



Clinical trial results:

A randomized, multicentre, phase III trial evaluating the interest of imatinib treatment maintenance or interruption after 3 years of adjuvant treatment in patients with Gastrointestinal Stromal Tumours (GIST)

Summary

EudraCT number	2013-001372-37
Trial protocol	FR
Global end of trial date	07 December 2023

Results information

Result version number	v1 (current)
This version publication date	15 November 2025
First version publication date	15 November 2025

Trial information

Trial identification

Sponsor protocol code	ET13-024
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Centre Léon Bérard
Sponsor organisation address	28 Rue Laënnec, Lyon, France,
Public contact	SEVERINE METZGER, CENTRE LEON BERARD, +33 0478782786 , severine.metzger@lyon.unicancer.fr
Scientific contact	SEVERINE METZGER, CENTRE LEON BERARD, +33 0478782786 , severine.metzger@lyon.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	17 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 December 2023
Global end of trial reached?	Yes
Global end of trial date	07 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical impact, in terms of Disease-Free Survival (DFS), of interruption versus maintenance of imatinib adjuvant treatment beyond 3 years, in patients with resected primary GIST at high risk of recurrence

Protection of trial subjects:

Information of patient and informed consent signature will be performed prior to any study-specific procedure. The patient will be orally provided by the investigator with the appropriate information; in addition, he will be given written information and an informed consent form. After a sufficient time to think, the patient will give his written consent, by dating and signing the informed consent form. This form will also be signed and dated by the investigator, preferentially on the same day, and a copy will be given to the patient (the original form will be archived in the patient medical file).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2014
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	France: 136
Worldwide total number of subjects	136
EEA total number of subjects	136

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)	136

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A screening visit should take place within 4 weeks (i.e. 28 days) prior to the programmed date of randomization, knowing that randomization (M0 visit) must be 36 months ($\pm$ 3 months) after the start date of imatinib adjuvant treatment.

Period 1

Period 1 title	Overall study period (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 1

Arm description:

Maintenance of imatinib at the last dose routinely taken by the patient in the 3-year period prior to randomization (either 300 or 400 mg/d)

Arm type	Standard treatment
Investigational medicinal product name	Glivec®
Investigational medicinal product code	
Other name	Imatinib mesilate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Imatinib mesilate (Glivec®, Novartis) is a selective inhibitor of KIT, PDGFRA and BCR-ABL protein tyrosine kinase activity and is commercialized by Novartis Pharma SAS. Imatinib (300, 400 or 800mg/d) must be taken orally with a meal and a large glass of water until PD or unacceptable toxicity as per Glivec SPC.

Arm title	Arm 2
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Arm description:

Interruption of imatinib treatment from the day of randomization.

Arm type	Interruption
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Arm 1	Arm 2
Started	71	65
Completed	71	65

Baseline characteristics

Reporting groups

Reporting group title	Arm 1
Reporting group description:	
Maintenance of imatinib at the last dose routinely taken by the patient in the 3-year period prior to randomization (either 300 or 400 mg/d)	
Reporting group title	Arm 2
Reporting group description:	
Interruption of imatinib treatment from the day of randomization.	

Reporting group values	Arm 1	Arm 2	Total
Number of subjects	71	65	136
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	71	65	136
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
median	62	63	
full range (min-max)	25 to 84	25 to 90	-
Gender categorical			
Units: Subjects			
Female	28	40	68
Male	43	25	68

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
Maintenance of imatinib at the last dose routinely taken by the patient in the 3-year period prior to randomization (either 300 or 400 mg/d)	
Reporting group title	Arm 2
Reporting group description:	
Interruption of imatinib treatment from the day of randomization.	

Primary: Disease Free survival

End point title	Disease Free survival ^[1]
End point description:	
Disease-Free Survival (DFS), will be analysed based on the data from the ITT population, according to the study arm and randomization strata to which patients were assigned. It will be measured from the date of randomization to the date of event defined as the first documented relapse or death due to any cause. Patients with no event at the time of the analysis will be censored at the date of the last adequate tumour assessment. The distribution of DFS will be estimated using the Kaplan-Meier method. The median DFS along with 95% CI will be presented by study arm. The primary efficacy analysis will be the comparison of the distribution of DFS between the two arms using a log-rank test stratified by randomization stratification factors at two-sided 5% level of significance. A Cox regression model stratified by randomization stratification factors will be used to estimate the hazard ratio (HR) of DFS, along with 95% CI	
End point type	Primary
End point timeframe:	
Disease-free survival was defined as the time from randomization to the first date of relapse or death from any cause. Patients without relapse were censored at the date of the last available tumor assessment. DFS after 3y of adjuvant imatinib treatment.	

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: Time to imatinib resistance was calculated as the time from randomization to first progression on imatinib or death. Seven patients in the maintenance arm relapsed while on treatment. In the interruption arm, five patients progressed after restarting treatment and three died without restarting treatment. The 3-year disease-free survival rates on imatinib were 93% and 96% in the maintenance and interruption arms, respectively.

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	65		
Units: Rechute				
Oui	15	28		
Non	56	37		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All period

Adverse event reporting additional description:

Adverse event (AE): any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product, and which does not necessarily have a causal relationship with this treatment. All AEs will be reported in the CRF.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Frequency threshold for reporting non-serious adverse events: 5 %

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: Regarding safety, 123 (90.4%) patients experienced at least one AE, 56 (86.2%) and 67 (94.4%) in the discontinuation and maintenance groups, respectively. The incidence of grade 3 or higher adverse events (AEs) was not significantly different between discontinuation and maintenance (n=19, [29.2%] vs. 13 [18.3%], $p>0.05$), with a similar number of serious AEs in both arms (13 [20.0%] vs. 13 [18.3%]). Myalgia was the only side effect significantly different between the two arms.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2014	• Modification des impératifs concernant la méthode de contraception à utiliser dans le cadre de l'étude (une méthode contraceptive au lieu de deux) et modification du critère d'inclusion I9 en conséquence • Signaler le changement de la personne de contact auprès du promoteur • Mise à jour de la liste des investigateurs : - Déclarer 3 nouveaux investigateurs : - Signaler le changement d'adresse d'un Centre
13 January 2015	• Déclarer un nouveau lieu de recherche • Mettre à jour la liste des investigateurs : - Déclarer un investigateur - Supprimer 3 investigateurs
28 April 2015	• Déclarer un nouveau lieu de recherche : • Mettre à jour la liste des investigateurs : Déclarer 6 investigateurs Supprimer un investigateur
08 March 2016	* Mise à jour de la liste des investigateurs : - Déclarer un nouveau lieu de recherche - Déclarer le changement d'investigateur principal - Supprimer un lieu de recherche - Déclarer 8 nouveaux investigateurs dans des lieux de recherche déjà déclarés - Supprimer un investigateur
07 June 2016	* Mise à jour de la liste des investigateurs - Déclarer un nouveau lieu de recherche
20 September 2016	Déclarer un nouveau lieu de recherche
13 June 2017	* Mise à jour de la liste des investigateurs : - Déclarer un nouveau lieu de recherche - Déclarer le changement d'investigateur principal - Déclarer 3 nouveaux investigateurs - Supprimer un investigateur
13 February 2018	• Prolongation de 2 ans de la durée des inclusions • Mise à jour de la liste des investigateurs : Déclarer un nouveau lieu de recherche : Déclarer de nouveaux investigateurs dans des lieux de recherche déjà déclarés

18 December 2018	• Réévaluation du nombre de patients à inclure : 134 patients au lieu des 256 initialement planifiés ; • Mise à jour de la section vigilance ; • Mise en conformité des documents de l'étude suite à la législation européenne (Règlement Général sur la Protection des Données « RGPD ») ; • Actualisation du paragraphe « Sponsor Responsibilities » selon les procédures du promoteur ; • Modification de certains termes suite à la loi Jardé ; • Actualisation de la liste des abréviations ; • Mise à jour de la liste des investigateurs : déclaration de 2 nouveaux investigateurs dans des lieux déjà déclarés et retrait d'un investigateur Déclaration nouveaux investigateurs : Retrait d'un investigateur :
15 October 2019	• Prolongation de 2 ans de la durée des inclusions initialement prévue (7 ans au lieu de 5 ans) et en conséquence de la durée totale de l'étude ainsi que la dernière visite du dernier patient (sans modification de la durée de traitement ni de suivi) ; • Actualisation des données du RGPD (durée archivage maximale).
14 January 2020	• Mise à jour de la liste des investigateurs (changement d'investigateur principal (IP) et déclaration d'un nouvel investigateur dans un lieu de recherche déjà déclaré) :
23 March 2021	• Mise à jour de la liste des investigateurs (changement d'investigateur principal (IP) et déclaration d'un nouvel investigateur dans un lieu de recherche déjà déclaré)
18 January 2022	• Prolongation de la durée d'inclusions ; • Mise à jour des documents de l'étude suite à la publication du Règlement Général sur la Protection des Données (RGPD) ; • Mise à jour de la liste des investigateurs.
21 June 2022	• Mise à jour de la liste des investigateurs : Changement du nom d'un centre Ajout d'un lieu de recherche
11 May 2023	• Mise à jour de la liste des investigateurs (changement d'investigateur principal « IP » dans un lieu de recherche déjà déclaré)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported