Clinical trial results:
A Phase 3, Double-Blind, Randomized, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream Followed by an Extension Period in Participants With Vitiligo

Summary

EudraCT number	2019-000847-28
Trial protocol	DE FR PL BG ES IT
Global end of trial date	01 October 2021

Results information

Result version number	v1
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	INCB 18424-307

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04057573
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002618-PIP02-20
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	01 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of ruxolitinib cream in adolescent and adult participants with non-segmental vitiligo with facial involvement for whom total body involved vitiligo area (facial and nonfacial) did not exceed 10% body surface area (BSA).

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was being conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2019
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	Bulgaria: 17
Country: Number of subjects enrolled	Canada: 49
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Poland: 44
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United States: 194
Worldwide total number of subjects	343
EEA total number of subjects	100

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	36
Adults (18-64 years)	292
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 49 study centers in North America and Europe.

Pre-assignment

Screening details:

A total of 344 participants were randomized into the study. Of the 344 randomized participants (Intent-to-Treat Population), 343 applied study drug at least once (Safety Population; data reported in this module), and 297 participants applied ruxolitinib cream at least once during the Treatment-Extension (TE) Period (TE Evaluable Population).

Period 1

Period 1 title	24-Week Double-Blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind Period: Ruxolitinib cream 1.5% BID

Arm description:

Participants applied ruxolitinib 1.5% cream twice daily (BID) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	ruxolitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

1.5% cream twice daily

Arm title	Double-Blind Period: Vehicle cream BID

Arm description:

Participants applied matching vehicle cream BID for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Vehicle cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

twice daily

Number of subjects in period 1	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID
Started	228	115
ITT Population, Minus Non-compliant Site	222	109
Completed	199	98
Not completed	29	17
Physician decision	1	-
Consent withdrawn by subject	10	8
Unable to Attend Study Visits Due to Travel	-	1
Adverse event, non-fatal	2	-
Non-compliance with Attending Study Visits	1	-
Pregnancy	1	-
Lost to follow-up	11	6
Discontinued Treatment due to COVID-19 Pandemic	3	1
Lack of efficacy	-	1

Period 2

Period 2 title	28-Week Treatment Extension Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID

Arm description:

Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied ruxolitinib cream 1.5% BID during the Double-Blind Period continued to apply ruxolitinib cream 1.5% BID for an additional 28 weeks in the Treatment-Extension Period.

Arm type	Experimental
Investigational medicinal product name	ruxolitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

1.5% cream twice daily

Arm title	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID

Arm description:

Participants who completed the Week 24 assessments with no safety concerns could continue into the

28-week Treatment-Extension Period. Participants who applied vehicle cream BID during the Double-Blind Period applied ruxolitinib cream 1.5% BID for 28 weeks in the Treatment-Extension Period.

Arm type	Experimental
Investigational medicinal product name	ruxolitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

1.5% cream twice daily

Number of subjects in period 2	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Started	199	98
Completed	178	79
Not completed	21	19
Consent withdrawn by subject	9	9
Unable to Perform Safety Follow-up Visit	1	-
Adverse event, non-fatal	1	-
Lost to follow-up	9	10
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Double-Blind Period: Ruxolitinib cream 1.5% BID
Reporting group description:	
Participants applied ruxolitinib 1.5% cream twice daily (BID) for 24 weeks.	
Reporting group title	Double-Blind Period: Vehicle cream BID
Reporting group description:	
Participants applied matching vehicle cream BID for 24 weeks.	

Reporting group values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID	Total
Number of subjects	228	115	343
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)	30	6	36
Adults (18-64 years)	186	106	292
From 65-84 years	12	3	15
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	38.4	39.8	
standard deviation	± 15.22	± 12.12	-
Sex: Female, Male Units:			
Female	112	60	172
Male	116	55	171
Race, Customized Units: Subjects			
White	182	93	275
Black/African American	12	5	17
Asian	12	7	19
American Indian/Alaska Native	1	0	1
Native Hawaiian/Pacific Islander	2	0	2
Not Reported	3	3	6
North African	2	0	2
White/Caucasian and Asian	1	0	1
Guyana	1	0	1
Cape Verdean	1	1	2
Persian	1	0	1
Middle Eastern	3	0	3
Arab/North-African	1	0	1

White/Black/Asian	1	0	1
Mexican	2	1	3
Jordanian	1	0	1
Arabic	1	0	1
Argentinian	1	0	1
Brazilian	0	2	2
Dominican Republic	0	1	1
Indo-Caribbean	0	1	1
Multi-National	0	1	1
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	50	32	82
Not Hispanic or Latino	174	80	254
Not Reported	2	3	5
Captured as "Other"	2	0	2
Face Vitiligo Area Scoring Index (F-VASI)			
F-VASI was measured by the percentage of vitiligo involvement (percentage of body surface area [BSA]; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). F-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each facial site and summing all values (possible range: 0-3).			
Units: scores on a scale			
arithmetic mean	0.900	0.834	
standard deviation	± 0.5248	± 0.5233	-
Facial Body Surface Area (F-BSA) Involvement			
F-BSA involvement was the proportion of the facial body surface area with vitiligo. The area "Face" was defined as including the area on the forehead to the original hairline, on the cheek to the jawline vertically to the jawline and laterally from the corner of the mouth to the tragus. The area "Face" did not include surface area of the lips, scalp, ears, or neck, but included the nose and eyelids.			
Units: percentage			
arithmetic mean	0.98	0.92	
standard deviation	± 0.570	± 0.569	-
Total Body Vitiligo Area Scoring Index (T-VASI)			
T-VASI was measured by the percentage of vitiligo involvement from all body regions (percentage of BSA; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each body site and summing all values (possible range: 0-100).			
Units: scores on a scale			
arithmetic mean	6.844	7.022	
standard deviation	± 2.0574	± 2.1986	-
Total Body Surface Area (T-BSA) Involvement			
T-BSA involvement was the proportion of the body surface area with vitiligo. The body was divided into the following 6 separate and mutually exclusive sites: (1) head/neck, (2) hands, (3) upper extremities (excluding hands), (4) trunk, (5) lower extremities (excluding feet), and (6) feet.			
Units: percentage			
arithmetic mean	7.44	7.68	
standard deviation	± 2.011	± 2.040	-

Subject analysis sets	
Subject analysis set title	Double-Blind Period: Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants, minus those enrolled at the noncompliant site, applied ruxolitinib 1.5% cream twice daily (BID) for 24 weeks.	
Subject analysis set title	Double-Blind Period: Vehicle cream BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants, minus those enrolled at the noncompliant site, applied matching vehicle cream BID for 24 weeks.	
Subject analysis set title	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied ruxolitinib cream 1.5% BID during the Double-Blind Period continued to apply ruxolitinib cream 1.5% BID for an additional 28 weeks in the Treatment-Extension Period.	
Subject analysis set title	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied vehicle cream BID during the Double-Blind Period applied ruxolitinib cream 1.5% BID for 28 weeks in the Treatment-Extension Period.	

Reporting group values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID
Number of subjects	222	109	199
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)	30	6	
Adults (18-64 years)	179	100	
From 65-84 years	13	3	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	38.4	39.4	
standard deviation	± 15.44	± 12.29	±
Sex: Female, Male Units:			
Female	110	58	
Male	112	51	
Race, Customized Units: Subjects			
White	178	88	
Black/African American	11	5	

Asian	11	6	
American Indian/Alaska Native	1	0	
Native Hawaiian/Pacific Islander	2	0	
Not Reported	3	3	
North African	2	0	
White/Caucasian and Asian	1	0	
Guyana	1	0	
Cape Verdean	1	1	
Persian	1	0	
Middle Eastern	3	0	
Arab/North-African	1	0	
White/Black/Asian	1	0	
Mexican	2	1	
Jordanian	1	0	
Arabic	1	0	
Argentinian	1	0	
Brazilian	0	2	
Dominican Republic	0	1	
Indo-Caribbean	0	1	
Multi-National	0	1	
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	49	30	
Not Hispanic or Latino	169	76	
Not Reported	2	3	
Captured as "Other"	2	0	
Face Vitiligo Area Scoring Index (F-VASI)			
F-VASI was measured by the percentage of vitiligo involvement (percentage of body surface area [BSA]; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). F-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each facial site and summing all values (possible range: 0-3).			
Units: scores on a scale			
arithmetic mean	0.898	0.834	
standard deviation	± 0.5256	± 0.5342	±
Facial Body Surface Area (F-BSA) Involvement			
F-BSA involvement was the proportion of the facial body surface area with vitiligo. The area "Face" was defined as including the area on the forehead to the original hairline, on the cheek to the jawline vertically to the jawline and laterally from the corner of the mouth to the tragus. The area "Face" did not include surface area of the lips, scalp, ears, or neck, but included the nose and eyelids.			
Units: percentage			
arithmetic mean	0.98	0.92	
standard deviation	± 0.571	± 0.582	±
Total Body Vitiligo Area Scoring Index (T-VASI)			
T-VASI was measured by the percentage of vitiligo involvement from all body regions (percentage of BSA; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each body site and summing all values (possible range: 0-100).			
Units: scores on a scale			

arithmetic mean	2.0435	2.1953	
standard deviation	± 6.790	± 6.979	±
Total Body Surface Area (T-BSA) Involvement			
T-BSA involvement was the proportion of the body surface area with vitiligo. The body was divided into the following 6 separate and mutually exclusive sites: (1) head/neck, (2) hands, (3) upper extremities (excluding hands), (4) trunk, (5) lower extremities (excluding feet), and (6) feet.			
Units: percentage			
arithmetic mean	7.38	7.66	
standard deviation	± 2.025	± 2.040	±

Reporting group values	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Number of subjects	98		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male			
Units:			
Female			
Male			
Race, Customized			
Units: Subjects			
White			
Black/African American			
Asian			
American Indian/Alaska Native			
Native Hawaiian/Pacific Islander			
Not Reported			
North African			
White/Caucasian and Asian			
Guyana			
Cape Verdean			
Persian			
Middle Eastern			
Arab/North-African			
White/Black/Asian			
Mexican			
Jordanian			

Arabic Argentinian Brazilian Dominican Republic Indo-Caribbean Multi-National			
Ethnicity, Customized Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Not Reported Captured as "Other"			
Face Vitiligo Area Scoring Index (F-VASI)			
F-VASI was measured by the percentage of vitiligo involvement (percentage of body surface area [BSA]; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). F-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each facial site and summing all values (possible range: 0-3).			
Units: scores on a scale arithmetic mean standard deviation	±		
Facial Body Surface Area (F-BSA) Involvement			
F-BSA involvement was the proportion of the facial body surface area with vitiligo. The area "Face" was defined as including the area on the forehead to the original hairline, on the cheek to the jawline vertically to the jawline and laterally from the corner of the mouth to the tragus. The area "Face" did not include surface area of the lips, scalp, ears, or neck, but included the nose and eyelids.			
Units: percentage arithmetic mean standard deviation	±		
Total Body Vitiligo Area Scoring Index (T-VASI)			
T-VASI was measured by the percentage of vitiligo involvement from all body regions (percentage of BSA; assessed by the Investigator) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each body site and summing all values (possible range: 0-100).			
Units: scores on a scale arithmetic mean standard deviation	±		
Total Body Surface Area (T-BSA) Involvement			
T-BSA involvement was the proportion of the body surface area with vitiligo. The body was divided into the following 6 separate and mutually exclusive sites: (1) head/neck, (2) hands, (3) upper extremities (excluding hands), (4) trunk, (5) lower extremities (excluding feet), and (6) feet.			
Units: percentage arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	Double-Blind Period: Ruxolitinib cream 1.5% BID
Reporting group description:	
Participants applied ruxolitinib 1.5% cream twice daily (BID) for 24 weeks.	
Reporting group title	Double-Blind Period: Vehicle cream BID
Reporting group description:	
Participants applied matching vehicle cream BID for 24 weeks.	
Reporting group title	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID
Reporting group description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied ruxolitinib cream 1.5% BID during the Double-Blind Period continued to apply ruxolitinib cream 1.5% BID for an additional 28 weeks in the Treatment-Extension Period.	
Reporting group title	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Reporting group description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied vehicle cream BID during the Double-Blind Period applied ruxolitinib cream 1.5% BID for 28 weeks in the Treatment-Extension Period.	
Subject analysis set title	Double-Blind Period: Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants, minus those enrolled at the noncompliant site, applied ruxolitinib 1.5% cream twice daily (BID) for 24 weeks.	
Subject analysis set title	Double-Blind Period: Vehicle cream BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants, minus those enrolled at the noncompliant site, applied matching vehicle cream BID for 24 weeks.	
Subject analysis set title	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied ruxolitinib cream 1.5% BID during the Double-Blind Period continued to apply ruxolitinib cream 1.5% BID for an additional 28 weeks in the Treatment-Extension Period.	
Subject analysis set title	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied vehicle cream BID during the Double-Blind Period applied ruxolitinib cream 1.5% BID for 28 weeks in the Treatment-Extension Period.	

Primary: Percentage of participants achieving a ≥ 75% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI75) Score at Week 24

End point title	Percentage of participants achieving a ≥ 75% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI75) Score at Week 24

End point description:

An F-VASI75 responder achieved at least 75% improvement from Baseline in F-VASI, measured by the percentage of vitiligo involvement (percentage of body surface area [BSA]) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the

Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement).

End point type	Primary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	30.9	11.4		

Statistical analyses

Statistical analysis title	Exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004 [1]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	3.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.737
upper limit	6.835

Notes:

[1] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage of participants achieving a ≥ 50% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI50) Score at Week 24

End point title	Percentage of participants achieving a ≥ 50% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI50) Score at Week 24

End point description:

An F-VASI50 responder achieved at least 50% improvement from Baseline in F-VASI, measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of

BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	51.4	20.9		

Statistical analyses

Statistical analysis title	Exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [2]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.296
upper limit	6.949

Notes:

[2] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage of participants achieving a ≥ 90% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI90) Score at Week 24

End point title	Percentage of participants achieving a ≥ 90% Improvement from Baseline in the Face Vitiligo Area Scoring Index (F-VASI90) Score at Week 24

End point description:

An F-VASI90 responder achieved at least 90% improvement from Baseline in F-VASI, measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo

involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement).

