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SHORT PAPER

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# Use of dupilumab in a patient with atopic dermatitis, severe asthma, and HIV infection

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## Abstract

Dupilumab is a monoclonal antibody against interleukin 4 (IL-4) receptor α that blocks signaling from IL-4 and IL-13, essential mediators of T helper 2 (Th2) pathway. To date, all clinical trials investigating the use of dupilumab excluded patients with human immunodeficiency virus. Herein, we describe the safe and successful use of dupilumab in a patient with atopic dermatitis, severe therapy resistant asthma, and HIV infection.

**KEYWORDS**

asthma, atopic dermatitis, dupilumab, HIV

## 1 | CASE DESCRIPTION

We describe a 41-year-old Caucasian male who has suffered from generalized severe atopic dermatitis since childhood. Personal history included well-controlled HIV infection, severe therapy resistant asthma, and polyvalent allergy, with dominating house dust mite and cat allergy.

The asthma symptoms in the patient occurred from 3 years of age together with pollen rhinitis and peaked during his adolescence and then again after 2012. Since 2012, he has been on treatment corresponding to the highest step of Global Initiative for Asthma (GINA) guidelines, that is, treatment with high doses inhaled corticosteroids and long-acting beta-2 agonists, plus antileucotriene. Then thiotropium was added to the treatment, but despite that, the control of asthma was not achieved, and frequent exacerbations and gradual declination of lung function were observed.

HIV infection was diagnosed in 2006. Before antiretroviral therapy (ART, emtricitabine, tenofovir alafenamide, and darunavir), HIV laboratory values were CD4 650/μl, viral load 407,000c/ml and since then the patient has been repeatedly treated. The pre-dupilumab CD4 count was 800/μl and CD4/CD8 ratio was 1.82 (range 0.6-3).

The patient had previously received high-potency topical corticosteroids with an only temporary or insufficient clinical response for his skin disorder. He could not be treated with any systemic immunosuppressants on a long term basis due to HIV-infection, so dupilumab was his first systemic treatment, as it was not contraindicated in HIV patients. The treatment was initiated in November 2019 using the standard dosing regimen of a 600 mg induction dose subcutaneously followed by 300 mg dose every 2 weeks (Figure 1A,B). The patient responded with an immediate improvement of atopic dermatitis and bronchial asthma after the first dose.

Clinical improvement was evaluated by measuring the eczema area and severity index (EASI), SCORing atopic dermatitis (SCORAD) and body surface area (BSA). The patient's quality of life was assessed by the Dermatology Life Quality Index (DLQI) and visual analogue scale (VAS) to evaluate severity of itching and pain. The patient's initial EASI score was 39, BSA 72%, SCORAD 82.4, DLQI 12, and VAS 10. After the initial 16 weeks of therapy, the patient achieved EASI 1.8, BSA 6%, SCORAD 16,3, DLQI 4, and VAS 1 (Figure 2).

The laboratory parameters before dupilumab starting were as follows: total IgE 19 000 kU/l, specific IgE to house dust mite, cat and grass pollen—all above 100 kU/l, eosinophilia 600 abs., eosinophil cationic protein (ECP) 185.0 mcg/l, fraction of exhaled nitric oxide (FeNO) 170 ppb. As to lung function, Forced expiratory volume (FEV1) was 2.3 L (58% predicted). Asthma control test (ACT) 5 points from total 25. Parameters after 4 months treatment with dupilumab: total IgE 11800kU/l, eosinophilia and ECP were not significantly changed, FENO 34 ppb, FEV1 3.1 L (78% predicted), ACT 21 points, CD4 count 840/μl, and CD4/CD8 ratio 1.56.

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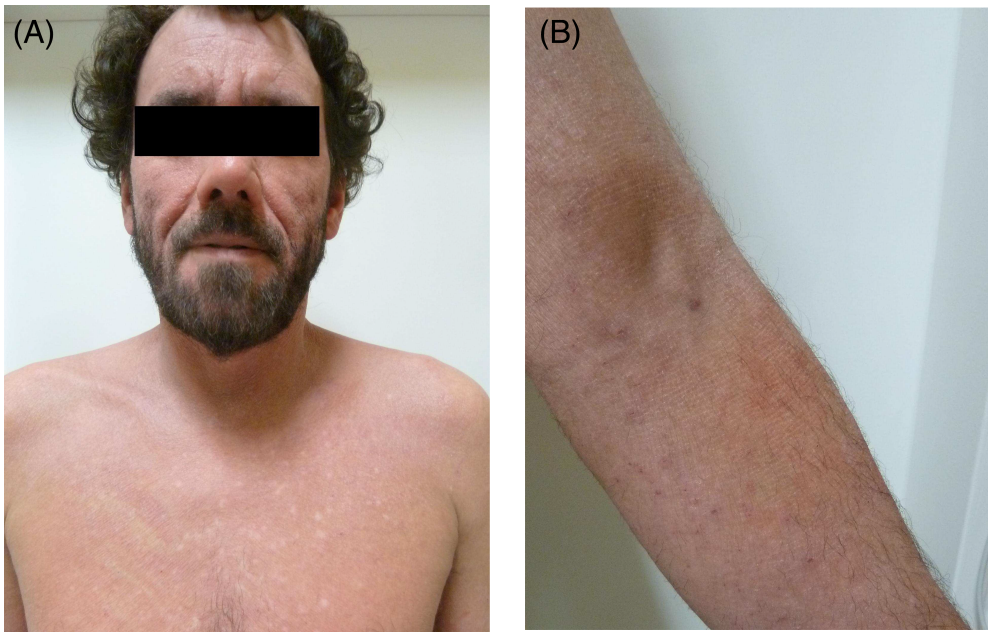



**FIGURE 1** A and B, Before treatment with dupilumab



**FIGURE 2** After 16 weeks of therapy with dupilumab

Nowadays, the patient is still treated with dupilumab for 33 weeks and no side effects or adverse events have been reported. Treatment with dupilumab significantly improved the patient's quality of life, itching, sleep, and symptoms of anxiety and depression.

## 2 | DISCUSSION

Atopic dermatitis (AD) is a common inflammatory skin condition. Pruritus is the essential feature of AD. Incidences of chronic itch and prurigo nodularis (PN) are higher in patients with HIV.[1,2]

Dupilumab is a fully human monoclonal antibody directed against the interleukin (IL)-4 receptor α that blocks the binding of IL-4 and IL 13, which are the key drivers of Th2 immune diseases, including AD. IL-4, and IL-13 have a direct effect on the epidermis by effecting the keratinocytes differentiation, production of filaggrin, and cell adhesion molecules. Furthermore, IL-4 and IL-13 induce Th2 cell activation and survival, promote IgE class switching, and stimulate eosinophil recruitment.

Dupilumab is the first biological agent approved for the treatment of patients with inadequately controlled moderate to severe AD.[3] Unfortunately, the effects of dupilumab in patients who are HIV-positive are unknown, as these patients were excluded from clinical trials if they had known or suspected history of immunosuppression, recurrent, or prolonged infections, a history of HIV infection or positive HIV serology at the screening.[3]

Last year, Mollanazar et al described the first four patients with HIV with concomitant AD or PN that were treated safely and successfully with dupilumab.[4] A couple of months later, Marks et al published another case on the use of dupilumab in the atopic patient with HIV.[5] All reported patients, including our case, experienced rapid and substantial improvement in AD and itch severity while HIV laboratory values remained stable.

Patients with AD have an increased risk of ocular comorbidities, especially keratoconjunctivitis, that could be controlled with artificial tears, antihistamine eye drops, or topical treatment with anti-inflammatory ointment on the eyelids. Other relatively frequently reported side effects during dupilumab treatment are headache, injection site reaction, and gastrointestinal complaints.[6-8] Transient eosinophilia was also observed in clinical trials, including patients treated with dupilumab for asthma, chronic sinusitis, and nasal polyposis.[3,6,7,8] This fact supports the hypothesis that dupilumab inhibits the migration of eosinophils into the tissues by suppressing the IL-4 and IL-13-stimulated production of eotaxins without influencing the production or migration from the bone marrow.[9] Eotaxins are released from endothelial cells that have been stimulated with IL-4 and IL-13 and

attract eosinophils and other inflammatory cells. Eosinophils stimulate the production of Th2-associated cytokines by T-lymphocytes, which in turn prolong the survival and mediate the activation and migration of eosinophils.[9] Dupilumab has shown to normalize the RNA expression of Th2-related inflammatory molecules and reverse skin barrier abnormalities in biopsies from AD patients treated with dupilumab.[10]

The current dupilumab package insert does not list HIV status as a contraindication.[7] Nevertheless, IL-4 may impact HIV co-receptor expression and immune dysregulation and so IL-4 can also play a role in HIV infection and disease advancement.[11] Additionally, Zheng et al showed that antiretroviral therapy leads to reduced IL-4 levels that were otherwise increased in untreated subjects. This may indicate a role for IL-4 in HIV replication.[12] Ranasinghe et al discussed the theory of using IL-4/13 blockade as a possibility for HIV vaccination.[13] The clinical relevance of these data for the use of dupilumab is still unclear. Possible interactions between dupilumab and the drugs used to treat HIV infection should also be considered. However, the Summary of Product Characteristics does not mention interaction with antiretrovirals.

## 3 | CONCLUSION

In our patient after 33 weeks of treatment, dupilumab has provided a rapid and substantial improvement in both bronchial asthma and atopic dermatitis. The cases of patients reported so far offer preliminary evidence that dupilumab is safe in patients who are HIV-positive and does not instigate disease progression, although our knowledge is limited by the relatively short duration of follow-up and further studies are necessary to investigate long-term effects.

As an immunomodulator of the Th2 inflammatory pathway, dupilumab is unique from other biological drugs and does not have any known relevant pharmacokinetic interactions to validate the exclusion of patients with HIV. Ultimately, it remains up to the treating physician to make a benefit/risk analysis and decide upon the best treatment for such a patient in light of the full clinical picture.

### CONFLICT OF INTEREST

None.

### AUTHORS' CONTRIBUTIONS

Petra Brodska and Petra Cetkovska: substantial contributions, collected data, performed the analysis, wrote the paper, final approval of the version to be published. Petr Panzner: collected data, performed the analysis. Dalibor Sedlacek: contributed data. Milan Terl: contributed data.

### DATA AVAILABILITY STATEMENT

Data available on request from the authors

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