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 occurrences (all)	50 / 50 (100.00%) 50	53 / 53 (100.00%) 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