



## Clinical trial results:

### Phase II study with cetuximab, irinotecan and sunitinib (CIS) for patients with treatment resistant colorectal cancer.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2007-004232-22 |
| Trial protocol           | DK             |
| Global end of trial date | 07 May 2009    |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 18 March 2021 |
| First version publication date | 18 March 2021 |

#### Trial information

##### Trial identification

|                       |     |
|-----------------------|-----|
| Sponsor protocol code | SIC |
|-----------------------|-----|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Odense University Hospital   |
| Sponsor organisation address | J. B. Winsløvs Vej 2, entrance 140, basement, Odense C, Denmark, 5000              |
| Public contact               | Ida Coordt Elle, Odense University Hospital, +45 29335922, ida.coordt.elle@rsyd.dk |
| Scientific contact           | Per Pfeiffer, Odense University Hospital, +45 26283844, per.pfeiffer@rsyd.dk       |

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:

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**Results analysis stage**

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 01 June 2010 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 07 May 2009  |
| Was the trial ended prematurely?                     | No           |

Notes:

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**General information about the trial**

Main objective of the trial:

To investigate the combination of Cetuximab, Irinotecan and Sunitinib (CIS or SIC) for treatment of patients with treatment-resistant colorectal cancer.

Protection of trial subjects:

Administration of pre-medication to minimize adverse reactions.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 04 January 2008 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 55 |
| Worldwide total number of subjects   | 55          |
| EEA total number of subjects         | 55          |

Notes:

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**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 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 40 |
| From 65 to 84 years                       | 15 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

November 2007-January 2009.

Follow-up until disease progression.

Expected number of patients: 55.

### Pre-assignment

Screening details:

In Denmark, approximately 150 patients per year will be of adequate performance status to be offered 3rd line chemotherapy. Before the introduction of Cetuximab and Irinotecan, there was no 3rd line treatment to offer these patients. Adding Sunitinib to the regimen is expected to prolong PFS and thereby quality of life for these patients.

### Period 1

|                              |                               |
|------------------------------|-------------------------------|
| Period 1 title               | Trial period (overall period) |
| Is this the baseline period? | Yes                           |
| Allocation method            | Not applicable                |
| Blinding used                | Not blinded                   |

### Arms

|           |              |
|-----------|--------------|
| Arm title | Experimental |
|-----------|--------------|

Arm description:

Cetuximab 500 mg/m<sup>2</sup> i.v. day 1 every 2 weeks.

Irinotecan 180 mg/m<sup>2</sup> i.v. day 1 every 2 weeks.

Sunitinib 25 mg p.o. daily for 4 weeks and afterwards 37.5 mg daily.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Cetuximab  |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

500 mg/m<sup>2</sup> on day 1 every two weeks.

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | Irinotecan                        |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solvent for solution for infusion |
| Routes of administration               | Intravenous use                   |

Dosage and administration details:

180 mg/m<sup>2</sup> on day 1 every two weeks.

|  |           |
|--|-----------|
| Investigational medicinal product name | Sunitinib |
| Investigational medicinal product code |           |
| Other name                             | Sutent    |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

25 mg per day for 4 weeks and then 37.5 mg per day.

| <b>Number of subjects in period 1</b> | Experimental |
|---------------------------------------|--------------|
| Started                               | 55           |
| Completed                             | 55           |

## Baseline characteristics

### Reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | Trial period |
| Reporting group description: - |              |

| Reporting group values                             | Trial period | Total |  |
|--|--------------|-------|--|
| Number of subjects                                 | 55           | 55    |  |
| Age categorical                                    |              |       |  |
| Units: Subjects                                    |              |       |  |
| In utero   | 0            | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0            | 0     |  |
| Newborns (0-27 days)                               | 0            | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0            | 0     |  |
| Children (2-11 years)                              | 0            | 0     |  |
| Adolescents (12-17 years)                          | 0            | 0     |  |
| Adults (18-64 years)                               | 40           | 40    |  |
| From 65-84 years                                   | 15           | 15    |  |
| 85 years and over                                  | 0            | 0     |  |
| Gender categorical                                 |              |       |  |
| Units: Subjects                                    |              |       |  |
| Male   | 30           | 30    |  |
| Female   | 25           | 25    |  |

### Subject analysis sets

|                                   |               |
|-----------------------------------|---------------|
| Subject analysis set title        | Patients      |
| Subject analysis set type         | Full analysis |
| Subject analysis set description: |               |
| All patients in the study.        |               |

| Reporting group values                             | Patients |  |  |
|--|----------|--|--|
| Number of subjects                                 | 55       |  |  |
| Age categorical                                    |          |  |  |
| Units: Subjects                                    |          |  |  |
| In utero   | 0        |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0        |  |  |
| Newborns (0-27 days)                               | 0        |  |  |
| Infants and toddlers (28 days-23 months)           | 0        |  |  |
| Children (2-11 years)                              | 0        |  |  |
| Adolescents (12-17 years)                          | 0        |  |  |
| Adults (18-64 years)                               | 40       |  |  |
| From 65-84 years                                   | 15       |  |  |
| 85 years and over                                  | 0        |  |  |

|                    |    |  |  |
|--------------------|----|--|--|
| Gender categorical |    |  |  |
| Units: Subjects    |    |  |  |
| Male               | 30 |  |  |
| Female             | 25 |  |  |

## End points

### End points reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Experimental |
|-----------------------|--------------|

Reporting group description:

Cetuximab 500 mg/m<sup>2</sup> i.v. day 1 every 2 weeks.

Irinotecan 180 mg/m<sup>2</sup> i.v. day 1 every 2 weeks.

Sunitinib 25 mg p.o. daily for 4 weeks and afterwards 37.5 mg daily.

|                            |          |
|----------------------------|----------|
| Subject analysis set title | Patients |
|----------------------------|----------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All patients in the study.

### Primary: Progression-free survival

|                 |  |
|-----------------|--|
| End point title | Progression-free survival <sup>[1]</sup> |
|-----------------|--|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

24 months

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 study was not deemed publishable; therefore no thorough analysis of the data was performed.

| End point values                 | Experimental    | Patients             |  |  |
|----------------------------------|-----------------|----------------------|--|--|
| Subject group type               | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed      | 20              | 20                   |  |  |
| Units: months                    |                 |                      |  |  |
| median (confidence interval 95%) | 3 (0 to 8)      | 3 (0 to 8)           |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Last treatment+30 days.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Patients |
|-----------------------|----------|

Reporting group description: -

| Serious adverse events                               | Patients         |  |  |
|--|------------------|--|--|
| Total subjects affected by serious adverse events    |                  |  |  |
| subjects affected / exposed                          | 20 / 55 (36.36%) |  |  |
| number of deaths (all causes)                        | 19               |  |  |
| number of deaths resulting from adverse events       | 0                |  |  |
| Cardiac disorders                                    |                  |  |  |
| Acute myocardial infarction                          |                  |  |  |
| subjects affected / exposed                          | 1 / 55 (1.82%)   |  |  |
| occurrences causally related to treatment / all      | 1 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| General disorders and administration site conditions |                  |  |  |
| Febrile neutropenia                                  |                  |  |  |
| subjects affected / exposed                          | 2 / 55 (3.64%)   |  |  |
| occurrences causally related to treatment / all      | 2 / 2            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Febrile infection                                    |                  |  |  |
| subjects affected / exposed                          | 5 / 55 (9.09%)   |  |  |
| occurrences causally related to treatment / all      | 5 / 5            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Blood and lymphatic system disorders                 |                  |  |  |
| Thrombosis   |                  |  |  |
| subjects affected / exposed                          | 3 / 55 (5.45%)   |  |  |
| occurrences causally related to treatment / all      | 3 / 3            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Gastrointestinal disorders                      |                |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 2 / 55 (3.64%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 3 / 55 (5.45%) |  |  |
| occurrences causally related to treatment / all | 3 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ileus   |                |  |  |
| subjects affected / exposed                     | 1 / 55 (1.82%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Infection                                       |                |  |  |
| subjects affected / exposed                     | 4 / 55 (7.27%) |  |  |
| occurrences causally related to treatment / all | 4 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Patients         |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 45 / 55 (81.82%) |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Fatigue   |                  |  |  |
| subjects affected / exposed                           | 40 / 55 (72.73%) |  |  |
| occurrences (all)                                     | 40               |  |  |
| Gastrointestinal disorders                            |                  |  |  |
| Diarrhoea   |                  |  |  |
| subjects affected / exposed                           | 18 / 55 (32.73%) |  |  |
| occurrences (all)                                     | 18               |  |  |
| Nausea  |                  |  |  |
| subjects affected / exposed                           | 20 / 55 (36.36%) |  |  |
| occurrences (all)                                     | 24               |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported