Clinical trial results:
Pre-emptive cycline treatment on Cetuximab-induced skin toxicity in patients with metastatic colorectal cancer treated with an intensified FOLFIRI.

Summary

EudraCT number	2010-019140-39
Trial protocol	FR
Global end of trial date	10 October 2016

Results information

Result version number	v1 (current)
This version publication date	02 December 2021
First version publication date	02 December 2021

Trial information

Trial identification

Sponsor protocol code	CPP-450

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01317433
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut de Cancérologie de l'Ouest
Sponsor organisation address	15 rue André Boquel, Angers, France, 49055
Public contact	Marine TIGREAT, Institut de Cancérologie de l'Ouest, +33 240679878, marine.tigreat@ico.unicancer.fr
Scientific contact	Marine TIGREAT, Institut de Cancérologie l'Ouest, +33 240679878, marine.tigreat@ico.unicancer.fr

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	10 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 October 2016
Global end of trial reached?	Yes
Global end of trial date	10 October 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

30% decrease in the incidence of acneiform rash type skin toxicity of G >= 2 during preventive treatment with cyclins for 6 weeks.
The toxicity is evaluated at each consultation and graded according to the NCI CTCAE v4.0 criteria

Protection of trial subjects:

In order to ensure the protection of the rights and safety of trial subjects, this clinical trial was performed in compliance with the principles laid down in the declaration of Helsinki, good clinical practice and European regulation

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 December 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	11
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

It must be performed before the start of anticancer treatment with regard to tumor evaluation and pharmacogenetics, at the latest 15 days before randomization for laboratory assessment and within 7 days before randomization for clinical assessment.

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	Arm A : experimental

Arm description:

Intensified FOLFIRI plus Cetuximab + Doxycycline + skin moisturizers, sun protection.

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

Dosage and administration details:

100 mg daily per os o start 7 days before Cetuximab for 6 weeks

Arm title	Arm B : control

Arm description:

Intensified FOLFIRI plus Cetuximab + skin moisturizers (Dexeryl), sun protection.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Arm A : experimental	Arm B : control
Started	13	12
Completed	10	12
Not completed	3	0
Adverse event, serious fatal	1	-
Adverse event, non-fatal	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	25	25	
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)	11	11	
From 65-84 years	14	14	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	18	18	

End points

End points reporting groups

Reporting group title	Arm A : experimental
Reporting group description: Intensified FOLFIRI plus Cetuximab + Doxycycline + skin moisturizers, sun protection.	
Reporting group title	Arm B : control
Reporting group description: Intensified FOLFIRI plus Cetuximab + skin moisturizers (Dexeryl), sun protection.	

Primary: Patient with at least grade > or = 2 acne-like skin rash

End point title	Patient with at least grade > or = 2 acne-like skin rash
End point description:	
End point type	Primary
End point timeframe: 6 weeks of pre-emptive cycline treatment	

End point values	Arm A : experimental	Arm B : control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: patients	1	5		

Statistical analyses

Statistical analysis title	Efficacy results
Comparison groups	Arm A : experimental v Arm B : control
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)

Notes:

[1] - Descriptive

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Adverse event reporting additional description:	
Only cutaneous toxicities have been reported	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTC AE
Dictionary version	4.0

Reporting groups	
Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B
Reporting group description: -	

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)	3 / 12 (25.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Inferior vena cava syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
dyspnea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Myocardial infarction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	12 / 12 (100.00%)	
Cardiac disorders			
Cheilitis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			

Rash erythematous			
subjects affected / exposed	3 / 13 (23.08%)	5 / 12 (41.67%)	
occurrences (all)	1	1	
Rash papulosquamous			
subjects affected / exposed	3 / 13 (23.08%)	2 / 12 (16.67%)	
occurrences (all)	1	1	
finger fissur			
subjects affected / exposed	6 / 13 (46.15%)	6 / 12 (50.00%)	
occurrences (all)	1	1	
Paronychia			
subjects affected / exposed	1 / 13 (7.69%)	5 / 12 (41.67%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	6 / 13 (46.15%)	10 / 12 (83.33%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	1	
follicular			
subjects affected / exposed	5 / 13 (38.46%)	6 / 12 (50.00%)	
occurrences (all)	1	1	
palmar-plantar erythrodysesthesia			
subjects affected / exposed	4 / 13 (30.77%)	4 / 12 (33.33%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2011	- increase the number of patients - create a specific consent for screening of DPD - update list of investigators
31 January 2011	Use a masterful preparation instead of dexeryl - update of the inclusion procedure - specify the deadline for inclusion
27 November 2012	all metastatic line can be included - prolongation of inclusions

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated prematurely due to a lack of inclusion
The logistical burden of this study and the many competing trials did not allow us to recruit the expected number of patients
The statistical analysis carried out was only descriptive

Notes: