# 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 | 2019-000846-37 |
| Trial protocol | FR PL DE BG ES IT |
| Global end of trial date | 21 October 2021 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 11 October 2022 |
| First version publication date | 05 May 2022 |
| Version creation reason | |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | INCB 18424-306 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04052425 |
| 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 18554633463, medinfo@incyte.com |
| Scientific contact | Study Director, Incyte Corporation, 1 18554633463, 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 | 21 October 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 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 | 20 September 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 | United States: 204 |
| Country: Number of subjects enrolled | Bulgaria: 17 |
| Country: Number of subjects enrolled | Canada: 16 |
| Country: Number of subjects enrolled | France: 19 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Poland: 63 |
| Country: Number of subjects enrolled | Spain: 4 |
| Worldwide total number of subjects | 330 |
| EEA total number of subjects | 110 |

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) | 265 |
| From 65 to 84 years | 29 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 45 study centers in North America and Europe.

### Pre-assignment

Screening details:

A total of 330 participants were randomized into the study. All randomized participants (Intent-to-Treat Population) applied study drug at least once (Safety Population), and 283 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 | Subject, Investigator, Monitor, 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 |
| 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 | 221 | 109 |
| Completed | 193 | 90 |
| Not completed | 28 | 19 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 9 | 10 |
| Adverse event, non-fatal | - | 1 |
| Discontinued Treatment Due to COVID-19 Pandemic | 3 | - |
| Lost to follow-up | 14 | 7 |
| Protocol deviation | 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 | Vehicle |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:
twice daily

| | |
|---|---|
| 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 | 193 | 90 |
| Completed | 174 | 80 |
| Not completed | 19 | 10 |
| Consent withdrawn by subject | 10 | 7 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 1 | - |
| Participant Moved | 1 | 1 |
| Lost to follow-up | 5 | 1 |
| Sponsor Opinion Due to Safety Reason | 1 | - |
| 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 | 221 | 109 | 330 |
| Age categorical<br>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) | 25 | 11 | 36 |
| Adults (18-64 years) | 180 | 85 | 265 |
| From 65-84 years | 16 | 13 | 29 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 40.5 | 39.7 | |
| standard deviation | ± 15.44 | ± 16.71 | - |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 136 | 50 | 186 |
| Male | 85 | 59 | 144 |
| Race, Customized<br>Units: Subjects | | | |
| White | 180 | 96 | 276 |
| Black/African American | 11 | 4 | 15 |
| Asian | 5 | 4 | 9 |
| American Indian/Alaska Native | 1 | 0 | 1 |
| Not Reported | 16 | 3 | 19 |
| Latino | 3 | 1 | 4 |
| Hispanic or Latino | 1 | 0 | 1 |
| Iranian | 1 | 0 | 1 |
| Indian | 1 | 1 | 2 |
| Hispanic | 1 | 0 | 1 |
| Black-Hispanic | 1 | 0 | 1 |
| Ethnicity, Customized<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Hispanic or Latino | 53 | 20 | 73 |
| Not Hispanic or Latino | 151 | 86 | 237 |
| Not Reported | 15 | 3 | 18 |
| Unknown | 1 | 0 | 1 |
| Captured as "Other" | 1 | 0 | 1 |
| 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% (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), 100% (no pigment). F-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each facial site and summing all values (range: 0-3; higher values=worse outcome). | | | |
| Units: scores on a scale | | | |
| arithmetic mean | 0.932 | 0.999 | |
| standard deviation | ± 0.5813 | ± 0.5942 | - |
| 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 of facial surface area | | | |
| arithmetic mean | 1.05 | 1.15 | |
| standard deviation | ± 0.692 | ± 0.710 | - |
| 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; Investigator assessed) and the degree of depigmentation: 0% (no depigmentation), 10% (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), 100% (no pigment). T-VASI was derived by multiplying the vitiligo involvement values by the percentage of affected skin for each site and summing all values (possible range: 0-100; higher values=worse outcome). | | | |
| Units: scores on a scale | | | |
| arithmetic mean | 6.489 | 6.424 | |
| standard deviation | ± 2.0228 | ± 1.9241 | - |
| 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 of total body surface area | | | |
| arithmetic mean | 7.28 | 7.22 | |
| standard deviation | ± 2.033 | ± 2.008 | - |

## 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 | 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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 29.8 | 7.4 | | |

**Statistical analyses**

| Statistical analysis title | exact logistic regression |
|---|---|
| Comparison groups | Double-Blind Period: Vehicle cream BID v Double-Blind Period: Ruxolitinib cream 1.5% BID |
| Number of subjects included in analysis | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 [1] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.341 |
| upper limit | 11.903 |

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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 51.2 | 16.9 | | |

**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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 [2] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.831 |
| upper limit | 9.482 |

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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 15.3 | 2.2 | | |

**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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0038 [3] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 8.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.997 |
| upper limit | 36.048 |

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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 20.6 | 5.1 | | |

### 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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.002 [4] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.795 |
| upper limit | 13.566 |

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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 24.5 | 3.3 | | |

**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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0002 [5] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 9.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.9 |
| upper limit | 31.29 |

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 | 221 | 109 | | |
| Units: percentage change | | | | |
| least squares mean (standard error) | -28.9 (± 2.22) | -9.5 (± 3.25) | | |

**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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 [6] |
| Method | ANCOVA |
| Parameter estimate | least squares mean difference |
| Point estimate | -19.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -27.05 |
| upper limit | -11.64 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.93 |

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 | 221 | 109 | | |
| Units: participants | 101 | 42 | | |

### 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 | 193 | 90 | | |
| Units: participants | 65 | 31 | | |

### 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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 69.8 | 30.0 | | |

**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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [7] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.226 |
| upper limit | 9.578 |

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 | 173 | 82 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| F-VASI25 | 89.6 | 74.4 | | |
| F-VASI50 | 75.1 | 56.1 | | |
| F-VASI75 | 52.6 | 26.8 | | |
| F-VASI90 | 32.9 | 12.2 | | |

## 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 | 195 | 90 | | |
| Units: percentage change | | | | |
| least squares mean (standard error) | -47.79 (± 2.43) | -17.18 (± 3.53) | | |

**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 | 285 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | mixed-effect model; repeated measurement |
| Parameter estimate | least squares mean difference |
| Point estimate | -30.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -39.03 |
| upper limit | -22.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.28 |

**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 | 173 | 82 | | |
| Units: percentage change | | | | |
| arithmetic mean (standard deviation) | -67.24 (± 33.660) | -52.98 (± 30.174) | | |

## 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 | 173 | 82 | | |
| Units: percentage change | | | | |
| arithmetic mean (standard deviation) | -44.87 (± 43.954) | -32.40 (± 30.068) | | |

## 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 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). 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 | 195 | 90 | | |
| Units: percentage change | | | | |
| least squares mean (standard error) | -27.60 (± 1.81) | -10.62 (± 2.64) | | |

### 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 | 285 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | mixed-effect model; repeated measurement |
| Parameter estimate | least squares mean difference |
| Point estimate | -16.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.28 |
| upper limit | -10.68 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.2 |

## 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 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). 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 | 173 | 82 | | |
| Units: percentage change | | | | |
| arithmetic mean (standard deviation) | -49.23 (± 26.366) | -29.85 (± 37.832) | | |

### 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 | 195 | 90 | | |
| Units: percentage change | | | | |
| least squares mean (standard error) | -13.08 (± 1.40) | -4.02 (± 2.05) | | |

**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 | 285 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0003 |
| Method | mixed-effect model; repeated measurement |
| Parameter estimate | least squares mean difference |
| Point estimate | -9.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.96 |
| upper limit | -4.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.49 |

**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 | 173 | 82 | | |
| Units: percentage change | | | | |
| arithmetic mean (standard deviation) | -27.39 (± 25.705) | -11.83 (± 34.654) | | |

## 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 | 221 | 109 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| T-VASI25 | 48.8 | 23.8 | | |
| T-VASI75 | 4.1 | 1.8 | | |
| T-VASI90 | 0.5 | 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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 [8] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.746 |
| upper limit | 5.307 |

