Clinical trial results:
Everolimus and temozolomide as first-line treatment in advanced gastrointestinal neuroendocrine carcinoma (G3) with a Ki67 of 20-55%

Summary

EudraCT number	2013-002524-16
Trial protocol	SE DK
Global end of trial date	01 December 2019

Results information

Result version number	v1 (current)
This version publication date	08 May 2021
First version publication date	08 May 2021

Trial information

Trial identification

Sponsor protocol code	240562-2013-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Oncology, Hauekalnd Univ Hospital
Sponsor organisation address	Jonas Lies v, Bergen, Norway,
Public contact	Dept of Oncology. Haukeland Univ, Nordic Neuroendocrine Tumor Group, halfdan.sorbye@helse-bergen.no
Scientific contact	Dept of Oncology. Haukeland Univ, Nordic Neuroendocrine Tumor Group, halfdan.sorbye@helse-bergen.no

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	21 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To study the efficacy of everolimus combined with temozolomide as first-line treatment in advanced gastrointestinal neuroendocrine carcinoma with a Ki67 of 20-55%, measured as disease control rate (non-progressive disease) at 6 months.

Protection of trial subjects:

Dose reduction plan if side effects

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 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	Sweden: 6
Country: Number of subjects enrolled	Denmark: 24
Country: Number of subjects enrolled	Norway: 8
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	23
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started 14NOv14 and stopped 20DEC17. 39 cases recruited. 1 casewronlgy included and deleted.

Pre-assignment

Screening details:

1 patient excluded as reclassified as adenoicarcinom and not neuroendcorine carcinoma

Period 1

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

Arms

Arm title	Temozolomide and everolimus

Arm description: -

Arm type	experimental
Investigational medicinal product name	everolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg daily

Investigational medicinal product name	temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg daily

Number of subjects in period 1	Temozolomide and everolimus
Started	38
Completed	38

Baseline characteristics

Reporting groups	
Reporting group title	Baseline period

Reporting group description: -

Reporting group values	Baseline period	Total	
Number of subjects	38	38	
Age categorical Units: Subjects			
Adults (18-64 years)	25	25	
From 65-84 years	13	13	
Gender categorical Units: Subjects			
Female	18	18	
Male	20	20	

End points

End points reporting groups

Reporting group title	Temozolomide and everolimus
Reporting group description: -	
Subject analysis set title	PFS 6 m
Subject analysis set type	Per protocol
Subject analysis set description: All correctly included patients	

Primary: PFS 6 m

End point title	PFS 6 m
End point description:	
End point type	Primary
End point timeframe: Last update 2020	

End point values	Temozolomide and everolimus	PFS 6 m		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	38	38		
Units: months				
number (not applicable)	38	38		

Statistical analyses

Statistical analysis title	PFS 6 m
Comparison groups	Temozolomide and everolimus v PFS 6 m
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Fleming one stage

Notes:
[1] - PFS 6 m

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2014-2017 on active treatment

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Adverse avents

Reporting group description: -

Serious adverse events	Adverse avents		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 38 (18.42%)		
number of deaths (all causes)	28		
number of deaths resulting from adverse events	0		
Nervous system disorders			
TIA	Additional description: 1 case		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain management			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Trombocytepenia			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adverse avents		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 38 (7.89%)		
Blood and lymphatic system disorders			
Trombocytopenia			
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	3		

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