# A Phase 3, Open-Label, Randomized, Active-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib Versus Gemcitabine Plus Cisplatin Chemotherapy in First-Line Treatment of Participants With Unresectable or Metastatic Cholangiocarcinoma With FGFR2 Rearrangement (FIGHT-302)

Published: 17-04-2019
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This study has been transitioned to CTIS with ID 2024-513513-12-00 check the CTIS register for the current data. Primary ObjectivesEvaluate the efficacy of pemigatinib versus gemcitabine plus cisplatin in the first-line treatment of participants...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Hepatobiliary neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52434

**Source**
ToetsingOnline

**Brief title**
INCB54828-302 (FIGHT-302)

## Condition

- Hepatobiliary neoplasms malignant and unspecified

**Synonym**
Bile duct cancer, Cholangiocarcinoma

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Incyte Corporation
**Source(s) of monetary or material Support:** pharmaceutical industry

## Intervention

**Keyword:** FGFR2 Rearrangement, First-Line Treatment, Phase 3, Unresectable or Metastatic Cholangiocarcinoma

## Outcome measures

### Primary outcome

Progression Free Survival: defined as the time from date of randomization until

date of disease progression (according to RECIST v1.1 and assessed by an ICR)

or death, whichever occurs first.

### Secondary outcome

• Overall Response rate (complete response(CR) + Partial Response(PR)): defined

as the proportion of participants with best overall response of CR or PR per

RECIST v1.1 as assessed by an ICR.

• Overall Survival: defined as the time from date of randomization until death

due to any cause.

# Study description

## Background summary

Pemigatinib is an inhibitor of the FGFR family of receptor tyrosine kinases that is proposed for the treatment of cholangiocarcinoma. Aberrant signaling through FGFR resulting from gene amplification or mutation, chromosomal translocation, and ligand-dependent activation of the receptors has been demonstrated in multiple types of human cancers. Fibroblast growth factor receptor signaling contributes to the development of malignancies by promoting tumor cell proliferation, survival, migration, and angiogenesis. Incyte is proposing to study pemigatinib for the treatment of cholangiocarcinoma. Refer to the IB for additional background information on pemigatinib.

## Study objective

This study has been transitioned to CTIS with ID 2024-513513-12-00 check the CTIS register for the current data.

Primary Objectives
Evaluate the efficacy of pemigatinib versus gemcitabine plus cisplatin in the first-line treatment of participants with cholangiocarcinoma with FGFR2 rearrangement.

Secundary Objectives
Evaluate the efficacy of pemigatinib versus gemcitabine plus cisplatin in the first-line treatment of participants with cholangiocarcinoma with FGFR2 rearrangement.

## Study design

This is a Phase 3, open-label, randomized, active-controlled study of pemigatinib versus gemcitabine plus cisplatin as first-line treatment of participants with unresectable and/or metastatic cholangiocarcinoma with FGFR2 rearrangement. The study will enroll approximately 432 participants in a 1:1 randomization ratio stratified by geographic region (Western [NA and EU] vs APAC vs ROW) and by tumor burden (locally advanced vs distant metastasis) into 1 of the following 2 treatment groups:
• Treatment Group A: Pemigatinib (13.5 mg QD) administered as continuous therapy schedule (a cycle is 3 weeks).
• Treatment Group B: Gemcitabine (1000 mg/m2) and cisplatin (25 mg /m2) administered as an intravenous infusion on Days 1 and 8 of every 3-week cycle for up to 8 cycles.

Participants will be required to have documented FGFR2 rearrangement through the sponsor's central laboratory to confirm eligibility.

## Intervention

• Treatment Group A: Pemigatinib (13.5 mg per day) administered as continuous therapy schedule (a cycle is 3 weeks).
• Treatment Group B: Gemcitabine (1000 mg/m2) plus cisplatin (25 mg/m2) administered as intravenous infusion on Days 1 and 8 of every 3-week cycle for up to 8 cycles.

**Study burden and risks**

Cholangiocarcinoma continues to be a rare and lethal disease where there is a high unmet need for new therapies. Thus, a targeted agent with a manageable safety profile that can provide a significant DCR in a molecularly defined population would provide a meaningful clinical benefit.
Gemcitabine-platinum combination regimens are the best evaluated first-line treatment for cholangiocarcinoma and have been shown to extend survival. However, the toxicities and long-term sequelae associated with chemotherapy administration are significant and typically contribute to dose modifications and discontinuations of treatment due to lack of tolerability.
As of 25 NOV 2018, a total of 105 participants (99.1%) who received pemigatinib monotherapy (all doses and dose regimens combined) in Study INCB 54828-101 had TEAEs, and, consistent with the expected pharmacological effect of FGFR inhibition on serum phosphate levels, the most frequently reported TEAE was hyperphosphatemia (74 participants [69.8%]; serum phosphate > 5.5 mg/dL). Other frequently reported TEAEs included fatigue in 43 participants (40.6%), dry mouth in 39 participants (36.8%), and alopecia in 35 participants (33.0%). Treatment-emergent AEs occurring in >= 10% of participants who received pemigatinib monotherapy (Parts 1 and 2 combined) are presented by dose and dose regimen and overall in Table 8 of the protocol.
Forty-five participants (42.5%) who received pemigatinib monotherapy had at least 1 SAE; the overall incidence of SAEs for the continuous dose regimen (56.7%) was higher than was seen for the interval dose regimen (36.8%). Pneumonia in 7 participants (6.6%) was the most frequently occurring SAE. Other SAEs occurring in more than 1 participant included back pain and disease progression in 4 participants (3.8%) each; abdominal pain, dehydration, fatigue, hyponatremia, and acute renal failure in 3 participants (2.8%) each; and blood bilirubin increased, cerebrovascular accident, constipation, hypotension, pain in extremity, pleural effusion, and pyrexia in 2 participants (1.9%) each. Within the eye disorders SOC, a single participant had an SAE of ocular hyperemia (Grade 2), which was considered unrelated to pemigatinib by the investigator.
A total of 11 participants (10.4%), 7 participants (9.2%) on an interval dose regimen and 4 participants (13.3%) on a continuous dose regimen, had SAEs with a fatal outcome: disease progression in 4 participants (3.8%) and pneumonia, malignant neoplasm progression (ie, disease progression), cerebrovascular accident, intracranial hemorrhage, multiorgan failure, esophageal varices hemorrhage, pneumonia, respiratory failure, and acute respiratory failure secondary to acute anemia (verbatim term) in 1 participant (0.9%) each. None of these fatal events were assessed as related to pemigatinib by the investigator.

Eleven participants (10.4%) discontinued pemigatinib monotherapy due to TEAEs; pneumonia in 3 participants (2.8%) and dehydration and small intestinal obstruction in 2 participants (1.9%) each were the only TEAEs leading to discontinuation of pemigatinib that occurred in more than 1 participant.

# 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

Participants are eligible to be included in the study only if all of the following criteria apply:
1. Ability to comprehend and willingness to sign a written ICF for the study.
2. Male and female participants at least 18 years of age at the time of signing the ICF; a legally minor participant from Japan needs written parental consent.
3. Histologically or cytologically confirmed cholangiocarcinoma that is

previously untreated and considered unresectable and/or metastatic (Stage IV per the AJCC Cancer Staging Manual [AJCC 2010]).
4. Radiographically measurable or evaluable disease by CT or MRI per RECIST v1.1 criteria.
5. ECOG performance status 0 to 1.
6. Documented FGFR2 rearrangement.

## Exclusion criteria

Participants are excluded from the study if any of the following criteria apply:
1. Received prior anticancer systemic therapy for unresectable and/or metastatic disease (not including adjuvant/neoadjuvant treatment completed at least 6 months prior to enrollment, and participants that have received treatment for locally advanced disease with trans-arterial chemoembolization or selective internal radiation therapy, if clear evidence of radiological progression is observed before enrollment, or enrolled as of Amendment 6 and the participant received 1 cycle of gemcitabine plus cisplatin [the start of study drug {Cycle 1 Day 1} must be at least 14 days and <= 4 weeks {28 days} from the last dose of gemcitabine plus cisplatin]).
2. In participants with liver cirrhosis, Child-Pugh B and C (Note: Ascites attributed to cholangiocarcinoma rather than liver dysfunction (eg, in the presence of peritoneal metastases) should not be taken into consideration when scoring).
3. Toxicities related to prior therapy(ies) must be CTCAE v5.0 <= Grade 1 at the time of screening.
4. Concurrent anticancer therapy (eg, chemotherapy, radiation therapy, surgery, immunotherapy, biologic therapy, hormonal therapy, investigational therapy, or tumor embolization), other than the therapies being tested in this study.
5. Participant is a candidate for potentially curative surgery.
6. Current evidence of clinically significant corneal (including but not limited to bullous/band keratopathy, corneal abrasion, inflammation/ulceration, and keratoconjunctivitis) or retinal disorder (including but not limited to central serous retinopathy, macular/retinal degeneration, diabetic retinopathy, retinal detachment) as confirmed by ophthalmologic examination.
7. Radiation therapy administered within 4 weeks of enrollment/randomization/ first dose of study treatment. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. Evidence of fibrosis within a radiation field from prior radiotherapy is permitted with medical monitor approval. A 2-week washout is permitted for palliative radiation to non-CNS disease.
8. Known CNS metastases or history of uncontrolled seizures. Participants with treated brain metastases are eligible if there is no evidence of progression for at least 4 weeks after CNS-directed treatment, as ascertained by clinical examination and brain imaging (MRI or CT scan) during the screening period, and they are on stable or decreasing dose of corticosteroids for at least 1 week.

9. Known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 06-04-2020 |
| Enrollment: | 12 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Cisplatin |
| Generic name: | Cisplatin |
| Registration: | Yes - NL outside intended use |
| Product type: | Medicine |
| Brand name: | Gemcitabine |
| Generic name: | Gemcitabine Hydrochloride |
| Registration: | Yes - NL outside intended use |
| Product type: | Medicine |

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|---|---|
| Brand name: | Not yet available |
| Generic name: | Pemigatinib |

## Ethics review

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| Approved WMO Date: | 17-04-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-07-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 30-09-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 30-10-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-05-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-08-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-08-2020 |
| Application type: | Amendment |

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|---|---|
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-11-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-12-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-04-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-07-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 27-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-09-2023 |
| Application type: | Amendment |

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| Approved WMO Date: | 13-02-2024 |
| Application type: | Amendment |
| Review commission: | MEC Academisch Medisch Centrum (Amsterdam)<br>Kamer G4-214<br>Postbus 22660<br>1100 DD Amsterdam<br>020 566 7389<br>mecamc@amsterdamumc.nl |
| Approved WMO Date: | 23-02-2024 |
| Application type: | Amendment |
| Review commission: | MEC Academisch Medisch Centrum (Amsterdam)<br>Kamer G4-214<br>Postbus 22660<br>1100 DD Amsterdam<br>020 566 7389<br>mecamc@amsterdamumc.nl |
| Approved WMO Date: | 01-03-2024 |

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# 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 |
|---|---|
| EU-CTR | CTIS2024-513513-12-00 |
| EudraCT | EUCTR2018-002894-23-NL |
| ClinicalTrials.gov | NCT03656536 |
| CCMO | NL67456.018.19 |