# A phase 1 first-in-human study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of AMG232 in adult subjects with advanced solid tumors or multiple myeloma

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In this study, we examine whether the new drug AMG232 is safe and tolerable for patients with advanced solid tumors. In addition, the pharmacokinetic and pharmacodynamic properties of AMG232 are evaluated.

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON44939

**Source**
ToetsingOnline

**Brief title**
Phase 1 study with AMG232 in adults with solid tumors or multiple myeloma

### Condition

- Other condition

**Synonym**
tumor in the organs

**Health condition**

solide tumoren

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Amgen
**Source(s) of monetary or material Support:** Amgen

## Intervention

**Keyword:** Advanced solid tumors, AMG232, Multiple Myeloma, Phase 1

## Outcome measures

**Primary outcome**

- To evaluate the safety and tolerability of AMG232 after multiple oral

administrations in subjects with advanced solid tumors

- To evaluate the pkarmacokinetics of AMG232

- To determine the MTD of AMG232

**Secondary outcome**

- To evaluate tumor response assessed by CT or MRI or Macdonald criteria (GMB

subjects)

- To evaluate the pharmacokinetics of the acyl glucuronide metabolite of AMG232

in plasma

- To evaluate the pharmacodynamic effects of AMG232 exposure on serum MIC-1

levels, p21 induction and/or evidence of apoptosis

- To evaluate the efficacy of AMG 232

# Study description

## Background summary

In this study AMG232 is studied. The safety and tolerability are evaluated in subjects with advanced solid tumors. The pharmacokinetics and pharmacodynamics are also being evaluatied in this patient population.

AMG232 blocks the interaction between MDM2 and p53 proteins.

AMG232 is considered as an experimental drug. AMG232 is not approved by any regulatory organization (such as the Food and Drug Administration, FDA) to treat any type of cancer.

About 155 patients will participate in this study in the US, France and The Netherlands. Amgen Inc. is funding this clinical study.

## Study objective

In this study, we examine whether the new drug AMG232 is safe and tolerable for patients with advanced solid tumors. In addition, the pharmacokinetic and pharmacodynamic properties of AMG232 are evaluated.

## Study design

This phase 1 study is performed in several hospitals in The Netherlands, US and France.
Patients start the study after signing the Informed Consent with the screenings phase. When the patient is eligible the patient starts with the treatment phase (for about 6 months). Four weeks after the last intake of AMG232 the End of Study visit will be performed.

During part 1a of the study, patients will receive 7days treatment in every 3 week cycle with a specific dose of AMG232. This is done to determine the Maximum Tolerated Dose (MTD).
During part 1b of the study, patients will receive 3 days treatment in every 3 week cycle with a specific higher dose of AMG232. This is done to determine the tolerability of daily doses AMG232 at of higer than the part 1a MTD.
During part 1c of the study, patients will receive 7 days, 2x a day treatment in every 3 week cycle with a specific higher dose of AMG232. This is done to determine the tolerability of daily doses AMG232 at of higer than the part 1a MTD.

The dose and schedule for part 2 are dependent of the results from part 1a.

## Intervention

Patients will receive divers doses of AMG232 every 7 (part 1a) or 3 (part 1b)

or 7 days (2x a day, part 1c) days every 3 weeks.
The dose and schedule for part 2 is dependent of the results from part 1a.

**Study burden and risks**

Risk:
Adverse events of the study medication AMG232. During the visits to the hospital the subjects will be monitored for adverse events.

Burden:
Maximum duration is about 7,5 months. The duration of each visit will be about 5 hours.

## Contacts

**Public**
Amgen

Minervum 7061
Breda 4800 DH
NL
**Scientific**
Amgen

Minervum 7061
Breda 4800 DH
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

Men or women >/<= 18 years old;Pathologically documented, definitively diagnosed, advanced solid tumor that is refractory to standard treatment or for which no standard therapy is available or the subject refuses standard therapy;Subjects with tumors showing evidence of wild-type p53.;ECOG performance status of 3 months, in the opinion of the investigator.;Able to take oral medications.;Voor een volledig overzicht van alle inclusiecriteria verwijs ik u naar paragraaf 4.1 van het 20120106 protocol

### Exclusion criteria

Prior bone marrow transplant;History or presence of hematological malignancies;Myocardial infarction within 6 months of study day 1, symptomatic congestive heart failure, unstable angina or cardiac arrhythmia requiring medication.;Active infection requiring intravenous antibiotics within 2 weeks of study enrollment (day 1).;Major surgery within 28 days of study day 1.;Voor een volledig overzicht van alle exclusiecriteria verwijs ik u naar paragraaf 4.2 van het 20120106 protocol

## 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: | Recruitment stopped |
| Start date (anticipated): | 24-06-2013 |
| Enrollment: | 42 |
| Type: | Actual |

## Ethics review

Approved WMO

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|---|---|
| Date: | 28-01-2013 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-04-2013 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 11-07-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 30-08-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 23-09-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 31-10-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 29-11-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 17-12-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam |

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| | (Rotterdam) |
| Approved WMO Date: | 31-07-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 07-08-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-09-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-10-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-02-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 25-03-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 23-04-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 15-07-2015 |

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| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-07-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 16-09-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 17-09-2015 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 25-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 07-04-2016 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 14-03-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 28-03-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

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| Approved WMO Date: | 14-06-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-06-2017 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 | EUCTR2012-002908-41-NL |
| ClinicalTrials.gov | NCT01723020 |
| CCMO | NL41417.078.12 |