6-2-2021

Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial

Iltefat H. Hamzavi
Henry Ford Health, ihamzav1@hfhs.org

David Rosmarin

John E. Harris

Amit G. Pandya

Mark Lebwohl

See next page for additional authors

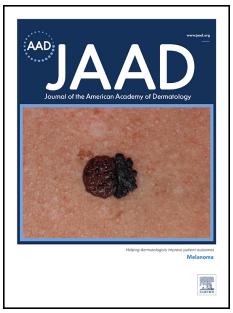
Recommended Citation

Hamzavi I, Rosmarin D, Harris JE, Pandya AG, Lebwohl M, Gottlieb AB, Butler K, Kuo FI, Sun K, and Grimes P. Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial. J Am Acad Dermatol 2021.

Authors

Iltefat H. Hamzavi, David Rosmarin, John E. Harris, Amit G. Pandya, Mark Lebwohl, Alice B. Gottlieb, Kathleen Butler, Fiona I. Kuo, Kang Sun, and Pearl Grimes

Journal Pre-proof



Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial

Iltefat Hamzavi, MD, David Rosmarin, MD, John E. Harris, MD, PhD, Amit G. Pandya, MD, Mark Lebwohl, MD, Alice B. Gottlieb, MD, PhD, Kathleen Butler, MD, Fiona I. Kuo, PhD, Kang Sun, PhD, Pearl Grimes, MD

PII: S0190-9622(21)01043-4

DOI: https://doi.org/10.1016/j.jaad.2021.05.047

Reference: YMJD 16049

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 4 September 2020

Revised Date: 24 May 2021

Accepted Date: 26 May 2021

Please cite this article as: Hamzavi I, Rosmarin D, Harris JE, Pandya AG, Lebwohl M, Gottlieb AB, Butler K, Kuo FI, Sun K, Grimes P, Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial, *Journal of the American Academy of Dermatology* (2021), doi: https://doi.org/10.1016/j.jaad.2021.05.047.

Efficacy of Ruxolitinib Cream in Vitiligo by Patient Characteristics and Affected Body Areas: Descriptive Subgroup Analyses From a Phase 2, Randomized, Double-Blind Trial

Iltefat Hamzavi, MD,[1] David Rosmarin, MD,[2] John E. Harris, MD, PhD,[3] Amit G. Pandya, MD,[4,5] Mark Lebwohl, MD,[6] Alice B. Gottlieb, MD, PhD,[6] Kathleen Butler, MD,[7] Fiona I. Kuo, PhD,[7] Kang Sun, PhD,[7] Pearl Grimes, MD[8]

[1]Henry Ford Medical Center, Detroit, MI; [2]Tufts Medical Center, Boston, MA; [3]University of Massachusetts Medical School, Worcester, MA; [4]Palo Alto Foundation Medical Group, Mountain View, CA; [5]University of Texas Southwestern Medical Center, Dallas, TX; [6]Icahn School of Medicine at Mount Sinai, New York, NY; [7]Incyte Corporation, Wilmington, DE; [8]The Vitiligo & Pigmentation Institute of Southern California, Los Angeles, CA

Corresponding Author: Iltefat Hamzavi, MD
Department of Dermatology
Henry Ford Medical Center
3031 West Grand Blvd
Detroit, MI 48202
Phone: (313) 916-2151
Email: IHamzavi@hamzavi.com

Manuscript word count: 453 words (limit, 500)

References: 4 (limit, 5)

Figures/Tables: 1/1 (limit, 2)

IRB approval statement: The study protocol was approved by each site's institutional review board.

Clinical trials registration: Clinicaltrials.gov: NCT03099304

Keywords: Janus kinase, pigmentation, ruxolitinib cream, subgroup analysis, vitiligo, Vitiligo Area Scoring Index

Funding sources: Support for this study was provided by Incyte Corporation.

Conflicts of interest: IH has served as an advisory board member for AbbVie; a consultant for Incyte Corporation, Pfizer, and UCB; a principal investigator for AbbVie, Allergan, Bayer, Clinuvel Pharmaceuticals, Estée Lauder, Ferndale Laboratories, Galderma Laboratories LP, GE Healthcare, Incyte Corporation, Janssen, Janssen Biotech, Johnson & Johnson, Lenicura, LEO Pharma, Pfizer, and Unigen; a subinvestigator for Amgen, Bristol Myers Squibb, Foamix Pharmaceuticals, and Janssen; president of the HS Foundation; and cochair of the Global Vitiligo Foundation. DR has received honoraria as a consultant for AbbVie, Celgene, Dermavant Sciences, Dermira, Eli Lilly and Company, Janssen, Kyowa Kirin, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharmaceuticals, UCB, and VielaBio; research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly and Company, Incyte Corporation, Janssen, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi. JEH has served as a consultant for AbbVie, Aclaris Therapeutics, BiologicsMD, EMD Serono, Genzyme/Sanofi, Janssen, Pfizer, Rheos Medicines, Sun Pharmaceuticals, TeVido BioDevices, The Expert Institute, 3rd Rock Ventures, and Villaris Therapeutics; has served as an investigator for Aclaris Therapeutics, Celgene, Dermira, EMD Serono, Genzyme/Sanofi, Incyte Corporation, LEO Pharma, Pfizer, Rheos Medicines, Stiefel/GSK, Sun Pharmaceuticals, TeVido BioDevices, and Villaris Therapeutics; holds equity in Rheos Medicines, TeVido BioDevices, and Villaris Therapeutics; is a scientific founder of Villaris Therapeutics; and has patents pending for IL-15 blockade for treatment of vitiligo, JAK inhibition with light therapy for vitiligo, and CXCR3 antibody depletion for treatment of vitiligo. AGP has served as an investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte Corporation, and Pfizer; a consultant for Arcutis, Avita Medical, Chromaderm, Immune Tolerance Network, Incyte Corporation, Pfizer, Viela Bio, and Villaris; and a board member who also holds stock options for Clarify Medical and Tara Medical. ML is an employee of Mount Sinai Hospital, which receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte Corporation, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc; and is a consultant for Aditum Bio, Almirall, AnaptysBio, Arcutis, Aristea, Arrive Technology, Avotres Therapeutics, BioMX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics,

Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, and Verrica. ABG has received honoraria as an advisory board member and consultant for AnaptysBio, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Incyte Corporation, Janssen, LEO Pharma, Novartis, Sun Pharmaceuticals, and UCB; has stock options in Xbiotech; and has received institutional research/educational grants from Boehringer Ingelheim, Incyte Corporation, Janssen, Novartis, UCB, Xbiotech, and Sun Pharmaceuticals to Mount Sinai School of Medicine. KB, FIK, and KS are employees and shareholders of Incyte Corporation. PG has served as a consultant for Aclaris Therapeutics, Clarify Medical, DermaForce, Incyte Corporation, Proctor & Gamble, and Versicolor Technologies and a principal investigator for Aclaris Therapeutics, Allergan/SkinMedica, Clinuvel Pharmaceuticals, Incyte Corporation, Johnson & Johnson, L'Oreal, Merz Pharma, Pfizer, Thync Global Inc., and VT Cosmetics.

To the Editor: Vitiligo is a chronic autoimmune disease resulting in patches of depigmented skin[1] and reduced quality of life.[2] In a randomized, dose-ranging phase 2 study (NCT03099304) in 157 adult patients, the Janus kinase (JAK) 1/JAK2 inhibitor ruxolitinib cream produced substantial repigmentation of facial and total body vitiligo lesions after 24 weeks, with continued improvement through Week 52, and was well tolerated.[3] Here we present treatment response subanalyses from the phase 2 trial.

The proportion of patients receiving 1.5% ruxolitinib cream twice daily (BID) who achieved ≥50% improvement in facial Vitiligo Area Scoring Index (F-VASI50) at Week 24 was assessed by demographics and baseline clinical characteristics. In addition, the proportion of patients initially randomized to 1.5% ruxolitinib cream once daily (QD) or BID who achieved ≥50% and ≥75% improvement from baseline in total VASI (T-VASI50 and T-VASI75, respectively) at Week 52 was assessed by affected body area. Because ruxolitinib cream application was limited to ≤20% of total body surface area (T-BSA; limit for practicality of application), total body analyses were conducted only in patients with vitiligo affecting ≤20% of T-BSA at baseline. Data were analyzed using descriptive statistics.

Among 33 patients who received 1.5% ruxolitinib cream BID, a larger proportion of F-VASI50 responders at 24 weeks were aged ≤50 years compared with >50 years (58.8% vs 31.3%; **Figure 1**). A larger proportion of female versus male patients (60.0% vs 33.3%) were F-VASI50 responders. A larger proportion of responders had ≤1.5% affected baseline facial BSA, disease duration >20 years, and previous treatment with phototherapy. There were no substantial differences between responders based on race, skin type, baseline T-BSA, or disease status.

Among patients with vitiligo affecting ≤20% of T-BSA at baseline, both doses of ruxolitinib cream (1.5% QD and BID) produced notable T-VASI50 and T-VASI75 responses at Week 52 (**Table 1**). The 1.5% ruxolitinib cream BID dose produced the highest proportion of T-VASI50 responders in the head/neck region (60.0%), followed by upper and lower extremities (52.9% and 52.6%, respectively). T-VASI50 of the hands and feet was noted for 15.0% and 29.4% of patients, respectively, who received 1.5% ruxolitinib cream BID.

In summary, ruxolitinib cream demonstrated trends for clinical activity in the treatment of vitiligo across demographics and clinical characteristics, including in patients with longstanding and extensive disease. F-VASI50 responses were observed in >40% of patients previously treated with topical corticosteroids or topical calcineurin inhibitors and in two-thirds of patients who received prior phototherapy. Ruxolitinib cream also produced clinically meaningful repigmentation of all body areas, including acral areas that are notoriously difficult to repigment.[4]

Overall, these findings support the use of ruxolitinib cream in the treatment of vitiligo. Reported analyses were descriptive and sample sizes were small, warranting confirmation of results in larger populations.

Acknowledgments

The study was funded by Incyte Corporation (Wilmington, DE). Writing assistance was provided by Laurie Orloski, PharmD, of ICON (North Wales, PA) and was funded by Incyte Corporation.

References

1. Taïeb A, Picardo M. Clinical practice. Vitiligo. N Engl J Med 2009;360:160-9.
2. Morrison B, Burden-Teh E, Batchelor JM, Mead E, Grindlay D, Ratib S. Quality of life in people with vitiligo: a systematic review and meta-analysis. Br J Dermatol 2017;177:e338-e9.
3. Rosmarin D, Pandya AG, Lebwohl M, Grimes P, Hamzavi I, Gottlieb AB, et al. Ruxolitinib cream for treatment of vitiligo: a randomised, controlled, phase 2 trial. Lancet 2020;396:110-20.
4. Esmat SM, El-Tawdy AM, Hafez GA, Zeid OA, Abdel Halim DM, Saleh MA, et al. Acral lesions of vitiligo: why are they resistant to photochemotherapy? J Eur Acad Dermatol Venereol 2012;26:1097-104.

Table 1. Proportion of Patients Who Applied 1.5% Ruxolitinib Cream and Achieved T-VASI50 or T-VASI75 Responses at Week 52*

	Ruxolitinib Cream	
Responders, n/N (%)	**1.5% QD**	**1.5% BID**
T-VASI50†	7/19 (36.8)	9/20 (45.0)
Head/neck	6/19 (31.6)	12/20 (60.0)
Trunk	7/18 (38.9)	5/17 (29.4)
Upper extremities	7/18 (38.9)	9/17 (52.9)
Lower extremities	6/18 (33.3)	10/19 (52.6)
Hands	4/19 (21.1)	3/20 (15.0)
Feet	5/19 (26.3)	5/17 (29.4)
T-VASI75†	2/19 (10.5)	3/20 (15.0)
Head/neck	5/19 (26.3)	11/20 (55.0)
Trunk	4/18 (22.2)	2/17 (11.8)
Upper extremities	3/18 (16.7)	4/17 (23.5)
Lower extremities	3/18 (16.7)	5/19 (26.3)
Hands	4/19 (21.1)	1/20 (5.0)
Feet	4/19 (21.1)	3/17 (17.6)

BID, twice daily; QD, once daily; T-BSA, total body surface area; T-VASI50, ≥50% improvement from baseline in total Vitiligo Area Scoring Index; T-VASI75, ≥75% improvement from baseline in total Vitiligo Area Scoring Index.

* T-VASI50 and T-VASI75 responses are reported for the subset of patients with baseline T-BSA ≤20% because treatment was limited to lesions constituting ≤20% of T-BSA.

† Percentage change from baseline differs for each body region, and the value for all body regions is based on the sum of all regions; binary outcomes (ie, yes/no) for T-VASI50 may not follow the distribution of percentage change from baseline.

Figure Legend

Figure 1. F-VASI50 Response to 1.5% Ruxolitinib Cream BID at Week 24 by Patient Demographics and Clinical Characteristics. * Disease duration was not available for 1 patient; † Determination of disease stability was based on investigator judgment. ‡ Patients could have used ≥1 previous therapy. BID, twice daily; F-BSA, facial body surface area; F-VASI50, ≥50% improvement from baseline in facial Vitiligo Area Scoring Index; SE, standard error; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; T-BSA, total body surface area.