# A Phase 1, Open-label Clinical Study to Assess the Pharmacokinetics (Distribution, Metabolism,;and Excretion) of 14C-Vosaroxin in Patients with Advanced Solid Tumors

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The primary objective of the study is to quantitatively determine the PK (distribution, metabolism, and excretion) of 14C-vosaroxin and its metabolites in patients with advanced solid tumors.The secondary objective is to evaluate safety and…

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

## Summary

### ID

NL-OMON42076

**Source**
ToetsingOnline

**Brief title**
VOS-ADME-101

### Condition

- Other condition

**Synonym**
Solid tumors

**Health condition**

advanced solid tumors (ie, breast, lung, head/neck,colorectal, melanoma, and sarcoma)

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Sunesis Pharmaceuticals, Inc.
**Source(s) of monetary or material Support:** Sunesis Pharmaceuticals Inc.

## Intervention

**Keyword:** Open-label, Phase1, Solid Tumors, Vosaroxin

## Outcome measures

### Primary outcome

Since this is a Phase 1 PK study, there are no primary or secondary endpoint right now. The primary objective for this study is: To quantitatively determine the pharmacokinetics (distribution, metabolism, and excretion) of 14C-vosaroxin and its metabolites in patients with advanced solid tumors.

### Secondary outcome

Since this is a Phase 1 PK study, there are no primary or secondary endpoint right now. Secondary objective for this study is: To evaluate safety and tolerability of vosaroxin in patients with advanced solid tumors.

# Study description

### Background summary

Vosaroxin is a non-anthracycline, first-in-class quinolone derivative that induces replication-dependent deoxyribonucleic acid (DNA) damage by intercalating DNA and inhibiting topoisomerase II, leading to apoptosis. In contrast to the classic topoisomerase II agents, vosaroxin anticancer activity appears to result exclusively from intercalation of DNA and inhibition of topoisomerase II.

Vosaroxin causes site-selective DNA double-stranded breaks (DSB) in G/C-rich

sequences that are characteristic of quinolone-induced DNA cleavage, distinct from the extensive DNA damage caused by other topoisomerase II poisons such as the anthracyclines and epipodophyllotoxins. Vosaroxin does not produce significant free radicals via metabolism, or the reactive oxygen species (ROS) that have been implicated in the
cumulative cardiotoxicity seen with anthracyclines.

Vosaroxin is currently in clinical development by Sunesis Pharmaceuticals, Inc. (Sunesis) as a treatment in combination with cytarabine for patients with relapsed/refractory acute myeloid leukemia (AML). Vosaroxin has been evaluated in 6 clinical studies, including 1 extension study, in patients with advanced solid tumors and 4 studies in hematologic malignancies, including the pivotal Phase 3 VALOR study of vosaroxin/placebo in combination with cytarabine in patients with relapsed/refractory AML.

**Study objective**

The primary objective of the study is to quantitatively determine the PK (distribution, metabolism, and excretion) of 14C-vosaroxin and its metabolites in patients with advanced solid tumors.

The secondary objective is to evaluate safety and tolerability of vosaroxin in patients with advanced solid tumors.

**Study design**

This is a Phase 1, open-label, non-randomized study to determine the mass balance, blood distribution, PK, and metabolite profiling of vosaroxin in adult patients with advanced solid tumors. Up to 10 patients with advanced solid tumors will be enrolled to ensure that a minimum of 6 patients complete Assessment Period A of the study.

The study consists of a screening period of up to 28 days, followed by an open-label treatment period of up to four 28-day cycles, and a final assessment to occur approximately 28±7 days after the end of the last treatment cycle.

The open-label treatment period will consist of 2 assessment periods:

Assessment Period A (PK sampling period):
Days 1 through 8 of Cycle 1; single radiolabeled 14C-vosaroxin dose 60 mg/m2 (up to a maximum BSA of 1.67 m2 or 100 µCi
total dose of radioactivity, specific activity 1 µCi/mg) administered on Day 1 Cycle 1 as a short IV infusion (over a period of <=10 minutes), followed by 8 days (168 hours) of PK sampling on an inpatient basis.

Assessment Period B:

Day 9 of Cycle 1 through Day 28 of Cycle 4; non-radiolabeled vosaroxin 60 mg/m2 (up to a maximum BSA of 2.0 m2) on Day 1 of Cycles 2 through 4. Safety assessments performed weekly (±1 day).

**Intervention**

Assessment period 1 (Cycle 1 : days 1-8). On the first day of treatment: 14C vosaroxin (single dose). Hospital admission 9 nights, for blood collection and collection of urine and feces. Assessment period B (Cycle 1 / day 9 to Cycle 4 / day 28). On the first day of each cycle: vosaroxin.
Weekly visits to the hospital.

**Study burden and risks**

The side effects listed below represent side effects seen in patients treated with vosaroxin who had leukemia or other kinds of cancer.
Very Common Side Effects have occurred in over 25% of the people who have received vosaroxin:
• Decreased appetite
• Fatigue
• Fever by itself or with low white blood cell count (which may lead to infections)
• Low red blood cell count (anemia)
• Nausea, vomiting and diarrhea
• Upper gastrointestinal mucositis (for example, sores and swelling of the mouth, throat and lip)
Common Side Effects have occurred in 10 - 25% of the people who have received vosaroxin:
• Blood electrolyte imbalances (for example, low levels of potassium requiring a supplement)
• Constipation
• Hair loss (alopecia)
• Infections, including infections of the blood and pneumonia
• Low platelet count which may lead to an increase in bruising or bleeding
•
This is a Phase 1 study and there is a chance that the subject will benefit from the study treatment, however this cannot be guaranteed.

# Contacts

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US
**Scientific**
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US

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Able to understand and provide written informed consent;
2. At least 18 years old at the time of informed consent;
3. Histologically or cytologically confirmed diagnosis of advanced solid tumors (ie, breast, lung, head/neck, colorectal, melanoma, and sarcoma). The malignancy must be considered unresponsive to accepted available therapies;
4. ECOG performance status of 0, 1, or 2;
5. Life expectancy of >= 3 months;
6. Acceptable recovery from clinically significant nonhematologic toxicity after prior therapy;
7. If female, must be surgically or biologically sterile or postmenopausal (amenorrheic for at least 12 months) or if of childbearing potential, must have a negative urine or serum pregnancy test within 14 days before randomization, and must agree to use an adequate method of contraception during the study until 30 days after the last treatment. Males must be surgically or biologically sterile or agree to use an adequate method;
of contraception during the study until 30 days after the last treatment;
8. Adequate renal function (normal to mild dysfunction), with a serum creatinine value of >1.5 x the upper limit of normal (ULN) and with a calculated creatinine clearance (CLCR) of >=40 mL/minute;
9. Adequate hepatic function defined as follows;
- total bilirubin <= 1.5 x ULN, unless due to Gilbert*s syndrome;

- aspartate aminotransferase (AST) <= 2.5 x ULN;
- alanine aminotransferase (ALT) <= 2.5 x ULN;
10. Willing and able to comply with study restrictions and to remain at the study center for the required duration during Assessment Period A;
11. Able to tolerate a high fiber diet (at least 25 g/day).

### Exclusion criteria

1. Prior chemotherapy, radiotherapy, radioimmunotherapy, or immunotherapy within 28 days of the first dose of study treatment or has not recovered from adverse events (AEs) due to any agents administered previously;
2. Presence of known brain metastases or active central nervous system (CNS) disease;
3. Prior treatment with vosaroxin within 60 days of enrollment;
4. Prior treatment with any hematopoietic growth factors within 14 days of study entry (patients on chronic erythropoiesis stimulating agents are allowed);
5. New York Heart Association Class 3 or 4 heart disease, active ischemia, or any uncontrolled, unstable cardiac condition for which treatment for the condition is indicated but is not controlled despite adequate therapy, including angina pectoris, cardiac arrhythmia, hypertension, or congestive heart failure;
6. Myocardial infarction within the previous 12 weeks;
7. Active, uncontrolled systemic infection considered opportunistic, life threatening, or clinically significant at the time of treatment;
8. Pregnant or lactating;
9. Known positive test result for hepatitis B surface antigen (HBsAg) or hepatitis C antibodies (HC Ab) or has a known positive test result for human immunodeficiency virus (HIV) or a history of HIV disease.;10. Presence of inflammatory bowel disease, occlusion of the gastrointestinal tract, significant constipation, or any condition resulting in clinically significant obstruction of the gastrointestinal tract.;11. History of biliary obstruction or cholecystectomy.;12. Any condition resulting in a clinically significant obstruction of the urinary tract.;13. Known hypersensitivity to vosaroxin or any other components of the study treatment.;14. Serious medical or psychiatric condition that, in the opinion of the Investigator, should preclude the patient from participating in the study.

## Study design

### Design

**Study type:** Interventional

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 12-11-2014 |
| Enrollment: | 6 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | [14C]Vosaroxin |
| Generic name: | [14C]SNS595 |
| Product type: | Medicine |
| Brand name: | Vosaroxin |
| Generic name: | SNS-595 |

# Ethics review

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| Approved WMO Date: | 14-05-2014 |
| Application type: | First submission |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 05-08-2014 |
| Application type: | First submission |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 03-07-2015 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 07-08-2015 |
| Application type: | Amendment |

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| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |

# 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 | EUCTR2014-001344-38-NL |
| CCMO | NL48788.031.14 |