Clinical safety study on 5-Aminolevulinic acid (5-ALA) in children and adolescents with brain tumors

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This study has been transitioned to CTIS with ID 2024-517575-20-00 check the CTIS register for the current data. This study proposes a safety study in children in which tumors are operated on using fluorescence-guided resection which are similar to...

Ethical review	Approved WMO
Status	Pending
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON52327

Source
ToetsingOnline

Brief title
5-ALA in children and adolescents

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumors

Research involving
Human

Sponsors and support

Primary sponsor: Universität Münster
Source(s) of monetary or material Support: Ministerie van OC&W,Medac,photonamic GmbH & Co

Intervention

Keyword: 5-ALA, Brain tumors, Pediatric

Outcome measures

Primary outcome

Toxicological and clinical safety by measuring the incidence of adverse events of CTCAE grade III, IV or V (excluding chemotherapy-associated toxicities) during and after 5-ALA fluorescence-guided resections in children and adolescents with unifocal, contrast-enhancing intra-axial brain tumors, (first diagnosis with unknown histology, recurrent with malignant neuroepithelial histology).

Secondary outcome

1. True positive rate of fluorescence for indicating tumor.

2. Extent of resection as assessed on early post-operative MRI

3. Pharmacokinetics (determination of protoporphyrin IX 3 times within 12h after 5-ALA administration)

Study description

Background summary

5-ALA, a biochemical precursor of heme, is specifically converted into fluorescent porphyrins within malignant glioma cells via a series of enzymatic reactions. These porphyrins exhibit strong fluorescence. Since malignant brain tumors often grow by infiltrating surrounding brain, it is often difficult to distinguish them from healthy brain tissue. By virtue of the fluorescence, which can be visualized with a specific filter integrated into the microscope, pathological tumor tissue and in particular residual tumor tissue become more easily visible and, depending on the assessment of the surgeon regarding resectability, can be removed. Thus, 5-ALA serves the purpose of an intra-operative visualization aid. In contradistinction to other methods for

intra-operative identification of tumor tissue, identification is performed in real-time, i.e. interruptions of the course of surgery are not necessary.

European and later, US approval, was preceded by a number of studies in adults, which could show amongst others, that 5-ALA could be safely used with minimal side effects, accumulated specifically in malignant glioma cells and provided sufficient fluorescence in doses of 20 mg/kg. This intraoperative imaging tool, which is now widely regarded as beneficial for brain tumor surgery in adults, is often perceived as possibly beneficial in children and adolescents with brain tumors as well.

Study objective

This study has been transitioned to CTIS with ID 2024-517575-20-00 check the CTIS register for the current data.

This study proposes a safety study in children in which tumors are operated on using fluorescence-guided resection which are similar to those tumors usually operated on in adults.
Based on previous findings regarding safety and the positive experience with adults using fluorescence-guided resections with 5-ALA, the aim with this present study protocol is to provide a more solid data basis for extending this method to children and adolescents with brain tumors, so that they can benefit also.

Study design

The 5-ALA study protocol is a prospective, open, single-armed, multicenter, phase II study

Intervention

Single administration of 5-ALA prior to planned resection

Study burden and risks

It is not yet certain that 5-ALA has the same desired effect in children as in adults. That is one of the questions of this study. Since it has yet to be shown that 5-ALA also specifically stains tumor tissue in children, only tumor tissue that would also be removed under white light will be removed during the study. The administration of 5-ALA is therefore considered complementary. On the other hand, the fluorescent tissue will make the surgeon aware of potentially leftover resectable tissue that might otherwise have gone unnoticed. This tissue can then be carefully examined with white light, after which a choice can still be made on the basis of white light to remove this tissue.

Treatment under this study may lead to previously unknown side effects/risks.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Age 3 - <18 years.
- First radiological diagnosis of intra-axial, contrast-enhancing tumor on MRI or recurrent intra-axial brain tumor (malignant glioma, astrocytoma, malignant ependymoma, astroblastoma, AT/RT, Oligodendroglioma, etc.).
- Resection is part of therapeutic strategy with an emphasis on neurological safety.
- Informed consent by the parents or guardians and if possible assent of the patient after education of purpose and risks of study. Patients that are able

to understand should provide assent to participate in the trial.
-Female adolescents: not pregnant (pregnancy test required for adolescents of child-bearing age) and not breast-feeding (for at least 24 hours after Gliolan intake). Female patients of childbearing potential and male patients who are sexually active must be practising a highly effective method of birth control up to 6 weeks after the tumor operation consistent with local regulations regarding the use of birth control methods for subjects participating in clinical trials.

Exclusion criteria

- Extra-axial tumors such as craniopharyngeoma.
- Entities precluding surgical resection.
- Acute or chronic porphyria.
- Hypersensitivity to 5-ALA or porphyrins.
- Renal insufficiency: serum creatinine > 2x upper limit of normal (ULN).
- Hepatic insufficiency: serum bilirubine > 2x ULN, serum γ-GT > 2,5 x ULN, alanine transaminase (ALT) and aspartate transaminase (AST)> 2,5 ULN.
- Blood clotting: INR out of acceptable limits.
- Other malignant disease.
- Patients with pre-existing cardiovascular diseases.
- Co-administration with other potentially phototoxic substances (e.g. tetracyclines, sulfonamides, fluoroquinolones, hypericin extracts).
- Planned administration of potentially hepatotoxic substances within 24 hours after 5-ALA administration.

Study design

Design

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

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-07-2022
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Gliolan
Generic name:	5-Aminolevulinic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-05-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-10-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-12-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-08-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-10-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	CTIS2024-517575-20-00
EudraCT	EUCTR2014-005669-54-NL
ClinicalTrials.gov	NCT04738162
CCMO	NL77803.000.22