



## Clinical trial results: PREVENTING CHOLESTASIS IN PREMATURE INFANTS USING SMOFLIPID

### Summary

EudraCT number	2011-005456-33
Trial protocol	AT
Global end of trial date	17 November 2017

### Results information

Result version number	v1 (current)
This version publication date	29 April 2018
First version publication date	29 April 2018

### Trial information

#### Trial identification

Sponsor protocol code	v 1.3
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01585935
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Medical University Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Dr. Repa, Medical University Vienna, andreas.repa@meduniwien.ac.at
Scientific contact	Dr. Repa, Medical University Vienna, andreas.repa@meduniwien.ac.at

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	13 November 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 November 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare a mixed parenteral lipid emulsion containing fish oil (SMOFlipid®) with a soybean oil based lipid emulsion (Intralipid®) for its effect on the occurrence of parenteral nutrition associated cholestasis in extremely low birth weight infants.

Protection of trial subjects:

Only routine blood samples and testing was used.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 230
Worldwide total number of subjects	230
EEA total number of subjects	230

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	230
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 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This double-blind randomized trial of 230 ELBW infants was recruiting from June 2012 to July 2015 in a single center in Vienna, Austria.

### Pre-assignment

Screening details:

Eligible participants were preterm Infants born below 1 kg and admitted before 24 hours of life. Infants with cholestasis (conjugated bilirubin > 1.5 mg/dL [25 µmol/L]) before intervention and higher order multiples were not eligible. Infants with conditions associated with cholestasis independent of parenteral nutrition were excluded.

### Pre-assignment period milestones

Number of subjects started	230
Number of subjects completed	230

### Period 1

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

Blinding implementation details:

The investigational products were visually indistinguishable white fluids.

The glass containers were masked using opaque labels designated "A" or "B."

Labels were resistant to detachment and discarded containers were controlled for blinding integrity.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	SMOF

Arm description:

Infants received the mixed lipid emulsion (SMOFlipid)

Arm type	Experimental
Investigational medicinal product name	SMOFlipid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for suspension for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

1-3 g /kg/d continuous over 24 hours

<b>Arm title</b>	Intralipid
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Arm description:

Patients received the soybean oil based lipid emulsion

Arm type	Active comparator
Investigational medicinal product name	Intralipid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intravenous drip use

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Dosage and administration details:  
1-3 g /kg/d continuous over 24 hours

<b>Number of subjects in period 1</b>	SMOF	Intralipid
Started	113	117
Completed	113	117

## Baseline characteristics

### Reporting groups

Reporting group title	SMOF
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Reporting group description:

Infants received the mixed lipid emulsion (SMOFlipid)

Reporting group title	Intralipid
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Reporting group description:

Patients received the soybean oil based lipid emulsion

Reporting group values	SMOF	Intralipid	Total
Number of subjects	113	117	230
Age categorical			
Infants are preterm infants born below 1 kg birth weight			
Units: Subjects			
Preterm newborn infants (gestational age < 37 wks)	113	117	230
Gender categorical			
Units: Subjects			
Female	49	44	93
Male	64	73	137

## End points

### End points reporting groups

Reporting group title	SMOF
Reporting group description: Infants received the mixed lipid emulsion (SMOFlipid)	
Reporting group title	Intralipid
Reporting group description: Patients received the soybean oil based lipid emulsion	

### Primary: Cholestasis

End point title	Cholestasis
End point description:	
End point type	Primary
End point timeframe: Birth to discharge from hospital	

End point values	SMOF	Intralipid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	113		
Units: Subjects	11	18		

### Statistical analyses

Statistical analysis title	Univariate Analysis
Comparison groups	SMOF v Intralipid
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From allocation to discharge from hospital

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	2.0
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### Reporting groups

Reporting group title	SMOF
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Reporting group description:

Infants received the mixed lipid emulsion (SMOFlipid)

Reporting group title	Intralipid
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Reporting group description:

Patients received the soybean oil based lipid emulsion

Serious adverse events	SMOF	Intralipid	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 110 (27.27%)	21 / 113 (18.58%)	
number of deaths (all causes)	8	8	
number of deaths resulting from adverse events	1	0	
Nervous system disorders			
Intraventricular haemorrhage neonatal	Additional description: Severe Grade 3/4		
subjects affected / exposed	12 / 110 (10.91%)	9 / 113 (7.96%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinopathy of prematurity	Additional description: Severe retinopathy of prematurity requiring treatment		
subjects affected / exposed	9 / 110 (8.18%)	10 / 113 (8.85%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Necrotising enterocolitis neonatal			
subjects affected / exposed	8 / 110 (7.27%)	8 / 113 (7.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

<b>Non-serious adverse events</b>	<b>SMOF</b>	<b>Intralipid</b>	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 110 (100.00%)	113 / 113 (100.00%)	
Cardiac disorders			
Persistent foetal circulation	Additional description: PDA requiring treatment		
subjects affected / exposed	56 / 110 (50.91%)	68 / 113 (60.18%)	
occurrences (all)	56	68	
Bradycardia neonatal			
subjects affected / exposed	110 / 110 (100.00%)	113 / 113 (100.00%)	
occurrences (all)	110	113	
Respiratory, thoracic and mediastinal disorders			
Bronchopulmonary dysplasia	Additional description: Oxygen need after 36 weeks PMA		
subjects affected / exposed	19 / 110 (17.27%)	21 / 113 (18.58%)	
occurrences (all)	19	21	
Pulmonary hypertension			
subjects affected / exposed	23 / 110 (20.91%)	31 / 113 (27.43%)	
occurrences (all)	23	31	
Infections and infestations			
Sepsis	Additional description: Blood culture positive sepsis		
subjects affected / exposed	24 / 110 (21.82%)	26 / 113 (23.01%)	
occurrences (all)	24	26	
Metabolism and nutrition disorders			
Hyperlipidaemia	Additional description: Triglycerides > 250 mg/dl		
subjects affected / exposed	39 / 110 (35.45%)	38 / 113 (33.63%)	
occurrences (all)	39	38	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29269199>