Clinical, Cosmetic and Investigational Dermatology

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CASE SERIES

Managing Atopic Dermatitis with Dupilumab in Special Populations: A Case Series Study

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin disorder with skin barrier disruptions and heightened T helper (Th) 2-mediated inflammation. Dupilumab, a monoclonal antibody targeting interleukin-4 and −13 pathways, has shown efficacy in treating AD and other type 2 inflammatory diseases. However, its safety and effectiveness in special populations (SP) like kidney transplant recipients, cancer patients, and individuals with neurological conditions remain unclear.

Materials and Methods: This retrospective case series includes 12 representative cases of SP treated with dupilumab, featuring cases of a kidney transplant recipient, a metastatic melanoma patient, a non-functioning pituitary adenoma patient, and an individual with multiple sclerosis (MS). Clinical data were collected, and outcomes were assessed using various indices.

Results: Dupilumab provided significant AD symptom improvement across all cases, with no adverse effects or recurrence of underlying conditions.

Conclusion: Dupilumab shows promise for managing AD in SP, but careful monitoring and further research are necessary to address safety concerns and optimize treatment strategies. Larger studies with longer follow-ups are needed to fully evaluate its safety and efficacy in SP and those with comorbidities. These findings support the need for personalized treatments and ongoing research to enhance outcomes in patients with complex medical histories.

Keywords: atopic dermatitis, dupilumab, special populations, melanoma, kidney transplant, multiple sclerosis

Introduction

Atopic dermatitis (AD) represents a chronic inflammatory skin disorder characterized by disruptions in the skin barrier and hyperactivation of T helper (Th) 2-mediated inflammation.[1] Atopic dermatitis takes the form of an extremely common skin disorder: around 101.27 million adults and 102.78 million children worldwide have AD, corresponding to prevalence rates of 2.0% (95% UI 1.4–2.6) and 4.0% (95% UI 2.8–5.3), respectively.[2] Females were more likely to suffer from AD than males. Clinically, AD manifests as eczema accompanied by pruritus and commonly affects individuals across all age groups, with a higher prevalence observed in children. Within the pathophysiology of atopic dermatitis, aberrant activation of the Th2 pathway results in the overexpression of specific inflammatory cytokines, notably interleukin-4 (IL-4) and IL-13.[3,4] The list of factors that can potentially trigger or contribute to atopic dermatitis is extensive, ranging from genetic factors, family history, dietary choices, immune triggers, and environmental factors.[5] Dupilumab, a recombinant human IgG4 monoclonal antibody, effectively targets interleukin-4 and interleukin-13 signal transduction pathways.[6,7] By blocking IL-4 signal transduction through the type I receptor (IL-4Rα/γc) and both IL-4 and IL-13 signal transduction through the type II receptor (IL-4Rα/IL-13Rα), dupilumab demonstrates therapeutic efficacy in managing AD and related type 2 inflammatory diseases such as asthma and chronic rhinosinusitis with nasal polyps (CRSwNP).[8] Recent systemic therapies for AD include innovative biologics and JAK inhibitors (JAKi) beyond dupilumab.[9] Upadacitinib and abrocitinib, both JAK1 selective inhibitors, have demonstrated rapid and potent efficacy,

Received: 24 November 2024
Accepted: 30 April 2025
Published: 30 October 2025

with upadacitinib showing excellent short-term results, especially in reducing AD-related symptoms severity.[10,11] Baricitinib, another JAKi, has also shown sustained efficacy in AD, with ongoing studies highlighting its potential for both monotherapy and in combination with topical therapies.[9,12] Additionally, tralokinumab, a selective IL-13 inhibitor, has shown promising long-term efficacy with improvements in pruritus and quality of life, while lebrikizumab, also targeting IL-13, demonstrated superior efficacy compared to placebo in both adolescents and adults.[13,14] Both biologics offer an alternative approach to IL-13 targeting, differing in their mechanisms of action but sharing similar clinical benefits. These treatments, alongside JAKi, provide new options for patients seeking alternatives to traditional therapies.

In clinical practice, certain patient groups, including patients with medical comorbidities and elderly, are significantly underrepresented in clinical trials.[15] The exclusion of special populations (SPs) from clinical research creates an unmet medical need when new drugs enter the market, as their safety and efficacy profiles remain largely uncertain. Despite the well-documented effectiveness and safety of many therapies in both clinical trials and real-world settings, studies specifically addressing SPs remain scarce. Clinical trials often implement strict inclusion and exclusion criteria, which limit the representation of patients with complex medical conditions, disabilities, or concurrent treatments.[16] As a result, most available data on drug safety and efficacy in SPs originate from post-marketing studies.[16,17] These real-world data are crucial, as they reflect a broader spectrum of patient characteristics and better capture the heterogeneity observed in everyday clinical practice. SPs require particular attention due to physiological variations, clinical complexities, and potential drug interactions that can influence metabolism, treatment response, and the risk of adverse drug reactions (ADRs).[15,18] Addressing the needs of these populations is essential to ensure equitable healthcare and optimize therapeutic strategies. An approach that acknowledges the diversity of SPs while promoting individualized treatment strategies is needed to reduce disparities in medical care and improve patient outcomes. Recently, an expert consensus on the treatment of atopic dermatitis in special populations evaluated the optimal therapeutic strategies across six specific scenarios: (1) comorbid asthma, (2) ocular surface disease (OSD), (3) history of cancer, (4) past or ongoing infections of interest, (5) pregnancy and lactation, and (6) elderly patients.[19] However, we believe that a broader range of patient subgroups with atopic dermatitis should be considered to ensure the most comprehensive and personalized therapeutic approach. In recent years, special populations of patients with atopic dermatitis have been gaining increasing attention within the scientific community.[16,17,20] In this article, SPs refer to underrepresented groups in clinical trials who face unmet medical needs when new therapies become available. These include individuals with malignant neoplasms, organ insufficiencies, autoimmune diseases, connective tissue disorders, chronic infections, transplant recipients and pregnant women. This study aims to address the disparity between clinical trial outcomes and real-world experiences by conducting a comprehensive retrospective analysis of twelve patient records with atopic dermatitis, including those with significant comorbidities. Additionally, it seeks to evaluate the real-world effectiveness of dupilumab in routine clinical practice.

Materials and Methods

Study Population

This is a retrospective monocentric study included 12 patients affected by moderate-to-severe AD who received dupilumab treatment and attended the outpatient clinic. The inclusion criteria comprised individuals aged ≥18 years with a diagnosis of moderate-to-severe AD who had undergone dupilumab treatment for a minimum of 24 weeks and had one or more severe comorbidities, allowing them to be classified as part of "special populations." These special populations, typically excluded from approval trials, included cancer patients, transplant recipients, and individuals with chronic conditions. Moreover, selected patients presented comorbidities like infections, tumours, renal transplant, autoimmune diseases and genetic syndromes. Comorbidities were defined as "severe" when they significantly impact a patient's overall health, complicate the treatment of the primary condition, or increase the risk of adverse outcomes. Exclusion criteria were history of allergy to any component of dupilumab, absence of a severe comorbidity which does not allow to categorize these patients as SP. Patients were treated with dupilumab administered subcutaneously (SC); all patients initially received the dosing regimen approved for atopic dermatitis: 600 mg SC initially followed by 300 mg SC every other week. No specific washout period was required for patients to switch from immunosuppressive medication to

dupilumab. Data collected for the study included gender, medical history, previous treatments for AD, concomitant medications and clinical characteristics of the skin lesions. Skin improvement was assessed by Eczema Area and Severity Index (EASI), Pruritus Numeric Rating Scale (Pruritus-NRS), Sleep Numeric Rating Scale (Sleep-NRS), and Dermatology Life Quality Index (DLQI). For safety data, any new clinical symptoms reported by the patient or detected during physical exams were recorded at each visit and evaluated for possible side effects.

Statistical Analysis

Continuous variables were reported as median with range and mean ± SD. Categorical variables were summarized as frequencies and percentages of the study population and by subgroups, where appropriate. Statistical significance of clinical improvement (EASI, P-NRS, DLQI) at the last patient observation as compared with baseline was evaluated by using Student's *t*-test. Statistical analyses were performed using R version 4.0.2 and RStudio version 1.2.5033 (The R Foundation for Statistical Computing, Vienna, Austria), with significance set at $p < 0.05$.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. It was approved by the "Lazio 2" Ethics Committee (protocol number 0054579/2022, dated 09/03/2022) and registered in the AIFA (Agenzia Italiana del Farmaco) registry for observational studies. Written informed consent was obtained from all participants for the collection and use of their personal and clinical data. Patient information was extracted from electronic medical records and entered into a secure, password-protected, anonymized electronic database to ensure confidentiality and data protection.

Results

Population Description

A total of 142 patients were screened. Of these, 70 (49.29%) had a follow-up period of at least 24 weeks. Then, 72 (50.70%) subjects were excluded since they did not respect inclusion criteria. Finally, 12 patients were included in the study, respecting all the inclusion and exclusion criteria, as detailed in Table 1. Of these patients, 7 were female and 4 were male, age ranging from 12 to 87 years (mean age: 51.83 ± 27.45, mode: 75, median: 51). The cohort included individuals suffered from various comorbidities: 2 patients had genetic syndromes (Down syndrome and Kabuki syndrome), 3 had autoimmune diseases (multiple sclerosis, undifferentiated connectivitis, and Sjogren's syndrome), 4 had neoplastic diseases (thyroid carcinoma, metastatic melanoma, lung carcinoma, and pituitary adenoma), one had HIV-HCV co-infection, and one had chronic renal failure, one patient was a kidney transplant recipient. The interval between the diagnosis of the comorbidities and the initiation of dupilumab therapy varied significantly, ranging from 5 months to 43 years.

Efficacy and Safety Data

At baseline, the mean Eczema Area and Severity Index (EASI) score was 26.36 ± 5.09, while the Dermatology Life Quality Index (DLQI) was 21.8 ± 6.17, and the Pruritus Numeric Rating Scale (Pruritus-NRS) was 7.9 ± 2.66, indicating substantial disease burden and impact on quality of life (Figure 1). Considerable improvement of all scores was observed at the end of follow up period. In particular, a statistically significant reduction of EASI was observed at the last observation (1.67 ± 2.39, $p < 0.0001$) as compared with baseline. Similarly, DLQI significantly decrease (1.2 ± 1.57, $p < 0.0001$). As regards the impact of dupilumab on itch, p-NRS significantly reduced at the last visit (0.6 ± 0.86, $p < 0.0001$).

Here are the most interesting clinical cases categorized by themes.

Dupilumab in Kidney Diseases and Kidney Transplant Recipient

A 30-year-old Caucasian man, who had been diagnosed with AD since childhood, experienced a moderate-to-severe flare. He underwent kidney transplantation 15 years ago due to bilateral renal dysplasia. Post-transplant, the patient maintained good clinical status and commenced an immunosuppressive regimen with cyclosporine at a dosage of 3 mg/

https://doi.org/10.2147/CCID.S508359

Table 1 Demographic and Clinical Characteristics of Patients

N°	Sex (M/F)	Age (Years)	Relevant Disease	Date of Relevant Disease Diagnosis	Management of Relevant Comorbidity.	Prior and Concomitant Therapy for AD	Date of Dupilumab Treatment Start	EASI at Baseline	DLQI at Baseline	Pruritus-NRS at Baseline	Date of Last Observation	EASI at Last Observation	DLQI at Last Observation	Pruritus-NRS at Last Observation	Dupilumab-Related Adverse Events
1	F	43	Down Syndrome	Birth	Follow-up and citalopram	Prior: PhT, Cys Concomitant: TCSs	Jul-2021	20	10	5	May-2024	0	0	0	No
2	M	22	Multiple Sclerosis	Oct-2020	Teriflunomide	Concomitant: TCSs	Jan-2022	26	20	7	Oct-2024	0	0	0	No
3	M	82	Metastatic Melanoma	Oct-2018	Pembrolizumab (discontinued), dabrafenib and trametinib	Prior: PhT, TCIs, TCSs	Oct-2021	40	30	8	Mar-2024	0	0	0	No
4	M	87	Lung Cancer	Nov-2017	Osimertinib	Prior: PhT, TCIs Concomitant: TCSs	Mar-2022	30	25	9	Jun-2024	5	0	2	No
5	F	23	Pituitary Adenoma	Apr-2020	Follow-up	Prior: TCSs, Cys, TCIs	Sep-2021	24	30	7	Jun-2024	0	0	0	No
6	F	26	Papillary Thyroid Cancer	Oct-2020	Levotiroxine	Prior: TCSs, Cys	Feb-2021	25	20	8	Jul-2024	5	5	2	No
7	F	12	Kabuki Syndrome	Birth	Follow-up and speech therapy	Concomitant: TCSs	May-2023	20	30	8	Oct-2024	0	0	0	No
8	F	75	Undifferentiated Connective Tissue Disease	Apr-2013	Azathioprine	Prior: Cys, PhT, TCSs Concomitant: TCIs	Sep-2022	26	20	10	Oct-2024	0	0	0	No
9	M	87	Renal Failure	Jun-2012	Dialysis	Prior: TCSs, PhT	Feb-2023	30	20	10	Sep-2023	4	2	2	No
10	F	60	HIV and HCV	Jan-2012	Sofosbuvir (discontinued), Bictegravir/ Emtricitabine/ Tenofovir	Prior: Pht, TCSs	Jul-2021	25	20	10	Aug-2024	0	0	0	No
11	F	75	Sjogren Syndrome	Dec-2010	Courses of methylprednisolone, artificial tears	Prior: Cys, TCIs Concomitant: TCSs	Feb-2021	24	15	5	Nov-2024	0	0	0	No
12	M	30	Kidney transplant recipient	Jul- 2009	Tacrolimus, mycophenolate mofetil, and prednisone	Prior: TCSs	Sep- 2020	28	15	10	Sep-2024	6	3	1	No

Abbreviations: AD, Atopic Dermatitis; M, Male; F, Female; HIV, Human Immunodeficiency Virus; HCV, Hepatitis C Virus; Cys, Cyclosporine; PhT, Phototherapy; CCS, Corticosteroids; TCSs, topical corticosteroids; TCIs, Topical Calcineurin Inhibitors.

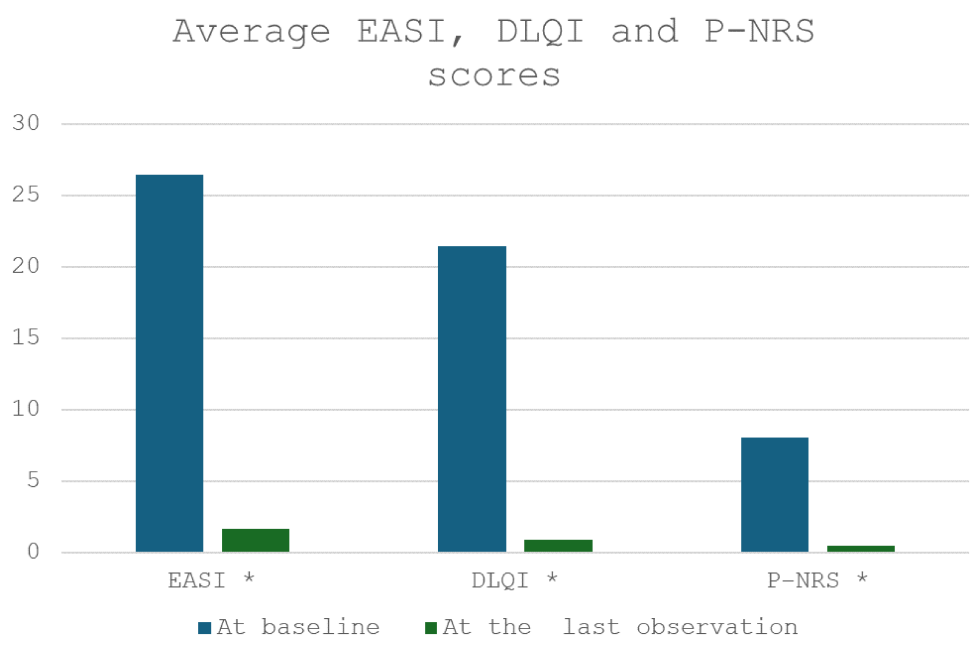

Figure 1 Improvement of EASI, DLQI, and p-NRS Scores from Baseline to Last Observation. * statistically significant ($p < 0.05$).
Abbreviations. EASI, Eczema Area Severity Index; DLQI, Dermatology Life Quality Index; P-NRS, Pruritus – Numerical Rating Scale.

kg/day. However, due to the onset of arterial hypertension, he transitioned to tacrolimus at a daily dosage of 2 mg, mycophenolate mofetil at 360 mg daily, and prednisone at 6 mg every other day after 7 years. He presented subsequently with a severe AD, reflected by an EASI 28, a Pruritus-NRS 10, a Sleep-NRS 10, and a DLQI 15, despite the ongoing immunosuppressive regimen. He had previously undergone approximately six months of topical therapy (corticosteroid and emollient) and oral antihistamines, resulting in only a partial response. In agreement with the transplant team, treatment with Dupixent was initiated. Initially, the patient received two subcutaneous injections (600 mg each), followed by administration every two weeks at a dosage of 300 mg. After 4 weeks of treatment, significant improvement was observed, with a reduction in EASI score from 28 to 6 and an improvement in DLQI from 15 to 3. By the end of the second month of treatment, the patient achieved complete resolution of dermatitis, which was sustained at the one-year follow-up visit. No adverse effects related to dupilumab, or deterioration of the transplanted organ were observed.

The second patient was an 85-year-old male with a history of severe atopic dermatitis (AD), chronic kidney disease (CKD) likely due to hypertensive nephrosclerosis. His complex medical background made management challenging. The patient had previously undergone treatment with potent topical corticosteroids and phototherapy, but these interventions provided limited clinical benefit in managing his severe atopic dermatitis. He presented with a severe AD, reflected by an EASI 30, a Pruritus-NRS 10, a Sleep-NRS 9, and a DLQI 20. Despite the comorbidity and the severe AD, after one year of treatment with dupilumab, there was a significant improvement in his AD scores, reflecting an effective management of his skin condition. Renal function remained stable throughout this period, with no noticeable decline. However, due to the advanced stage of his renal disease, the patient required dialysis 5 months after starting dupilumab treatment. Notably, the initiation of dialysis did not necessitate any modification of his dupilumab dosage. Over the subsequent 12-month follow-up period, while undergoing dialysis, the patient continued to show excellent control of his AD symptoms, with dupilumab maintaining its efficacy. No adverse effects were reported, and his renal function did not deteriorate further during this period.

Dupilumab in Patients with Neoplastic Diseases

An 82-year-old Caucasian man with metastatic nodular melanoma, initially on pembrolizumab then dabrafenib/trametinib, developed severe atopic dermatitis refractory to topicals/antihistamines and achieved rapid, sustained control with dupilumab from October 2021 without adverse events; this case has already been reported by Tolino et al, 2024.[21]

An 87-year-old male with advanced lung cancer, on ongoing osimertinib since November 2017, developed chronic eczematous dermatitis compatible with treatment-associated atopic dermatitis. Prior therapies included phototherapy and topical calcineurin inhibitors, with inadequate control; topical corticosteroids were continued concomitantly. At presentation (March 2022), disease severity scores were SCORAD 30, EASI 25, and pruritus-NRS 9, indicating moderate–severe activity with intense itch and sleep disturbance. Given suboptimal response to topical measures and the need to avoid systemic immunosuppression in an oncologic patient, dupilumab was initiated. Progressive improvement was observed, reaching SCORAD 5, EASI 0, and pruritus-NRS 2 by June 2024, with sustained clinical remission on maintenance dosing. No adverse events attributable to dupilumab were reported.

A 26-year-old female patient presented with significant eczematous lesions, severe pruritus, and sleep disturbances. Histological examination confirmed the diagnosis of atopic dermatitis (AD). At the time of diagnosis, the patient had an ASI score of 25, an NRS pruritus score of 8, and a DLQI of 20. She was initially treated with potent topical corticosteroids and systemic cyclosporine, but the cyclosporine therapy was discontinued due to hypertensive episodes. The patient was then started on dupilumab therapy. Follow-up visits showed significant improvement in her skin condition and a marked reduction in symptoms. However, 12 months after starting dupilumab therapy, a neck ultrasound revealed suspicious thyroid nodules. The patient underwent total thyroidectomy, resulting in a diagnosis of papillary thyroid carcinoma, and subsequent radioiodine therapy. The patient chose to discontinue dupilumab during the perioperative period (about 6 weeks), during which a mild flare of atopic dermatitis occurred. After completing radioiodine therapy, dupilumab was reintroduced, and the patient achieved control of her skin condition again. There were no signs of recurrence of thyroid pathology, and no adverse events related to dupilumab were reported. The patient is currently on levothyroxine therapy and maintains good control of her atopic dermatitis.

Dupilumab in Patients with Neurological Disorders

A 23-year-old female patient presented with severe atopic dermatitis and non-functioning pituitary adenoma. The patient has been suffering from atopic dermatitis since the age of one year. Over the years, the patient has been treated with topical therapy based on corticosteroids and emollients. At the age of 19, following a head trauma, she underwent a head CT scan, during which a pituitary adenoma was accidentally discovered confirmed by MRI. Laboratory evaluations were negative, allowing a diagnosis of non-functioning pituitary adenoma. Approximately 2 years after the adenoma was detected, the patient began to experience worsening atopic dermatitis (EASI 24, NRS-pruritus 7, NRS-sleep 10, DLQI 30). The patient underwent therapy with topical calcineurin inhibitors and cyclosporine with limited therapeutic benefits. In agreement with neurosurgeons and endocrinologists, subcutaneous dupilumab therapy was initiated. At 16 weeks from the start of treatment, a marked clinical improvement was observed (EASI 8, NRS-pruritus 4, NRS-sleep 5, DLQI 5). At the last follow-up, there was no increase in the size of the adenoma, and the hormonal profile was within normal limits. No adverse events related to dupilumab therapy were reported.

A 21-year-old male patient with a history of AD since childhood presented with severe rash and pruritus exacerbated recently. Physical examination revealed diffuse and severe xerosis, excoriated erythematous papules on the extremities and trunk, as well as localized hyperpigmentation on the extremities and trunk. The face was heavily involved. Laboratory tests at baseline showed elevated levels of IgE and lactate dehydrogenase. EASI was 26, while the Dermatology Life Quality Index (DLQI) was 20. The patient reported severe pruritus (NRS-pruritus 7/10) and sleep disturbances (NRS-sleep 5/10). Two years prior, he developed isolated paraesthesia in his left hand, followed by limb weakness, unstable walking and diplopia. Based on clinical history, MRI, and CSF examination, a diagnosis of multiple sclerosis (MS) was made. The patient was treated with teriflunomide and remained stable clinically and radiologically over the following two years. After multidisciplinary consultation, the patient started dupilumab therapy, which led to rapid and progressive improvement of AD signs and symptoms. At 16 weeks, significant improvement was observed in AD severity, pruritus, sleep disturbances, and quality of life (EASI 5, NRS-pruritus 2/10, NRS-sleep 0/10, DLQI 5). The patient continued dupilumab therapy, and more than two years later, he remains in complete remission of AD, with no relapses (EASI 0, NRS-pruritus 0, NRS-sleep 0 and DLQI 0) or dupilumab related adverse effects. Neurological evaluations and MRI scans confirm stable MS status.

Discussion

Dupilumab is one of the most effective and safe immunomodulating therapies available for treating moderate-to-severe AD and symptoms associated, including itching, poor sleep quality, anxiety, and depression.[22] The evidence from an increasing number of trials suggests that the benefits of dupilumab far outweigh its side effects. In clinical practice, certain patient groups, termed "special populations" (SP), are often underrepresented in clinical trials, including children, elderly individuals, patients with renal/hepatic impairment, pregnant women, and those with rare disabilities or clinical disorders. Insights into the effects of drugs within these populations primarily derive from postmarketing studies, as they may exhibit differential treatment responses and varying frequencies and severities of adverse drug reactions (ADRs) due to physiological variations and clinical complexities.[23]

This paper reports representative cases of special populations treated with dupilumab, focusing on the cases of a kidney transplant recipient, a metastatic melanoma patient, a patient with a non-functioning pituitary adenoma, and a patient suffering from multiple sclerosis.

In the case of the kidney transplant recipient, despite ongoing immunosuppressive therapy, the patient experienced a severe exacerbation of AD, which was effectively managed with dupilumab without adverse effects or organ deterioration. Several hypotheses have been proposed regarding why transplant recipients are at an increased risk of experiencing atopic dermatitis and allergic manifestations. It is believed that immunosuppressive drugs, particularly oral calcineurin inhibitors like tacrolimus, affect the Th1 response and inhibit IL-2 production, leading to a significant reduction in the control of the Th2 pathway by Treg lymphocytes.[24,25] This selective inhibition of the Th1 response may shift the immune response towards a Th2-type response, making transplant patients more susceptible to developing or worsening atopic dermatitis or other allergic manifestations. In this case, indeed, there was exacerbation of atopic dermatitis following the switch from cyclosporine to tacrolimus, which has greater selectivity in inhibiting the Th1 response. There are only seven case reports in the literature treating the use of dupilumab in the transplant patients: three cases involving heart transplant recipients aged 18, 29, and 12 years respectively,[25–27] two cases of liver transplant recipients aged 38 and 18 years,[28,29] and two cases of adult kidney transplant recipients aged 52 and 32 years.[28,30] Based on our study, we have found that dupilumab is a safe and effective option for treating moderate-to-severe atopic dermatitis in the post-transplant setting. A rapid and complete resolution of the disease without any discernible side effects or damage to the transplanted organ was observed.

In the metastatic melanoma patient treated with combined anti-BRAF/MEK targeted therapy, the onset of AD posed challenges due to safety concerns with systemic immunosuppressors. Dupilumab therapy proved effectiveness in managing AD symptoms without compromising cancer treatment outcomes. In the patient with a non-functioning pituitary adenoma, dupilumab therapy led to marked clinical improvement in AD symptoms without exacerbating the adenoma or affecting hormonal profiles. To date there are no reports regarding the correlation between the use of dupilumab and cancer.

A systematic review observed intricate and conflicting outcomes following modulation of the IL-13/IL-4 pathway concerning malignancy risk.[31] Predominantly, preclinical investigations have unveiled detrimental effects associated with both IL-13, both independently and in conjunction with IL-4, on malignancy, which conceivably could be mitigated through therapeutic pathway inhibition. Nonetheless, a minority of studies have indicated protective attributes of these pathways, the benefits of which might be compromised by targeted IL-13/IL-4 interventions. Adding to the complexity, a study by Ingram et al has revealed that blocking IL-4Rα, thereby inhibiting the IL-13 and IL-4 pathways, could exert either beneficial or deleterious effects contingent upon the cancer progression stage.[32] The apparent inconsistencies in these findings are likely attributable, at least in part, to the diverse experimental models and cell lines employed across studies. Furthermore, the heterogeneity of cancer types and the intricate molecular landscape of their respective tumor microenvironments may also contribute to these discrepancies. While safety profiles of drugs targeting the IL-13 and IL-4 pathway are generally favorable, it is imperative to acknowledge that the duration of many clinical trials may not have been sufficient to discern malignancy risks adequately.[31] Moreover, the external validity of existing clinical trials may be questioned due to the exclusion of patients with comorbidities and those on certain concomitant medications, potentially predisposing them to safety risks. Finally, no malignancy safety signals associated with modulation of the IL-13/IL-4 pathways were found. However, larger prospective studies with longer follow-up are needed to further assess this topic.

The case of the patient with multiple sclerosis (MS) who underwent treatment with dupilumab for atopic dermatitis represents a noteworthy instance of therapeutic success without exacerbation of the neurological condition.

The association between multiple sclerosis (MS) and atopic dermatitis (AD) remains controversial, with limited assessment of atopy prevalence in MS patients. Some research suggests a lower incidence of atopic disorders among MS patients, potentially linked to reduced T helper cell type 2 (Th2) cytokine release observed in MS.[33] There's speculation that a history of atopic allergies, notably asthma, might confer protection against MS.[34] However, reports of MS cases emerging or worsening during dupilumab therapy, an AD treatment, have surfaced.[35] Dupilumab suppresses Th2 activity by blocking the shared receptor subunit for interleukin-4 (IL-4) and interleukin-13 (IL-13), potentially promoting a shift towards Th1/Th17 polarization implicated in autoimmune diseases like psoriasis and MS.[36] One documented case noted a temporal association between relapsing-remitting MS flare-up and dupilumab treatment in an AD patient with long-standing untreated MS.[37] This suggests dupilumab's use in genetically predisposed individuals might trigger or exacerbate Th1/Th17-related diseases like MS. However, attributing direct causality between dupilumab and MS development or worsening is complex.[36] MS exhibits a variable course with relapses and remissions, especially in younger patients. Therefore, while these associations raise intriguing questions about the interplay between atopic disorders, immune modulation, and MS, further research is needed to clarify the mechanisms and potential risks associated with dupilumab or similar treatments in individuals predisposed to autoimmune diseases.

Limitations

This study presents several limitations that should be considered when interpreting the results. First, the sample size is relatively small, with only 12 patients included, which limits the generalizability of the findings. The diversity of the patient population, encompassing various comorbidities such as kidney transplant, metastatic melanoma, non-functioning pituitary adenoma, and multiple sclerosis, makes it difficult to draw definitive conclusions applicable to each condition individually. Moreover, the retrospective design of this study introduces potential biases, including selection bias and the reliance on pre-existing clinical records. Furthermore, the absence of a control group limits the ability to compare the effects of dupilumab against alternative treatments or placebo. The follow-up period was also relatively short, and this may not be sufficient to detect long-term safety concerns.

Conclusion

In summary, the findings from this study provide promising evidence regarding the safety and effectiveness of dupilumab in special populations, such as kidney transplant recipients, cancer patients, and individuals with neurological disorders like multiple sclerosis. However, the limitations discussed above highlight the need for further research. Future studies should involve larger, multicenter cohorts with longer follow-up periods to better evaluate the long-term safety and efficacy of dupilumab, particularly in special populations. Additionally, prospective studies with control groups would provide more robust comparisons and help address potential biases inherent in retrospective designs. Careful monitoring for adverse outcomes, including malignancy and autoimmune flare-ups, is necessary in these patient groups, and personalized treatment protocols should be developed to optimize outcomes. Ongoing research into the mechanisms underlying dupilumab's effects in these populations will further clarify its role in managing complex cases of atopic dermatitis and other comorbid conditions.

Informed Consent Statement

The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors.

Institutional Review Board Statement

The study was conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. It was approved by the "Lazio 2" Ethics Committee (protocol number 0054579/2022, dated 09/03/2022).

Data Sharing Statement

All data reported in the present manuscript will be available on request from the authors.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

The present study was not supported by any funds.

Disclosure

The authors declare no conflict of interest.

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