



Clinical trial results:

FLOX + Erbitux. 1. line treatment to patients with metastatic colorectal cancer and wild type K-RAS tumor. A phase II study.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-007834-21 |
| Trial protocol | DK SE |
| Global end of trial date | 01 May 2011 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 11 March 2021 |
| First version publication date | 11 March 2021 |
| Summary attachment (see zip file) | ASCO 2012 NORDIC 7.5 poster (ASCO 2012 N75 PP Final LT.ppt) |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 08.04 |
|-----------------------|-------|

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. Winsløws 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:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 28 May 2012 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 May 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim was to complement the data of the NORDIC VII trial, arm C (Tveit et al, JCO 2012). Specifically, the goal was to substantiate efficacy and safety of biweekly cetuximab as maintenance therapy and to assess time to failure of strategy (TFS) as an end-point in maintenance therapy studies.

The NORDIC-7.5 trial was an investigator-initiated, multicenter single-arm phase II trial to evaluate intermittent chemotherapy and cetuximab every second week¹⁴ followed by maintenance cetuximab every second week in first-line treatment of mCRC. Results of the NORDIC-7.5 should add to the aims of the NORDIC-VII trial¹² to investigate how cetuximab every second week might safely and conveniently be added to an intermittent treatment strategy.

Protection of trial subjects:

Pre-medication to minimize nausea, allergic reactions etc.

Use of heating pad when administering i.v. chemotherapy.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 01 July 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Norway: 28 |
| Country: Number of subjects enrolled | Sweden: 66 |
| Country: Number of subjects enrolled | Denmark: 58 |
| Worldwide total number of subjects | 152 |
| EEA total number of subjects | 152 |

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 months) | 0 |

| | |
|---------------------------|-----|
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 130 |
| From 65 to 84 years | 22 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

July 2008-September 2010.

Pre-assignment

Screening details:

The inclusion criteria were as in NORDIC-VII except that only patients with KRAS (exon 2) wild type tumors were included.

Patients eligible for inclusion were 18 to 75 years of age, had previously untreated mCRC, at least 1 measurable lesion according to RECIST criteria, and Performance status 0-2.

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: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Cetuximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received 8 courses of Nordic FLOX (oxaliplatin 85 mg/m²) over 1 hour on day 1, and 5-fluorouracil 500 mg/m²) as a bolus injection, followed 30 minutes later with bolus folinic acid 60 mg/m²) on days 1 and 2). Cetuximab was administered every 2 weeks at a dose of 500 mg/m²) for 16 weeks followed by cetuximab as maintenance therapy until disease progression.

| | |
|---------------------------------------|--------------|
| Number of subjects in period 1 | Experimental |
| Started | 152 |
| Completed | 152 |

Baseline characteristics

Reporting groups

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

| Reporting group values | Trial period | Total | |
|---|--------------|-------|--|
| Number of subjects | 152 | 152 | |
| 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) | 130 | 130 | |
| From 65-84 years | 22 | 22 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 61 | 61 | |
| Male | 91 | 91 | |

Subject analysis sets

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

| Reporting group values | Patients | | |
|---|----------|--|--|
| Number of subjects | 152 | | |
| 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) | 130 | | |
| From 65-84 years | 22 | | |
| 85 years and over | 0 | | |

| | | | |
|--------------------|----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 61 | | |
| Male | 91 | | |

End points

End points reporting groups

| | |
|-------------------------------------|---------------|
| Reporting group title | Experimental |
| Reporting group description: - | |
| Subject analysis set title | Patients |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All patients included in the trial. | |

Primary: Response rate

| | |
|------------------------|------------------------------|
| End point title | Response rate ^[1] |
| 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: Please see attached publication for analysis.

| End point values | Experimental | Patients | | |
|----------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 152 | 152 | | |
| Units: % | | | | |
| number (confidence interval 95%) | 62 (54 to 69) | 62 (54 to 69) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Last drug administration + 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 | 6 / 152 (3.95%) | | |
| number of deaths (all causes) | 12 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 152 (3.95%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Patients | | |
|---|---------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 152 / 152 (100.00%) | | |
| Nervous system disorders | | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 89 / 152 (58.55%) | | |
| occurrences (all) | 89 | | |
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 52 / 152 (34.21%) | | |
| occurrences (all) | 52 | | |
| Neutropenia | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thrombocytopenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>60 / 152 (39.47%)</p> <p>60</p> <p>40 / 152 (26.32%)</p> <p>40</p> | | |
| <p>General disorders and administration site conditions</p> <p>Nail toxicity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>47 / 152 (30.92%)</p> <p>47</p> <p>84 / 152 (55.26%)</p> <p>84</p> | | |
| <p>Immune system disorders</p> <p>Allergic reaction to excipient</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>18 / 152 (11.84%)</p> <p>18</p> | | |
| <p>Gastrointestinal disorders</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>59 / 152 (38.82%)</p> <p>59</p> <p>71 / 152 (46.71%)</p> <p>71</p> <p>31 / 152 (20.39%)</p> <p>31</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Skin reaction</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>91 / 152 (59.87%)</p> <p>91</p> | | |
| <p>Infections and infestations</p> <p>Infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Stomatitis</p> | <p>33 / 152 (21.71%)</p> <p>33</p> | | |

| | | | |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 53 / 152 (34.87%) | | |
| occurrences (all) | 53 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 26 November 2008 | 1. New information about participating departments/investigators. 2. Elaboration of the section about biomarkers. 3. Definition of events not to be treated as SAEs. 4. Correction of dose modifications at skin reactions. 5. Sanofi Avensis deleted from the protocol. 6. In section 4.2.2 we added a possible correlation between AE grade and treatment efficacy, as well as a possible correlation between serum magnesium and treatment efficacy. 7. Grammatical/spelling errors corrected. |
| 13 October 2009 | Inclusion of 120 patients instead of the originally planned 86. |
| 23 April 2010 | Inclusion of 150 patients instead of 120. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25956187>