Journal of Dermatology and Skin Science

Mini Review Article Open Access

Patient Journey in Atopic Dermatitis: The Real-world Scenario

Jose Manuel Carrascosa[1], Francisco José Rebollo[2*]

[1]Hospital Universitario Germans Trias I Pujol, Badalona, Spain
[2]Pfizer SLU, Madrid, Spain

Article Info

Article Notes
Received: January 12, 2022
Accepted: March 22, 2022

***Correspondence:**
*Dr. Francisco José Rebollo, Pfizer SLU, Avenida Europa 20B, Parque Empresarial La Moraleja, 28108 Madrid, Spain; Email: francisco.rebollo@pfizer.com.

Atopic dermatitis (AD) is a chronic skin disease associated with a heterogenous clinical presentation[1]. This diversity extends to the patient age at disease onset, intensity of disease signs and symptoms, disease trajectory, and emergence of comorbid conditions during the "atopic march"[1], the progression of atopic conditions from AD to allergic rhinitis and asthma in young patients[2]. AD treatment guidelines[3-5] have been developed to guide clinicians in decision-making when treating patients with this disease; however, there are inconsistencies among these guidelines[6]. Heterogeneity in disease presentation, divergent treatment guidelines, and an increasingly broad therapeutic landscape can result in ambiguity with regards to diagnosis and treatment in a real-world clinical setting. The clinical variability in the diagnosis, treatment, and management of AD in Asia, Africa, North America, Latin America, Europe, and the Middle East has been described in the literature[7-16]. Here, we discuss an analysis to investigate the consistency of the AD patient journey in Spain, from the perspective of dermatologists in a real-world clinical setting[17].

Carrascosa et al[17] evaluated the perception of a group of dermatologists in Spain regarding the diagnosis, treatment, and long-term management of AD. After conducting a systematic literature review to identify statements regarding AD diagnosis and treatment, the authors convened a scientific committee to discuss the outcomes of this review and propose a list of items for inclusion in a Delphi questionnaire. The Delphi questionnaire was then distributed online to a panel of Spanish dermatologists to assess their consensus on various topics. The degree of consensus on each topic was determined based on an analysis of the responses and an established consensus threshold from the Delphi survey technique guidelines[18].

A total of 17 dermatologists completed the survey. Despite the existence of detailed guidelines for the diagnosis of AD and the treatment of patients with AD[3-5, 19], Carrascosa et al revealed a lack of consensus among the dermatologists in Spain concerning essential aspects of routine diagnosis and treatment[17]. Of the 58 items included in the Delphi questionnaire, consensus was reached on 22 items (37.9%), including 5 of 22 items (22.7%) on patient presentation and diagnosis, 11 of 27 items (19.0%) on therapeutic approaches to managing AD, and 6 of 7 items (86.0%) on long-term management and flare treatment (**Table 1**). Consensus was not reached on many clinical aspects of AD, including Delphi items regarding diagnostic criteria and severity rating scales, and treatment[17].

Table 1. Items in the Delphi Questionnaire for which a consensus was reached. Reproduced from Carrascosa et al 2021[7]

