ForPatients
by Roche

Acute Lymphoblastic Leukemia (ALL)NeuroblastomaSolid TumorsAcute Myeloid LeukemiaAcute Lymphocytic Leukemia

A clinical trial to find a safe and suitable dose of idasanutlin, and to see how well idasanutlin works when given with chemotherapy or venetoclax, in children and young adults with leukemia or solid tumours

A Study Evaluating the Safety, Tolerability, Pharmacokinetics and Preliminary Activity of Idasanutlin in Combination With Either Chemotherapy or Venetoclax in Treatment of Pediatric and Young Adult Participants With Relapsed/Refractory Acute Leukemias or Solid Tumors

Trial Status	Trial Runs In	Trial Identifier
Terminated	6 Countries	NCT04029688 2018-004579-11 GO40871

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase I/II, Multicenter, Open-Label, Multi-Arm Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Preliminary Activity of Idasanutlin in Combination With Either Chemotherapy or Venetoclax in the Treatment of Pediatric and Young Adult Patients With Relapsed/Refractory Acute Leukemias or Solid Tumors

Trial Summary:

This is a Phase I/II, multicenter, open-label, multi-arm study designed to evaluate the safety, tolerability, pharmacokinetics, and preliminary efficacy of idasanutlin, administered as a single agent or in combination with chemotherapy or venetoclax, in pediatric and young adult participants with acute leukemias or solid tumors. This study is divided into three parts: Part 1 will begin with dose escalation of idasanutlin as a single agent in pediatric participants with relapsed or refractory solid tumors to identify the maximum tolerated dose (MTD)/maximum administered dose (MAD) and to characterize dose-limiting toxicities (DLTs). Following MTD/MAD identification, three separate safety run-in cohorts in neuroblastoma, acute myeloid leukemia (AML), and acute lymphoblastic leukemia (ALL) will be conducted to identify the recommended Phase 2 dose (RP2D) of idasanutlin in each combination, with chemotherapy or venetoclax. Part 2 will evaluate the safety and early efficacy of idasanutlin in combination with chemotherapy or venetoclax in newly enrolled pediatric and young adult participants in neuroblastoma, AML,and ALL cohorts at idasanutlin RP2D. Part 3 will potentially be conducted as an additional

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expansion phase of the idasanutlin combination cohorts in neuroblastoma, AML, or ALL for further response and safety assessment.

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Sponsor

Phase 1/Phase 2
Phase

NCT04029688 2018-004579-11 GO40871
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	**#0 Years & # 30 Years**	**No**

How does the iMATRIX idasa clinical trial work?

This clinical trial is recruiting children and young adults who have a type of blood cancer called leukemia, or cancer of any tissue or organs that form solid tumours. In order to take part, patients with leukemia must have either acute myeloid leukemia (or AML) or acute lymphocytic leukemia (or ALL). All patients, including those with solid tumours, must have disease that has not gone into remission after treatment or that has come back after going into remission.

The purpose of the first part of this clinical trial is to find a safe and suitable dose of idasanutlin for children.

The purpose of the second part of this clinical trial is to compare the effects, good or bad, of idasanutlin plus other medicines in patients with leukemia or a particular type of solid tumour called neuroblastoma. If you join the second part of the trial, you will get either idasanutlin plus chemotherapy or idasanutlin plus venetoclax.

How do I take part in this clinical trial? To be able to take part in this clinical trial, you must have been diagnosed with AML, ALL, or any type of solid tumour that has not gone into remission after treatment or that has come back after going into remission.

You must not have previously been given idasanutlin (or venetoclax if you are in a group that can be given this drug in the clinical trial) and you cannot join the trial if you are pregnant or breastfeeding.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

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You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial? This clinical trial will be split into 3 parts. You will only be able to join Part 1 or Part 2/3.

Part 1

Only people with solid tumours under the age of 18 will be able to join Part 1.

Part 1 will find a safe and suitable dose of idasanutlin for children. If you are enrolled in Part 1, you will receive idasanutlin given as a tablet or a drink to swallow every day for the first 5 days of a 4 week treatment cycle.

If idasanutlin does not make you too sick after 4 weeks, you will have the following options:

- Continue to receive idasanutlin given as a tablet or a drink to swallow every day for the first 5 days of each 4 week treatment cycle
- OR receive idasanutlin given as a tablet or a drink to swallow and chemotherapy (cyclophosphamide and topotecan) given as an infusion into your vein (all treatments given every day for the first 5 days of each 4 week treatment cycle)

If idasanutlin makes you too sick during the first cycle of treatment, you will receive idasanutlin every day for the first 5 days of each 4 week treatment cycle, but at a lower dose.

Once a suitable dose of idasanutlin has been found, the trial will try to find the best dose of idasanutlin when given with chemotherapy or venetoclax in patients with solid tumours, AML and ALL. You may be given idasanutlin plus chemotherapy or idasanutlin plus venetoclax depending on your type of cancer. If you have AML or ALL, you will also be given chemotherapy directly into your spine with a lumbar puncture.

The trial will then move on to Part 2.

Part 2

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Everyone who joins Part 2 of this clinical trial will be split into groups based on whether they have acute myeloid leukemia (or AML), acute lymphocytic leukemia (or ALL), or a specific type of solid tumour called neuroblastoma.

AML

Everyone with AML will be split into 2 groups and given either:

- idasanutlin given as a tablet or a drink to swallow and chemotherapy (fludarabine and cytarabine) given as an infusion into your vein (treatments given every day for the first 5 days of each 4 week treatment cycle)
- OR idasanutlin given as a tablet or a drink to swallow every day for the first 5 days of each 4 week treatment cycle, and venetoclax given as a tablet or a drink to swallow every day.

Your doctor will tell you which treatment you will receive. You might be placed in a treatment group randomly (like flipping a coin). If this is the case, you will have an equal chance of being placed in either group. You will also be given chemotherapy directly into your spine with a lumbar puncture, regardless of which treatment you are given.

ALL

Everyone with ALL will be given idasanutlin given as a tablet or a drink to swallow every day for the first 5 days of each 4 week treatment cycle, and venetoclax given as a tablet or a drink to swallow every day. You will also be given chemotherapy directly into your spine with a lumbar puncture.

Neuroblastoma

Everyone with neuroblastoma will be split into 2 groups and given either:

- idasanutlin given as a tablet or a drink to swallow and chemotherapy (cyclophosphamide and topotecan) given as an infusion into your vein (treatments given every day for the first 5 days of each 4 week treatment cycle)
- **OR** idasanutlin given as a tablet or a drink to swallow every day for the first 5 days of each 4 week treatment cycle, and venetoclax given as a tablet or a drink to swallow every day.

Your doctor will tell you which treatment you will receive. You might be placed in a treatment group randomly (like flipping a coin). If this is the case, you will have an equal chance of being placed in either group.

Part 3

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If Part 2 shows that the drug works well, more patients may be added to the clinical trial and given the same treatments as in Part 2.

How often will I be seen in follow-up appointments, and for how long?

You will be given the treatment for as long as it can help you. You are free to stop this treatment at any time. After being given your last treatment, the clinical trial doctor will see you after 1 month and then you will be contacted every 3 months. These checks will monitor how you are responding to the treatment and any side effects that you may be having.

What happens if I am unable to take part in this clinical trial? If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT04029688?term=GO40871&rank=1

Trial-identifier: NCT04029688

Inclusion Criteria:

- The participants ages are < 18 for part 1a, < 30 for Parts 1b. 2 and 3
- Study Part 1 (single-agent therapy dose escalation): histologically confirmed diagnosis of neuroblastoma or other solid tumor that has progressed or recurred despite standard therapy, and for which there is no therapy proven to prolong survival with an acceptable quality of life
- Study Part 1 (combination safety run-in), Study Part 2 (initial expansion), and Study Part 3 (additional expansion): histologically confirmed diagnosis of neuroblastoma, AML, or precursor-B ALL that has progressed or recurred despite, or is refractory to, standard therapy
- Adequate performance status: Participants <16 years of age: Lansky greater than or equal to (#)50%; Patients #16 years of age: Karnofsky #50%
- Adequate end-organ function, as defined in the protocol
- For females of childbearing potential: agreement to remain abstinent, use contraception, agreement to refrain from donating eggs. Females must remain abstinent or use two methods of contraception with a failure rate of <1% per year during the treatment and follow-up period (variable depending on the combination agent) or in accordance with national prescribing information guidance regarding abstinence, contraception
- For males: agreement to remain abstinent or use a condom, and agreement to refrain from donating sperm, with a female partner of childbearing potential or pregnant female partner, males must remain abstinent or use a condom during the treatment period and for follow-up period (variable, depending on the combination agent) or in accordance with national prescribing information guidance regarding abstinence, contraception

Additional Inclusion Criteria for Participants with Solid Tumors (including Neuroblastoma)

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- At least one evaluable or measurable radiological site of disease as defined by standard criteria for the participant's tumor type, or measurable bone marrow disease by morphology
- Adequate hematologic end-organ function, as defined in the protocol
- Tumor tissue from relapsed disease

Additional Inclusion Criteria for Patients with Leukemia

- Bone marrow with #5% lymphoblasts by morphologic assessment at screening
- Available bone marrow aspirate or biopsy from screening

Exclusion Criteria:

- Primary Central Nervous System (CNS) tumors
- Symptomatic CNS metastases that result in a neurologically unstable clinical state or require increasing doses of corticosteroids or local CNS-directed therapy to control the CNS disease
- CNS3 leukemia
- Acute promyelocytic leukemia
- White blood cell count >50 × 10^9 cells/Liter (L)
- Down syndrome, Li-Fraumeni syndrome, history of severe aplastic anemia, or any known bone marrow failure predisposition syndrome
- Burkitt-type acute lymphoblastic leukemia
- T-cell lymphoblastic leukemia
- Prior treatment with a MDM2 antagonist
- Prior treatment with venetoclax (if potential for enrollment in a venetoclax arm)
- Infection considered by the investigator to be clinically uncontrolled or of unacceptable risk to the participant
- Any uncontrolled medical condition or other identified abnormality that precludes the patient's safe participation in and completion of the study
- Systemic anticancer therapy within 28 days or 5 half-lives, whichever is shorter, prior to initiation of study treatment
- Treatment with monoclonal antibodies, antibody drug conjugates, or cellular therapy for anti-neoplastic intent within 30 days prior to initiation of study treatment
- I-131 meta-iodobenzylguanidine (MIBG) therapy within 6 weeks prior to initiation of study treatment
- Myeloablative therapy with autologous or allogeneic hematopoietic stem cell rescue within 100 days of study treatment initiation
- Immunosuppressive therapy for treatment of graft-versus-host disease within 2 weeks of study treatment initiation
- Radiotherapy within 3 weeks prior to study treatment initiation
- Specific restrictions are applicable for patients treated with drugs interacting with CYP2C8, CYP3A4, OATP1B1/B3, and P-gp
- Received anti-coagulant or anti-platelet agent within 7 days or 5 half-lives prior to study treatment initiation
- Underwent major surgical procedure within 21 days of study treatment initiation, or anticipate need for major surgical procedure during the course of the study

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