



## Clinical trial results: Use of acetylsalicylic acid (ASA) for enhanced early detection of colorectal neoplasms

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-005603-32  |
| Trial protocol           | DE              |
| Global end of trial date | 27 January 2017 |

### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 27 January 2023   |
| First version publication date    | 27 January 2023   |
| Summary attachment (see zip file) | Trial results (ASTER_End of Trial Report_V2.0_2020_03_10_final.pdf) |

### Trial information

#### Trial identification

|                       |      |
|-----------------------|------|
| Sponsor protocol code | K357 |
|-----------------------|------|

#### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN)   | - |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | German Cancer Research Center (DKFZ)   |
| Sponsor organisation address | Im Neuenheimer Feld 280, Heidelberg, Germany, 69120  |
| Public contact               | German Cancer Research Center, German Cancer Research Center, +49 6221421349, k.tikk@dkfz.de |
| Scientific contact           | German Cancer Research Center, German Cancer Research Center, +49 6221421349, k.tikk@dkfz.de |

Notes:

### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 10 March 2020   |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 27 January 2017 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 27 January 2017 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate diagnostic performance (sensitivity, specificity, positive and negative predictive values, likelihood ratios, area under the curve) of 2 immunochemical Fecal Occult Blood Tests (iFOBTs) for detecting advanced colorectal neoplasms after a single dose of acetylsalicylic acid as compared to placebo

Protection of trial subjects:

Candidate-participants in the study will be excluded if they use potentially interacting medication or have illnesses that may be worsened by participation in this study (for details, see exclusion criteria). In the study information documents, participants will be informed about all relevant potential adverse effects.

Before being asked to participate in the study, the participants have all decided to undergo colonoscopy as a screening or diagnostic procedure. The time between drug intake and the planned colonoscopy allows for recovery of haemostatic functions (see below). Thus, the colonoscopy is not considered to be a part of the study.

In case of an emergency situation, in which a treating physician feels that information on whether the participant received acetylsalicylic acid or placebo is needed for adequate medical treatment of the participant, it is possible to unblind the randomization information

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 18 June 2013 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |               |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Germany: 2422 |
| Worldwide total number of subjects   | 2422          |
| EEA total number of subjects         | 2422          |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23          | 0 |

|                           |      |
|---------------------------|------|
| months)                   |      |
| Children (2-11 years)     | 0    |
| Adolescents (12-17 years) | 0    |
| Adults (18-64 years)      | 1788 |
| From 65 to 84 years       | 634  |
| 85 years and over         | 0    |

## Subject disposition

### Recruitment

Recruitment details:

Men and women aged 40 to 80 years with no recent use of aspirin or other drugs with antithrombotic effects were recruited when visiting 1 of 18 trial centers in Germany for a pre-colonoscopy appointment.

### Pre-assignment

Screening details:

Inclusion criteria: Age 40 to 80 years (both males and females), planned screening or diagnostic colonoscopy, no antithrombotic drug intake, able to speak and understand German sufficiently to give informed consent

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator          |

### Arms

|                              |       |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Verum |

Arm description:

participants receiving trial medication

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | Acetylsalicylic acid |
| Investigational medicinal product code |                      |
| Other name                             | ASS; ASA; aspirin    |
| Pharmaceutical forms                   | Coated tablet        |
| Routes of administration               | Oral use             |

Dosage and administration details:

ASS-ratiopharm, 300 mg, single oral dose of administration

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Participants receiving Placebo

|  |               |
|--|---------------|
| Arm type                               | Placebo       |
| Investigational medicinal product name | Placebo       |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Coated tablet |
| Routes of administration               | Oral use      |

Dosage and administration details:

Single oral dose

| <b>Number of subjects in period 1</b> | Verum | Placebo |
|---------------------------------------|-------|---------|
| Started                               | 1208  | 1214    |
| Completed                             | 1075  | 1059    |
| Not completed                         | 133   | 155     |
| Physician decision                    | 20    | 35      |
| Drop-out                              | 77    | 61      |
| no stool samples                      | 32    | 56      |
| Protocol deviation                    | 4     | 3       |

## Baseline characteristics

### Reporting groups

|   |         |
|---|---------|
| Reporting group title   | Verum   |
| Reporting group description:<br>participants receiving trial medication |         |
| Reporting group title   | Placebo |
| Reporting group description:<br>Participants receiving Placebo          |         |

| Reporting group values                                | Verum | Placebo | Total |
|---|-------|---------|-------|
| Number of subjects                                    | 1208  | 1214    | 2422  |
| Age categorical<br>Units: Subjects                    |       |         |       |
| In utero  | 0     | 0       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0     | 0       | 0     |
| Newborns (0-27 days)                                  | 0     | 0       | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0     | 0       | 0     |
| Children (2-11 years)                                 | 0     | 0       | 0     |
| Adolescents (12-17 years)                             | 0     | 0       | 0     |
| Adults (18-64 years)                                  | 801   | 780     | 1581  |
| From 65-84 years                                      | 274   | 279     | 553   |
| 85 years and over                                     | 0     | 0       | 0     |
| DropOut   | 133   | 155     | 288   |
| Gender categorical<br>Units: Subjects                 |       |         |       |
| Female  | 528   | 531     | 1059  |
| Male  | 547   | 528     | 1075  |
| Drop-Out  | 133   | 155     | 288   |

### Subject analysis sets

|  |                 |
|--|-----------------|
| Subject analysis set title   | Per Protocol    |
| Subject analysis set type  | Per protocol    |
| Subject analysis set description:<br>final analysis per protocol                   |                 |
| Subject analysis set title   | Safety          |
| Subject analysis set type  | Safety analysis |
| Subject analysis set description:<br>subjects in safety follow up after medication |                 |

| Reporting group values             | Per Protocol | Safety |  |
|------------------------------------|--------------|--------|--|
| Number of subjects                 | 2134         | 2134   |  |
| Age categorical<br>Units: Subjects |              |        |  |
| In utero                           | 0            | 0      |  |

|   |      |      |  |
|---|------|------|--|
| Preterm newborn infants<br>(gestational age < 37 wks) | 0    | 0    |  |
| Newborns (0-27 days)                                  | 0    | 0    |  |
| Infants and toddlers (28 days-23<br>months)           | 0    | 0    |  |
| Children (2-11 years)                                 | 0    | 0    |  |
| Adolescents (12-17 years)                             | 0    | 0    |  |
| Adults (18-64 years)                                  | 1581 | 1581 |  |
| From 65-84 years                                      | 553  | 553  |  |
| 85 years and over                                     | 0    | 0    |  |
| DropOut   | 0    | 0    |  |
| Gender categorical                                    |      |      |  |
| Units: Subjects                                       |      |      |  |
| Female  | 1059 | 1059 |  |
| Male  | 1075 | 1075 |  |
| Drop-Out  | 0    | 0    |  |

## End points

### End points reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | Verum           |
| Reporting group description:<br>participants receiving trial medication            |                 |
| Reporting group title  | Placebo         |
| Reporting group description:<br>Participants receiving Placebo                     |                 |
| Subject analysis set title   | Per Protocol    |
| Subject analysis set type  | Per protocol    |
| Subject analysis set description:<br>final analysis per protocol                   |                 |
| Subject analysis set title   | Safety          |
| Subject analysis set type  | Safety analysis |
| Subject analysis set description:<br>subjects in safety follow up after medication |                 |

### Primary: Sensitivity and Specificity of iFOBT 10 µg Hb

|   |  |
|---|--|
| End point title   | Sensitivity and Specificity of iFOBT 10 µg Hb <sup>[1]</sup> |
| End point description:<br>Sensitivity and Specificity of immunochemical FOBT (fecal occult blood test) at cutoff 10.2 µg Hemoglobin / g stool |  |
| End point type  | Primary  |
| End point timeframe:<br>2 days after tablet intake  |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical analyses used in the trial were not compatible with the selectable parameters. Information on statistical analyses is provided in the attached Study Report.

| End point values            | Verum           | Placebo         | Per Protocol         |  |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type          | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed | 1075            | 1059            | 2134                 |  |
| Units: cutoff               |                 |                 |                      |  |
| number (not applicable)     | 40.2            | 30.4            | 9.8                  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Sensitivity and Specificity of iFOBT 17µg

|   |  |
|---|--|
| End point title   | Sensitivity and Specificity of iFOBT 17µg <sup>[2]</sup> |
| End point description:<br>Sensitivity and Specificity of immunochemical FOBT (fecal occult blood test) at cutoff 17 µg Hemoglobin / g stool |  |
| End point type  | Primary  |



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End point timeframe:

2 days after tablet intake

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Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical analyses used in the trial were not compatible with the selectable parameters. Information on statistical analyses is provided in the attached Study Report.

| <b>End point values</b>     | Verum           | Placebo         | Per Protocol         |  |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type          | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed | 1075            | 1059            | 2134                 |  |
| Units: cutoff               |                 |                 |                      |  |
| number (not applicable)     | 28.6            | 22.5            | 6.0                  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

overall trial

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | Safety |
|-----------------------|--------|

Reporting group description: -

| Serious adverse events                            | Safety           |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 2 / 2134 (0.09%) |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |
| Gastrointestinal disorders                        |                  |  |  |
| Appendicitis                                      |                  |  |  |
| subjects affected / exposed                       | 1 / 2134 (0.05%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Cholangitis acute                                 |                  |  |  |
| subjects affected / exposed                       | 1 / 2134 (0.05%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |

Frequency threshold for reporting non-serious adverse events: 0.01 %

| Non-serious adverse events                            | Safety           |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 3 / 2134 (0.14%) |  |  |
| Nervous system disorders                              |                  |  |  |
| Migraine  |                  |  |  |
| subjects affected / exposed                           | 1 / 2134 (0.05%) |  |  |
| occurrences (all)                                     | 1                |  |  |
| Headache  |                  |  |  |

|  |                       |  |  |
|--|-----------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 2134 (0.05%)<br>1 |  |  |
| Immune system disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 2134 (0.05%)<br>1 |  |  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 1 / 2134 (0.05%)<br>1 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 16 November 2012 | <ul style="list-style-type: none"><li>- inclusion and exclusion criteria were changed with respect to pregnancy</li><li>- study duration was updated</li><li>- shipment of colonoscopy reports was specified</li><li>- list of medication taken by the patient beforehand was specified</li><li>- list of responsibilities of the investigators were deleted</li><li>- check for completeness and plausibility of source documents was specified</li><li>- the causality of an AE was changed from "unclassified" and "unclassifiable" to "not assessable"</li><li>- reporting of SAEs by investigator was specified</li></ul> |
| 11 March 2013    | <ul style="list-style-type: none"><li>- Change of LKP</li><li>- Responsibilities for data management and analysis were specified</li><li>- terminology was specified</li><li>- definition of drop-outs was specified</li></ul>   |
| 01 July 2013     | Change of LKP within the same study center   |
| 14 August 2015   | <ul style="list-style-type: none"><li>- Study duration prolonged</li><li>- inclusion criteria changed</li><li>- number of stool samples changed</li><li>- observation period for AEs changed</li><li>financial incentive for study centers was changed</li></ul>   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported