well-informed and have full access to the range of treatment options. Clinicians counselling patients regarding rates of incomplete excision for BCC should consider the specialty as a potential factor that may influence their advice on the likelihood of complete excision. The present data suggest that patients who require referral to plastic surgery have approximately twice the risk of incomplete excision.

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Dupilumab in adolescents with moderate to severe atopic dermatitis: a 32-week real-world experience during the COVID-19 pandemic

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Dear Editor,

Real-life data concerning dupilumab effectiveness and safety in adolescents (aged ≥ 12 to <18 years) with moderate to severe atopic dermatitis (AD) are rarely reported.[1] In two adolescence studies, the phase III randomized, placebo-controlled, clinical trial (LIBERTY AD ADOL)[2] and the phase IIa and subsequent phase III open-label extension (LIBERTY AD PED-OLE)[3] dupilumab produced significant improvement in signs and symptoms at Week 16, with a good safety profile. We report our real-life experience in using dupilumab to treat AD in adolescents.

This was a 32-week prospective real-life study. The study was approved by the ethics committees of the participating institutions, and informed consent from patients and parents were obtained.

Nine adolescents (mean age 15.7 years) with moderate to severe AD who were started on dupilumab from January to October 2020 under the Italian Medicine Agency compassionate use programme were included in this study. Data on demographics and AD clinical characteristics at baseline are reported in Table 1.

Eight patients (weight ≥ 60 kg were treated every 2 weeks with dupilumab 300 mg) and the ninth (weight < 60 kg) with 200 mg. Moisturizers and mild topical corticosteroids (TCS) were allowed. AD characteristics, TCS use and adverse events (AEs) were assessed at Weeks 16 and 32.

All patients completed the full 32-week course of dupilumab. At Weeks 16 and 32, 100% of patients reached 75% reduction in Eczema Area and Severity Index (EASI75), 44.4% reached EASI90 and 22.2% reached EASI100 (Table 2), with an EASI reduction at Weeks 16 and 32 of 84.7% and 83.0%, respectively. At Week 16, there was a 77.4% reduction in the Children's Dermatology Life Quality Index (cDLQI), which reduced from 20.4 to 4.6, a 5.9-point reduction in Numerical Rating Scale (NRS) itch score (from 8.0 to 2.1) and an 87.5% reduction (from 7.2 to 0.9) in NRS

Table 1 Demographics and clinical characteristics at baseline of nine adolescents with moderate to severe atopic dermatitis.

Patient	Sex	Age, years	BMI	Age at AD onset, years	Clinical course	Atopic comorbidities	Prior systemic medications	Clinical phenotype	EASI	cDLQI	NRS itch score	NRS sleep-loss score
1	F	15	31.9	1	P	–	AH, CsA, PT, SCS	DE	42	28	9	8
2	M	17	22.2	1	R	A, Rh	AH, CsA, PT, SCS	FE, HNE, HE	26	21	7	6
3	M	14	25.6	2	R	–	CsA, SCS	DE	36	24	9	9
4	M	15	23.2	1	R	A, C, Rh	AH, CsA, SCS	DE	55	28	4	4
5	M	16	21.2	1	P	A, Rh	CsA, SCS	DE	36	30	9	9
6	F	16	22.0	5	P	–	–	FE, HNE	42	25	9	7
7	F	15	19.3	1	R	–	AH, SCS	FE, HNE, HE	27	8	7	6
8	F	16	28.6	2	P	A	AH, PT, SCS	FE, HNE, HE	24	5	9	8
9	F	17	25.1	12	P	Rh	AH, CsA, SCS	DE	30	25	9	8

A, asthma, AD, atopic dermatitis; AH antihistamines; C, conjunctivitis, cDLQI, Children's Dermatology Life Quality Index; CsA. ciclosporin A; DE, diffuse eczema; EASI, Eczema Area and Severity Index; FE, flexural eczema, HE, hand eczema; HNE, head and neck eczema, NRS, Numerical Rating Scale; P, persistent, PT, phototherapy; R, relapsing; Rh, rhinitis; SCS, systemic corticosteroids.

Table 2 Dupilumab effectiveness at Weeks 16 and 32 by sex, baseline body mass index (< 25 and ≥ 25) and baseline Eczema Area and Severity Index (< 30 and ≥ 30).

		Sex		Baseline BMI		Baseline EASI	
EASI reduction	All patients (n = 9)	Male (n = 4)	Female (n = 5)	BMI < 5 (n = 5)	BMI ≥ 25 (n = 4)	EASI < 30 (n = 3)	EASI ≥ 30 (n = 6)
Week 16, *n* (%)							
EASI75	9 (100)	4 (100)	5 (100)	5 (100)	4 (100)	3 (100)	6 (100)
EASI90	4 (44.4)	1 (25.0)	3 (60.0)	3 (60.0)	1 (25.0)	1 (33.3)	3 (50.0)
EASI100	2 (22.2)	0	2 (40.0)	1 (20.0)	0	1 (33.3)	1 (16.7)
Week 32, *n* (%)							
EASI75	9 (100)	4 (100)	5 (100)	5 (100)	4 (100)	3 (100)	6 (100)
EASI90	4 (44.4)	2 (50.0)	2 (40.0)	4 (80.0)	0	1 (33.3)	3 (50.0)
EASI100	2 (22.2)	0	2 (40.0)	2 (40.0)	0	1 (33.3)	1 (16.7)

BMI, body mass index; EASI, Eczema Area and Severity Index.

sleep-loss score. Overall, the therapeutic outcome was maintained at Week 32.

The two patients who reached EASI100 at Week 16 were both female. Adolescents with a body mass index (BMI) of < 25 were more likely than those with a BMI of ≥ 25 to achieve EASI90 or EASI100 at Weeks 16 and 32. Patients with EASI of ≥ 30 at baseline were more likely than those with baseline EASI < 30 to achieve EASI90 at Weeks 16 and 32 (Table 2).

All patients stopped TCS at a mean of 15.3 days (range 1–24 days) after the beginning of dupilumab therapy. One patient contracted asymptomatic SARS-CoV-2 infection at Week 10, and one developed mild conjunctivitis at Week 12 treated with dexamethasone ointment; both continued on dupilumab.

In this real-life experience of adolescent AD treated with dupilumab, we documented an excellent therapeutic response with the drug, better than that reported in the 16-week LIBERTY AD ADOL[2] and the 52-week LIBERTY AD PED-OLE[3] studies. In fact, all of our patients reached EASI75 at Week 16, compared with 41.5%[2] and 68.4%[3] of patients in the previous two trials. Similarly, 44.4% of our patients reached EASI90 compared with 23.2%[2] and 52.6[3] of the previous trials. Two of our patients (22.2%) achieved completely clear skin, compared with none of patients included in the previous trials.[2,3] Additionally, we observed a greater improvement in patients with low BMI and high EASI at baseline.

Other AD characteristics also presented a better outcome in our study compared with the two clinical trials: at Week 16 we observed a reduction from baseline in cDLQI score (77.4% vs. 64.9%[3]), NRS itch score (5.9 vs. 3.6[2] and 5.0[3] points), and NRS sleep-loss score (87.5% vs. 47.9%[2]), and all of these meaningful improvements were maintained at Week 32, with a further decrease in NRS sleep-loss score (giving a 94.4% reduction from baseline).

We confirmed the excellent tolerability and safety of dupilumab, even in the SARS-CoV-2 infected patient. The issue of dupilumab therapy was under debate during COVID-19 pandemic first wave.[4] In the Italian experience on 1576 patients under dupilumab treatment, 15 patients contracted SARS-CoV-2 infection with a good clinical outcome, confirming that dupilumab should be continued during the COVID-19 pandemic.[5] Nevertheless, systematic studies are needed to evaluate the effect of dupilumab in patients with SARS-CoV-2 infection.

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Localized Darier disease: three cases of Type 1 segmental mosaicism

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Dear Editor,

Darier disease (DD) is an autosomal dominant acantholytic dermatosis with an estimated prevalence of 1 in 30 000–100 000.[1] Onset is during childhood or adolescence,[2] and the disease is characterized by keratotic, crusted red–brown papules in a seborrhoeic distribution, nail changes (longitudinal erythronychia, longitudinal ridges and distal breakage with V-shaped notches) and palmar/plantar pits.[1] A localized form of DD was first described by Kreibich in 1906 and is thought to account for 10% of all cases.[2] A number of clinical variants have been reported including: unilateral, linear, segmental or zosteriform DD.[2] We present a case series of three patients with localized DD.

The three patients (2 women, 1 man; age range 21–79 years) presented with varying clinical manifestations (Fig. 1, Table 1). One of our patients was younger and one older than the usual age range for localized DD, which generally develops in the third or fourth decade.[3]

The lesions of localized DD are clinically and histologically indistinguishable from those of classic DD.[1] Nail manifestations are usually diminished or absent.[1] Diagnosis is often delayed due to confusion with other conditions such as an inflammatory linear verrucous naevus (ILVEN) or herpesvirus infection (seen in our Patient 2). Our patients all displayed histological findings of acantholytic dermatosis, and all had negative results for direct immunofluorescence (Fig. 2).

Like the generalized form, localized DD can be difficult to manage. Treatment options include topical corticosteroids, topical retinoids, topical 5-fluorouracil, oral retinoids and physical therapies (surgical excision, dermabrasion, CO_2 laser ablation).[4] Patients 1 and 3 were treated with a moderate-potency topical steroid and a topical retinoid (adapalene), while Patient 2 received an oral retinoid (acitretin) but unfortunately she developed progression of metastatic breast cancer and was referred for palliative treatment.

Localized DD is an example of segmental mosaicism,[5] in which the distribution of the affected area closely follows the lines of Blaschko, which are segmental divisions of the skin thought to represent the linear migration of divergent cell lines during embryogenesis.[1] Two types of segmental mosaicism have been described. In Type 1, a postzygotic mutation occurs at an early developmental stage in an otherwise healthy embryo,[5] and the affected segment reflects the outgrowth of a clone that is heterozygous for the mutation (ATP2A2).[5] In Type 2, a postzygotic mutation occurs in a heterozygous embryo[5] (i.e. an embryo that already has the DD genotype), and manifests as generalized DD with segmental areas of increased severity.[1] In our cases, the diagnosis of Type 1 segmental mosaicism was made on a clinical basis due to: (i) the absence of a positive family history of DD, (ii) the segmental distribution of typical DD lesions and (iii) histological findings typical for DD.

It is important to determine the type of segmental mosaicism present as this has an impact on the risk of transmission to offspring; in Type 1 segmental mosaicism, there is a low but definite risk of offspring developing generalized DD due to the possibility of gonadal mosaicism,[5] whereas Type 2 occurs in the setting of classic autosomal dominant DD and carries a 50% risk