Delphi Questionnaire Item	Strength of consensus (median)
Block 1: Patient Presentation and Diagnosis	
Patient Journey	
The dermatologist is the professional who usually makes the differential diagnosis of moderate-to-severe forms of AD	10
In addition to the dermatologist, the following specialists should typically be involved in the management of patients with mild AD: pediatricians, allergists, general practitioner	8
Assessment of risk factors	
[No items reached consensus]	
Diagnosis Criteria and Severity Rating Scales	
For the diagnosis of AD, the specialist's opinion prevails over other criteria, such as rating indexes and scales	8
Measures that assess the patient's quality of life should be added to adopt a comprehensive approach to the management of patients with AD	10
Mobile phone apps featuring disease severity scales are useful in usual clinical practice	8
Block 2: Therapeutic Approaches to the Management of AD	
Emollient recommendation	
In routine clinical practice, patients with atopic dermatitis are usually prescribed a specific emollient	8
Hygienic measures	
In terms of bathing practices as nonpharmacological measures for the treatment of atopic dermatitis, a daily frequency is recommended	8
Educational actions	
At the office visit, patient involvement in the treatment of atopic dermatitis is usually sought to ensure good therapeutic results	9
Educational measures are usually implemented in clinical practice to achieve greater patient involvement in the treatment of AD and the prevention of flare	8
Scope of nonpharmacological treatment	
Adjuvant nonpharmacological treatment is essential to achieve good therapeutic results, even with the new generation of drugs used for AD	9
In mild–moderate forms of atopic dermatitis, or between flares, non-pharmacological measures are typically proactively supplemented with preventive pharmacological treatments	8
Topical treatment	
Lesion location is more relevant than age of the patient for determining the potency of a topical corticosteroid	8
Corticosteroid wet wrap therapy is a common strategy in the management of moderate–severe AD in children	8
Topical calcineurin inhibitors are used as second-line therapy after corticosteroids for the topical treatment of AD	9
Phototherapy	
[No items reached consensus]	
Systemic therapy	
Antihistamines are commonly prescribed in patients with moderate–severe AD	8
Based on the data available at the moment, systemic therapy with Janus kinase (JAK) inhibitors could potentially have a relevant role in the systemic treatment of patients with moderate–severe atopic dermatitis	9
Assessment of effectiveness	
[No items reached consensus]	
Block 3: Long-Term Management and Flare Treatment	
Proactive (maintenance treatment)	
The intermittent use of topical corticoids as maintenance therapy is common in clinical practice	9
The use of calcineurin inhibitors as maintenance therapy is common in clinical practice	9
Pharmacological approach to the treatment of flares	
Stress is frequently a triggering factor in an AD flare	8
In the dermatological visit during a flare, factors such as a lack of treatment compliance, infection, or contact dermatitis are assessed before intensifying treatment	9
Patient commitment	
''Steroid phobia'' (the rejection of corticosteroids due to safety concerns) often compromises patient compliance with treatment involving these drugs	9
Low treatment compliance is a common obstacle in the long-term management of AD	9

Items were rated on a 10-point scale, where 1 meant "totally disagree" and 10 "totally agree"

Table reproduced with permission from Carrascosa JM, de la Cueva P, de Lucas R, Fonseca E, Martín A, Vicente A, et al. Patient journey in atopic dermatitis: the real-world scenario. Dermatol Ther. 2021;11(5):1693-705.

Although there was limited consensus surrounding aspects of AD symptoms and diagnosis, consensus was reached on the role and variety of specialists involved in patient management and the importance of the role of medicated topical treatments (topical corticosteroids [TCS] and topical calcineurin inhibitors [TCI]) for long-term maintenance of disease control. By contrast, there was a lack of consensus around the use of severity scales and indices for scaling up therapy, suggesting that scales developed for clinical trials may not be applicable to clinical practice.

In patients with moderate-to-severe AD, regular use of TCS and TCI may not be sufficient to control disease[20]. Guidelines recommend scaling up therapy to include the use of advanced systemic therapies in these patients, which includes phototherapy and oral immunosuppressants[5, 20]. This study did not find a consensus on the timing or use of these systemic therapies, which may reflect the increasing adoption of biologic therapies for treating patients with moderate-to-severe AD. Until recently, biologic therapy was limited to the injectable interleukin-4 receptor α antibody, dupilumab[21, 22]. The therapeutic potential of Janus kinase (JAK) inhibition has now become a focus of research. Oral JAK inhibitors, including baricitinib (JAK1/2)[23-25], upadacitinib (JAK1/2/3/tyrosine kinase 2 inhibitor with preference for JAK1)[26-29], and abrocitinib (JAK1)[30-34] have shown efficacy and safety in the treatment of moderate-to-severe AD in pivotal phase 2b and phase 3 clinical trials. Approval for use in moderate-to-severe AD has been granted for baricitinib (Olumiant™), upadacitinib (Rinvoq™), and abrocitinib (Cibinqo™) in the European Union[35-37], Korea[35, 38, 39], Japan[40-42], and Great Britain[43-45] among other countries. Upadacitinib and abrocitinib were recently approved for use by eligible patients with moderate-to-severe AD in the United States,[46, 47] while the FDA decision on baricitinib is pending[48]. Real-world data describing the safety and efficacy of JAK inhibitors in the treatment of patients with moderate-to-severe AD are limited. Regardless, most dermatologists surveyed in this study agreed upon the significant near-term potential of JAK inhibitors for the treatment of moderate-to-severe AD.

Carrascosa et al extends upon a previous Delphi analysis of dermatologists and allergologists in Spain[49] but with a dermatologist-only sample. Although Delphi questionnaires used in previous studies were designed to evaluate consensus on guideline statements[50], the aim of this study was to assess consensus on the practical aspects of real-world clinical scenarios. One important aspect of AD diagnosis, treatment, and long-term maintenance that was highlighted by this study was the central role of the patient throughout the disease course. Surveyed dermatologists agreed on the importance of considering patient quality of life when establishing a management plan, as well as the need for health education and patient commitment to therapy. Together, these findings highlight the importance of involving patients in their treatment.

Carrascosa et al also found discrepancies in dermatologists' perspectives that aligned closely with discrepancies across AD guidelines. For example, although a consensus was reached among the surveyed dermatologists on the importance of frequent bathing for patients with AD, the addition of bath additives was not agreed upon, reflecting disparate recommendations on this topic across AD guidelines[3, 4].

The results of Carrascosa et al are promising and provide valuable insight into the views of dermatologists who interact with AD patients in real-world clinical settings in Spain[17]. Nevertheless, there are limitations to the generalizability of the findings. The analysis included only dermatologists, even though multiple specialists are routinely involved in the treatment of AD[20]. In addition, a relatively small number of dermatologists in Spain answered the Delphi questionnaire. Replicating this analysis in a larger sample of clinicians in other countries could provide a deeper understanding of the global applicability of the results.

Current understanding of the AD patient trajectory in the real-world clinical setting is limited. Although this study suggests a lack of consensus among dermatologists treating AD in Spain, further research is needed to determine how best to address this lack of consensus in a real-world clinical setting. A more unified approach to the development of AD diagnostic and treatment guidelines to address the complexities of diagnosis and management in the real world will become especially necessary as new treatment options for AD continue to emerge.

Abbreviations

AD, atopic dermatitis; JAK, Janus kinase; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids.

Conflicts of Interest

JMC has received honoraria or fees as investigator, speaker, and/or advisor from Pfizer, Sanofi, Lilly, AbbVie, LEO Pharma, and UCB. **FJR** is an employee and shareholder of Pfizer Inc.

Acknowledgements

Editorial/medical writing support under the guidance of authors was provided by Megan K. Elder, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med*. 2015;163:461-464).

References

1. Amat F, Soria A, Tallon P, et al. New insights into the phenotypes of atopic dermatitis linked with allergies and asthma in children: An overview. Clin Exp Allergy. 2018; 48(8): 919-34.
2. Bantz SK, Zhu Z, Zheng T. The atopic march: Progression from atopic dermatitis to allergic rhinitis and asthma. J Clin Cell Immunol. 2014; 5(2):pii: 202.
3. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014; 71(1): 116-32.
4. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. J Allergy Clin Immunol. 2013; 131(2): 295-9.e1-27.
5. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol. 2014; 71(2): 327-49.
6. Eichenfield LF, Ahluwalia J, Waldman A, et al. Current guidelines for the evaluation and management of atopic dermatitis: A comparison of the Joint Task Force Practice Parameter and American Academy of Dermatology guidelines. J Allergy Clin Immunol. 2017; 139(4S): S49-S57.
7. Katoh N, Ohya Y, Ikeda M, et al. Japanese guidelines for atopic dermatitis 2020. Allergol Int. 2020; 69(3): 356-69.
8. Sinclair W, Aboobaker J, Jordaan F, et al. Management of atopic dermatitis in adolescents and adults in South Africa. SAMJ: South African Medical Journal. 2008; 98(4): 303-20.
9. Weinstein M, Barber K, Bergman J, et al. Atopic dermatitis: a practical guide to management. Health Care Provid Resour. 2016; 12: 1-12.
10. Aoki V, Lorenzini D, Orfali RL, et al. Consensus on the therapeutic management of atopic dermatitis-Brazilian Society of Dermatology. Anais Brasileiros de Dermatologia. 2019; 94: 67-75.
11. Russo F, Milanesi N, Iannone M, et al. Tuscan Consensus on the diagnosis, treatment and follow up of adult atopic dermatitis. G Ital Dermatol Venereol. 2020; 155: 253-60.
12. Poveda-Montoyo I, García-Doval I, Descalzo M, et al. Quality Indicators in Care of Patients With Atopic Dermatitis: Consensus Document of the Spanish Academy of Dermatology and Venereology. Actas Dermo-Sifiliográficas (English Edition). 2020; 111(7): 567-73.
13. Tan SH, Yew YW. Editorial on guidelines for the management of atopic dermatitis in Singapore. Ann Acad Med Singap. 2016; 45: 437-8.
14. Rubel D, Thirumoorthy T, Soebaryo RW, et al. Consensus guidelines for the management of atopic dermatitis: An Asia–Pacific perspective. J Dermatol. 2013; 40(3): 160-71.
15. Reda AM, Elgendi A, Ebraheem AI, et al. A practical algorithm for topical treatment of atopic dermatitis in the Middle East emphasizing the importance of sensitive skin areas. J Dermatol Treat. 2019; 30(4): 366-73.
16. Lopez Carrera YI, Al Hammadi A, Huang Y-H, et al. Epidemiology, diagnosis, and treatment of atopic dermatitis in the developing countries of Asia, Africa, Latin America, and the Middle East: a review. Dermatol Ther. 2019; 9(4): 685-705.
17. Carrascosa JM, de la Cueva P, de Lucas R, et al. Patient journey in atopic dermatitis: The real-world scenario. Dermatol Ther (Heidelb). 2021; 11(5): 1693-705.
18. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. J Adv Nurs. 2000; 32(4): 1008-15.
19. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014; 70(2): 338-51.
20. Boguniewicz M, Fonacier L, Guttman-Yassky E, et al. Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape. Ann Allergy Asthma Immunol. 2018; 120(1): 10-22.e2.
21. Regeneron Pharmaceuticals Inc. DUPIXENT® (dupilumab) injection, for subcutaneous use. 03/2019. Regeneron Pharmaceuticals Inc.: Tarrytown, NY; 2019. p. 48.
22. Ratchataswan T, Banzon TM, Thyssen JP, et al. Biologics for treatment of atopic dermatitis: Current status and future prospect. J Allergy Clin Immunol Pract. 2021; 9(3): 1053-65.
23. Guttman-Yassky E, Silverberg JI, Nemoto O, et al. Baricitinib in adult patients with moderate-to-severe atopic dermatitis: A phase 2 parallel, double-blinded, randomized placebo-controlled multiple-dose study. J Am Acad Dermatol. 2019; 80(4): 913-21.e9.
24. Simpson EL, Forman S, Silverberg JI, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis: Results from a randomized monotherapy Phase 3 trial in the United States and Canada (BREEZE-AD5). J Am Acad Dermatol. 2021.
25. Simpson EL, Lacour JP, Spelman L, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: results from two randomized monotherapy phase III trials. Br J Dermatol. 2020; 183(2): 242-55.
26. Blauvelt A, Teixeira HD, Simpson EL, et al. Efficacy and safety of upadacitinib vs dupilumab in adults with moderate-to-severe atopic dermatitis: A randomized clinical trial. JAMA Dermatol. 2021; 157(9): 1047-55.
27. Guttman-Yassky E, Teixeira HD, Simpson EL, et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. Lancet. 2021; 397(10290): 2151-68.
28. Guttman-Yassky E, Thaci D, Pangan AL, et al. Upadacitinib in Adults With Moderate-to-Severe Atopic Dermatitis: 16-Week Results From a Randomized, Placebo-Controlled Trial. J Allergy Clin Immunol. 2019.
29. Reich K, Teixeira HD, de Bruin-Weller M, et al. Safety and efficacy of upadacitinib in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis (AD Up): results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2021; 397(10290): 2169-81.
30. Silverberg JI, Simpson EL, Thyssen JP, et al. Efficacy and safety of abrocitinib in patients with moderate-to-severe atopic dermatitis: a randomized clinical trial. JAMA Dermatol. 2020; 156(8): 863-73.
31. Gooderham MJ, Forman SB, Bissonnette R, et al. Efficacy and safety of oral janus kinase 1 inhibitor abrocitinib for patients with atopic dermatitis: a phase 2 randomized clinical trial. JAMA Dermatol. 2019; 155(12): 1371-9.
32. Bieber T, Simpson EL, Silverberg JI, et al. Abrocitinib versus placebo or dupilumab for atopic dermatitis. N Engl J Med. 2021; 384(12): 1101-12.
33. Blauvelt A, Silverberg JI, Lynde CW, et al. Abrocitinib induction, randomized withdrawal, and retreatment in patients with moderate-to-severe atopic dermatitis: Results from the JAK1 Atopic Dermatitis Efficacy and Safety (JADE) REGIMEN phase 3 trial. J Am Acad Dermatol. 2022; 86(1): 104-112.
34. Eichenfield LF, Flohr C, Sidbury R, et al. Efficacy and Safety of abrocitinib in combination with topical therapy in adolescents with moderate-to-severe atopic dermatitis: The JADE TEEN randomized clinical trial. JAMA Dermatol. 2021; 157(10): 1165-73.
35. European commission approves pfizer's cibinqo® (abrocitinib) for the treatment of adults with moderate-to-severe atopic dermatitis [press release]. New York, NY: Pfizer Inc., 12/10/2021. https://www.pfizer.com/news/press-release/press-release-detail/european-commission-approves-pfizers-cibinqor-abrocitinib

