Clinical trial results:
The effects of acetylsalicylic acid on immunoparalysis following human endotoxemia.

Summary

EudraCT number	2016-001971-61
Trial protocol	NL
Global end of trial date	02 November 2016

Results information

Result version number	v2 (current)
This version publication date	23 September 2020
First version publication date	01 February 2020
Version creation reason	• New data added to full data set first time did not work, new attempt

Trial information

Trial identification

Sponsor protocol code	SALYCENDO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02922673
WHO universal trial number (UTN)	-
Other trial identifiers	CMO number: 2016-2550, ABR: 57410.091.16

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein 10, Nijmegen, Netherlands,
Public contact	Research IC, office of Guus Leijte, Radboudumc, +31 0243668420, guus.leijte@radboudumc.nl
Scientific contact	Research IC, office of Guus Leijte, Radboudumc, +31 0243668420, guus.leijte@radboudumc.nl

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	08 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2016
Global end of trial reached?	Yes
Global end of trial date	02 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To determine whether acetylsalicylic acid treatment can reverse endotoxin tolerance, which is expressed as a decrease in pro-inflammatory cytokine levels between the first and second endotoxin challenge.

Protection of trial subjects:

Subjects were carefully instructed during the trial.

Background therapy:

All subjects underwent an endotoxin challenge twice, with an interval of one week in-between.

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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	Netherlands: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy male subjects will be recruited by posters at several faculties on the campus of the Radboud University Nijmegen and using the Radboud University website.

Pre-assignment

Screening details:

All subjects gave written informed consent and medical history, physical examination, laboratory tests, and a 12-leads electrocardiogram did not reveal any abnormalities.

Period 1

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

Blinding implementation details:

Subjects will be randomly allocated to prophylaxis, treatment or control group using a sealed envelope opened by a research nurse not involved in the study. The allocated study medication will be delivered in identical packs, as identical capsules, by an independent nurse. The randomization will only be broken only if necessary for safety reasons. The investigators and participating subjects will be blinded for treatment allocation until all study endpoint are known and the database is locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description:

control group receiving placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Enteral use

Dosage and administration details:

Oral use

Arm title	Treatment group

Arm description:

80 mg acetylsalicylic acid daily for the 7-d period in-between both endotoxin challenges

Arm type	Experimental
Investigational medicinal product name	Acetylsalicylic acid
Investigational medicinal product code	PR1
Other name	Aspirin
Pharmaceutical forms	Dispersible tablet
Routes of administration	Enteral use

Dosage and administration details:

80 milligram per day, oral use

Investigational medicinal product name	Placebo
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Enteral use

Dosage and administration details:

Oral use

Arm title	Prophylaxis group

Arm description:

80 mg acetylsalicylic acid daily for a 14-d period,starting 7 d before the first endotoxin challenge

Arm type	Experimental
Investigational medicinal product name	Acetylsalicylic acid
Investigational medicinal product code	PR1
Other name	Aspirin
Pharmaceutical forms	Dispersible tablet
Routes of administration	Enteral use

Dosage and administration details:

80 milligram per day, oral use

Number of subjects in period 1	Control group	Treatment group	Prophylaxis group
Started	10	10	10
Completed	10	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Control group
Reporting group description:	
control group receiving placebo	
Reporting group title	Treatment group
Reporting group description:	
80 mg acetylsalicylic acid daily for the 7-d period in-between both endotoxin challenges	
Reporting group title	Prophylaxis group
Reporting group description:	
80 mg acetylsalicylic acid daily for a 14-d period,starting 7 d before the first endotoxin challenge	

Reporting group values	Control group	Treatment group	Prophylaxis group
Number of subjects	10	10	10
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	22	23	22
standard deviation	± 2	± 3	± 3
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	10	10	10

Reporting group values	Total		
Number of subjects	30		
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			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	0		
Male	30		

End points

End points reporting groups	
Reporting group title	Control group
Reporting group description: control group receiving placebo	
Reporting group title	Treatment group
Reporting group description: 80 mg acetylsalicylic acid daily for the 7-d period in-between both endotoxin challenges	
Reporting group title	Prophylaxis group
Reporting group description: 80 mg acetylsalicylic acid daily for a 14-d period,starting 7 d before the first endotoxin challenge	

Primary: Area under the TNFa concentration time curve	
End point title	Area under the TNFa concentration time curve
End point description: Area under the TNFa concentration time curve	
End point type	Primary
End point timeframe: TNF concentration is determined on challenge days from baseline (just before endotoxin administration) up to 8 hours post challenge.	

End point values	Control group	Treatment group	Prophylaxis group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: pg/mL				
arithmetic mean (standard error)	23590 (± 4384)	36086 (± 6648)	33257 (± 8312)	

Statistical analyses

Statistical analysis title	Two-way ANOVA for primary endpoint
Statistical analysis description: Two-way ANOVA for cytokine concentration data over time.	
Comparison groups	Treatment group v Control group v Prophylaxis group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigator will report all SAEs to the sponsor without undue delay after obtaining knowledge of the events.

Adverse event reporting additional description:

The sponsor will report the SAEs through the web portal ToetsingOnline to the accredited METC that approved the protocol.

Assessment type	Non-systematic

Dictionary used

Dictionary name	ToetsingOnline
Dictionary version	1

Reporting groups

Reporting group title	Did not have any AE during this study

Reporting group description:

Did not have any AE during this study

Serious adverse events	Did not have any AE during this study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Did not have any AE during this study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Investigations			
Did not have any AE during this study	Additional description: Did not have any AE during this study.		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported