Clinical trial results:
Efficacité et tolérance d'un traitement de première intention par tocilizumab dans la maladie de Takayasu: étude française multicentrique prospective

Summary

EudraCT number	2013-005039-26
Trial protocol	FR
Global end of trial date	01 February 2019

Results information

Result version number	v1 (current)
This version publication date	29 June 2022
First version publication date	29 June 2022
Summary attachment (see zip file)	Résumé du rapport final (TOCITAKA_resume-rapport-final_20200210_DRC.pdf)

Trial information

Trial identification

Sponsor protocol code	P130404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02101333
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS
Sponsor organisation address	4 Avenue Victoria, PARIS, France, 75004
Public contact	Yannick VACHER, ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS, yannick.vacher@aphp.fr
Scientific contact	Pr Olivier FAIN, ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS, yannick.vacher@aphp.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 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2019
Global end of trial reached?	Yes
Global end of trial date	01 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Etudier l'influence d'un traitement par tocilizumab pendant 6 mois sur le nombre de patients bons répondeurs ayant pu arrêter les corticoïdes.

Protection of trial subjects:

Le déroulement de la recherche dans les centres investigateurs et la prise en charge des sujets sera fait conformément à la déclaration d'Helsinki et les Bonnes Pratiques en vigueur.
Cette recherche a obtenu l'avis favorable du CPP Ile de France X le 16/01/2014

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 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: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

L'étude a été conçue comme une étude multicentrique avec 27 sites investigateurs en France. 15 patients atteints de la Maladie de Takayasu devait être inclus dans l'étude. Une MS a augmenté le nombre de sujets à inclure afin d'avoir 15 patients analysables

Pre-assignment

Screening details:

17 patients ont été inclus dans la recherche dans 12 centres en France

Period 1

Period 1 title	Patients inclus
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Patients ayant signé le consentement

Arm description:

Signature du consentement

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Patients ayant signé le consentement
Started	17
Completed	14
Not completed	3
Physician decision	3

Period 2

Period 2 title	Patients ayant initié le traitement
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Bras unique

Arm description:

Administration de Tocilizumab pendant au minimum un mois

Arm type	Experimental
Investigational medicinal product name	RoActemra
Investigational medicinal product code	86045397
Other name	TOCILIZUMAB
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tous les patients bénéficieront d'un traitement par tocilizumab, qui sera administré selon les recommandations en vigueur, à 8 mg/kg en une injection intraveineuse sur 1 heure associé à la surveillance habituelle prévue. Le tocilizumab sera administré selon les mêmes modalités à M0, puis de façon mensuelle pendant 6 mois.

Number of subjects in period 2	Bras unique
Started	14
Completed	13
Not completed	1
Protocol deviation	1

Period 3

Period 3 title	Patients ayant été traité 6 mois
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Patients analysés

Arm description:

Administration du Tocilizumab pendant les 6 premiers mois de l'étude

Arm type	Experimental
Investigational medicinal product name	RoActemra
Investigational medicinal product code	86045397
Other name	TOCILIZUMAB
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tous les patients bénéficieront d'un traitement par tocilizumab, qui sera administré selon les recommandations en vigueur, à 8 mg/kg en une injection intraveineuse sur 1 heure associé à la surveillance habituelle prévue. Le tocilizumab sera administré selon les mêmes modalités à M0, puis de façon mensuelle pendant 6 mois.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: 3 patients inclus n'ont reçu aucune perfusion de Tocilizumab et 1 patient a été inclus à tord

mais a reçu une perfusion de Tocilizumab
la Période baseline correspond aux patients ayant reçu au moins une perfusion de Tocilizumab et n'ayant pas été inclus à tord

Number of subjects in period 3[2]	Patients analysés
Started	13
Completed	13

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 3 patients inclus n'ont reçu aucune perfusion de Tocilizumab et 1 patient a été inclus à tord mais a reçu une perfusion de Tocilizumab
la Période baseline correspond aux patients ayant reçu au moins une perfusion de Tocilizumab et n'ayant pas été inclus à tord

Baseline characteristics

Reporting groups

Reporting group title	Patients ayant été traité 6 mois

Reporting group description: -

Reporting group values	Patients ayant été traité 6 mois	Total	
Number of subjects	13	13	
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)	13	13	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	32		
full range (min-max)	19 to 45	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	1	1	
Origine ethnique Units: Subjects			
Caucasienne	7	7	
Afrique du Nord	4	4	
Autre	2	2	

End points

End points reporting groups

Reporting group title	Patients ayant signé le consentement
Reporting group description: Signature du consentement	
Reporting group title	Bras unique
Reporting group description: Administration de Tocilizumab pendant au minimum un mois	
Reporting group title	Patients analysés
Reporting group description: Administration du Tocilizumab pendant les 6 premiers mois de l'étude	

Primary: Nombre de bons répondeurs en rémission complète ayant arrêté les corticoïdes après 6 mois de traitement par tocilizumab

End point title	Nombre de bons répondeurs en rémission complète ayant arrêté les corticoïdes après 6 mois de traitement par tocilizumab[1]
End point description: La rémission complète étant définie par l'absence d'activité clinique, biologique et radiologique à 6 mois	
End point type	Primary
End point timeframe: 6 mois après le début du traitemen	

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: L'étude TOCITAKA n'est pas une étude comparative

End point values	Patients analysés			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Nombre de patients				
Succès	6			
Echec	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

18 mois et 21 jours

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Bras unique

Reporting group description: -

Serious adverse events	Bras unique		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vasospasm cerebral			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral artery stenosis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
acute pancreatitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
Polyarthritis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
polyarthralgia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
perianal abcess			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
infectious colitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Bras unique		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)		
Blood and lymphatic system disorders			
asymptomatic neutropenia			
alternative dictionary used: NA NA			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Otitis			
alternative dictionary used: NA NA			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	3		
Gastrointestinal disorders			

viral gastroenteritis alternative dictionary used: NA NA subjects affected / exposed occurrences (all) acute pancreatitis alternative dictionary used: NA NA subjects affected / exposed occurrences (all)	 2 / 13 (15.38%) 0 1 / 13 (7.69%) 1		
Respiratory, thoracic and mediastinal disorders rhinopharyngitis alternative dictionary used: NA NA subjects affected / exposed occurrences (all)	 3 / 13 (23.08%) 3		
Infections and infestations urinary tract infection alternative dictionary used: NA NA subjects affected / exposed occurrences (all) Thoracic zona alternative dictionary used: NA NA subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2014	- ajout d'un nouveau centre - mise à jour du formulaire de notification d'EIG
15 December 2014	Ajout du centre 024 (service de Médecine interne, Diabète et Maladies métaboliques, CHRU de Strasbourg)
12 February 2015	Centre 023: déménagement du Pr Olivier Fain (investigateur coordonnateur de l'étude) à l'hôpital Saint-Antoine qui devient investigateur principal au niveau du centre
29 June 2015	- prolongation de la période d'inclusion. La durée totale de la recherche passe ainsi de 30 mois à 54 mois - ajout du centre 025: service de médecine interne et maladies infectieuses, CHU de Bordeaux - ajout de la possibilité de faire un angio-scanner à la place de l'angio-IRM
28 September 2015	Ajout d'un nouveau centre : Service de Médecine Interne, CHU de Tours o Investigateur principal : Dr Bertrand LIOGER
03 May 2017	Prolongation de la période d'inclusion et de l'étude de 6 mois Augmentation du nombre de patients à inclure à 20 afin d'avoir 15 patients évaluables (qui ont été traités)
25 September 2017	Modification du lieu de conditionnement secondaire du Tocilizumab. o La société Movianto (Gonesse) remplace le Site Logistique Roche (Rosny sous Bois) Modification du lieu de certification du Tocilizumab o Certification à Roche Boulogne-Billancourt (à la place de Roche - Rosny-sous-Bois)
01 February 2018	- Suppression du Comité de Surveillance Indépendant - Modification de l'investigateur principal du centre 003 (Henri Mondor) o Le Dr Nicolas LIMAL remplace le Pr GODEAU - Modification de l'investigateur principal du centre 026 (Tours) o Le Dr Nicole FERREIRA remplace le Dr LIOGER
22 February 2018	Modification de l'investigateur principal dans le centre 004 (Médecine Interne 1 - Hôpital Pitié Salpetrière). Le Pr Saadoun remplace le Pr Cacoub
17 May 2018	- Ajout d'un nouveau centre : o Service de Médecine vasculaire, CHU de Montpellier o Investigateur principal : Pr Isabelle QUERE

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32943098