



Clinical trial results:

Phase III, multicentre, randomised, double blind, parallel-group, clinical trial to evaluate the efficacy and safety of a new medicated nail lacquer for the treatment of toenail fungal infection

Summary

EudraCT number	2016-003784-19
Trial protocol	ES LV
Global end of trial date	16 December 2019

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	RJ-CPX01
-----------------------	----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Laboratorio Reig Jofre, SA
Sponsor organisation address	C/Gran Capità, 10, San Joan Despí, Barcelona, Spain, 08970
Public contact	Clinical R&D, Laboratorio Reig Jofre, SA, 0034 93 480 67 10 , Jordi.Picas@reigjofre.com
Scientific contact	Clinical R&D, Laboratorio Reig Jofre, SA, 0034 93 480 67 10 , Jordi.Picas@reigjofre.com

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	21 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2019
Global end of trial reached?	Yes
Global end of trial date	16 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of RJ-0265, in terms of complete cure (defined as complete replacement of the diseased nail by new healthy nail and conversion to negative on Dermatophyte Test Strip (DTS) and on culture), in comparison with placebo, for the treatment of toenail onychomycosis due to dermatophyte fungi, at week 52.

Protection of trial subjects:

The protocol and consent forms were submitted to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent forms (if applicable) after initial IEC/IRB approval were submitted to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki. Local regulations at each participating country were also followed.

Background therapy:

None (not applicable)

Evidence for comparator:

Onytec is the active comparator. Onytec is a currently marketed ciclopirox nail lacquer 80mg/g. The investigational product, RJ-0265, is a new ciclopirox nail lacquer 80 mg/g

Actual start date of recruitment	03 August 2017
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	Spain: 201
Country: Number of subjects enrolled	Latvia: 101
Country: Number of subjects enrolled	Mexico: 79
Worldwide total number of subjects	381
EEA total number of subjects	302

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)	285
From 65 to 84 years	96
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started on 03-Aug-17 (first patient first visit) and finished on 16-Dec-19 (last patient last visit). The countries contributed recruiting patients for this clinical trial: Spain, Latvia and Mexico

Pre-assignment

Screening details:

A total of 1430 subjects were screened to reach 381 analysed for safety, 376 for efficacy and 255 completers

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RJ-0265

Arm description:

RJ-0265 applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

Arm type	Experimental
Investigational medicinal product name	RJ-0265
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Applied once daily (in the evening) as a thin layer

Arm title	Active control (Ony-Tec)
------------------	--------------------------

Arm description:

Ony-Tec applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

Arm type	Active comparator
Investigational medicinal product name	Ony-Tec
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Applied once daily (in the evening) as a thin layer

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

Arm description:

Applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

Arm type	Placebo
----------	---------

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Applied once daily (in the evening) as a thin layer

Number of subjects in period 1	RJ-0265	Active control (Ony-Tec)	Placebo
Started	127	128	126
Completed	83	88	84
Not completed	44	40	42
Consent withdrawn by subject	5	2	6
Physician decision	5	4	5
Adverse event, non-fatal	1	2	-
Subject's decision	30	28	25
undefined	2	-	5
undifined	-	4	-
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	RJ-0265
Reporting group description: RJ-0265 applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	
Reporting group title	Active control (Ony-Tec)
Reporting group description: Ony-Tec applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	
Reporting group title	Placebo
Reporting group description: Applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	

Reporting group values	RJ-0265	Active control (Ony-Tec)	Placebo
Number of subjects	127	128	126
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)	99	93	93
From 65-84 years	28	35	33
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.3	55.6	54.9
standard deviation	± 11.1	± 12.7	± 12.7
Gender categorical Units: Subjects			
Female	63	57	54
Male	64	71	72
Race Units: Subjects			
White	105	105	107
American Indian or Alaska Native	22	22	19
Black or African American	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	91	90	90
Not Hispanic or Latino	36	38	36

Reporting group values	Total		
Number of subjects	381		

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)	285		
From 65-84 years	96		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	174		
Male	207		
Race Units: Subjects			
White	317		
American Indian or Alaska Native	63		
Black or African American	1		
Ethnicity Units: Subjects			
Hispanic or Latino	271		
Not Hispanic or Latino	110		

End points

End points reporting groups

Reporting group title	RJ-0265
Reporting group description: RJ-0265 applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	
Reporting group title	Active control (Ony-Tec)
Reporting group description: Ony-Tec applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	
Reporting group title	Placebo
Reporting group description: Applied once daily (in the evening) as a thin layer, for a period of 48 weeks.	

Primary: Rate of complete cure assessed by an independent evaluator at week 52 (comparison between RJ-0265 and placebo)

End point title	Rate of complete cure assessed by an independent evaluator at week 52 (comparison between RJ-0265 and placebo)
End point description: The primary endpoint (complete cure rate) was evaluated testing the superiority contrast, RJ-0265 versus placebo. The primary analysis was done in the ITT population, using techniques of missing imputation. The comparison between RJ-0265 and placebo employed Fisher's exact test. Two-sided p- values were obtained and statistically significant results declared if $p < 0.05$.	
End point type	Primary
End point timeframe: Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	10.4 (9.99 to 12.46)	11.1 (10.69 to 13.16)	11.2 (10.79 to 13.26)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo

Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.839
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	7.1

Secondary: Complete cure rate (%) assessed by independent evaluator (W52)

End point title	Complete cure rate (%) assessed by independent evaluator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	10.4 (9.92 to 12.82)	11.1 (10.65 to 13.29)	11.2 (10.79 to 13.26)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.839
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	7.1

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.856
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	7.2

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.982
Method	Fisher exact
Parameter estimate	Percentage Difference
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	7.9

Secondary: Complete cure rate (%) assessed by independent investigator (W52)

End point title	Complete cure rate (%) assessed by independent investigator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	9.6 (9.13 to 12.11)	10.3 (9.86 to 12.55)	10.4 (10 to 12.5)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.833
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	6.9

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	7

Statistical analysis title	Ony-Tec vs. Placebo
-----------------------------------	---------------------

Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.983
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	7.7

Secondary: Complete cure rate (%) assessed by independent evaluator (W48)

End point title	Complete cure rate (%) assessed by independent evaluator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	7.2 (6.65 to 10.64)	9.5 (9.08 to 11.82)	9.6 (9.31 to 11.39)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.493
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-2.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	4.8

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.505
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	4.8

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.984
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	7.5

Secondary: Complete cure rate (%) assessed by investigator (W48)

End point title	Complete cure rate (%) assessed by investigator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	9.6 (9.13 to 12.11)	10.3 (9.92 to 12.16)	12 (11.66 to 13.74)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.541
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	5.5

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	7

Statistical analysis title	Ony-Tec vs. Placebo
-----------------------------------	---------------------

Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.672
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	6.3

Secondary: Responder's rate (%) assessed by independent evaluator (W52)

End point title	Responder's rate (%) assessed by independent evaluator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	14.4 (14.2 to 16.07)	11.9 (11.52 to 13.57)	14.4 (13.91 to 16.44)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	8.8

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	11

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	11

Secondary: Responder's rate (%) assessed by investigator (W52)	
End point title	Responder's rate (%) assessed by investigator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	17.6 (17.21 to 19.14)	14.3 (13.75 to 16.66)	12.8 (12.07 to 15.77)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.29
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	13.8

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	12.5

Statistical analysis title	Ony-Tec vs. Placebo
-----------------------------------	---------------------

Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.731
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	10.1

Secondary: Responder's rate (%) assessed by independent evaluator (W48)

End point title	Responder's rate (%) assessed by independent evaluator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	10.4 (9.87 to 12.99)	11.9 (11.47 to 13.86)	12.8 (12.44 to 14.52)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.553
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-2.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	5.7

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.705
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	6.5

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.829
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	7.4

Secondary: Responder's rate (%) assessed by investigator (W48)

End point title	Responder's rate (%) assessed by investigator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	16 (15.36 to 18.39)	19 (18.28 to 21.76)	14.4 (13.83 to 16.68)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.725
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	10.6

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.525
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	6.4

Statistical analysis title	Ony-Tec vs. Placebo
-----------------------------------	---------------------

Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.323
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	13.9

Secondary: Improvement rate (%) assessed by independent evaluator (W52)

End point title	Improvement rate (%) assessed by independent evaluator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: percentage of participants				
number (confidence interval 95%)	27.2 (26.81 to 28.4)	20.6 (20.09 to 22.33)	21.6 (20.84 to 24.04)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.302
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	5.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	16.1

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.222
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	17

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.851
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	9.1

Secondary: Improvement rate (%) assessed by investigator W52)	
End point title	Improvement rate (%) assessed by investigator W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	25.6 (25.16 to 27.02)	21.4 (20.81 to 23.43)	20 (19.24 to 22.51)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.291
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	15.9

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.436
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	14.6

Statistical analysis title	RJ-0265 vs. Placebo
-----------------------------------	---------------------

Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	11.4

Secondary: Improvement rate (%) assessed by independent evaluator W48)

End point title	Improvement rate (%) assessed by independent evaluator W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	21.6 (20.94 to 23.74)	24.6 (23.85 to 27.13)	19.2 (18.57 to 21.36)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.638
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	2.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	12.4

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.572
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	7.4

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	15.5

Secondary: Improvement rate (%) assessed by investigator (W48)	
End point title	Improvement rate (%) assessed by investigator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	24 (23.15 to 26.58)	31.7 (30.55 to 35.46)	18.4 (17.64 to 21)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	15.6

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.171
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.6
upper limit	3.3

Statistical analysis title	Ony-Tec vs. Placebo
-----------------------------------	---------------------

Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	23.7

Secondary: Decrease of disease nail area (%) to <10% of total assessed by independent evaluator (W52)

End point title	Decrease of disease nail area (%) to <10% of total assessed by independent evaluator (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	21.8 (21.37 to 23.31)	18.4 (17.85 to 20.42)	17.6 (16.9 to 20.06)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.407
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	4.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	14

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.506
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	13.3

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.869
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	10.4

Secondary: Decrease of disease nail area (%) to <10% of total assessed by investigator (W52)

End point title	Decrease of disease nail area (%) to <10% of total assessed by investigator (W52)
End point description:	
End point type	Secondary

End point timeframe:

Week 52

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	34.8 (34.32 to 36.35)	22.2 (21.63 to 24.09)	21.6 (20.94 to 23.77)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.549
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	13.6

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	13

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.905
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	10.8

Secondary: Decrease of disease nail area (%) to <10% of total assessed by independent evaluator (W48)

End point title	Decrease of disease nail area (%) to <10% of total assessed by independent evaluator (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	15.3 (14.84 to 17.17)	14.4 (13.96 to 16.17)	16 (15.52 to 17.89)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo

Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.883
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	8.5

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.838
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	9.9

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.725
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	7.4

Secondary: Decrease of disease nail area (%) to <10% of total assessed by

investigator (W48)

End point title	Decrease of disease nail area (%) to <10% of total assessed by investigator (W48)
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Week 48

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	21.6 (21.06 to 23.41)	21.4 (20.83 to 23.31)	20.8 (20.23 to 22.73)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.887
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	10.9

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.974
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	10.3

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.903
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	10.7

Secondary: Conversion to negative KOH/DTS rate (W52)	
End point title	Conversion to negative KOH/DTS rate (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	40 (39.38 to 41.69)	40.5 (39.57 to 43.13)	30.4 (29.49 to 32.98)	

Statistical analyses	
Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo

Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	21.1

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.939
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	11.5

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	21.5

Secondary: Conversion to negative KOH/DTS rate (W48)

End point title	Conversion to negative KOH/DTS rate (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	34.4 (33.62 to 36.57)	40.5 (39.72 to 42.67)	34.4 (33.81 to 36.09)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	11.6

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-6.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.7
upper limit	5.8

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	17.7

Secondary: Conversion to negative to dermatophyte by culture rate (W52)	
End point title	Conversion to negative to dermatophyte by culture rate (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	47.2 (46.62 to 48.77)	46 (45.02 to 48.72)	34.4 (33.37 to 37.25)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo

Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	24.5

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.853
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	13.3

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	11.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	23.3

Secondary: Conversion to negative to dermatophyte by culture rate (W48)

End point title	Conversion to negative to dermatophyte by culture rate (W48)
End point description:	
End point type	Secondary
End point timeframe:	
Week 48	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	59.2 (57.35 to 64.41)	69 (68.08 to 71.59)	32 (29.2 to 40.15)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	27.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.9
upper limit	38.3

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-9.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.3
upper limit	2

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	37
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.9
upper limit	47.6

Secondary: Conversion to negative to dermatophyte by culture and negative to KOH/DTS rate (%) (W52)

End point title	Conversion to negative to dermatophyte by culture and negative to KOH/DTS rate (%) (W52)
End point description:	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	32 (31.55 to 33.35)	27 (26.31 to 29.18)	23.2 (22.31 to 25.94)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	19.6

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.383
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	16.1

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	14.4

Secondary: nConversion to negative to dermatophyte by culture and negative to KOH/DTS rate (%) (48)

End point title	nConversion to negative to dermatophyte by culture and negative to KOH/DTS rate (%) (48)
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Week 48

End point values	RJ-0265	Active control (Ony-Tec)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	126	125	
Units: Percentage of participants				
number (confidence interval 95%)	31.2 (30.31 to 33.73)	40.5 (39.13 to 44.62)	22.4 (21.5 to 25.18)	

Statistical analyses

Statistical analysis title	RJ-0265 vs. Placebo
Comparison groups	RJ-0265 v Placebo
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	19.5

Statistical analysis title	RJ-0265 vs. Ony-Tec
Comparison groups	RJ-0265 v Active control (Ony-Tec)

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.125
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	-9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.8
upper limit	2.6

Statistical analysis title	Ony-Tec vs. Placebo
Comparison groups	Active control (Ony-Tec) v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Fisher exact
Parameter estimate	Percentage Difference
Point estimate	18.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.6
upper limit	28.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From written informed consent to the end of the study (whatever the reason is) [maximum 1 year and 6 weeks]

Adverse event reporting additional description:

The Safety Analysis Set included all randomized participants

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	RJ-0265
-----------------------	---------

Reporting group description:

RJ-0265 applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

Reporting group title	Active control (Ony-Tec)
-----------------------	--------------------------

Reporting group description:

Ony-Tec applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

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

Reporting group description:

Applied once daily (in the evening) as a thin layer, for a period of 48 weeks.

Serious adverse events	RJ-0265	Active control (Ony-Tec)	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 127 (2.36%)	6 / 128 (4.69%)	2 / 126 (1.59%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic cancer			

subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Bladder cancer			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory Tract Infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
post surgical infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			

subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	RJ-0265	Active control (Ony-Tec)	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 127 (17.32%)	24 / 128 (18.75%)	23 / 126 (18.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected neoplasm			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Dental implantation			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	2	0	1
Cataract operation			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia repair			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	2
Knee operation			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	2
Tooth extraction			

subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Wisdom teeth removal subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
General disorders and administration site conditions			
Malaise subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	2 / 128 (1.56%) 2	0 / 126 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Immune system disorders			
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	1 / 126 (0.79%) 2
Reproductive system and breast disorders			
Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Asthma subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 127 (0.00%)	2 / 128 (1.56%)	1 / 126 (0.79%)
occurrences (all)	0	2	1
Depression			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	1	0	1
Dental restoration failure			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	2
Limb injury			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Meniscus injury			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	2	0	0
Traumatic haematoma			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 127 (2.36%)	1 / 128 (0.78%)	2 / 126 (1.59%)
occurrences (all)	5	2	7

Sciatica			
subjects affected / exposed	1 / 127 (0.79%)	1 / 128 (0.78%)	1 / 126 (0.79%)
occurrences (all)	1	1	1
Perineurial cyst			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1
Intestinal congestion			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Onychalgia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	2 / 126 (1.59%)
occurrences (all)	0	1	3
Nail discolouration			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	2	0	1
Dermatitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Rash			

subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 3	0 / 126 (0.00%) 0
Rosacea subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	2 / 128 (1.56%) 3	2 / 126 (1.59%) 2
back pain subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
neck pain subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Periarthritis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Periostitis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 2	0 / 126 (0.00%) 0
Rotator cuff syndrome			

subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
Tendonitis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 2	0 / 126 (0.00%) 0
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	4 / 127 (3.15%) 4	4 / 128 (3.13%) 4	4 / 126 (3.17%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 127 (3.15%) 4	2 / 128 (1.56%) 3	3 / 126 (2.38%) 4
Ear infection subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	3 / 128 (2.34%) 3	0 / 126 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	1 / 126 (0.79%) 1
Cellulitis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0
Dengue subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Gastroenteritis viral subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	0 / 128 (0.00%) 0	1 / 126 (0.79%) 1
Gingivitis subjects affected / exposed occurrences (all)	0 / 127 (0.00%) 0	1 / 128 (0.78%) 1	1 / 126 (0.79%) 1
Pharyngitis subjects affected / exposed occurrences (all)	2 / 127 (1.57%) 2	0 / 128 (0.00%) 0	0 / 126 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	1 / 127 (0.79%) 1	1 / 128 (0.78%) 1	0 / 126 (0.00%) 0

Conjunctivitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
gastroenteritis			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1
Helicobacter infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 128 (0.78%)	0 / 126 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 128 (0.00%)	0 / 126 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 127 (0.00%)	0 / 128 (0.00%)	1 / 126 (0.79%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2017	<p>The amendment consisted of the following changes:</p> <ul style="list-style-type: none">- Change of one of the protocol's diagnostic test (from KOH-based microscopic examination to Diafactory Tinea Unguium commercial test kit) to increase the sensitivity and reduce examiner subjectivity. It also provided an immediate diagnostic.- Participant's age extended from 70 to 75 years.- Change in the number and distribution of participating centres (from 30 to 31). <p>Taking advantage of this amendment, the study calendar was updated, and typographic errors of the previous version were corrected.</p>

Notes:

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.

Elevated number of screening failures (90.8%) due to lack of a positive culture at screening before randomization

Notes: