Participant Flow

Recruitment Details	Recruitment period from 14/05/2019 to 15/10/2021.
Pre-assignment Details	Screening based on Uridine diphosphate-GlucuronosylTransferase (UGT1A1) status and DiHydroPyrimidine Dehydrogenase (DHPD) status with serum uracile < 16 ng/ml.

Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products is unchanged. Oxaliplatin, 5 FU Bolus and 5FU continuous are at 85 mg/m², 400 mg/m² and 2400 mg/m² respectively.	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib. The dosage of the others products is unchanged. Oxaliplatin, 5FU Bolus and 5FU continuous are at 85 mg/m², 400 mg/m² and 2400 mg/m² respectively.	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib. The dosage of the others products is unchanged. Oxaliplatin, 5 FU Bolus and 5FU continuous are at 85 mg/m², 400 mg/m² and 2400 mg/m² respectively.
Period Title: **Overall Study**			—
Started	3	6	4
Completed	3	6	4
Not Completed	0	0	0

Arm/Group Title	Experimental Irinotecan 150 mg/m² (IV) and Regorafenib 120 mg/m² (PO)	Experimental Irinotecan 180 mg/m² (IV) and Regorafenib 120 mg/m² (PO)	Experimental Irinotecan 180 mg/m² (IV) and Regorafenib 160 mg/m² (PO)	Total
Arm/Group Description	Cohort 1 : Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged i.e Oxaliplation at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged i.e Oxaliplation at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged i.e Oxaliplation at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Total of all reporting groups
Overall Number of Baseline Participants	3	6	4	13
Baseline Analysis Population Description	[Not Specified]			

Age, Continuous

Median (Inter-Quartile Range) | Unit of measure: years

	3 participants	6 participants	4 participants	13 participants
Number Analyzed				
	53 (49 to 65)	69 (40 to 76)	64.5 (49 to 76)	65 (40 to 76)

Sex: Female, Male Measure Type: Count of Participants | Unit of measure: Participants				
Number Analyzed	3 participants	6 participants	4 participants	13 participants
Female	2 66.7%	3 50.0%	2 50.0%	7 53.8%
Male	1 33.3%	3 50.0%	2 50.0%	6 46.2%

Race (NIH/OMB) Measure Type: Count of Participants | Unit of measure: Participants				
Number Analyzed		6 participants	4 participants	13 participants
American Indian or Alaska Native	%	0 0.0%	0 0.0%	0 0.0%
Asian	%	0 0.0%	0 0.0%	0 0.0%
Native Hawaiian or Other Pacific Islander	%	0 0.0%	0 0.0%	0 0.0%
Black or African American	%	0 0.0%	0 0.0%	0 0.0%
White	%	6 100.0%	4 100.0%	13 100.0%
More than one race	%	0 0.0%	0 0.0%	0 0.0%
Unknown or Not Reported	%	0 0.0%	0 0.0%	0 0.0%

Region of Enrollment Measure Type: Number | Unit of measure: participants				
Number Analyzed		6 participants	4 participants	13 participants
France		6	4	13

Assessment of the patient's general condition using the ECOG scale[1] Measure Type: Number | Unit of measure: participants				
Number Analyzed		6 participants	4 participants	13 participants
0		2	3	6
1		4	1	7

[1] Measure Description:
The physician determines the general condition of patient by using the scale ECOG.

ECOG 0 : Fully active patient, able to perform the same pre-morbid activities without restriction. Very good general condition.

ECOG 1 : Patient restricted in physical activities, but ambulatory and able to perform light or sedentary activities, e.g. light housework or administrative tasks. Good general condition.

Weight

Median (Inter-Quartile Range) | Unit of measure: Kilograms

Number Analyzed		6 participants	4 participants	13 participants
		69 (42 to 96)	78 (57 to 106)	69 (42 to 106)

Body Mass Index

Median (Inter-Quartile Range) | Unit of measure: kg/m²

Number Analyzed		6 participants	4 participants	13 participants
		27.2 (16 to 34)	24.3 (19.7 to 31.7)	27 (16 to 34)

Systolic blood pressure

Median (Inter-Quartile Range) | Unit of measure: mm/hg

Number Analyzed		6 participants	4 participants	13 participants
		127 (113 to 146)	140.5 (133 to 158)	130 (113 to 158)

Diastolic blood pressure

Median (Inter-Quartile Range) | Unit of measure: mm/hg

Number Analyzed		6 participants	4 participants	13 participants
		73 (64 to 87)	82 (73 to 85)	79 (64 to 89)

Tumor location

Measure Type: Number | Unit of measure: participants

Number Analyzed		6 participants	4 participants	13 participants
Right colon		1	0	2
Left colon		1	0	1
Transverse colon		1	0	1
Recto-sigmoid junction		1	1	2
Rectum		2	3	7

Lymph node dissection

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed		6 participants	4 participants	13 participants
Lymph node dissection done	%	5 83.3%	3 75.0%	11 84.6%
Lymph node dissection not done	%	1 16.7%	1 25.0%	2 15.4%

Adenocarcinoma type

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed		6 participants	4 participants	13 participants
well/moderately differentiated	%	4 66.7%	0 0.0%	5 38.5%
Poorly differentiated/ undifferentiated	%	2 33.3%	4 100.0%	6 46.2%
Unknown	%	0 0.0%	0 0.0%	2 15.4%

Depth of tumoral invasion in the wall of colon/rectum determined by pathologist[1]

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed		6 participants	4 participants	13 participants
T3	%	1 16.7%	1 25.0%	2 15.4%
T4b	%	1 16.7%	0 0.0%	1 7.7%
TX (not operated)	%	4 66.7%	3 75.0%	9 69.2%
Unknown	%	0 0.0%	0 0.0%	1 7.7%

[1] Measure Description:

T1: The cancer has grown through the muscularis mucosa into the submucosa. Locally advanced tumor. Very good pronostic.

T2 : The cancer have grown into the muscularis propria. Good pronostic. T3: The cancer has grown into the outermost layers of the colon or rectum but has not gone through them. Bad pronostic.

T4a: The cancer has grown through the wall of the colon or rectum but has not grown into other organs. Very bad pronostic.

T4b: The cancer has grown through the wall of the colon or rectum and is attached to or has grown into other nearby tissues or organs.Very bad pronostic.

Comparison of number of patients with positive nodes versus negative nodes [1]

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed		6 participants	4 participants	13 participants
N0	%	0 0.0%	1 25.0%	1 7.7%
N1	%	2 33.3%	1 25.0%	3 23.1%
N2	%	1 16.7%	0 0.0%	1 7.7%
NX (not operated)	%	3 50.0%	2 50.0%	7 53.8%
Unknown	%	0 0.0%	0 0.0%	1 7.7%

[1] Measure Description: N0 means there are no lymph nodes containing cancer cells.Very good prognosis. N1 means there are cancer cells in 1 to 3 lymph nodes. Intermediate prognosis. N2 means means there are cancer cells in more than 4 lymph nodes.Bad prognosis.

Comparison of number of metastatic patients versus metastasis-free patients [1]

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed		6 participants	4 participants	13 participants
M0	%	1 16.7%	1 25.0%	2 15.4%
M1	%	5 83.3%	2 50.0%	10 76.9%
M1a	%	0 0.0%	1 25.0%	1 7.7%

[1] Measure Description: M0 : metastasis-free patient. Good prognosis. M1: metastatic patient. Bad prognosis.

Metastatic location

Measure Type: Number | Unit of measure: metastatic sites

Number Analyzed		6 participants	4 participants	13 participants
Brain		1	0	1
Liver		5	4	12
Lymphatic nodes		2	1	3
Bone		0	0	0
Lung		3	1	5
Peritoneum		1	0	2

Outcome Measures

1. Number of Participants With Pre-specified Treatment-related Adverse Events Type: Primary | Time Frame: At the end of cycle 1 to 3 (each cycle is 14 days)			
Description	The physician determines pre-specified treatment-related toxicities and grades them by using the Common Terminology Criteria for Adverse Events (NCI-CTC Version 5). 1 - Mild: 2 - Moderate: 3 - Severe: 4 - Life-threatening: 5 - Death. Th evaluation is realized during the first three cycles.		
Time Frame	At the end of cycle 1 to 3 (each cycle is 14 days)		
Analysis Population Description	Evaluable population for Dose-limiting toxicity (DLT). The list of DLTs is pre-specified in the protocol.		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² and Regorafenib 120 mg	Experimental : Irinotecan 180 mg/m² and Regorafenib 120 mg	Experimental : Irinotecan 180 mg/m² and Regorafenib 160 mg
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2 : Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3 : Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Measure Type: Number | Unit of Measure: participants	3	5	3

2. Progression-free Survival (PFS)

Type: Secondary | Time Frame: From baseline of patient until the first observed disease progression

Description	Progression-free survival (PFS), defined as the time from date of inclusion to date of first observed disease progression (investigator's radiological or clinical assessment) or death due to any cause, if death occurs before progression is documented. . A central review of CT-scans is planned for patients found progression-free at 48 weeks. Patients without tumor progression or death at the time of analysis will be censored at their last date of tumor assessment.		
Time Frame	From baseline of patient until the first observed disease progression		
Analysis Population Description	Intention to treat		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Median (Full Range) | Unit of Measure: Month	12.5 (8.7 to 15.4)	8.2 (3.1 to 9.1)	5.1 (3.4 to 7.7)

3. Number of Patients With Disease Control

Type: Secondary | Time Frame: Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).

Description	The disease control corresponds to stable, partial and complete responses determined by RECIST criteria. Criteria recist are based on lesions measurement determined by radiologist. Calculation : the values at the baseline minus the lowest values (nadir)		
Time Frame	Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).		
Analysis Population Description	Intention to treat		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Measure Type: Count of Participants | Unit of Measure: Participants	3 100.0%	6 100.0%	4 100.0%

4. Number of Participants With Objective Response

Type: Secondary | Time Frame: Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).

Description	The objective response corresponds to partial and complete responses determined by RECIST criteria. Criteria recist are based on lesions measurement determined by radiologist. Calculation : The values at the baseline minus the lowest values (nadir)		
Time Frame	Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).		
Analysis Population Description	Intention to treat		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Measure Type: Number | Unit of Measure: participants	2	3	4

5. Overall Survival (OS) Type: Secondary | Time Frame: From baseline to date of patient death			
Description	[Not Specified]		
Time Frame	From baseline to date of patient death		
Analysis Population Description	Intention to treat		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Median (Full Range) | Unit of Measure: Month	16.7 (15.6 to 18)	13.3 (7 to 20)	10.7 (7.2 to 15)

6. The Median of Regression of Tumor Size

Type: Secondary | Time Frame: Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).

Description	The percentage of regression of tumor size to its lowest value (nadir), compared with the pre-treatment tumor size (baseline), according to RECIST criteria (this is the reference method for evaluating cancer treatments based on the measurement of lesions by radiologist).		
Time Frame	Up to 6 months, from baseline of patient to the point where the values are the lowest (nadir).		
Analysis Population Description	Intention to treat		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	3	6	4
Median (Full Range) | Unit of Measure: Percentage	55.3 (21.7 to 64.7)	40.85 (1.1 to 61.7)	60.75 (40.6 to 73)

7. Maintenance Treatment With Regorafenib Alone

Type: Secondary | Time Frame: Up to 16 weeks (after 12 cycles of Folfirinox-R)

Description	Description by cycles of Regorafenib maintenance treatment after 12 cycles of Folfirinox-R
Time Frame	Up to 16 weeks (after 12 cycles of Folfirinox-R)
Analysis Population Description	Population by step and evaluable for safety
Arm/Group Title	Folfirinox-R
Arm/Group Description	Folfirinox + regorafenib Folfirinox + regorafenib: folfirinox : from day 1 to day 3 regorafenib : day 4 to day 10 a cycle during 14 days
Overall Number of Participants Analyzed	13
Step 1 : IRINOTECAN 150 / REGORAFENIB 120	
Number Analyzed	3 participants
2 cycles received *Measure Type: Count of Participants | Unit of Measure: Participants	0 0.0%
3 cycles received *	0 0.0%
4 cycles received *	0 0.0%
6 cycles received *	0 0.0%
8 cycles received *	0 0.0%
No cycles received *	3 100.0%

Step 2 : IRINOTECAN 180 / REGORAFENIB 120	
Number Analyzed	6 participants
2 cycles received *	1 16.7%
3 cycles received *	0 0.0%
4 cycles received *	1 16.7%
6 cycles received *	0 0.0%
8 cycles received *	1 16.7%
No cycles received *	3 50.0%
Step 3 : IRINOTECAN 180 / REGORAFENIB 160	
Number Analyzed	4 participants
2 cycles received *	0 0.0%
3 cycles received *	1 25.0%
4 cycles received *	0 0.0%
6 cycles received *	1 25.0%
8 cycles received *	0 0.0%
No cycles received *	2 50.0%

All steps		
Number Analyzed	13 participants	
2 cycles received *	1	7.7%
3 cycles received *	1	7.7%
4 cycles received *	1	7.7%
6 cycles received *	1	7.7%
8 cycles received *	1	7.7%
No cycles received *	8	61.5%

* Measure Type: Count of Participants | Unit of Measure: Participants

8. Determination of Circulating Free DNA Concentration (Not Available)

Type: Secondary | Time Frame: Baseline, 8 weeks, 16 weeks etc. through the end of treatment

Description	From baseline of first patient until the end of treatment		
Time Frame	Baseline, 8 weeks, 16 weeks etc. through the end of treatment		
Analysis Population Description	Blood samples were not analyzed because the number of patients per cohort was too low. Consequently, the data is not available and cannot be populated.		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	0	0	0

No data displayed because Outcome Measure has zero total analyzed.

