A Phase I/II study of Brigatinib in pediatric and young adult patients with ALK+ Anaplastic Large Cell Lymphoma, Inflammatory Myofibroblastic Tumors or other solid tumors

Published: 14-10-2021
Last updated: 09-11-2024

This study has been transitioned to CTIS with ID 2024-513412-10-00 check the CTIS register for the current data. Phase 1: • To determine the MTD/RP2D regimen of brigatinib monotherapy when administered in pediatric and AYA patients with ALK+ ALCL or...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50304

Source
ToetsingOnline

Brief title
BrigaPED

Condition

- Other condition
- Leukaemias

Synonym
ALK positive tumors

Health condition

ALK+ ALCL, IMT en andere ALK+ tumoren

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Takeda

Intervention

Keyword: ALK+ tumor, brigatinib, Fase I/II, pediatric and young adults

Outcome measures

Primary outcome

Phase 1:

• Dose-limiting toxicities (DLTs) during the first course of therapy.

• Brigatinib plasma PK parameters to be determined:

o maximum observed concentration (Cmax),

o time of first occurrence of maximum observed concentration (Tmax),

o area under the concentration-time curve from time 0 to the time of the last quantifiable concentration (AUClast).

• The RP2D will be selected by the DSMB and will be based on the dose that results in equivalent (approximately ±20% of the adult values) PK exposure to the adult comparator and with <2 out of 6 patients at this dose level present with a DLT and taking into account responses observed in phase 1.

Phase 2:

In Cohort B1, ALK+ IMT :

• Overall response rate (ORR), defined as the percentage of patients with CR or PR according to RECIST 1.1 after 1 course and best ORR during brigatinib treatment.

In Cohort B2, ALK+ ALCL:

• EFS (using the IPNHL response criteria), defined as the time between start of study treatment and first event being progressive disease, relapse, death of any cause and second malignancies, whatever happens first. Patients consolidated with HSCT will be censored.

Secondary outcome

Phase 1:

Safety

• Adverse events (AEs), as characterized by type, frequency, severity (graded using CTCAE v5.0), including ocular, pulmonary, endocrine AEs, and height, weight or growth abnormalities, timing and relation to the study therapy, during the first and subsequent courses of therapy.

• Occurrence of toxic death, i.e. death attributable to brigatinib therapy, as well as other causes of death.

• Laboratory abnormalities as characterized by type, frequency, severity and timing.

• The cumulative incidence of non-relapse mortality, with time calculated between start of study treatment and death.

• Palatability questionnaire during two years of treatment (for frequency see SOE table).

• Acceptability: diary reporting number of times a dose was not effectively administered.

• Occurrence of any long-term toxicity during the off-therapy period up to 5 years after study inclusion with special attention to ocular, pulmonary,

endocrine AEs, and height, weight or growth abnormalities .

• Collection of grade 3 or higher AEs and AESIs, suspected by the investigator to be related to brigatinib after the start of new anticancer therapy.

Activity/efficacy

• ORR, defined as CR or PR, by RECIST 1.1 for solid tumors (other than neuroblastoma or brain tumors), by IPNHL (International Pediatric revised Response Criteria for Malignant Lymphoma) for ALCL, by NANT (New Approaches to Neuroblastoma Therapy) response criteria for neuroblastoma, by RANO (Responses Assessment in Neuro-Oncology) criteria for brain tumors, measured after 1 course and as best response during brigatinib treatment,

• Time to best response, defined as the time between achieving the best response and the start of treatment with brigatinib For patients with ALCL; qualitative minimal residual disease (MRD) measured at multiple timepoints during treatment, including the percentage of patients who become MRD-negative, and time to MRD negativation.

• Cumulative incidence of non-response or relapse and/or non-relapse mortality or patient withdrawal due to side effects in a competing risk model.

• Duration of response (DOR), defined as the time between achieving response (CR or PR) after starting study treatment and documented disease progression, relapse or death.

• EFS, defined as the time between start of study treatment and first event: relapse, progressive disease, death of any cause and second malignancies, whichever happens first.

• OS, defined as time to death following start of study treatment.

• Number of patients with IMT that undergo a complete (microscopic radical R0) resection after treatment with brigatinib.

• Comparison of survival estimates for ALCL patients consolidated with SCT with patients that did not receive consolidation for SCT, and describe response versus duration of MRD negativity..

• ORR, defined as CR or PR, (by IPNHL), measured after 1 course and as best response during brigatinib treatment (re-induction) in patients with ALCL that relapse after brigatinib discontinuation and that are subsequently re-challenged with brigatinib.

• Number and percentage of IMT patients with completely necrotic tumors by pathology evaluation.

• Duration of on treatment survival, defined as time from first treatment date to disease progression, death, or discontinuation of treatment for any reason (e.g., toxicity, patient/physician preference, or initiation of a new treatment without documented progression, usingapplicable response criteria as specified in section 11).).

Phase 2 :

Safety (in both cohorts)

• Adverse events (AEs), as characterized by type, frequency, severity (graded using CTCAE v5.0), including pulmonary, ocular, endocrine AEs and height, weight or growth abnormalities, timing and relation to the study therapy, during brigatinib treatment.

• Occurrence of toxic death, i.e. death attributable to brigatinib therapy as

well as other causes of death.

• Laboratory abnormalities as characterized by type, frequency, severity and timing.

• The cumulative incidence of non-relapse mortality, defined as the cumulative probability of non-relapse mortality, with time calculated between start of study treatment and death.

• Palatability questionnaire during two years of treatment (for frequency see SOE table).

• Acceptability: diary reporting number of times a dose was not effectively administered.

• Brigatinib plasma PK parameters

o maximum observed concentration (Cmax),

o time of first occurrence of maximum observed concentration (Tmax),

o area under the concentration-time curve from time 0 to the time of the last quantifiable concentration (AUClast).

• Occurrence of any long-term toxicity during the off-therapy period up to 5 years after study inclusion) with special attention pulmonary, ocular, endocrine AEs and height, weight or growth abnormalities.

• Collection of grade 3 or higher AEs and AESIs, suspected by the investigator to be related to brigatinib after the start of new anticancer therapy.

Activity/efficacy

In Cohort B1, ALK+ IMT:

• Time to best response, defined as the time between achieving the best response and the start of treatment with brigatinib.

• Duration of response (DOR), defined as the time between achieving response (CR or PR according to RECIST 1.1) after starting study treatment and documented relapse or death.

• The number of IMT patients that undergo a (curative) resection after treatment with brigatinib.

• Cumulative incidence of non-response or relapse and/or non-relapse mortality or patient withdrawal due to side effects in a competing risk model.

• Number of patients relapsing after electively stopping brigatinib after 24 cycles of brigatinib therapy, and to report the 1 and 2 year cumulative incidence of relapse after stopping brigatinib in these patients.

• EFS (using RECIST criteria), defined as the time between start of study treatment and first event: relapse, progressive disease, death of any cause and second malignancies, whichever happens first.

• OS, defined as time to death of any cause following start of study treatment.

• Duration of on treatment survival, defined as time from first treatment date to disease progression, death, or discontinuation of treatment for any reason (e.g., toxicity, patient preference, or initiation of a new treatment without documented progression, using RECIST 1.1 criteria).

• Number and percentage of IMT patients with completely necrotic tumors by pathology evaluation

In Cohort B2, ALK+ ALCL:

• ORR, defined as CR or PR, by IPNHL, measured after 1 course and as best response during brigatinib treatment.

• Time to best response, defined as the time between achieving the best

response and the start of treatment with brigatinib.

• Duration of response (DOR), defined as the time between achieving response (according to IPNHL) after starting study treatment and documented relapse or death.

• Cumulative incidence of non-response or relapse and/or non-relapse mortality or patient withdrawal due to side effects in a competing risk model.

• Number of patients relapsing after electively stopping brigatinib after 24 cycles of brigatinib therapy, and to report the 1 and 2 year cumulative incidence of relapse after stopping brigatinib in these patients.

• OS, defined as time to death of any cause following start of study treatment.

• Duration of on treatment survival, defined as time from first treatment date to disease progression, death, or discontinuation of treatment for any reason (e.g., toxicity, patient preference, or initiation of a new treatment without documented progression, using IPNHL response criteria.

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Study description

Background summary

Brigatinib is a second generation novel, orally administered, tyrosine kinase inhibitor (TKI) that potently inhibits activated variants of ALK and to a lesser extent ROS1. Currently, brigatinib is approved by FDA and EMA as a treatment for adult patients with locally advanced or metastatic ALK+ non-small cell lung cancer (NSCLC), both in ALK inhibitor naïve patients as well as after previous treatment with crizotinib. Brigatinib is well tolerated in adults at the recommended flat fixed dose of 180 mg QD, with a 7-day lead-in of 90 mg QD. Compared to some other ALK-inhibitors, it has a more favorable safety profile and it penetrates into the CNS. Recently, crizotinib was approved by the FDA for pediatric and young adult patients with ALCL. In Europe, there are

currently no ALK inhibitors registered for children, and besides brigatinib there are no other ALK inhibitors (that we are aware of) with a pediatric investigational plan (PIP) approved with a focus on ALCL and IMT. Adult studies in patients with NSCLC have shown that brigatinib is more potent than crizotinib, can overcome resistance mutations that crizotinib cannot overcome, and has superior intracranial efficacy over crizotinib for treating NSCLC brain metastases due to the CNS penetration.
Apart from NSCLC, ALK is rearranged, mutated, or amplified in a variety of tumors relevant to the pediatric population including neuroblastoma, IMT, infants with brain tumors and ALCL. Although IMTs can also harbor ROS1 rearrangements, ROS1 is less sensitive to brigatinib than ALK, and therefore ROS1 rearranged IMTs will not be eligible for this study. Other, potentially more potent ROS1 inhibitors, are currently in development in pediatric malignancies.
IMT is a very rare solid tumor characterized by spindle-shaped myofibroblastic cells with a chronic inflammatory component that mostly occurs in children and adolescents, primarily in the lung, soft tissues, and the abdominal region. Chromosomal translocations leading to ALK activation are present in 50% to 70% of IMTs, and are more common at younger ages. IMT treatment is generally limited to surgical resection, and there are no standard approaches for metastatic/recurrent disease or when complete resection is deemed not feasible or may result in (severe) mutilation.
ALCL is a rare form of non-Hodgkin lymphoma (NHL) that occurs predominantly in children, adolescents, and young adults (AYA). ALCL is characterized by proliferation of lymphoid T cells that express CD30. Up to 90% of children with ALCL have ALK+ disease, whereas adult ALCL patients exhibit ALK positivity less frequently (50%). ALK+ ALCL is a chemo sensitive disease but 20-40% of the patients still suffer from relapse. The standard of care (SOC) for patients with recurrent ALCL comprises reinduction chemotherapy followed by hematopoietic stem cell transplantation (HSCT), with subsequent high risk of treatment-related morbidity and mortality, and with poor results. ALK inhibitors in this relapse setting could potentially improve outcome for these patients and, with two year of treatment, achieve deep CR, replacing the need for consolidation with HSCT and thereby reducing treatment-related morbidity and mortality induced by HSCT. More recently , another group of very high-risk ALCL patients was identified: patients with persistent positive MRD (by qualitative assessment) after the first chemotherapy course were shown to have an inferior prognosis with a 5-year event free survival (EFS) of ~20%. To date, there is no strategy to improve outcome of these very high risk patients and avoid relapse by alternative treatment regimens.
The present study evaluates the safety and efficacy of brigatinib monotherapy in pediatric and young adult patients with ALK+ ALCL, IMT or other solid tumors. The robust clinical efficacy of brigatinib observed in adult patients with ALK+ NSCLC, the promising proof-of-concept data available in the literature with use of other ALK inhibitors in ALK+ IMT and ALCL patients and the unmet medical needs described above, provide a scientific rationale to explore use of brigatinib in these cancers. There is currently no ALK inhibitor

recommended by the European Medicines Agency (EMA) in the European Union/European Economic Area for use in paediatric patients and brigatinib has a clear advantage as opposed to crizotinib (only other ALK inhibitor approved by FDA for ALCL in children and young adults), being more potent and penetrating the CNS. Overlap within the ITCC portfolio, with the other ALK-inhibitors studies is limited, where the other ALK inhibitors mainly focus on other disease indications, such as brain tumors or ROS-mutated tumors.

Study objective

This study has been transitioned to CTIS with ID 2024-513412-10-00 check the CTIS register for the current data.

Phase 1:
• To determine the MTD/RP2D regimen of brigatinib monotherapy when administered in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
• To characterize the PK of brigatinib administered as monotherapy in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
Note that:
o If the MTD is not reached at the highest proposed test dose, no further dose-escalation will be performed.
o Pediatric PK data, compared to exposure in adults, will be taken into consideration to determine the RP2D.
Phase 2:
• Cohort B1, ALK+ IMT:
To establish the anti-tumor activity of single agent brigatinib when administered to children with ALK+ IMT.

• Cohort B2, ALK+ ALCL:
To establish the efficacy of single agent brigatinib when administered to children with ALK+ ALCL without planned HSCT in consolidation.

Study design

This is an open-label, phase I-II dose-escalation and expansion study designed to define the recommended dose of brigatinib as monotherapy in pediatric and young adult patients with ALK+ ALCL, IMT or other solid tumors, and to evaluate the pharmacokinetics (PK), (long-term) safety and efficacy of brigatinib in these children.
Phase 1 will be a dose escalation study using a rolling six design, aiming to accrue a minimum of 6 and a maximum of 18 evaluable patients. Dose levels are given in the table below. Only patients >=1 and <18 years will be eligible for phase 1.
Phase 2 will be the tumor cohort expansion part of the study to further evaluate the safety, tolerability, and clinical activity/efficacy of brigatinib

as monotherapy in two tumor-specific cohorts:
• Cohort B1: ALK+ IMT
The planned sample size for Phase 2 is 28 patients with IMT. Patients who are included in the monotherapy Phase 1 IMT dose-escalation portion of the study treated at the RP2D will count towards the total sample size of 28 patients. At least 15 patients younger than 18 years of age (with a total of at least 28 patients) need to be evaluable for the primary analysis.
• Cohort B2: ALK+ ALCL
The planned sample size for Phase 2 is 22 patients with ALCL. Patients who are included in the monotherapy Phase 1 ALCL dose-escalation portion of the study and treated at the RP2D will count towards the total sample size of 22 patients. At least 11 patients younger than 18 years of age (with a total of at least 22 patients) need to be evaluable for the primary analysis.

Intervention

Brigatinib will be administered orally in 28-day cycles continuously at the assigned dose level in Phase 1 and the RP2D in Phase 2 and dosed based on body weight. Brigatinib may be taken with or without food. Each tablet should be swallowed separately with a sip of water. At initiation, the treatment begins by a lead-in phase of seven days with a decreased dose of brigatinib to minimize the risk of early pulmonary toxicity as described in NSCLC in adults. Brigatinib is available as a tablet(s) of 30 mg, 90 mg and 180 mg. At a later stage an age appropriate (liquid) formulation will be made available for younger children/those who cannot swallow tablets and added to this protocol by an amendment. The tablets cannot be crushed or given via a nasogastric tube.

Duration of treatment:
Patients with ALCL who completed the initial 24 cycles of treatment and, in the opinion of the investigator and confirmed by the sponsor, continue to experience a clinically meaningful benefit from brigatinib, may continue to receive brigatinib treatment on protocol, until a total of 24 cycles of continued MRD-negativity while on brigatinib treatment. In ALCL, continuation of treatment for 24 cycles after complete molecular remission (i.e. qualitative MRD negativation) is strongly advised before discontinuation of brigatinib treatment.

Patients with IMT or other solid tumor who have met the primary (and/or second endpoints of the study and in the opinion of investigator and confirmed by the sponsor, and continue to experience a clinical benfit may continue to receive brigatinib in an extension phase of this study, or a separate open-label rollover study, or through another appropriate access process. Follow-up of these patients shall be organized as per standard of care procedures.

Patients who relapsed after stopping brigatinib, may continue to receive brigatinib in an extension phase of this study, or a separate open-label rollover study, or through another appropriate access process. Follow-up of

these patients shall be organized as per standard of care procedures.

Study burden and risks

Risks of study participation mainly involve the potential side effects of brigatinib treatment. Previous (adult) studies have shown that brigatinib is relatively safe. Of special interest is the pneumonitis related to brigatinib treatment that has been described in adults with NSCLC. However, with the introduction of a 7 day lead-in phase, pneumonitis has become less frequent and mostly less severe. The side effects of brigatinib should be weighted against the risks of the currently available treatments. New side-effects may still appear as the number of patients treated with brigatinib is still limited and there is no experience in children yet.

IMT patients currently have no standardized systemic treatment. Surgery is the mainstay of treatment but due to close relation to vital structures or due to its infiltrating nature, a radical resection is often not possible without clinically relevant mutilation. Previously, ALK inhibitors have shown to be very effective in ALK+ IMT patients, but currently no ALK inhibitors are approved or available for treatment of IMT patients.
For patients with ALCL, CR achieved with re-induction treatment at relapse is often consolidated with allo-HSCT. As described previously, transplantation can be toxic, with treatment-related morbidity and mortality, with a mortality rate still around 10%. Like with IMT patients, previous ALK inhibitors have shown to be effective in patients with ALK+ ALCL patients, but until now, no ALK inhibitors are approved or available for treatment of pediatric ALCL patients in Europe. In the current study, it is recommended to avoid consolidation with allo-HSCT, with the rationale that early introduction of an ALK inhibitor combined with longer (two year) treatment may achieve deeper CR and may defer the need for allo-HSCT. Nevertheless, withholding consolidation with transplantation carries the risk of more patients relapsing upon treatment discontinuation. On the other hand, it has been observed that patients that do relapse after stopping treatment with ALK inhibitors remain sensitive for ALK inhibition when treatment is resumed, and could achieve a new CR.The cumulative incidence of relapse for patients not receiving HSCT will therefore be monitored closely within this study; including the response to re-exposure with brigatinib for patients that relapsed after treatment discontinuation. We therefore consider it justifiable to attempt to withhold HSCT as standard consolidation after 2 years of brigatinib therapy in the context of this study, with the aim to asses whether 2 years of TKI treatment may lead to continued complete remissions without HSCT. To mitigate risks, this study will include a safety stopping rule for ALCL patients to monitor the number of patients that relapse after brigatinib discontinuation.
Taking together, given the high medical need including the poor response for patients with relapsed/refractory ALCL and IMT, and the risk of surgical mutilation in IMTs that cannot be easily resected, we consider that the potential benefit of brigatinib outweighs the potential risks for this specific

patient population.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

1. Patients must be >=1 and < 26 years of age at the time of enrollment, and able to swallow brigatinib tablets
Note 1: for phase 1 only patients < 18 years old will be eligible, note a liquid formulation for children who cannot swallow tablets is in development.
Note 2: for the Netherlands only, minimum age is >= 5 years.
Note 3: for the Czech Republic only, minimum age is >= 4 years.

2. Patients must have a histologically confirmed diagnosis of cancer at baseline
3. Patients are required to provide prior results showing an activating ALK aberration in the tumor per local laboratory results, and material needs to be available for central laboratory confirmation of ALK status
4. For Phase 1:
• Patients with ALCL must be relapsed/refractory or intolerant to standard therapies. Refractory disease for ALCL is defined as:
o no response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD), and/or
o MRD-positivity by qualitative PCR for NPM-ALK after at least one course ALCL99/other standard of care chemotherapy (before the second course of chemotherapy).
• Patients with relapsed/refractory (R/R) or newly diagnosed IMT must not be suitable for curative surgical resection without causing severe mutilation or risk associated with organ involvement, or have metastatic disease.
• Patients with other solid tumors (excluding IMT) must have relapsed or refractory disease .
• Only patients >=1 and < 18 years will be eligible for phase 1. For the Netherlands only, minimum age is >= 5 years

5. For Phase 2, patients must have measurable and/or evaluable disease:
• Patients with ALCL must be relapsed/refractory as defined.
o No response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD), and/or
o MRD-positivity by qualitative PCR for NPM-ALK after at least one course of ALCL99/other standard of care chemotherapy (before the second course of chemotherapy).

• Patients with R/R IMT Relapsed/refractory IMT, or newly diagnosed, including locally advanced and metastatic IMT which cannot be surgically resected without causing mutilation.
6. Performance Status:
• Karnofsky performance status >=40% for patients >=16 years of age or Lansky Play Scale >=40% for patients <16 years of age for ALCL patients in phase 2.
• Karnofsky performance status >=50% for patients >=16 years of age or Lansky Play Scale >=50% for patients <16 years of age, for IMT and other solid tumors and for ALCL patients in phase 1.
7. Patients must not be receiving other investigational medications within 30 days of first dose of study drug or while on study.
9. Patients must have recovered to Grade <2 NCI CTCAE v5.0 or to baseline, from any nonhematologic toxicities
10. Patients must meet the organ function and system function requirements as stated below:
• Patients must have adequate renal and hepatic function
• No clinical, radiological or laboratory evidence of pancreatitis
• Absolute neutrophil count: >=0.75 × 10 9/L, except in case of macrophage activation syndrome (MAS) or bone marrow involvement.

• Platelet count
o In phase 1: Platelet count: >=75 × 10^9/ L, except in case of MAS or bone marrow involvement
o In phase 2: : Platelet count: >=75 × 10^9/ L, except in case of MAS or bone marrow involvement. For patients post SCT, platelet count >=50 × 10^9/ L is accepted.
o Hemoglobin >=8 g/dL or 5.0 mmol/L (red blood cell [RBC] transfusions to achieve this value are allowed
13. Have a life expectancy of >=3 months.
14. Female patients of childbearing potential must have a negative urine or serum pregnancy test confirmed prior to enrollment.
16. Contraception:
• Male and female patients of child-bearing potential must agree to use, an acceptable effective method for male and highly effective method for female

Remaining Inclusion criteria : see protocol

Exclusion criteria

1. Patients receiving systemic treatment with strong or moderate CYP3A inhibitors or inducers within 14 days or five half-lives, whichever the less, prior to the first dose of study drug (refer to Section 5.2 for a list of example medications).
2. Diagnosis of another concurrent primary malignancy.
3. Clinically significant cardiovascular disease, including any of the following:
• Myocardial infarction or unstable angina within 6 months of study entry.
• History of or presence of heart block, and/or clinically significant ventricular or atrial arrhythmias.
• Uncontrolled hypertension defined as persistent elevation of systolic and/or diastolic blood pressures to >=95th percentile based on age, sex, and height percentiles despite appropriate antihypertensive management.
4. Planned non-protocol chemotherapy, radiation therapy, another investigational agent, or immunotherapy while patient is on study treatment.
5. Any illness that affects gastrointestinal absorption.
6. Ongoing or active systemic infection, active seropositive HIV, or known active hepatitis B or C infection.
7. Any pre-existing condition or illness that, in the opinion of the investigator or sponsor, would compromise patient safety or interfere with the evaluation of the safety or efficacy of brigatinib.
8. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.
9. Patients with a history of cerebrovascular ischemia/hemorrhage with residual deficits are not eligible (patients with a history of cerebrovascular ischemia/hemorrhage remain eligible provided all neurologic deficits and

causative have resolved).
10. Uncontrolled seizure disorder (patients with seizure disorders that do not require antiepileptic drugs, or are well controlled with stable doses of antiepileptic drugs are eligible).
11. Patients with electrolytes imbalances >= grade 2 NCI CTCAE v5.0 are not eligible (supplementation or medical intervention is allowed to correct electrolyte imbalance before inclusion).
12. Patients with uncontrolled diabetes, i.e. patients with persistent hyperglycemia >= grade 2 NCI CTCAE v5.0 despite well conducted treatment with either oral anti glycemic agent and/or insulin are not eligible (patients with well controlled diabetes with either insulin or oral anti glycemic agents are eligible).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-08-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alunbrig
Generic name:	brigatinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	14-10-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-06-2024

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2024
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2024-513412-10-00
EudraCT	EUCTR2021-002713-34-NL
ClinicalTrials.gov	NCT04925609
CCMO	NL78938.041.21