Clinical trial results:
Tolerance of virucidal alcohol-based hand rubs - healthy volunteer trial

Summary

EudraCT number	2010-018624-20
Trial protocol	DE
Global end of trial date	17 January 2011

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	OPM-CIC-G-H-0902

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical Center - University of Freiburg
Sponsor organisation address	Breisacherstr. 153, Freiburg, Germany, 79110
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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	22 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2010
Global end of trial reached?	Yes
Global end of trial date	17 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Uncoated viruses such as adenovirus or norovirus are a challenge for infection control strategies since these pathogens are highly resistant to disinfectants. Hand hygiene is accepted to be an essential measure to prevent infections caused by adeno- or norovirus. In case of an adeno- or norovirus infection within the clinical setting it is strongly recommended to use a virucidal hand rub and to exchange conventional hand disinfectants by virucidal ones (German recommendation by the Robert Koch-Institute; www.rki.de). Disadvantage of virucidal hand rubs, however, might be limited skin-tolerability compared to conventional products. This in turn may impair hand hygiene compliance. The aim of this trial is to compare the tolerability of three different virucidal hand rubs and a reference conventional product. This is a cross-over trial with 4 periods.

Protection of trial subjects:

The safety, tolerability and acceptance of hand hygiene preparations impacts on compliance. In Germany, hand rub is classified as a drug, approval of which includes evaluation for efficacy, safety and tolerability. Nonetheless, few systematic scientific trials are available on the safety and tolerability of hand rubs. In particular, comparative data are missing for different preparations and their composition. The results obtained in this work on the safety and tolerability of four different virucidal hand rubs should provide important information to optimize their safety and tolerability.

Background therapy:

none

Evidence for comparator: -

Actual start date of recruitment	21 June 2010
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	Germany: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from students of the Medical Center, University of Freiburg, and nursing students of the Freiburg Academy of Medical Professions. Inclusion criteria were subject's written informed consent, age > 18 years; legal capacity; healthy in body and mind and not under medical treatment at the time of inclusion.

Pre-assignment

Screening details:

healthy volunteers

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	R - P1 - P3 - P2 / Period 1

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 1 received R in period 1.

Arm type	Active comparator
Investigational medicinal product name	Softa-Man® pure
Investigational medicinal product code	60998.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P1 - P2 - R - P3 / Period 1

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received P1 in period 1.

Arm type	Active comparator
Investigational medicinal product name	Softa-Man(R) acute
Investigational medicinal product code	61000.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P2 - P3 - P1 - R / Period 1

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received P2 in period 1.

Arm type	Active comparator
Investigational medicinal product name	Sterillium(R) virugard
Investigational medicinal product code	13814.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P3 - R - P2 - P1 / Period 1

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received P3 in period 4.

Arm type	Active comparator
Investigational medicinal product name	Manorapid(R) Synergy
Investigational medicinal product code	57801.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Number of subjects in period 1	R - P1 - P3 - P2 / Period 1	P1 - P2 - R - P3 / Period 1	P2 - P3 - P1 - R / Period 1
Started	5	6	6
Completed	5	6	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	P3 - R - P2 - P1 / Period 1
Started	5
Completed	4
Not completed	1
Consent withdrawn by subject	1

Period 2

Period 2 title	Intervention 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Blinding of products were done by the pharmacy using a working bench.

Arms

Are arms mutually exclusive?	Yes
Arm title	R - P1 - P3 - P2 / Period 2

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 1 received P1 in period 2.

Arm type	Active comparator
Investigational medicinal product name	Softa-Man(R) acute
Investigational medicinal product code	61000.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P1 - P2 - R - P3 / Period 2

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received P2 in period 2.

Arm type	Active comparator
Investigational medicinal product name	Sterillium(R) virugard
Investigational medicinal product code	13814.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P2 - P3 - P1 - R / Period 2

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received P3 in period 2.

Arm type	Active comparator
Investigational medicinal product name	Manorapid(R) Synergy
Investigational medicinal product code	57801.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P3 - R - P2 - P1 / Period 2

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received R in period 2.

Arm type	Active comparator
Investigational medicinal product name	Softa-Man® pure
Investigational medicinal product code	60998.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Number of subjects in period 2	R - P1 - P3 - P2 / Period 2	P1 - P2 - R - P3 / Period 2	P2 - P3 - P1 - R / Period 2
Started	5	6	6
Completed	5	5	6
Not completed	0	1	0
Consent withdrawn by subject	-	1	-
Joined	0	0	0
Restarting	-	-	-

Number of subjects in period 2	P3 - R - P2 - P1 / Period 2
Started	4
Completed	4
Not completed	1
Consent withdrawn by subject	1
Joined	1
Restarting	1

Period 3

Period 3 title	Intervention 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Blinding of products were done by the pharmacy using a working bench.

Arms

Are arms mutually exclusive?	Yes
Arm title	R - P1 - P3 - P2 / Period 3

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 1 received P3 in period 3.

Arm type	Active comparator
Investigational medicinal product name	Manorapid(R) Synergy
Investigational medicinal product code	57801.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P1 - P2 - R - P3 / Period 3

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received R in period 3.

Arm type	Experimental
Investigational medicinal product name	Softa-Man® pure
Investigational medicinal product code	60998.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P2 - P3 - P1 - R / Period 3

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received P1 in period 3.

Arm type	Experimental
Investigational medicinal product name	Softa-Man(R) acute
Investigational medicinal product code	61000.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P3 - R - P2 - P1 / Period 3

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received P2 in period 3.

Arm type	Active comparator
Investigational medicinal product name	Sterillium(R) virugard
Investigational medicinal product code	13814.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Number of subjects in period 3	R - P1 - P3 - P2 / Period 3	P1 - P2 - R - P3 / Period 3	P2 - P3 - P1 - R / Period 3
Started	5	5	6
Completed	3	5	5
Not completed	2	1	1
Consent withdrawn by subject	2	1	1
Joined	0	1	0
Restarted	-	1	-
Restarting	-	-	-

Number of subjects in period 3	P3 - R - P2 - P1 / Period 3
Started	4
Completed	4
Not completed	1
Consent withdrawn by subject	1
Joined	1
Restarted	-
Restarting	1

Period 4

Period 4 title	Intervention 4
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Blinding procedure took place within the pharmacy.

Arms

Are arms mutually exclusive?	Yes
Arm title	R - P1 - P3 - P2 / Period 4

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 1 received P2 in period 4.

Arm type	Experimental
Investigational medicinal product name	Sterillium(R) virugard
Investigational medicinal product code	13814.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Arm title	P1 - P2 - R - P3 / Period 4

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received P3 in period 4.

Arm type	Experimental
Investigational medicinal product name	Manorapid(R) Synergy
Investigational medicinal product code	57801.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P2 - P3 - P1 - R / Period 4

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received R in period 4.

Arm type	Experimental
Investigational medicinal product name	Softa-Man® pure
Investigational medicinal product code	60998.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (=total application of 90 mL per day).

Arm title	P3 - R - P2 - P1 / Period 4

Arm description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received P1 in period 4.

Arm type	Active comparator
Investigational medicinal product name	Softa-Man(R) acute
Investigational medicinal product code	61000.00.00
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

4 days with 30 hand disinfections each day; 3 mL per hand disinfection (= total application of 90 mL per day).

Number of subjects in period 4	R - P1 - P3 - P2 / Period 4	P1 - P2 - R - P3 / Period 4	P2 - P3 - P1 - R / Period 4
Started	3	5	5
Completed	5	5	4
Not completed	0	1	2
Consent withdrawn by subject	-	1	2
Joined	2	1	1
Restarted	2	1	1

Number of subjects in period 4	P3 - R - P2 - P1 / Period 4
Started	4
Completed	5
Not completed	0
Consent withdrawn by subject	-
Joined	1
Restarted	1

Baseline characteristics

Reporting groups	
Reporting group title	R - P1 - P3 - P2 / Period 1
Reporting group description:	
Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period. Arm 1 received R in period 1.	
Reporting group title	P1 - P2 - R - P3 / Period 1
Reporting group description:	
Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period. Arm 2 received P1 in period 1.	
Reporting group title	P2 - P3 - P1 - R / Period 1
Reporting group description:	
Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period. Arm 3 received P2 in period 1.	
Reporting group title	P3 - R - P2 - P1 / Period 1
Reporting group description:	
Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period. Arm 4 received P3 in period 4.	

Reporting group values	R - P1 - P3 - P2 / Period 1	P1 - P2 - R - P3 / Period 1	P2 - P3 - P1 - R / Period 1
Number of subjects	5	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	23	26.5	24.5
inter-quartile range (Q1-Q3)	23 to 24	23.5 to 31	23.25 to 25.75
Gender categorical Units: Subjects			
Female	3	5	3
Male	2	1	3

Reporting group values	P3 - R - P2 - P1 /	Total	

	Period 1		
Number of subjects	5	22	
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)	5	22	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	25		
inter-quartile range (Q1-Q3)	22 to 26	-	
Gender categorical Units: Subjects			
Female	4	15	
Male	1	7	

Subject analysis sets

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

All the analyses were performed in the safety population, including subjects who had started treatment in at least one period.

Reporting group values	Safety analysis		
Number of subjects	22		
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)	22		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
median	25		
inter-quartile range (Q1-Q3)	23 to 26		

Gender categorical Units: Subjects			
Female	15		
Male	7		

End points

End points reporting groups

Reporting group title	R - P1 - P3 - P2 / Period 1

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 1 received R in period 1.

Reporting group title	P1 - P2 - R - P3 / Period 1

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 2 received P1 in period 1.

Reporting group title	P2 - P3 - P1 - R / Period 1

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 3 received P2 in period 1.

Reporting group title	P3 - R - P2 - P1 / Period 1

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 4 received P3 in period 4.

Reporting group title	R - P1 - P3 - P2 / Period 2

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 1 received P1 in period 2.

Reporting group title	P1 - P2 - R - P3 / Period 2

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 2 received P2 in period 2.

Reporting group title	P2 - P3 - P1 - R / Period 2

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 3 received P3 in period 2.

Reporting group title	P3 - R - P2 - P1 / Period 2

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 4 received R in period 2.

Reporting group title	R - P1 - P3 - P2 / Period 3

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout period.
Arm 1 received P3 in period 3.

Reporting group title	P1 - P2 - R - P3 / Period 3

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received R in period 3.

Reporting group title	P2 - P3 - P1 - R / Period 3

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received P1 in period 3.

Reporting group title	P3 - R - P2 - P1 / Period 3

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received P2 in period 3.

Reporting group title	R - P1 - P3 - P2 / Period 4

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 1 received P2 in period 4.

Reporting group title	P1 - P2 - R - P3 / Period 4

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 2 received P3 in period 4.

Reporting group title	P2 - P3 - P1 - R / Period 4

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 3 received R in period 4.

Reporting group title	P3 - R - P2 - P1 / Period 4

Reporting group description:

Healthy volunteers received three different virucidal hand rubs (P1-P3) and a reference product (R) in randomized sequence over a period of four days each with a washout
period.
Arm 4 received P1 in period 4.

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

All the analyses were performed in the safety population, including subjects who had started treatment in at least one period.

Primary: Transepidermal water loss (TEWL)

End point title	Transepidermal water loss (TEWL)

End point description:

The primary endpoint was skin barrier function measured by transepidermal water loss (TEWL) in g/hm2 at the end of the 4-day application period.

End point type	Primary

End point timeframe:

Measured at the end of the 4-day application period

End point values	R - P1 - P3 - P2 / Period 1	P1 - P2 - R - P3 / Period 1	P2 - P3 - P1 - R / Period 1	P3 - R - P2 - P1 / Period 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	6	4
Units: g/hm2				
arithmetic mean (standard deviation)	26.93 (± 5.07)	21.26 (± 4.92)	19.25 (± 6.17)	13.93 (± 3.39)

End point values	R - P1 - P3 - P2 / Period 2	P1 - P2 - R - P3 / Period 2	P2 - P3 - P1 - R / Period 2	P3 - R - P2 - P1 / Period 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	4
Units: g/hm2				
arithmetic mean (standard deviation)	17.92 (± 2.63)	19.94 (± 9.41)	15.48 (± 3.08)	23.98 (± 6.39)

End point values	R - P1 - P3 - P2 / Period 4	P1 - P2 - R - P3 / Period 4	P2 - P3 - P1 - R / Period 4	P3 - R - P2 - P1 / Period 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	3	4
Units: g/hm2				
arithmetic mean (standard deviation)	13.40 (± 2.72)	20.67 (± 1.33)	23.74 (± 8.20)	28.03 (± 12.99)

End point values	R - P1 - P3 - P2 / Period 3	P1 - P2 - R - P3 / Period 3	P2 - P3 - P1 - R / Period 3	P3 - R - P2 - P1 / Period 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	5
Units: g/hm2				
arithmetic mean (standard deviation)	17.08 (± 5.09)	21.50 (± 6.95)	24.08 (± 3.26)	13.02 (± 2.11)

Statistical analyses

Statistical analysis title	Analysis of TEWL in SAF, P1 vs R

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	R - P1 - P3 - P2 / Period 1 v P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3

	- R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.42
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.33
upper limit	2.26

Notes:

[1] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P1 vs R.

Statistical analysis title	Analysis of TEWL in SAF, P2 vs R

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	R - P1 - P3 - P2 / Period 1 v P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3 - R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.45
upper limit	-3.96

Notes:

[2] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P2 vs R.

Statistical analysis title	Analysis of TEWL in SAF, P3 vs R

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v R - P1

	- P3 - P2 / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3 - R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.45
upper limit	-3.9

Notes:

[3] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P3 vs R.

Statistical analysis title	Analysis of TEWL in SAF, P1 vs P2

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	R - P1 - P3 - P2 / Period 1 v P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3 - R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0013
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.54
upper limit	9.79

Notes:

[4] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P1 vs P2.

Statistical analysis title	Analysis of TEWL in SAF, P1 vs P3

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	R - P1 - P3 - P2 / Period 1 v P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3 - R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.38
upper limit	9.89

Notes:

[5] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P1 vs P3.

Statistical analysis title	Analysis of TEWL in SAF, P2 vs P3

Statistical analysis description:

This is a cross-over trial with 4 periods in 22 patients. The analysis was performed in the safety population (SAF) including all patients who started treatment in at least one of the 4 intervention period.

Comparison groups	R - P1 - P3 - P2 / Period 1 v P1 - P2 - R - P3 / Period 1 v P2 - P3 - P1 - R / Period 1 v P3 - R - P2 - P1 / Period 1 v R - P1 - P3 - P2 / Period 2 v P1 - P2 - R - P3 / Period 2 v P2 - P3 - P1 - R / Period 2 v P3 - R - P2 - P1 / Period 2 v R - P1 - P3 - P2 / Period 4 v P1 - P2 - R - P3 / Period 4 v P2 - P3 - P1 - R / Period 4 v P3 - R - P2 - P1 / Period 4 v R - P1 - P3 - P2 / Period 3 v P1 - P2 - R - P3 / Period 3 v P2 - P3 - P1 - R / Period 3 v P3 - R - P2 - P1 / Period 3
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.99
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.69
upper limit	3.64

Notes:

[6] - The effects of the different agents on TEWL were analyzed in linear models including 'agent', 'period', 'randomized sequence' and baseline measurement as fixed effects, and 'subject within sequence' as random effect. Differences between mean results per agent were estimated with 95% confidence intervals. This is the analysis of P2 vs P3.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Each day during the intervention period the volunteer was questioned about adverse events.	
Adverse event reporting additional description:	
The percentage of subjects experiencing at least one adverse event	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13

Reporting groups	
Reporting group title	P1 Group
Reporting group description:	
P1 = Investigational Product 1: Softa-Man® acute	
Reporting group title	P2 Group
Reporting group description:	
P2 = Investigational Product 2: Sterillium® virugard	
Reporting group title	P3 Group
Reporting group description:	
P3 = Investigational Product 3: Manorapid® Synergy	
Reporting group title	R Reference
Reporting group description:	
R = Reference: Softa-Man® pure	

Serious adverse events	P1 Group	P2 Group	P3 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	R Reference		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	P1 Group	P2 Group	P3 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 21 (85.71%)	5 / 20 (25.00%)	16 / 18 (88.89%)
Injury, poisoning and procedural complications			
Skin injury			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Application site pruritus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	13 / 21 (61.90%)	5 / 20 (25.00%)	14 / 18 (77.78%)
occurrences (all)	13	5	14
Skin reaction			

subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Non-serious adverse events	R Reference		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 18 (55.56%)		
Injury, poisoning and procedural complications			
Skin injury			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Application site pruritus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin exfoliation			

subjects affected / exposed	8 / 18 (44.44%)		
occurrences (all)	8		
Skin reaction			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

none

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26448861