



Clinical trial results:

Traitement de l'insuffisance surrénale secondaire à un traumatisme crânien grave.

Etude multicentrique, contrôlée, randomisée portant sur un médicament.

- Etude Corti-TC"

Summary

EudraCT number	2010-019178-33
Trial protocol	FR
Global end of trial date	06 December 2013

Results information

Result version number	v1 (current)
This version publication date	08 September 2022
First version publication date	08 September 2022

Trial information

Trial identification

Sponsor protocol code	BRD/10/1-L
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01093261
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Nantes
Sponsor organisation address	5 allée de l'île gloriante, Nantes, France,
Public contact	Anne Omnes, CHU de Nantes, +33 0253482835, bp-prom-regl@chu-nantes.fr
Scientific contact	Anne Omnes, CHU de Nantes, +33 0253482835, bp-prom-regl@chu-nantes.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	25 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2013
Global end of trial reached?	Yes
Global end of trial date	06 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

L'objectif principal est de tester, dans une population de patients traumatisés crâniens l'efficacité d'un traitement de l'IS par hydrocortisone et fludrocortisone sur la prévention des pneumopathies nosocomiales à J28.

Protection of trial subjects:

Patients were informed in complete and faithful terms and in understandable language of the objectives and constraints of the study, the potential risks, the required observation and safety measures, and their right to refuse to participate in the study or to revoke their consent at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2010
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: 328
Worldwide total number of subjects	328
EEA total number of subjects	328

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)	328
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The recruitment is carried out from the hospital reception of head trauma patients with severity criteria. According to the local organization of the investigating centers, the selection took place: in the emergency department or in the anesthesia and intensive care department.

Period 1

Period 1 title	Period 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

treatment versus Placebo

All members of the surgical unit, including the anesthesiologist and surgeon, will remain blind to the assigned treatment group as well as the patient

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Treatment
------------------	-----------

Arm description:

Hydrocortisone : ivse : 200 mg/j pendant 10 jours + po :fludrocortisone 50 microg/j.

Arm type	Experimental
Investigational medicinal product name	Hydrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

Continuous intravenous administration at a dose of 200 mg/day for 10 days

Investigational medicinal product name	Fludrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

The dose of 50 µg / day during the stay in intensive care (10 days maximum)

Arm title	Placebo
------------------	---------

Arm description:

Excipients : phosphate disodique, phosphate monosodique

Arm type	Placebo
Investigational medicinal product name	Placebo de l'hydrocortisone : phosphate disodique, phosphate monosodique
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion

Routes of administration	Concentrate for solution for infusion
Dosage and administration details:	
Continuous intravenous administration at a dose of 200 mg/day	
Investigational medicinal product name	Placebo de la Fludrocortisone : cellulose microcristalline, magnésium stéarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

Once-daily enteral administration

Number of subjects in period 1	Treatment	Placebo
Started	165	163
Completed	165	163

Baseline characteristics

Reporting groups

Reporting group title	Period 1 (overall period)
-----------------------	---------------------------

Reporting group description: -

Reporting group values	Period 1 (overall period)	Total	
Number of subjects	328	328	
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)	328	328	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
18-65			
Units: years			
arithmetic mean	36.05		
full range (min-max)	15 to 65	-	
Gender categorical			
Units: Subjects			
Female	54	54	
Male	274	274	

Subject analysis sets

Subject analysis set title	Groupe treatment
----------------------------	------------------

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

The main analysis of the primary outcome used a multivariate Cox proportional hazards model that included 2 predefined covariates: mechanism, Glasgow coma score, age, and arterial pressure (MGAP) score and Glasgow Coma Scale (GCS) score.

Subject analysis set title	Traitement placebo
----------------------------	--------------------

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

The main analysis of the primary outcome used a multivariate Cox proportional hazards model that included 2 predefined covariates: mechanism, Glasgow coma score, age, and arterial pressure (MGAP) score and Glasgow Coma Scale (GCS) score.

Reporting group values	Groupe treatment	Traitement placebo	
Number of subjects	165	163	

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)	165	163	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
18-65			
Units: years			
arithmetic mean	36	31	
full range (min-max)	24 to 49	22 to 47	
Gender categorical			
Units: Subjects			
Female	27	27	
Male	138	136	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: Hydrocortisone : ivse : 200 mg/j pendant 10 jours + po :fludrocortisone 50 microg/j.	
Reporting group title	Placebo
Reporting group description: Excipients : phosphate disodique, phosphate monosodique	
Subject analysis set title	Groupe treatment
Subject analysis set type	Full analysis
Subject analysis set description: The main analysis of the primary outcome used a multivariate Cox proportional hazards model that included 2 predefined covariates: mechanism, Glasgow coma score, age, and arterial pressure (MGAP) score and Glasgow Coma Scale (GCS) score.	
Subject analysis set title	Traitement placebo
Subject analysis set type	Full analysis
Subject analysis set description: The main analysis of the primary outcome used a multivariate Cox proportional hazards model that included 2 predefined covariates: mechanism, Glasgow coma score, age, and arterial pressure (MGAP) score and Glasgow Coma Scale (GCS) score.	

Primary: hazard ratio for HAP at day 28

End point title	hazard ratio for HAP at day 28
End point description: The first primary endpoint was the comparison of the rates of Nosocomial Pneumonia in the first 28 days after the trauma, i.e., during the period most at risk of developing this complication, between the two groups (hydrocortisone + fludrocortisone versus double placebo) in patients with adrenal insufficiency criteria.	
End point type	Primary
End point timeframe: 28 days	

End point values	Groupe treatment	Traitement placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	163		
Units: pourcent	165	163		

Statistical analyses

Statistical analysis title	Rates of Nosocomial Pneumonia in the first 28 days
Statistical analysis description: The final analysis will be conducted on a modified intention-to-treat (mITT) basis and will be performed as soon as the study has been stopped. It will be performed only on patients with criteria of adrenal insufficiency at the initial assessment. The mITT analysis is therefore defined a priori and is made necessary by the urgency of initiating study treatment when the results of the hormonal assessment are not yet available. results of the hormonal assessment are only obtained in 48 hours.	
Comparison groups	Groupe treatment v Traitement placebo

Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.07
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.03
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

They should be reported immediately (within 24 hours of its detection by the investigator) to the sponsor.

Adverse event reporting additional description:

Annual safety report once a year.

Pregnancy, overdose, misuse, errors or risk of medication errors make the subject of a report to the sponsor by the investigator even if there are no adverse reactions.

Some non-serious adverse events may be declared to the proponent (--> protocole).

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	15
--------------------	----

Reporting groups

Reporting group title	Traitement
-----------------------	------------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Serious adverse events	Traitement	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 165 (13.33%)	24 / 163 (14.72%)	
number of deaths (all causes)	24	20	
number of deaths resulting from adverse events	21	20	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	5 / 165 (3.03%)	5 / 163 (3.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 5	0 / 5	
Vascular disorders			
vascular disorders			
subjects affected / exposed	1 / 165 (0.61%)	2 / 163 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiac disorders			
Cardiac disorders			

subjects affected / exposed	3 / 165 (1.82%)	4 / 163 (2.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 3	
General disorders and administration site conditions			
Général disorders and administration site conditions			
subjects affected / exposed	10 / 165 (6.06%)	5 / 163 (3.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 10	0 / 5	
Immune system disorders			
Trouble du système immunitaire			
subjects affected / exposed	1 / 165 (0.61%)	4 / 163 (2.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
infections and infestations			
subjects affected / exposed	1 / 165 (0.61%)	3 / 163 (1.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 3	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Traitement	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 165 (3.64%)	6 / 163 (3.68%)	
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	0 / 165 (0.00%)	1 / 163 (0.61%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Général disorders and administration site conditions			
subjects affected / exposed	4 / 165 (2.42%)	2 / 163 (1.23%)	
occurrences (all)	0	0	
Immune system disorders			

Nervous system disorders subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 0	0 / 163 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Respiratory disorders and administration subjects affected / exposed occurrences (all)	1 / 165 (0.61%) 0	0 / 163 (0.00%) 0	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	1 / 163 (0.61%) 0	
Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0	2 / 163 (1.23%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2010	Adding centers
22 February 2011	Adding centers
31 May 2011	Adding centers
25 October 2011	Adding centers
29 November 2011	Suppression of centers
21 June 2012	Study extension
23 October 2012	Change of investigators

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/25066331>