36. New oral treatment for moderate to severe atopic dermatitis [press release]. Netherlands: European Medicines Agency, 09/18/2020. https://www.ema.europa.eu/en/news/new-oral-treatment-moderate-severe-atopic-dermatitis

37. European Commission Approves RINVOQ® (upadacitinib) as first JAK inhibitor in the European Union for the treatment of both adults and adolescents with moderate to severe atopic dermatitis [press release]. North Chicago, Illinois, U.S.A.: AbbVie, Inc., 08/24/2021. https://news.abbvie.com/news/press-releases/european-commission-approves-rinvoq-upadacitinib-as-first-jak-inhibitor-in-european-union-for-treatment-both-adults-and-adolescents-with-moderate-to-severe-atopic-dermatitis.htm

38. Olumiant's indication for atopic dermatitis has expanded [press release]. Seoul, Korea: Dailypharmkorea, 05/28/2021. http://www.dailypharmkorea.com/Users/News/NewsView.html?ID=2099

39. AbbVie's Rinvoq adds indications including atopic dermatitis [press release]. Seoul, Korea: Korea Biomedical Review, 10/16/2021. http://www.koreabiomed.com/news/articleView.html?idxno=12293

40. JAPAN'S MHLW approves PFIZER'S CIBINQO® (ABROCITINIB) for adults and adolescents with moderate to severe atopic dermatitis [press release]. New York, NY: Pfizer, Inc., 09/30/2021. https://www.pfizer.com/news/press-release/press-release-detail/japans-mhlw-approves-pfizers-cibinqor-abrocitinib-adults

41. MHLW approves label expansions for olumiant, gardasil, lynparza and more [press release]. Japan: JIHO, Inc., 12/28/2020. https://pj.jiho.jp/article/243552

42. Japan approves Forxiga for CKD, rinvoq's atopic dermatitis use and more [press release]. Japan: JIHO, Inc., 08/26/2021. https://pj.jiho.jp/article/245071

43. UK'S MHRA grants marketing authorisation for Pfizer's CIBINQO® (abrocitinib) for adults and adolescents with moderate to severe atopic dermatitis [press release]. New York, NY: Pfizer Inc., 09/09/2021. https://www.pfizer.com/news/press-release/press-release-detail/uks-mhra-grants-marketing-authorisation-pfizers-cibinqor

44. NICE approval for Olumiant, a new class of treatment for atopic eczema [press release]. London, UK: The Pharma Letter, 03/03/2021. https://www.thepharmaletter.com/article/nice-approval-for-olumiant-a-new-class-of-treatment-for-atopic-eczema

45. MHRA nod for AbbVie's Rinvoq for adults and adolescents with eczema [press release]. Surrey, UK: PharmaTimes Media Limited: Virtual, 09/01/2021. https://www.pharmatimes.com/news/mhra_nod_for_abbvies_rinvoq_for_adults_and_adolescents_with_eczema_1376101

46. U.S. FDA approves Pfizer's CIBINQO® (abrocitinib) for adults with moderate-to-severe atopic dermatitis [press release]. New York, NY: Pfizer, Inc., 01/14/2022. https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-pfizers-cibinqor-abrocitinib-adults

47. U.S. FDA approves RINVOQ® (upadacitinib) to treat adults and children 12 years and older with refractory, moderate to severe atopic dermatitis [press release]. New York, NY: PR Newswire, 01/14/2022. https://www.prnewswire.com/news-releases/us-fda-approves-rinvoq-upadacitinib-to-treat-adults-and-children-12-years-and-older-with-refractory-moderate-to-severe-atopic-dermatitis-301461377.html

48. Impending regulatory approvals in atopic dermatitis (AD) [press release]. London, UK: Verdict Media Limited, 12/02/2021. https://www.pharmaceutical-technology.com/comment/impending-regulatory-approvals-atopic-dermatitis

49. Sastre J, Baldrich ES, Armario Hita JC, et al. Consensus on the clinical approach to moderate-to-severe atopic dermatitis in spain: A delphi survey. Dermatol Res Pract. 2020; 1524293.

50. Boguniewicz M, Alexis AF, Beck LA, et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: A multidisciplinary consensus addressing current and emerging therapies. J Allergy Clin Immunol Pract. 2017; 5(6): 1519-31.