



Clinical trial results:

LON-GAS

TRIFLURIDINE/TIPIRACIL (FTD/TPI) with or without Bevacizumab in patients with platinum-refractory esophago-gastric adenocarcinoma. A randomized phase III study

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2018-004845-18 |
| Trial protocol | DK |
| Global end of trial date | 31 October 2023 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 30 October 2024 |
| First version publication date | 30 October 2024 |
| Summary attachment (see zip file) | trial publication (longas artikel.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----|
| Sponsor protocol code | 1.4 |
|-----------------------|-----|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Rigshospitalet |
| Sponsor organisation address | Blegdamsvej 9, København Ø, Denmark, 2100 |
| Public contact | Dept of Oncology, Rigshospitalet, Lene Bæksgaard Jensen, 0045 35455072, lene.baeksgaard.jensen@regionh.dk |
| Scientific contact | Dept of Oncology, Rigshospitalet, Lene Bæksgaard Jensen, 0045 35455072, lene.baeksgaard.jensen@regionh.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 | 01 March 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 October 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and tolerability of Lonsurf with or without bevacizumab in Caucasian patients with platinum-refractory esophago-gastric adenocarcinoma. Primary objective is Progression Free Survival (PFS)

Protection of trial subjects:

According to protocol.

Background therapy:

NA. No products fit the description.

Evidence for comparator:

FTD/TPI significantly prolonged progressionfree survival and overall survival in patients with metastatic EGA in third or later line compared to placebo, based on the TAGS trial (Shitara K, Doi T, Dvorkin M, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2018;19:1437-1448.)

| | |
|---|---------------|
| Actual start date of recruitment | 01 March 2019 |
| 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 | Denmark: 103 |
| Worldwide total number of subjects | 103 |
| EEA total number of subjects | 103 |

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) | 33 |
| From 65 to 84 years | 70 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Main inclusion criteria were age at least 18 years, histologically confirmed esophagogastric adenocarcinoma and previous (perioperative or palliative) treatment with combination chemotherapy with a fluoropyrimidine (5-FU, capecitabine or S-1) and a platinum (cisplatin, oxaliplatin, or carboplatin).

Pre-assignment

Screening details:

153 patients were screened, 50 patients were ineligible, 34 not fulfilling the inclusion criteriae, 16 due to other reasons.

Period 1

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

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Intervention |

Arm description:

Trifluridine/tipiracil plus bevacizumab

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | trifluridine and tipiracil |
| Investigational medicinal product code | L01BC59 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trifluridine and tipiracil 35 mg/m² orally twice daily on days 1–5 and 8–12 every 28 days.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | bevacizumab |
| Investigational medicinal product code | L01F G01 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bevacizumab 5 mg/kg intravenously on days 1 and 15 every 28 days.

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description:

Control arm with trifluridine and tipiracil

| | |
|--|----------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | trifluridine and tipiracil |
| Investigational medicinal product code | L01BC59 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trifluridine and tipiracil 35 mg/m² orally twice daily on days 1–5 and 8–12 every 28 days.

| Number of subjects in period 1 | Intervention | Control |
|---------------------------------------|--------------|---------|
| Started | 50 | 53 |
| Completed | 50 | 53 |

Baseline characteristics

Reporting groups

| | |
|---|--------------|
| Reporting group title | Intervention |
| Reporting group description: Trifluridine/tipiracil plus bevacizumab | |
| Reporting group title | Control |
| Reporting group description: Control arm with trifluridine and tipiracil | |

| Reporting group values | Intervention | Control | Total |
|---|--------------|----------|-------|
| Number of subjects | 50 | 53 | 103 |
| 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| median | 64 | 66 | |
| full range (min-max) | 56 to 71 | 61 to 71 | - |
| Gender categorical Units: Subjects | | | |
| Female | 39 | 10 | 49 |
| Male | 11 | 43 | 54 |

Subject analysis sets

| | |
|---|---------------|
| Subject analysis set title | Full analysis |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All randomized and treated patients. | |

| Reporting group values | Full analysis | | |
|---|---------------|--|--|
| Number of subjects | 103 | | |
| Age categorical Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |

| | | | |
|---|----|--|--|
| Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years median full range (min-max) | | | |
| Gender categorical Units: Subjects | | | |
| Female | 21 | | |
| Male | 82 | | |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Intervention |
| Reporting group description: Trifluridine/tipiracil plus bevacizumab | |
| Reporting group title | Control |
| Reporting group description: Control arm with trifluridine and tipiracil | |
| Subject analysis set title | Full analysis |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All randomized and treated patients. | |

Primary: Progression-free survival

| | |
|--|---------------------------|
| End point title | Progression-free survival |
| End point description: | |
| End point type | Primary |
| End point timeframe: Progression-free survival calculated from the date of randomisation to the first date of radiological or clinical progression, time till death, or censored on cut-off date. | |

| End point values | Intervention | Control | | |
|----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 53 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.9 (3.0 to 6.3) | 3.1 (2.0 to 4.3) | | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | Kaplan-Meier |
| Comparison groups | Intervention v Control |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.05 |
| Method | Logrank |
| Parameter estimate | Cox proportional hazard |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Oct 1, 2019 to March 1st, 2023

Adverse event reporting additional description:

Adverse events were evaluated before each cycle and graded by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0. Nadir hematology was measured on day 14 on cycle one and two.

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

Dictionary used

| | |
|-----------------|-----------|
| Dictionary name | NCI-CTCAE |
|-----------------|-----------|

| | |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

Reporting groups

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

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | control |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Experimental | control | |
|--|---|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 50 (44.00%) | 21 / 53 (39.62%) | |
| number of deaths (all causes) | 49 | 51 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| General disorders and administration site conditions | | | |
| hospitalisation | Additional description: Serious adverse events, that all were due to hospitalisations, were observed in 21 patients (40%) in the FTD/TPI group and in 22 patients (44%) in the group receiving FTD/TPI plus bevacizumab | | |
| subjects affected / exposed | 22 / 50 (44.00%) | 21 / 53 (39.62%) | |
| occurrences causally related to treatment / all | 5 / 22 | 4 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Experimental | control | |
|---|--|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 50 (100.00%) | 53 / 53 (100.00%) | |
| General disorders and administration site conditions | | | |
| non-serious adverse event | Additional description: attached publication for further details on non-serious adverse events | | |

| | | | |
|-----------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 50 / 50 (100.00%) | 53 / 53 (100.00%) | |
| occurrences (all) | 50 | 53 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported