Clinical trial results:
Evaluation de l'efficacité d'une corticothérapie à faible dose, associée à l'acide mycophénolique (Myfortic) dans le traitement d'attaque du syndrome néphrotique à lésions glomérulaires minimes de l'adulte. Etude MSN

Evaluation of Low Dose Corticosteroids Efficiency, Associated With Myfortic ® in the Treatment of Nephrotic Syndrome (MSN)

Summary

EudraCT number	2009-011170-15
Trial protocol	FR
Global end of trial date	10 November 2015

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	P071226

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01197040
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS
Sponsor organisation address	4 Avenue Victoria, PARIS, France, 75004
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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	05 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2014
Global end of trial reached?	Yes
Global end of trial date	10 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

L'objectif principal est de comparer le taux de rémission complète à 4 semaines, obtenu sous corticoïdes seuls à pleine dose, 1mg/kg/j, par rapport au groupe sous l'association faible dose de corticoïdes 0,5 mg/kg/j et Myfortic® à la dose de 1440 mg/j.

evaluate efficacy of low dose steroid combined with mycophenolic acid (Myfortic) versus high dose steroid, at 4 weeks, in inducing remission in adults with minimal change nephrotic syndrome (MCNS)

Protection of trial subjects:

The study was carried out in accordance with the Declaration of Helsinki and the International Conference on Harmonization of Good Clinical Practice.The trial protocol was approved by the institutional review board (Comité de Protection des Personnes Ilede-France II # 2009-04-02.). Written informed consent was obtained from all patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2009
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: 117
Worldwide total number of subjects	117
EEA total number of subjects	117

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)	100
From 65 to 84 years	16
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Between November 2009 and June 2014, 117 patients met the inclusion criteria for this study

Pre-assignment

Screening details:

minimal change nephrotic syndrome in adults (MCNS) was based on appropriate renal biopsy examination

Period 1

Period 1 title	Overall trail (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental

Arm description:

Association of low dose corticosteroids 0.5 mg/kg/day and Myfortic ® at a dose of 1440 mg/day.

Arm type	Experimental
Investigational medicinal product name	mycophenolate sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

enteric-coated mycophenolate sodium 720 mg twice daily for 24 weeks

Investigational medicinal product name	prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone (0.5 mg/kg/day, maximum 40 mg/day) for 24 weeks

Arm title	Active Comparator

Arm description:

Monotherapy: treatment with only corticosteroids at doses usually 1 mg/kg/day,following a plan of reduction based on the degree of remission.

Arm type	Active comparator
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

oral prednisone (1 mg/kg/day, maximum 80 mg/day) for 24 weeks

Number of subjects in period 1[1]	Experimental	Active Comparator
Started	58	58
week 4	52	57
Completed	52	57
Not completed	6	1
Adverse event, serious fatal	1	1
Consent withdrawn by subject	1	-
outcome not available	4	-

Notes:

[1] - 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: 1 Consent withdrawal before randimazation, thus Excluded (n = 1)

Baseline characteristics

Reporting groups	
Reporting group title	Experimental
Reporting group description:	
Association of low dose corticosteroids 0.5 mg/kg/day and Myfortic ® at a dose of 1440 mg/day.	

Reporting group title	Active Comparator
Reporting group description:	
Monotherapy: treatment with only corticosteroids at doses usually 1 mg/kg/day,following a plan of reduction based on the degree of remission.	

Reporting group values	Experimental	Active Comparator	Total
Number of subjects	58	58	116
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	47.4	41.6	
inter-quartile range (Q1-Q3)	31.3 to 61.1	31.6 to 55.4	-
Gender categorical			
Units: Subjects			
Female	22	29	51
Male	36	29	65

End points

End points reporting groups

Reporting group title	Experimental

Reporting group description:

Association of low dose corticosteroids 0.5 mg/kg/day and Myfortic ® at a dose of 1440 mg/day.

Reporting group title	Active Comparator

Reporting group description:

Monotherapy: treatment with only corticosteroids at doses usually 1 mg/kg/day,following a plan of reduction based on the degree of remission.

Primary: Complete Remission rate after 4 weeks of treatment

End point title	Complete Remission rate after 4 weeks of treatment

End point description:

The primary endpoint was the complete remission (CR) rate after 4 weeks of treatment.
Complete remission was defined as urine protein-to-creatinine ratio (UPCR) < 30 mg/mmol or trace or negative results on repeat urine albumin dipstick tests, associated with an albumin level > 30 g/l.

End point type	Primary

End point timeframe:

4 weeks

End point values	Experimental	Active Comparator		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[1]	57		
Units: subjects	37	33		

Notes:

[1] - Analysis according to the intent-to-treat principle after imputation of missing data.

Statistical analyses

Statistical analysis title	Primary outcome, Week 4 Complete remission, ITT

Statistical analysis description:

Analysis according to the intent-to-treat principle after imputation of missing data. A multiple imputation approach was used for
handling missing data and limits attrition bias. We used the multiple multivariate imputation by chained equations procedure with the
missing at random assumption. We used both baseline covariates and outcome to impute the missing data values, and we independently
analyzed 20 copies of the data.

Comparison groups	Experimental v Active Comparator

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were followed up for 1 year after randomization (week 52). They attended follow-up visits every 2 weeks during the first 8 weeks after randomization, and then every 4 weeks until week 24, with a final visit at week 52.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Experimental

Reporting group description:

Association of low dose corticosteroids 0.5 mg/kg/day and Myfortic ® at a dose of 1440 mg/day.

Reporting group title	Active Comparator

Reporting group description:

Monotherapy: treatment with only corticosteroids at doses usually 1 mg/kg/day,following a plan of reduction based on the degree of remission.

Serious adverse events	Experimental	Active Comparator	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 58 (15.52%)	9 / 58 (15.52%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	2	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Suspicion of lung cancer			
subjects affected / exposed	0 / 58 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Hemorrhagic shock	Additional description: Two patients died between inclusion and primary outcome evaluation, due to a post-renal biopsy hemorrhage for 1 patient from experimental group and hemorrhagic shock related to stomach ulcer for 1 patient from control group.		
subjects affected / exposed	1 / 58 (1.72%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Gastrointestinal disorders			
Diarrhea			

subjects affected / exposed	0 / 58 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary embolism			
subjects affected / exposed	1 / 58 (1.72%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 58 (1.72%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Behavioral disorders			
subjects affected / exposed	1 / 58 (1.72%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
New-onset glucose intolerance	Additional description: New-onset glucose intolerance occurred in 2 patients from the control group, and none of the patients from the test group.		
subjects affected / exposed	0 / 58 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone fracture	Additional description: Two patients from the control group suffered bone fractures.		
subjects affected / exposed	0 / 58 (0.00%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock	Additional description: 1 patient from experimental group (39 weeks after inclusion) and 2 patients from control group (8 and 13 weeks after inclusion). The main cause of death in these patients was necrotizing fasciitis and severe community-acquired pneumonia in 2 cases		
subjects affected / exposed	1 / 58 (1.72%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	

Infectious episodes	Additional description: Nonfatal infectious episodes consisted in acute pyelonephritis in 3 patients, acute prostatitis in 1 case, viral diarrhea in 2 and an abscess after surgical intervention for carpal tunnel syndrome in the last.		
subjects affected / exposed	5 / 58 (8.62%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	1 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.01 %

Non-serious adverse events	Experimental	Active Comparator	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 58 (91.38%)	51 / 58 (87.93%)	
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	53 / 58 (91.38%)	51 / 58 (87.93%)	
occurrences (all)	251	238	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2009	MS1 1 Exclusion criteria modification; addition of fasting blood glucose assay at D1 ; modification of visit partial examination ; 2 New investigation sites added; principal investigator modification at Troyes Hospital
14 December 2009	MS2 Principal investigator modification at Necker Hospital (Paris, 75, France)
07 June 2010	MS3 Visit organisation modification; 1 inclusion criteria and 2 exclusion criteria modification; modification of forbidden drugs and treatment during protocol ; modification of synoptic table ; 3 investigation sites added
02 August 2010	MS4 Investigation site added
11 March 2013	MS5 Inclusion period extension (+6 months)
16 December 2013	MS6 Inclusion period extension (+12months) ; number of subjects needed decreased
02 February 2015	MS7 Inclusion period extension ; number of patients justified
09 November 2015	MS8 Principal investigator modification in 3 investigation sites ; declaration of number of patients included

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/30385039