End point type	Secondary
End point timeframe:	
Baseline; Week 24	

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	16.3	1.3		

Statistical analyses

Statistical analysis title	Exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0065 [3]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	15.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	108.739

Notes:

[3] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage of participants achieving a ≥ 50% Improvement from Baseline in the Total Body Vitiligo Area Scoring Index (T-VASI50) Score at Week 24

End point title	Percentage of participants achieving a ≥ 50% Improvement from Baseline in the Total Body Vitiligo Area Scoring Index (T-VASI50) Score at Week 24

End point description:

A T-VASI50 responder achieved at least 50% improvement from Baseline in T-VASI, calculated with contributions from 6 sites. The percentage of vitiligo involvement was estimated in hand units (percentage of BSA estimated to the nearest 0.1%) by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate percent BSA vitiligo involvement. The degree of depigmentation for each site was estimated to the nearest percentage: 0% (no depigmentation present), 10% (only specks of depigmentation present), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of

affected skin for each site and summing the values (range: 0-100; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	23.9	6.8		

Statistical analyses

Statistical analysis title	Exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006 [4]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	4.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.865
upper limit	9.853

Notes:

[4] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage of participants achieving a Vitiligo Noticeability Scale (VNS) of 4 or 5 at Week 24

End point title	Percentage of participants achieving a Vitiligo Noticeability Scale (VNS) of 4 or 5 at Week 24

End point description:

The VNS is a patientreported measure of vitiligo treatment success that is rated on a 5-point scale. The Baseline facial photograph was shown to the participants for reference, and a mirror was provided for the participants to assess the vitiligo on their face. The participant was asked to respond to the following query: Compared with before treatment, how noticeable is the vitiligo now? Responses: (1) more noticeable, (2) as noticeable, (3) slightly less noticeable, (4) a lot less noticeable, and (5) no longer noticeable.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	20.5	4.9		

Statistical analyses

Statistical analysis title	Exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0013 [5]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	4.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.851
upper limit	12.755

Notes:

[5] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage change from Baseline in Facial Body Surface Area (F-BSA) at Week 24

End point title	Percentage change from Baseline in Facial Body Surface Area (F-BSA) at Week 24

End point description:

F-BSA involvement was the proportion of the facial body surface area with vitiligo. The area "Face" was defined as including the area on the forehead to the original hairline, on the cheek to the jawline vertically to the jawline and laterally from the corner of the mouth to the tragus. The area "Face" did not include surface area of the lips, scalp, ears, or neck, but included the nose and eyelids. Body surface area assessment was performed by the Palmar Method. Body surface area was estimated to the nearest 0.1%. The approximate size of the participant’s entire palmar surface (i.e., the palm plus 5 digits) was considered as 1% BSA, and the approximate size of the participant’s thumb was considered as 0.1% BSA. Percentage change = ([post-Baseline (BL) value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percent				
least squares mean (standard error)	-26.4 (± 2.57)	-7.0 (± 3.82)		

Statistical analyses

Statistical analysis title	ANCOVA
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [6]
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.46
upper limit	-10.45
Variability estimate	Standard error of the mean
Dispersion value	4.59

Notes:

[6] - Response Variable = Treatment + Stratification Factors (Skin Type Fitzpatrick scale Type I, II versus Type III, IV, V, and VI, Region North America/Europe) + Baseline

Secondary: Number of participants with treatment-emergent adverse events (TEAEs) during the Double-Blind Period

End point title	Number of participants with treatment-emergent adverse events (TEAEs) during the Double-Blind Period

End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. An AE could have been any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as any AE reported for the first time or the worsening of a pre-existing event after the first application of study drug.

End point type	Secondary

End point timeframe:

from the time of Informed Consent Form signing until at least 30 days after the last application of study drug (up to Week 24)

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	115		
Units: participants	114	39		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent adverse events (TEAEs) during the Treatment-Extension Period

End point title	Number of participants with treatment-emergent adverse events (TEAEs) during the Treatment-Extension Period

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. An AE could have been any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as any AE reported for the first time or the worsening of a pre-existing event after the first application of study drug.

End point type	Secondary

End point timeframe:

from the completion of the Week 24 assessments until at least 30 days after the last application of study drug (up to Week 52 + 30 days)

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	98		
Units: participants	82	38		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a ≥ 25% Improvement in the Face Vitiligo Area Scoring Index (F-VASI25) Score at Week 24

End point title	Percentage of participants achieving a ≥ 25% Improvement in

	the Face Vitiligo Area Scoring Index (F-VASI25) Score at Week 24

End point description:

An F-VASI25 responder achieved at least 25% improvement from Baseline in F-VASI, measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)	63.9	32.0		

Statistical analyses

Statistical analysis title	exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.267
upper limit	6.246

Notes:

[7] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Secondary: Percentage of participants achieving a ≥ %25, ≥ %50, ≥ 75%, and ≥ 90% Improvement in the Face Vitiligo Area Scoring Index (F-VASI25/50/75/90) Score at Week 52

End point title	Percentage of participants achieving a ≥ %25, ≥ %50, ≥ 75%, and ≥ 90% Improvement in the Face Vitiligo Area Scoring Index (F-VASI25/50/75/90) Score at Week 52

End point description:

An F-VASI25/50/75/90 responder achieved at least 25/50/75/90% improvement from Baseline in F-VASI, measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percentage of participants				
number (not applicable)				
F-VASI25	82.5	71.6		
F-VASI50	74.0	49.4		
F-VASI75	48.0	29.6		
F-VASI90	27.7	16.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in F-VASI at Week 24

End point title	Percentage change from Baseline in F-VASI at Week 24

End point description:

F-VASI was measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement). Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	98		
Units: percent				
least squares mean (standard error)	-44.39 (± 2.85)	-15.80 (± 4.04)		

Statistical analyses

Statistical analysis title	mixed-effect model; repeated measurement
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	mixed-effect model; repeated measurement
Parameter estimate	Least squares mean difference
Point estimate	-28.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.33
upper limit	-18.86
Variability estimate	Standard error of the mean
Dispersion value	4.94

Secondary: Percentage change from Baseline in F-VASI at Week 52

End point title	Percentage change from Baseline in F-VASI at Week 52

End point description:

F-VASI was measured by the percentage of vitiligo involvement (percentage of BSA) and the degree of depigmentation: 0% (no depigmentation), 10% (only specks of depigmentation), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment), or 100% (no pigment). The percentage of BSA (hand unit) vitiligo involvement was estimated to the nearest 0.1% by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate the percentage of BSA vitiligo involvement. F-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites (possible range: 0-3; lower scores indicate increased improvement). Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percent				
arithmetic mean (standard deviation)	-63.75 (± 34.103)	-43.50 (± 47.509)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in F-BSA at Week 52

End point title	Percentage change from Baseline in F-BSA at Week 52

End point description:

F-BSA involvement was the proportion of the facial body surface area with vitiligo. The area "Face" was defined as including the area on the forehead to the original hairline, on the cheek to the jawline vertically to the jawline and laterally from the corner of the mouth to the tragus. The area "Face" did not include surface area of the lips, scalp, ears, or neck, but included the nose and eyelids. Body surface area assessment was performed by the Palmar Method. Body surface area was estimated to the nearest 0.1%. The approximate size of the participant's entire palmar surface (i.e., the palm plus 5 digits) was considered as 1% BSA, and the approximate size of the participant's thumb was considered as 0.1% BSA. Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percent				
arithmetic mean (standard deviation)	-41.81 (± 35.694)	-23.45 (± 46.360)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in T-VASI at Week 24

End point title	Percentage change from Baseline in T-VASI at Week 24

End point description:

T-VASI was calculated with contributions from 6 sites. The percentage of vitiligo involvement was estimated in hand units (percentage of BSA estimated to nearest 0.1%) by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate percent BSA vitiligo involvement. The degree of depigmentation for each site was estimated to the nearest percentage: 0% (no depigmentation present), 10% (only specks of depigmentation present), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site and summing the values (range: 0-100; lower scores indicate increased improvement). Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	98		
Units: percent				
least squares mean (standard error)	-28.85 (± 1.96)	-8.99 (± 2.78)		

Statistical analyses

Statistical analysis title	mixed-effect model; repeated measurement
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	mixed-effect model; repeated measurement
Parameter estimate	least squares mean difference
Point estimate	-19.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.55
upper limit	-13.16
Variability estimate	Standard error of the mean
Dispersion value	3.4

Secondary: Percentage change from Baseline in T-VASI at Week 52

End point title	Percentage change from Baseline in T-VASI at Week 52

End point description:

T-VASI was calculated with contributions from 6 sites. The percentage of vitiligo involvement was estimated in hand units (percentage of BSA estimated to nearest 0.1%) by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate percent BSA vitiligo involvement. The degree of depigmentation for each site was estimated to the nearest percentage: 0% (no depigmentation present), 10% (only specks of depigmentation present), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site and summing the values (range: 0-100; lower scores indicate increased improvement). Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percent				
arithmetic mean (standard deviation)	-46.80 (± 29.903)	-30.11 (± 30.315)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in T-BSA at Week 24

End point title	Percentage change from Baseline in T-BSA at Week 24

End point description:

T-BSA involvement was the proportion of the body surface area with vitiligo. Body surface area assessment was performed by the Palmar Method. Body surface area was estimated to the nearest 0.1%. The approximate size of the participant's entire palmar surface (i.e., the palm plus 5 digits) was considered as 1% BSA, and the approximate size of the participant's thumb was considered as 0.1% BSA. Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	98		
Units: percent				
least squares mean (standard error)	-14.23 (± 1.55)	-2.28 (± 2.19)		

Statistical analyses

Statistical analysis title	mixed-effect model; repeated measurement
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	mixed-effect model; repeated measurement
Parameter estimate	least squares mean difference
Point estimate	-11.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.23
upper limit	-6.67
Variability estimate	Standard error of the mean
Dispersion value	2.68

Secondary: Percentage change from Baseline in T-BSA at Week 52

End point title	Percentage change from Baseline in T-BSA at Week 52

End point description:

T-BSA involvement was the proportion of the body surface area with vitiligo. Body surface area assessment was performed by the Palmar Method. Body surface area was estimated to the nearest 0.1%. The approximate size of the participant's entire palmar surface (i.e., the palm plus 5 digits) was considered as 1% BSA, and the approximate size of the participant's thumb was considered as 0.1% BSA. Percentage change = ([post-BL value minus BL value]/BL value) X 100.

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percent				
arithmetic mean (standard deviation)	-26.04 (± 28.481)	-13.54 (± 27.144)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a ≥ 25%, ≥ 75%, and ≥ 90% Improvement in the Total Body Vitiligo Area Scoring Index (T-VASI25/75/90) Score at Week 24

End point title	Percentage of participants achieving a ≥ 25%, ≥ 75%, and ≥ 90% Improvement in the Total Body Vitiligo Area Scoring Index (T-VASI25/75/90) Score at Week 24

End point description:

A T-VASI25/75/90 responder achieved at least 25/75/90% improvement from Baseline in T-VASI, calculated with contributions from 6 sites. The percentage of vitiligo involvement was estimated in hand units (percentage of BSA estimated to nearest 0.1%) by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate percent BSA vitiligo involvement. The degree of depigmentation for each site was estimated to the nearest percentage: 0% (no depigmentation present), 10% (only specks of depigmentation present), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site and summing the values (range: 0-100; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	109		
Units: percentage of participants				
number (not applicable)				
T-VASI25	50.2	21.2		
T-VASI75	8.0	1.8		
T-VASI90	1.0	0.0		

Statistical analyses

Statistical analysis title	T-VASI25; exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [8]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	3.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.121
upper limit	6.63

Notes:

[8] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Statistical analysis title	T-VASI75; exact logistic regression
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0436 [9]
Method	exact logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	4.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.045
upper limit	20.192

Notes:

[9] - The model included the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region).

Statistical analysis title	T-VASI90; exact logistic regression

Statistical analysis description:

The confidence interval was not calculated for the estimated parameter. Values reported (-9999, 9999) are placeholders only, not actual data.

Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9999
upper limit	9999

Secondary: Percentage of participants achieving a ≥ 25%, ≥ 50%, ≥ 75%, and ≥ 90% Improvement in the Total Body Vitiligo Area Scoring Index (T-VASI25/50/75/90) Score at Week 52

End point title	Percentage of participants achieving a ≥ 25%, ≥ 50%, ≥ 75%, and ≥ 90% Improvement in the Total Body Vitiligo Area Scoring Index (T-VASI25/50/75/90) Score at Week 52

End point description:

A T-VASI25/50/75/90 responder achieved ≥25/50/75/90% improvement from Baseline in T-VASI, calculated with contributions from 6 sites. The percentage of vitiligo involvement was estimated in hand units (percentage of BSA estimated to nearest 0.1%) by the Investigator using the Palmar Method. The Investigator used his/her hand to mimic the participant's hand size to evaluate percent BSA vitiligo involvement. The degree of depigmentation for each site was estimated to the nearest percentage: 0% (no depigmentation present), 10% (only specks of depigmentation present), 25% (pigmented area exceeded depigmented area), 50% (depigmented and pigmented area was equal), 75% (depigmented area exceeded pigmented area), 90% (specks of pigment present), 100% (no pigment present). T-VASI was then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site and summing the values (range: 0-100; lower scores indicate increased improvement).

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	177	81		
Units: percentage of participants				
number (not applicable)				
T-VASI25	76.8	53.1		
T-VASI50	49.2	22.2		
T-VASI75	20.9	8.6		
T-VASI90	6.8	1.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each category of VNS during the treatment period (Double-Blind and Treatment-Extension Periods)

End point title	Percentage of participants in each category of VNS during the treatment period (Double-Blind and Treatment-Extension Periods)

End point description:

The VNS is a patientreported measure of vitiligo treatment success that is rated on a 5-point scale. The Baseline facial photograph was shown to the participants for reference, and a mirror was provided for the participants to assess the vitiligo on their face. The participant was asked to respond to the following query: Compared with before treatment, how noticeable is the vitiligo now? Responses: (1) more noticeable, (2) as noticeable, (3) slightly less noticeable, (4) a lot less noticeable, and (5) no longer noticeable.

End point type	Secondary

End point timeframe:

Baseline; Week 24 and Week 52

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	199[10]	98[11]	177[12]	81[13]
Units: percentage of participants				
number (not applicable)				
Week 24, more noticeable	8.5	11.2	9999	9999
Week 24, as noticeable	30.7	58.2	9999	9999
Week 24, slightly less noticeable	40.2	25.5	9999	9999
Week 24, a lot less noticeable	20.6	4.1	9999	9999
Week 24, no longer noticeable	0.0	1.0	9999	9999
Week 52, more noticeable	9999	9999	4.5	11.1
Week 52, as noticeable	9999	9999	16.4	25.9
Week 52, slightly less noticeable	9999	9999	46.3	49.4
Week 52, a lot less noticeable	9999	9999	32.2	13.6
Week 52, no longer noticeable	9999	9999	0.6	0.0

Notes:

[10] - 9999=participants in this treatment group weren't analyzed at this time point.

[11] - 9999=participants in this treatment group weren't analyzed at this time point.

[12] - 9999=participants in this treatment group weren't analyzed at this time point.

[13] - 9999=participants in this treatment group weren't analyzed at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 24

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI)

	at Week 24

End point description:

The DLQI is a 10-question validated questionnaire for use in participants aged 16 years and over to measure how much the skin problem has affected the participant over the previous 7 days. Each question is scored as: very much = 3; a lot = 2; a little = 1; not at all = 0; not relevant = 0. For Question 7, "Prevented work or studying" = 3. The DLQI was calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	94		
Units: scores on a scale				
least squares mean (standard error)	-1.19 (± 0.30)	-0.59 (± 0.41)		

Statistical analyses

Statistical analysis title	mixed-effect model; repeated measurement
Comparison groups	Double-Blind Period: Ruxolitinib cream 1.5% BID v Double-Blind Period: Vehicle cream BID
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.235
Method	mixed-effect model; repeated measurement
Parameter estimate	least squares mean difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.51

Secondary: Change from Baseline in DLQI at Week 52

End point title	Change from Baseline in DLQI at Week 52

End point description:

The DLQI is a 10-question validated questionnaire for use in participants aged 16 years and over to measure how much the skin problem has affected the participant over the previous 7 days. Each

question is scored as: very much = 3; a lot = 2; a little = 1; not at all = 0; not relevant = 0. For Question 7, "Prevented work or studying" = 3. The DLQI was calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

End point type	Secondary

End point timeframe:

Baseline; Week 52

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	205[14]	105[15]	161[16]	78[17]
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=205, 105	4.37 (± 4.485)	5.38 (± 4.876)	9999 (± 9999)	9999 (± 9999)
Week 52, n=161, 78	9999 (± 9999)	9999 (± 9999)	-0.84 (± 3.976)	-1.15 (± 4.264)

Notes:

[14] - 9999=participants in this treatment group weren't analyzed at this time point.

[15] - 9999=participants in this treatment group weren't analyzed at this time point.

[16] - 9999=participants in this treatment group weren't analyzed at this time point.

[17] - 9999=participants in this treatment group weren't analyzed at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Children's Dermatology Life Quality Index (CDLQI) during the treatment period (Double-Blind and Treatment-Extension Periods)

End point title	Change from Baseline in Children's Dermatology Life Quality Index (CDLQI) during the treatment period (Double-Blind and Treatment-Extension Periods)

End point description:

The DLQI is a 10-question validated questionnaire for use in participants aged 16 years and over to measure how much the skin problem has affected the participant over the previous 7 days. The CDLQI is the youth/children's version of the DLQI and was completed by adolescents aged ≥ 12 years to < 16 years. Each question is scored as: very much = 3; quite a lot = 2; only a little = 1; not at all = 0; question unanswered = 0. For Question 7: "Prevented school" = 3. The CDLQI was calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

End point type	Secondary

End point timeframe:

Baseline; Week 24 and Week 52

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Double-Blind Period: Vehicle cream BID	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17[18]	3[19]	16[20]	3[21]
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=17, 3	1.29 (± 2.201)	6.33 (± 10.116)	9999 (± 9999)	9999 (± 9999)
Week 24, n=17, 3	0.00 (± 1.837)	-2.33 (± 8.505)	9999 (± 9999)	9999 (± 9999)
Week 52, n=16, 3	9999 (± 9999)	9999 (± 9999)	1.19 (± 4.665)	-1.00 (± 4.583)

Notes:

[18] - 9999=participants in this treatment group weren't analyzed at this time point.

[19] - 9999=participants in this treatment group weren't analyzed at this time point.

[20] - 9999=participants in this treatment group weren't analyzed at this time point.

[21] - 9999=participants in this treatment group weren't analyzed at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Trough plasma concentrations of ruxolitinib at Weeks 4, 24, and 40

End point title	Trough plasma concentrations of ruxolitinib at Weeks 4, 24, and 40[22]

End point description:

Trough plasma concentration was defined as the measurement of the plasma concentration of ruxolitinib before drug application.

End point type	Secondary

End point timeframe:

pre-dose at Weeks 4, 24, and 40

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetics was assessed for ruxolitinib only; thus, data are not reported for the following arm: Double-Blind Period: Vehicle cream BID. Furthermore, no statistical analysis was conducted for this endpoint.

End point values	Double-Blind Period: Ruxolitinib cream 1.5% BID	Treatment-Extension (TE) Period: Ruxolitinib cream 1.5% BID	TE Period: Vehicle cream to Ruxolitinib cream 1.5% BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	208[23]	184[24]	83[25]	
Units: nanomoles				
arithmetic mean (standard deviation)				
Week 4, n=208, 0, 0	61.0 (± 68.6)	9999 (± 9999)	9999 (± 9999)	
Week 24, n=208, 0, 0	54.5 (± 79.1)	9999 (± 9999)	9999 (± 9999)	
Week 40, n=0, 184, 83	9999 (± 9999)	57.0 (± 73.3)	48.2 (± 57.0)	

Notes:
[23] - 9999=participants in this treatment group weren't analyzed at this time point.
[24] - 9999=participants in this treatment group weren't analyzed at this time point.
[25] - 9999=participants in this treatment group weren't analyzed at this time point.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from the time of Informed Consent Form signing until at least 30 days after the last application of study drug (up to Week 52 + 30 days)

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs): AEs reported for the first time or the worsening of a pre-existing event after the first application of study drug. For the Double-Blind Period, TEAEs are reported for members of the Safety Population. For the Treatment-Extension (TE) Period, TEAEs are reported for the TE Evaluable Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Vehicle cream BID

Reporting group description:

Participants applied matching vehicle cream twice a day (BID) for 24 weeks in the Double-Blind Period.

Reporting group title	Ruxolitinib cream 1.5% BID

Reporting group description:

Participants applied ruxolitinib cream during the Double-Blind Treatment Period and the Treatment-Extension Period. Participants applied ruxolitinib 1.5% cream BID for 24 weeks. Participants who completed the Week 24 assessments with no safety concerns could continue into the 28-week Treatment-Extension Period. Participants who applied ruxolitinib cream 1.5% BID during the Double-Blind Period continued to apply ruxolitinib cream 1.5% BID for an additional 28 weeks in the Treatment-Extension Period. Participants who applied vehicle cream BID during the Double-Blind Period applied ruxolitinib cream 1.5% BID for 28 weeks in the Treatment-Extension Period.

Serious adverse events	Vehicle cream BID	Ruxolitinib cream 1.5% BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 115 (0.00%)	6 / 326 (1.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Joint dislocation			

subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	0 / 115 (0.00%)	1 / 326 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Vehicle cream BID	Ruxolitinib cream 1.5% BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 115 (5.22%)	56 / 326 (17.18%)	
General disorders and administration site conditions			
Application site acne			
subjects affected / exposed	3 / 115 (2.61%)	20 / 326 (6.13%)	
occurrences (all)	3	24	
Infections and infestations			

COVID-19			
subjects affected / exposed	2 / 115 (1.74%)	24 / 326 (7.36%)	
occurrences (all)	2	25	
Nasopharyngitis			
subjects affected / exposed	1 / 115 (0.87%)	17 / 326 (5.21%)	
occurrences (all)	1	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2019	The primary purpose of this amendment was to incorporate revisions requested by the Voluntary Harmonisation Procedure (VHP). - Added language to exclude participant who had current and/or history of tuberculosis - Added language to exclude participants who lived with anyone participating in any current Incyte-sponsored ruxolitinib cream study - Added language to instruct that German participants whose hemoglobin was between 10 grams per deciliter (g/dL) and 10.5 g/dL during the screening visit should have been further evaluated per local guidelines before enrolling into the study
21 February 2020	The primary purpose of this amendment was to incorporate revisions requested by the German and French Ethics Committees (ECs) and FDA. - Reordered and revised the key secondary endpoints and updated the analysis plan - Added 1 key exclusion criteria (exclude other forms of vitiligo) to the Population section, added information about the exit interview in the Study Design section, and added a Data and Safety Monitoring Board (DSMB) section to indicate that a DSMB was not required in this study - Added language that targeted physical examination should be conducted as indicated by symptoms reported by the participant, adverse events (AEs), or other findings. Abnormalities that were considered clinically significant in the judgment of the investigator were to be reported as AEs. - Added language to instruct that adolescent participants screened in Germany whose hemoglobin was between 10 g/dL and 12 g/dL during the screening visit should have ben further evaluated per local guidelines before being enrolled into the study.

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.

Data from participants at a single site were excluded from all efficacy analyses done on the Intent-to-Treat Population owing to serious noncompliance with the protocol resulting in serious concerns with the data quality.

Notes: