Although it is possible for a KC to be clear in a plane, in fact, the distance of residual tumour to the inked surgical margin is examined. Hence, bread loaf sections are commonly used. Considerable improvement in hidradenitis suppurativa with oral roflumilast therapy.

DEAR EDITOR, Hidradenitis suppurativa (HS) is a chronic, inflammatory disease characterized by recurrent nodules, tunnels and excessive scarring in predominately inverse body sites. It is refined by the patient’s distress and social embarrassment, and costs society billions of dollars due to associated morbidity, healthcare expenditures, time lost from work, and reduced productivity. The disease is typically considered difficult to treat, and standard treatments include antibiotics, topical medications, systemic dapsone, isotretinoin, and surgery. Oral roflumilast, a selective phosphodiesterase 4 inhibitor, has demonstrated efficacy in improving inflammatory conditions. In this study, we evaluated the efficacy of oral roflumilast in improving HS symptoms. Our results indicate that oral roflumilast significantly reduced the frequency, size, and duration of HS flare-ups, as well as improved quality of life. These findings support the continued investigation of roflumilast as a potential treatment option for HS.

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regions. Moderate-to-severe HS is associated with various comorbidities, for example overweight and chronic obstructive pulmonary disease (COPD). Currently, adalimumab is the only biologic drug approved for HS by the European Medicines Agency. However, the drug survival time of adalimumab and other off-label biologics appears to be limited in HS. Therefore, alternative treatments are highly needed. We here present the first case of severe HS successfully treated with oral roflumilast, a selective phosphodiesterase (PDE)4 inhibitor.

In November 2020, a 54-year-old man was referred to our university dermatology clinic. Since 1995, he had experienced intermittent eruptions of boils and inflamed nodules in the intertriginous regions, and multiple systemic antibiotic courses of penicillin, dicloxacillin and doxycycline had been prescribed by his general practitioner. The patient had a 15-pack-year history of cigarette smoking and reported daily intake of a synthetic opioid (tramadol 50 mg, one to three times daily) due to skin pain. At clinical inspection, several inflamed interconnected tunnels, abscesses and excessive scarring were seen in inverse body regions, and the patient was diagnosed with Hurley stage 3 HS. In addition, moderate plaque psoriasis and obesity (body mass index 31.7 kg m\(^{-2}\)) were observed.

Biologic therapy with adalimumab (80 mg subcutaneously every 2 weeks) was initiated, but as disease control was not achieved in 6 months, treatment was shifted to infliximab (5 mg kg\(^{-1}\) intravenously, every 4 weeks). Despite this, severe HS flares continued [International Hidradenitis Suppurativa Severity Score System (IHS4) = 16], and infliximab was discontinued after 5 months. Monotherapy with oral roflumilast 500 µg once daily was initiated (Figure 1a). At the 3-month follow-up, the patient reported markedly improved quality of life, less intake of tramadol due to reduced HS activity (IHS4 = 9) and complete clearance of his psoriasis. In addition, he had achieved a 9-kg weight loss (body mass index 29.1 kg m\(^{-2}\)) (Figure 1b). Improvements were maintained after 5 months of treatment (IHS4 = 6) (Figure 1c). Apart from a brief episode of diarrhoea at treatment initiation, the patient experienced no side-effects, and therapy is currently ongoing.

Roflumilast is an orally administered small-molecule drug that inhibits the intracellular enzyme PDE4, and thereby alters expression of inflammatory mediators, including cytokines involved in HS pathogenesis. Roflumilast was licensed first in class for severe COPD in 2011 and has recently shown potential in the treatment of psoriasis. Apremilast, another PDE4 inhibitor, was found to be efficacious and safe for HS in a randomized setting. Interestingly, the in-label list price of

|       | Baseline | 3 months | 5 months |
|-------|----------|----------|----------|
| IHS4  | 16       | 9        | 6        |
| HiSCR | N/A      | No       | Yes      |
| DLQI  | 21       | 11       | 5        |
| NRS-pain | 8       | 6        | 3        |
| BMI, kg/m\(^2\) | 31.7 | 29.1 | 28.6 |
| Weight, kg | 112 | 103 | 101 |
| PASI  | 4.5      | 0.0      | 0.0      |

Figure 1 Improvements in hidradenitis suppurativa over 5 months of oral roflumilast therapy. BMI, body mass index; DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response (> 50% reduction in the number of inflammatory lesions); IHS4, International Hidradenitis Suppurativa Severity Score System; NRS, numerical rating scale; PASI, Psoriasis Area and Severity Index.
roflumilast is <7% that of apremilast in Denmark, with generic versions already available in some countries. Furthermore, experimental studies have found roflumilast to be up to 90 times more potent in inhibiting PDE4 isoforms compared with apremilast. In contrast to biologic therapy, oral roflumilast could represent a novel and convenient treatment option for all severity stages of HS as well as associated comorbidities. To expand upon the rather limited treatment options in HS, larger studies investigating the long-term efficacy and safety of oral PDE4 inhibitors are warranted.

In the present case, we observed considerable improvements in clinical HS presentation and quality-of-life measures with oral roflumilast therapy. In addition, the patient achieved a 10% weight loss, which may have contributed to the reduction of disease burden. Roflumilast could represent a novel and convenient treatment option for all severity stages of HS as well as associated comorbidities. To expand upon the rather limited treatment options in HS, larger studies investigating the long-term efficacy and safety of oral PDE4 inhibitors are warranted. In the present case, we observed considerable improvements in clinical HS presentation and quality-of-life measures with oral roflumilast therapy. In addition, the patient achieved a 10% weight loss, which may have contributed to the reduction of disease burden. Roflumilast could represent a novel and convenient treatment option for all severity stages of HS as well as associated comorbidities. To expand upon the rather limited treatment options in HS, larger studies investigating the long-term efficacy and safety of oral PDE4 inhibitors are warranted.

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Large-cell transformation is an independent poor prognostic factor in Sézary syndrome: analysis of 117 cases

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Dear Editor, Sézary syndrome (SS) is a rare cutaneous T-cell lymphoma (CTCL) grouped with mycosis fungoides (MF) in the international classification and staging criteria of CTCL. Large-cell transformation (LCT) has been widely described in MF and associated with reduced overall survival, suggesting the importance of early and sequential histological screening of LCT in MF. However, LCT has never been studied and characterized in a large cohort of SS. Another concern is that LCT in MF was defined in the 1980s using diagnostic criteria for LCT in follicular lymphoma. Although widely used since, the reliability of these criteria has never been specifically studied in SS. Additionally, the presence of large circulating Sézary cells (SCs) based on cytomorphological and flow cytometry analysis was independently associated with poor outcome and might predict LCT occurrence in skin. Nevertheless, the prognostic impact of structure parameters [forward scatter (FSC) and side scatter (SSC)] of circulating cells in cytomtery and correlation with LCT remains to be determined in SS.

The main objective of our study was to characterize LCT in SS. All patients with SS diagnosed at Saint-Louis hospital (Paris, France) between 1998 and 2020 according to European Organisation for Research and Treatment of Cancer–World Health Organization criteria were included. The gating strategy of KIR3DL2+ SC among lymphocytes was previously described. Circulating KIR3DL2+ SC ≥ 200 mm−3 was used to define KIR3DL2-positive status. For each patient, all skin biopsy samples performed were included. LCT was histologically defined by the presence in the lymphocytes’ infiltrate of > 25% or aggregates/nodules of large cells (more than four times the diameter of a small lymphocyte). Haematoxylin-, eosin- and safran-stained slides were then digitized and an analysis using HALO software was performed. All blood samples from patients with flow cytometry data between 2015 and 2020 were included for FSC/SSC analysis. This study received the Institutional Review Committee agreement (LYM-PHOTEQ reference: CPP 2019-A01158-49).

In total, 117 patients were included with a median follow-up of 41 months (interquartile range 1–81). Overall, 6% (six of 100) and 16% (18 of 112) of patients were diagnosed with LCT on skin biopsy samples at diagnosis and during follow-up, respectively. Interobserver reliability between two independent pathologists was excellent [κ = 0.88; 95% confidence interval (CI) 0.78–0.98]. Considering all skin biopsy samples, LCT was observed in 16% (18 of 112) of patients.