Clinical trial results:
Intrathecal Rituximab in Progressive Multiple Sclerosis

Summary

EudraCT number	2014-005493-11
Trial protocol	FR
Global end of trial date	02 September 2019

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022
Summary attachment (see zip file)	article publié de l'étude EFFRITE (MSI2021-8813498.pdf)

Trial information

Trial identification

Sponsor protocol code	CHPAU2014/01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02545959
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Hospitalier de Pau
Sponsor organisation address	4 Boulevard Hauterive, Pau, France, 64046 cedex
Public contact	URC - Information sur Essai EFFRITE, Centre Hospitalier de Pau, +33 559726801, stephane.debeugny@ch-pau.fr
Scientific contact	URC - Information sur Essai EFFRITE, Centre Hospitalier de Pau, +33 559726801, stephane.debeugny@ch-pau.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	18 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2018
Global end of trial reached?	Yes
Global end of trial date	02 September 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Our goal is to study the kinetics of action of a single dose of intrathecally-infused rituximab upon cerebro-spinal fluid (CSF) biological targets.
The main objective of the trial is to study the osteopontin level in CSF at d4 after a single intrathecal infusion of rituximab. CSF level is expected to normalize.

Protection of trial subjects:

- Avant la ponction lombaire : une prémédication par antihistaminique et 120 mg de méthylprednisolone sera préalablement administrée avant chaque injection de rituximab.

- Après la ponction lombaire : mise en position de Trendelenburg pendant 4 heures pour favoriser la diffusion du traitement vers l'encéphale et éviter les événements secondaires (douleurs, céphalées)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	7

From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Tous les patients ont été recrutés au CH de Pau de novembre 2015 à août 2018

Pre-assignment

Screening details:

Inclusion criteria:
Age ≥45 years, male or female
Secondary or primary progressive MS, in progressive phase since >2 years
EDSS ≥6.0
Absence of alternative therapy
Exclusion criteria:
Relapsing phase of MS
Contraindication to MRI, lumbar puncture
Active infection or immunosuppressive state or treatment
Dementia, severe psychiatric disorder

Period 1

Period 1 title	Inclusion 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	méthylprednisolone

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	méthylprednisolone
Investigational medicinal product code	H02AB04
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

120 mg milligrams for intravenous use

Arm title	Rituximab IT

Arm description: -

Arm type	Experimental
Investigational medicinal product name	rituximab
Investigational medicinal product code	L01XC02
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

20 mg milligrams Rituximab solution for injection in intrathecal use

Arm title	Rituximab IT + IV

Arm description: -

Arm type	Experimental

Investigational medicinal product name	rituximab
Investigational medicinal product code	L01XC02
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use, Intrathecal use

Dosage and administration details:

375 mg/m2 milligrams/square meter for intravenous use and 20 mg milligrams for intrathecal use

Number of subjects in period 1	méthylprednisolone	Rituximab IT	Rituximab IT + IV
Started	2	4	4
Completed	2	4	4

Baseline characteristics

End points

End points reporting groups

Reporting group title	méthylprednisolone
Reporting group description: -	
Reporting group title	Rituximab IT
Reporting group description: -	
Reporting group title	Rituximab IT + IV
Reporting group description: -	

Primary: Change in osteopontin level between D0 and D4

End point title	Change in osteopontin level between D0 and D4
End point description:	
End point type	Primary
End point timeframe:	
The primary end point consist to mesure changes in osteopontin level between D0 and D4	

End point values	méthylprednisolone	Rituximab IT	Rituximab IT + IV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	4	4	
Units: ng/ml				
arithmetic mean (standard deviation)	7.2 (± 26.9)	25.7 (± 26.0)	4.5 (± 23.2)	

Statistical analyses

Statistical analysis title	changes D0-D4 in osteopontin levels
Comparison groups	méthylprednisolone v Rituximab IT v Rituximab IT + IV
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.44
Method	Kruskal-wallis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Période de novembre 2015 à septembre 2019	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	méthylprednisolone
Reporting group description: -	
Reporting group title	Rituximab IT
Reporting group description: -	
Reporting group title	Rituximab IT+IV
Reporting group description: -	

Serious adverse events	méthylprednisolone	Rituximab IT	Rituximab IT+IV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	méthylprednisolone	Rituximab IT	Rituximab IT+IV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
Injury, poisoning and procedural complications			
Lumbar puncture abnormal	Additional description: one lumbar puncture failed after multiple attempts at M6 for a patient of the IV+IT group.		
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2018	Description : Proposition pour les patients inclus dans le groupe contrôle (corticothérapie IV seule), à l'issue de leur suivi, de poursuivre l'étude en étant randomisés dans un des groupes de traitement actif (Rituximab IT ou Rituximab IT+IV) Reason : Depuis le début de cette étude, le contexte thérapeutique s'est modifié en raison de la mise sur le marché de traitements de la forme progressive (biotine) ou d'une utilisation croissante off-label du Rituximab IV. Pour des raisons éthiques évidentes, nous souhaitons proposer aux patients du groupe contrôle (corticoïdes IV seuls) de pouvoir bénéficier secondairement, c'est à dire dans l'année suivant l'inclusion, d'un des traitements de l'étude (Rituximab IT ou Rituximab IT+IV). Ainsi ces patients seraient leurs propres témoins dans le cadre de l'étude.

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/33763241