9. Resection (R) Rates (Not Available)

Type: Secondary | Time Frame: Approximately at 6 months

Description	Through the treatment		
Time Frame	Approximately at 6 months		
Analysis Population Description	Blood samples were not analyzed because the number of patients per cohort was too low. Consequently, the data is not available and cannot be populated.		
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib 120 mg (PO)	Experimental : Irinotecan 180 mg/m² (IV) and Regorafenib 120 mg (PO)	Experimental : Irinotecan 180 mg/m² (IV) and Regorafenib 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2 : Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3 : Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatine at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².
Overall Number of Participants Analyzed	0	0	0

No data displayed because Outcome Measure has zero total analyzed.

Adverse Events

Time Frame	From the baseline up to one month after the last cycle of chemotherapy, up to 7 months (AE ans SAEs). From the baseline up to 20 months for all-cause mortality.
Adverse Event Reporting Description	[Not Specified]

Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) Cand Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
Arm/Group Description	Cohort 1: Participants were administered 150 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 2: Participants were administered 180 mg/m² of Irinotecan and 120 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².	Cohort 3: Participants were administered 180 mg/m² of Irinotecan and 160 mg of Regorafenib every 14 days. The dosage of the others products are unchanged. Oxaliplatin at 85 mg/m², 5FU Bolus at 400 mg/m² and 5FU continuous at 2400 mg/m².

All-Cause Mortality			
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) Cand Regorafenib at 120 mg (PO)	Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	3/3 (100.00%)	2/6 (33.33%)	0/4 (0.00%)

Serious Adverse Events

Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)		Experimental: Irinotecan 180 mg/m² (IV) Cand Regorafenib at 120 mg (PO)		Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	0/3 (0.00%)		4/6 (66.67%)		0/4 (0.00%)	
Blood and lymphatic system disorders						
Neutropenia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Cardiac disorders						
Atrial fibrillation †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Endocrine disorders						
Hyperparathyroidism primary †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Gastrointestinal disorders						
Intestinal subocclusive syndrom †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Decreased appetite †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Infections and infestations						
Device related sepsis †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Renal and urinary disorders						
Pyelonephritis acute †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

† Indicates events were collected by systematic assessment

1 Term from vocabulary, NCI-CTC Version 5

Other (Not Including Serious) Adverse Events						
Frequency Threshold for Reporting Other Adverse Events	0%					
Arm/Group Title	Experimental: Irinotecan 150 mg/m² (IV) and Regorafenib at 120 mg (PO)		Experimental: Irinotecan 180 mg/m² (IV) Cand Regorafenib at 120 mg (PO)		Experimental: Irinotecan 180 mg/m² (IV) and Regorafenib at 160 mg (PO)	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	3/3 (100.00%)		6/6 (100.00%)		4/4 (100.00%)	
Blood and lymphatic system disorders						
Anemia †1	0/3 (0.00%)	0	3/6 (50.00%)	8	2/4 (50.00%)	4
Hyperleukocytosis †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Lymphopenia †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Thrombopenia †1	1/3 (33.33%)	2	1/6 (16.67%)	2	0/4 (0.00%)	0
Thrombocytosis †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Cardiac disorders						
Arteriospasm coronary †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Ear and labyrinth disorders						
Vertigo †1	0/3 (0.00%)	0	0/6 (0.00%)	0	2/4 (50.00%)	2
Gastrointestinal disorders						
Abdominal pain †1	2/3 (66.67%)	2	2/6 (33.33%)	2	1/4 (25.00%)	2
Anorectal discomfort †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Aphtous ulcer †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Constipation †1	1/3 (33.33%)	1	2/6 (33.33%)	2	1/4 (25.00%)	1
Diarrhoea †1	3/3 (100.00%)	8	6/6 (100.00%)	25	4/4 (100.00%)	23
Dry mouth †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Dysepsia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Gingival bleeding †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Mouth ulceration †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Nausea †1	0/3 (0.00%)	0	5/6 (83.33%)	11	4/4 (100.00%)	7

Rectal syndrome †1	0/3 (0.00%)	0	0/6 (0.00%)	0	2/4 (50.00%)	4
Salivary hypersecretion †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Vomiting †1	1/3 (33.33%)	3	1/6 (16.67%)	1	2/4 (50.00%)	4
General disorders						
Asthenia †1	2/3 (66.67%)	9	6/6 (100.00%)	12	3/4 (75.00%)	10
Chest pain †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Mucosal inflammation †1	1/3 (33.33%)	1	2/6 (33.33%)	2	0/4 (0.00%)	0
Hepatobiliary disorders						
Cholestasis †1	0/3 (0.00%)	0	2/6 (33.33%)	2	1/4 (25.00%)	1
Hepatic pain †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Immune system disorders						
Anaphylactic reaction †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Drug hypersensitivy †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Hepatitis E †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Oral candidiasis †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Infections and infestations						
Cystitis †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	2
Erythema induratum †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Paronychia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Pharyngitis †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Urinary tract infection †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Investigations						
Blood alcaline phosphatase increased †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Blood lactatce dehydrogenase increased †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	2
Gammaglutamyl transferase increased †1	0/3 (0.00%)	0	1/6 (16.67%)	1	2/4 (50.00%)	4
Neutrophil count increased †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Weight decreased †1	1/3 (33.33%)	4	3/6 (50.00%)	4	3/4 (75.00%)	4
Transaminase increased †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Metabolism and nutrition disorders						
Decreased appetite †1	2/3 (66.67%)	2	4/6 (66.67%)	13	3/4 (75.00%)	3
Hypercalcemia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Hypoalbuminemia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Hypokalemia †1	0/3 (0.00%)	0	3/6 (50.00%)	4	1/4 (25.00%)	2
Hypomagnesemia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Hyponatremia [†1]	0/3 (0.00%)	0	2/6 (33.33%)	2	0/4 (0.00%)	0
Malnutrition [†1]	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Musculoskeletal and connective tissue disorders						
Arthralgia [†1]	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Back pain [†1]	0/3 (0.00%)	0	2/6 (33.33%)	4	0/4 (0.00%)	0
Pain in extremity [†1]	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Spinal pain [†1]	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Trismus [†1]	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Nervous system disorders						
Distal wekness [†1]	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Dizziness [†1]	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Dysgueusia [†1]	0/3 (0.00%)	0	2/6 (33.33%)	2	0/4 (0.00%)	0
Dysphonia [†1]	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Headache [†1]	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	2
Neuropathy peripheral [†1]	1/3 (33.33%)	3	4/6 (66.67%)	7	3/4 (75.00%)	9

Palmar-plantar erythrodysaesthesia syndrome †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Psychiatric disorders						
Anxiety †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Confusional state †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Insomnia †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Renal and urinary disorders						
Dysuria †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Hematuria †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1
Nocturia †1	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Proteinuria †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Renal failure †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Urinary retention †1	0/3 (0.00%)	0	1/6 (16.67%)	1	1/4 (25.00%)	1
Reproductive system and breast disorders						
Vulvovaginal dryness †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0

Vulvovaginal pruritus †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Respiratory, thoracic and mediastinal disorders						
Dyspnea †1	1/3 (33.33%)	2	0/6 (0.00%)	0	0/4 (0.00%)	0
Epistaxis †1	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Oropharyngeal pain †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Rhinorrhea †1	0/3 (0.00%)	0	1/6 (16.67%)	1	0/4 (0.00%)	0
Skin and subcutaneous tissue disorders						
Alopecia †1	2/3 (66.67%)	2	2/6 (33.33%)	2	2/4 (50.00%)	2
Dry skin †1	1/3 (33.33%)	1	1/6 (16.67%)	1	0/4 (0.00%)	0
Petechiae †1	1/3 (33.33%)	1	0/6 (0.00%)	0	0/4 (0.00%)	0
Vascular disorders						
Hypertension †1	1/3 (33.33%)	4	4/6 (66.67%)	6	4/4 (100.00%)	24
Thrombophlebitis superficial †1	0/3 (0.00%)	0	0/6 (0.00%)	0	1/4 (25.00%)	1

† Indicates events were collected by systematic assessment

1 Term from vocabulary, NCI-CTC Version 5

Conclusion :

Folfirinox-R is a Phase I/II trial that was halted at the end of Phase I following the recommendations of the independent scientific committee, which determined that there were too many cases of Grade 3 diarrhea at that dose level, even though this was not defined as a DLT. Consequently, the Phase II trial could not proceed to the recommended Phase II dose level.