Materials and Methods

Study Design and Setting

This was a multicenter, retrospective study designed to assess the efficacy and safety of adalimumab in patients with dissecting cellulitis of the scalp (DC). Data were collected across five European Dermatology Departments (Second Dermatology Department, Aristotle University of Thessaloniki, Thessaloniki, Greece; San Bortolo Hospital, Vicenza, Italy; Hospital Ruber de Juan Bravo, Madrid, Spain; IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; Salford Royal Foundation Trust, Manchester, United Kingdom; 2nd Department of Dermatology and Venereology, National and Kapodistrian University of Athens, Athens, Greece), all with dedicated inflammatory hair disorder clinics. The study period extended from January 2010 to June 2024.

The study protocol waived approval by the Institutional Review Boards/Ethics Committees of all participating centers. Data was anonymized in compliance with GDPR/ethical data protection regulations. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

Patient selection

All patients should meet the following inclusion criteria: 1. Adults ≥18 years with a clinical diagnosis of DC, confirmed by histopathological evaluation when required; 2. Treatment with adalimumab (prototype or biosimilar) for ≥12 consecutive weeks; 3. A minimum follow-up period of 16 weeks; and 4. Availability of baseline and at least one follow-up clinical assessment.

Exclusion criteria included: 1. Patients receiving other biologics for at least 6 months prior to; 2. Presence of uncontrolled systemic infections; 3. Concomitant immunosuppressive therapy; 4. Incomplete DC records preventing efficacy and/or safety evaluation.

Interventions

Patients received adalimumab according to the designated dosing schemes, either for hidradenitis suppurativa (HS) or psoriasis (Pso). According to the HS dosing scheme, for example, an induction dose of 160 mg subcutaneously at week 0, 80 mg at week 2 and at week 4 and thereafter, by a dose of 40 mg every week or 80 mg every other week. Those who were subscribed adalimumab under the Pso dosing scheme received an initial dose of 80 mg, followed by 40 mg every other week starting one week after the induction dose. Each patient was assigned to a specific dosage regimen as per standard clinical practice. Treatment response was assessed from 16 weeks onwards.

Concomitant topical treatments (antiseptic shampoos, corticosteroids, keratolytics) were permitted. Short antibiotic courses were allowed for superimposed bacterial infections.

Outcomes

The primary endpoint of the study was the change in disease activity; therefore, the efficacy of adalimumab was measured by a composite of clinical severity parameters, including: 1. The number of inflammatory nodules, abscesses, and presence of suppuration; 2. Pain level,

assessed using the Numeric Rating Scale (NRS, 11-point Likert scale), and 3. Physician Global Assessment (PGA) tool.

Since there is not a single, universally adopted severity score for DC of the scalp, assessments usually consider clinical features like the number and extent of nodules and abscesses, the presence of suppuration, sinus tracts and fibrosis, and the involvement of the scalp area. Our assessment was based on a proposed severity grading system by Lee. et al. of Stages I, II, and III depending on certain clinical and pathological features, with Stage I being mild and Stages II and III indicating more severe disease with scarring. For example:

- **Stage I (Mild):** Characterized by a single nodule or abscess.
- **Stage II (Severe):** Involves multiple nodules or abscesses with sinus tracts in one or more areas.
- **Stage III (Severe):** Includes multiple nodules, abscesses, sinus tracts, and the presence of fibrosis (scarring) in one or more scalp areas.

Regarding the evaluation of treatment outcomes, there is also a lack of widely accepted tools. Given that scarring is a non-reversible process, therapeutic outcome should consider clinical features related to disease activity, such as active inflammatory nodules, suppuration and new scarring in follow-up.

Considering the aforementioned limitations, the evaluation of response in our study considered the degree of inflammation and the presence/absence of new scarring. Complete response (CR), defined as the absence of inflammatory lesions and new scarring areas, and partial response (PR, defined as mild inflammatory lesions or flare-ups without new scarring areas, were additionally evaluated.

Secondary endpoints included: 1. Quality of life, measured by the Dermatology Life Quality Index (DLQI); 2. Trichoscopic findings over affected scalp areas pre- and post-treatment, as described below (standardized clinical photography).

Safety endpoints were: 1. The Frequency and type of adverse events (AEs) and serious adverse events (SAEs). Adverse events were recorded at each visit and classified according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0.; 2. Laboratory abnormalities (hematology, liver and renal function tests); 3. Infections, infusion reactions, and treatment discontinuations. Safety analysis included all patients who received at least one dose of adalimumab.

Data Collection and Follow-up

All patients underwent baseline evaluation, where demographics, biometrics, disease duration, previous systemic therapies, smoking status, and comorbidities (along with DC-related medical history, including but not limited to the presence of another disease of the “follicular occlusion tetrad”, namely hidradenitis suppurativa, acne conglobate and pilonidal sinus), adalimumab version (original or biosimilar) and dose regimen were extracted. Clinical follow-up was performed at a minimum of 16 weeks and onwards, with the last recorded visit taken into account for the treatment efficiency. Moreover, trichoscopy was performed, evaluating key scalp dermoscopic patterns using non-polarized light (x10 magnification) at each center, while laboratory monitoring (complete blood count, liver and renal function

tests) was periodically assessed. Latent tuberculosis and hepatitis B and C screening had been performed prior to treatment initiation.

Statistical Analysis

Descriptive statistics, t-test, chi-square and logistic regression were performed using the SPSS statistical analysis program (IBM, SPSS v.21.0). All tests were two-sided and statistically significant results were considered by a p-value < 0.05. Efficacy outcomes were adjusted for cofounding parameters, such as treatment duration, adalimumab version (original or biosimilar), demographics, dosing scheme and concominant medications.

Supp.Figure 1. (a) Clinical aspect and (b) close view of a patient with severe dissecting cellulitis, with visible, suppurative, tender nodules and disfiguring scarring alopecia. (c) Dermatoscopic aspect of the same patient at baseline, showing severe interfollicular erythema (black asterisks), “3D” yellow dots, also known as “soap bubble” (black arrow), yellow areas (green arrow), amorphous white areas (red asterisks) and yellow crusts (red arrows) due to suppuration. (d) Clinical aspect and (e) close view of the same patient one and half year after treatment with adalimumab at the dose of 40mg per week. There is a significant reduction of inflammation and suppuration that is highlighted in the (f) dermatoscopic picture, in which we observe only mild erythema and loss of follicular openings as a result of the scarring process.