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 | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2921 [9] |
| Method | exact logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.489 |
| upper limit | 10.823 |

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

| | |
|---|---|
| Number of subjects included in analysis | 330 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.49 |
| 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 | 173 | 82 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| T-VASI25 | 77.5 | 56.1 | | |
| T-VASI50 | 53.2 | 31.7 | | |
| T-VASI75 | 20.2 | 9.8 | | |
| T-VASI90 | 3.5 | 2.4 | | |

## 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 | 195[10] | 90[11] | 173[12] | 82[13] |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24, more noticeable | 6.2 | 14.4 | 9999 | 9999 |
| Week 24, as noticeable | 17.4 | 46.7 | 9999 | 9999 |
| Week 24, slightly less noticeable | 51.3 | 35.6 | 9999 | 9999 |
| Week 24, a lot less noticeable | 24.1 | 3.3 | 9999 | 9999 |
| Week 24, no longer noticeable | 1.0 | 0.0 | 9999 | 9999 |
| Week 52, more noticeable | 9999 | 9999 | 4.0 | 4.9 |
| Week 52, as noticeable | 9999 | 9999 | 9.2 | 15.9 |
| Week 52, slightly less noticeable | 9999 | 9999 | 46.8 | 59.8 |
| Week 52, a lot less noticeable | 9999 | 9999 | 39.3 | 19.5 |
| 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 | 178 | 87 | | |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -1.17 (± 0.27) | -0.85 (± 0.39) | | |

**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 | 265 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.497 |
| Method | mixed-effect model; repeated measurement |
| Parameter estimate | least squares mean difference |
| Point estimate | -0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.26 |
| upper limit | 0.62 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

## 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 | 204[14] | 105[15] | 204[16] | 105[17] |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline, n=204, 105 | 4.63 (± 4.446) | 4.59 (± 4.871) | 9999 (± 9999) | 9999 (± 9999) |
| Week 52, n=157, 79 | 9999 (± 9999) | 9999 (± 9999) | -1.40 (± 4.087) | -1.37 (± 3.617) |

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] | 4[19] | 17[20] | 4[21] |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline, n=16, 4 | 2.50 (± 2.805) | 1.25 (± 1.893) | 9999 (± 9999) | 9999 (± 9999) |
| Week 24, n=16, 3 | -0.25 (± 2.113) | 0.00 (± 0.000) | 9999 (± 9999) | 9999 (± 9999) |
| Week 52, n=15, 3 | 9999 (± 9999) | 9999 (± 9999) | -1.00 (± 2.507) | 0.00 (± 1.000) |

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 | 206[23] | 173[24] | 80[25] | |
| Units: nanomoles | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4, n=206, 0, 0 | 57.1 (± 61.4) | 9999 (± 9999) | 9999 (± 9999) | |
| Week 24, n=191, 0, 0 | 56.3 (± 69.4) | 9999 (± 9999) | 9999 (± 9999) | |
| Week 40, n=0, 173, 80 | 9999 (± 9999) | 55.5 (± 63.6) | 50.1 (± 55.8) | |

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[1]

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.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events occurred in at least 5% of participants in either treatment arm.

| Serious adverse events | Vehicle cream BID | Ruxolitinib cream 1.5% BID | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 109 (0.92%) | 8 / 311 (2.57%) | |
| 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) | | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| 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 | | | |
| Concussion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kidney contusion | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 109 (0.92%) | 0 / 311 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Subacute combined cord degeneration | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis infectious mononucleosis | | | |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 311 (0.32%) | |
| 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 | 0 / 109 (0.00%) | 0 / 311 (0.00%) | |

## 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).<br>- Added language to exclude participant who had current and/or history of tuberculosis<br>- Added language to exclude participants who lived with anyone participating in any current Incyte-sponsored ruxolitinib cream study<br>- 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.<br>- Reordered and revised the key secondary endpoints and updated the analysis plan<br>- 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<br>- Added language that targeted physical examination should have been 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.<br>- 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 been 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

None reported