that blocks phosphorylation of Signal Transducer and Activator of Transcription (STAT) proteins. pSTAT induces transcription of multiple genes involved in the progression of inflammatory disease. JNJ-64251330 has chemical properties that limits the amount of drug in the blood while delivering the drug to the tissues of the gut. Local inhibition of JAK in the gut may present a promising method to treat inflammatory diseases of the intestinal tract, such as FAP.

Study objective

The purpose of this study is to determine the effect of JNJ-64251330 in participants with Familial Adenomatous Polyposis (FAP) on colorectal polyp burden (sum of the polyp diameters).

Study design

The study consists of 3 phases: screening phase (30 days) a treatment phase (24 weeks), and follow-up visit (up to 30 days after last dose of study drug). The total duration of the study will be up to 32 weeks. Study evaluations will include efficacy via endoscopies, safety (monitoring of adverse events (AE), serious adverse events (SAEs), events of infections including tuberculosis (TB), clinical laboratory blood tests (complete blood count and serum

chemistries), vital signs, and concomitant medication review), pharmacokinetics, pharmacodynamic and biomarkers evaluations.

Intervention

JNJ-64251330 (Other name: Lorpucitinib): tablets will be administered orally.

Study burden and risks

See protocol and IB.

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

Inclusion Criteria:
- Genetic diagnosis of classical familial adenomatous polyposis (FAP) (adenomatous polyposis coli [APC] germline mutation or obligate carrier) with disease involvement of the colorectum
- At least 6 polyps greater than or equal to (>=) 2 millimeters (mm) in diameter in the rectum or colon
- A female participant of childbearing potential must have a negative highly sensitive pregnancy test at screening and within 72 hours prior to the first dose of study drug and must agree to further pregnancy tests during the study
- A male participant must agree not to donate sperm for the purpose of reproduction during the study and for a minimum of 90 days after receiving the last dose of study drug
- Must sign an informed consent form (ICF) indicating he or she understands the purpose of the study and procedures required for the study and is willing to participate in the study. Consent is to be obtained prior to the initiation of any study-related tests or procedures that are not part of standard of care for the participant*s disease

Exclusion criteria

Exclusion Criteria:
- Use of non-steroidal anti-inflammatory drugs (example, aspirin, ibuprofen) exceeding 5 days per month, or exceeding the nonprescription dose, unless completes a 4-week washout period prior to the first dose of study drug
- Treatment with other FAP-directed drug therapy (including sulindac or celecoxib), unless completes a 4-week washout period prior to the first dose of study drug- History of human immunodeficiency virus (HIV)
- History of severe, progressive, or uncontrolled renal, genitourinary, hepatic, hematologic, endocrine, cardiac, vascular (including increased risk of thrombosis), pulmonary, rheumatologic, neurologic, psychiatric, or metabolic disturbances, or signs and symptoms thereof
- A history of, or ongoing, chronic or recurrent infectious disease including latent or active tuberculosis (TB)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-11-2021
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-64251330 (lorpucitinib)
Generic name:	JNJ-64251330 (lorpucitinib)

Ethics review

Approved WMO Date:	07-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	15-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2022
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	EUCTR2021-001068-16-NL
ClinicalTrials.gov	NCT05014360
CCMO	NL78576.018.21