



Clinical trial results:

Etude de phase I associant la rapamycine et l'irinotecan dans toutes tumeurs solides réfractaires de l'enfant – RAPIRI

Summary

EudraCT number	2010-022329-13
Trial protocol	FR
Global end of trial date	31 March 2016

Results information

Result version number	v1 (current)
This version publication date	24 July 2026
First version publication date	24 July 2026

Trial information

Trial identification

Sponsor protocol code	4791
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01282697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hôpitaux Universitaires de Strasbourg- direction de la Recherche Clinique et des Innovations
Sponsor organisation address	1, place de l'Hôpital, , STRASBOURG, France, 67000
Public contact	Mme Sarah HUSTACHE, Hôpitaux Universitaires de Strasbourg- direction de la Recherche Clinique et des Innovations, dpidrci@chru-strasbourg.fr
Scientific contact	Pr Natacha ENTZ-WERLE, Hôpital de Hautepierre- Unité d'Onco-Hématologie Pédiatrique, dpidrci@chru-strasbourg.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	23 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2014
Global end of trial reached?	Yes
Global end of trial date	31 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Déterminer la dose maximale tolérée (DMT) de l'association thérapeutique d'irinotecan et de rapamycine dans toutes tumeurs solides réfractaires pédiatriques
- Evaluer la pharmacocinétique de la rapamycine et de l'irinotecan au cours du 1er cycle de chimiothérapie.

Protection of trial subjects:

Les enfants seront suivis pendant 12 mois à l'issue de leur traitement (si minimum deux mois de traitement effectués). La phase de suivi comprendra 4 visites (tous les 3 mois) et sera réalisée conformément aux recommandations habituelles de suivi dans les pathologies cancéreuses correspondantes.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 April 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Regulatory reason
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	18
Adolescents (12-17 years)	18
Adults (18-64 years)	6

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Potential subjects aged 1 to 21 years with recurrent or refractory solid tumors (including central nervous system tumors and sarcomas) who had exhausted standard therapeutic options were screened for eligibility. Screening criteria required adequate hematological, hepatic, and renal functions, a life expectancy of at least 8 weeks, and a ps >70%

Period 1

Period 1 title	Inclusion (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Rapamycin + Irinotecan
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Arm description:

Single-arm, 3+3 dose escalation study evaluating 10 dose levels of combined Rapamycin and Irinotecan in pediatric patients with refractory solid tumors

Arm type	Experimental
Investigational medicinal product name	IRINOTECAN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a 90-minute intravenous infusion on Day 1 and Day 15 of each 28-day cycle. The dosage depends on the dose-escalation level assigned to the patient (ranging from 125 mg/m² to 240 mg/m²)

Investigational medicinal product name	RAPAMUNE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Administered once daily, every day (from Day 1 to Day 28 of each cycle).

The first daily dose is administered at the end of the Irinotecan infusion.

Subsequent daily doses must be taken at a fixed time every day.

The dosage depends on the dose-escalation level (ranging from 0.5 mg/m²/day to 2.5 mg/m²/day)

Number of subjects in period 1	Rapamycin + Irinotecan
Started	42
Completed	42

Baseline characteristics

Reporting groups

Reporting group title	Inclusion
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Reporting group description: -

Reporting group values	Inclusion	Total	
Number of subjects	42	42	
Age categorical			
Age >=1 an et <= 21 ans			
Units: Subjects			
Children (2-11 years)	23	23	
Adolescents (12-17 years)	17	17	
Adults (18-64 years)	2	2	
Gender categorical			
Units: Subjects			
Female	16	16	
Male	26	26	

End points

End points reporting groups

Reporting group title	Rapamycin + Irinotecan
Reporting group description: Single-arm, 3+3 dose escalation study evaluating 10 dose levels of combined Rapamycin and Irinotecan in pediatric patients with refractory solid tumors	

Primary: Dose-Limiting Toxicities

End point title	Dose-Limiting Toxicities ^[1]
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End point description:

End point type	Primary
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End point timeframe:

First 28 days (Cycle 1) of treatment combination exposure

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Single arm study descriptive analysis

End point values	Rapamycin + Irinotecan			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: number of patient	3			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Tolerated Dose

End point title	Maximum Tolerated Dose ^[2]
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End point description:

Determine the maximum tolerated dose (MTD) of irinotecan and rapamycin combination in children with refractory solid tumors.

The Dose-Limiting Toxicity (DLT) of the drug combination is determined during the first cycle (J1 to J28) of treatment. MTD will be defined as the dose level immediately below the dose level at which 2 patients in a cohort of 3 to 6 patients will have experienced a DLT.

No MTD was reached. (Dose Max IRINOTECAN 240mg/m² / RAPAMYCIN 2,5mg/m²/day)

End point type	Primary
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End point timeframe:

J1-J28

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No MTD reached

End point values	Rapamycin + Irinotecan			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: mg/m2				
number (not applicable)	240			

Statistical analyses

No statistical analyses for this end point

Primary: AUC

End point title	AUC ^[3]
End point description:	AUC RAPAMYCIN D8
End point type	Primary
End point timeframe:	J8

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Single arm study descriptive analysis

End point values	Rapamycin + Irinotecan			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: min.mg/L				
number (not applicable)	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

During overall study participation

Adverse event reporting additional description:

old study, no possibility of MedDRA coding for non-serious AE

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	experimental
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Old study, no possibility of MedDRA coding for AE

Serious adverse events	experimental		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 42 (40.48%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
pyrexia			

subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Pneumothorax			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachypnoea			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Aplasia pure red cell			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular fibrillation			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in jaw			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Hyperkalaemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	experimental		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2010	Modification de la date de démarrage de l'étude: janvier 2011 ajout au cours du 1er cycle: l'étude de pharmacodynamie (quantification des progéniteurs endothéliaux circulants et dosage de marqueurs angiogéniques protéiques (cytokines et chimiokines))
27 October 2011	Modification des modalités de pré-inclusion et d'inclusion modification paragraphe V.3.2: contre-indications thérapeutiques

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported