XXIII CONVEGNO NAZIONALE

DERMATOLOGIA PER IL PEDIATRA

La terapia...
un dono grande

26-27 Maggio 2023

Palazzo dei Congressi, Riccione

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Nuove terapie all'orizzonte

Prof.ssa Annalisa Patrizi

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Upadacitinib for Successful Treatment of Alopecia Universalis in a Child: A Case Report and Literature Review

Acta Derm Venereol 2023; 103: 5578.

Dianhe YU and Yunqing REN*

- La terapia dell'alopecia areata totale o universale nell'infanzia ed adolescenza ha avuto finora limitate possibilità terapeutiche.

- I trattamenti convenzionali comprendono l'antralina, il Minoxidil topico o sistemico, gli steroidi topici o sistemici, gli immunosoppressori in particolare metotressato, azatioprina e ciclosporina e la sensibilizzazione con dibutilestere dell'acido squarico (SADBE) o difenilciprone.

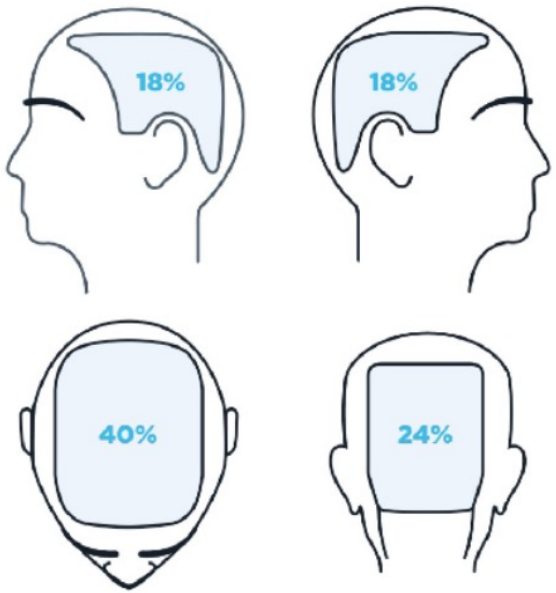
- Di recente sono usciti articoli sull'efficacia degli inibitori di Janus Kinasi (JAK) sia applicati localmente che per via orale sia in adolescenti, che come utilizzo of label in bambini da o sotto i 12 anni di età.

- Ad oggi non vi sono casi in letteratura trattati con Upadacitinib un JAK1 inibitore in pazienti sotto i 12 anni di età, anche se vi è uno studio in atto su pazienti pediatrici da 2 a 12 anni con dermatite atopica grave (NCT03646604).

- Questo studio fa una revisione della letteratura e trova 5 reports di pazienti con AA trattati con tale farmaco.: in 4 casi era associata DA grave e 5 erano adulti. Questi pazienti non avevano risposto a steroidi, ciclosporina, metotressato e azatioprina. In 3 casi l'AA non aveva risposto neppure a terapia con Dupilumab. In tutti , il dosaggio di Upadacitinib fu 30 mg/die e il trattamento fu ben tollerato in tutti i soggetti

The Severity of Alopecia Tool (SALT)

SALT Score



Percentages are quadrant surface area.

The SALT score is calculated by[1]:

- Multiplying the percentage of hair loss in each of the 4 quadrants of the scalp by the quadrant surface area
- Adding the 4 values together for a composite score

Maximum SALT score of **100** indicates complete scalp hair loss

Minimum SALT score of **0** indicates no hair loss

Anti JAK di interesse dermatologico approvati in Italia da AIFA al 2023

Baricitinib per AR, DA, Alopecia areata

Upadacitinib per AR, DA, Artrite psoriasica

Tofacitinib per AR, Artrite psoriasica

Baricitinib un anti JAK1/2 è approvato da AIFA e rimborsato per pazienti adulti di età > 18 anni con AA

Upadacitinib è an anti JAK1

Tofacitinib è un anti JAK1/3

Upadacitinib for Successful Treatment of Alopecia Universalis in a Child: A Case Report and Literature Review

Dianhe YU and Yunqing REN*

Acta Derm Venereol 2023; 103: 5578.

CASE REPORT

A 9-year-old female child (weighing 33 kg) presented with a 7-year history of alopecia universalis. She did not report any pain or pruritus of the scalp. Treatment with topical potent steroids, minoxidil, tacrolimus and oral compound glycyrrhizin tablets, and glucocorticoids was ineffective. The patient also had mild AD and her father had previously been diagnosed with allergic rhinitis. Phy-

Una bambina di 9 anni (peso 33 Kg) consultò per AA universale presente da 7 anni. La pz era asintomatica. Terapia topica con steroidi potenti, minoxidil, tacrolimus e con glicirizzina e steroidi orali furono inefficaci. Soffriva anche di DA lieve e il padre presentava rinite allergica.

Considering the lesser side-effects and the patients' unwillingness to have injection therapy, oral upadacitinib was administered off-label at a dosage of 15 mg per day after obtaining informed consent

In base ad un rifiuto di terapia iniettiva ed agli scarsi effetti collaterali degli inibitori di JAK riportati in letteratura, la pz fu trattata con Upadacitinib (anti KAK/1) alla dose di 15 mg/die.

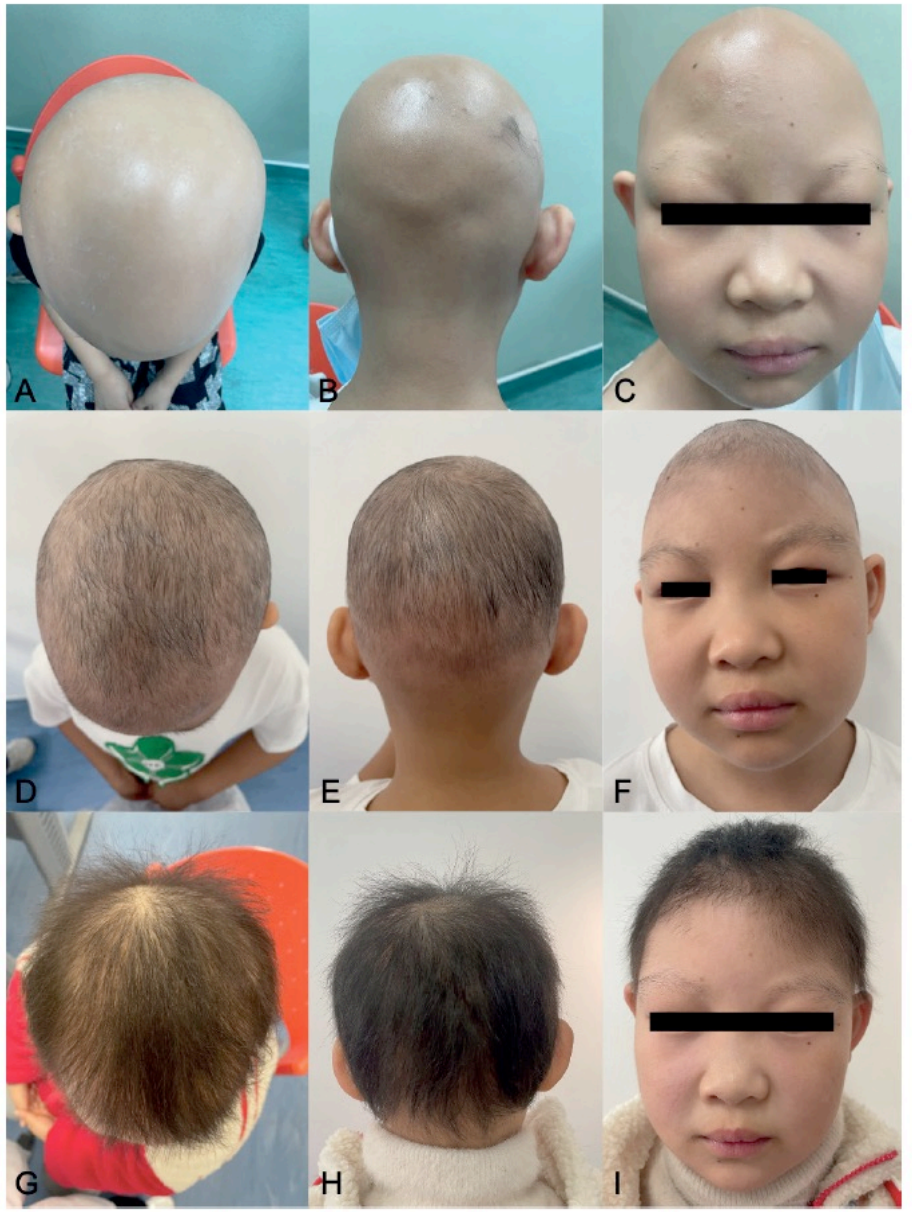


Fig. 1. (A–C) Hair loss over the entire scalp and sparse eyebrows and eyelashes (Severity of Alopecia Tool (SALT), 98) before treatment with upadacitinib. Only localized coin-sized patches of hair were seen. (D–F) Diffuse regrowth hair and thicker eyebrows and eyelashes (SALT score, 12) after 6 weeks' treatment with upadacitinib. Longer thick hair (G–I) (SALT score, 9) after 3 months' oral upadacitinib and 2 months' discontinuation.

Upadacitinib for the treatment of alopecia areata and severe atopic dermatitis in a paediatric patient: A case report

2022

SAGE Open Medical Case Reports
JCMS Case Reports
Volume 10: 1–5

Adrienn N Bourkas[1,2] and Cathryn Sibbald[2,3]

In 2021, RINVOQ® (upadacitinib), an oral, once-daily selective Janus kinase (JAK) 1 inhibitor was approved in Canada for the treatment of adults and adolescents over 12 years of age with refractory moderate-to-severe AD.[5]

JAK inhibitors are a promising new treatment for AA, especially in those with chronic, severe types.[6] Limited information is available on upadacitinib in paediatric AD cases with concurrent AA. We report the case of a 14-year-old adolescent with AA and AD treated successfully with upadacitinib.

Case report

A 14-year-old male with Fitzpatrick phototype IV skin and a 13-year history of AA and a positive family history for alopecia presented to our dermatology clinic for evaluation of his hair loss. A full physical exam was deferred as the sparing the eyelashes. A year prior, he was previously treated with intralesional corticosteroid injections with minimal improvement. He was also prescribed high potency topical corticosteroids and 0.1% protopic cream for the scalp. The patient also had concurrent eczema of the skin, later diagnosed as AD, and exhibited the atopic triad, with allergenic rhinitis and asthma.

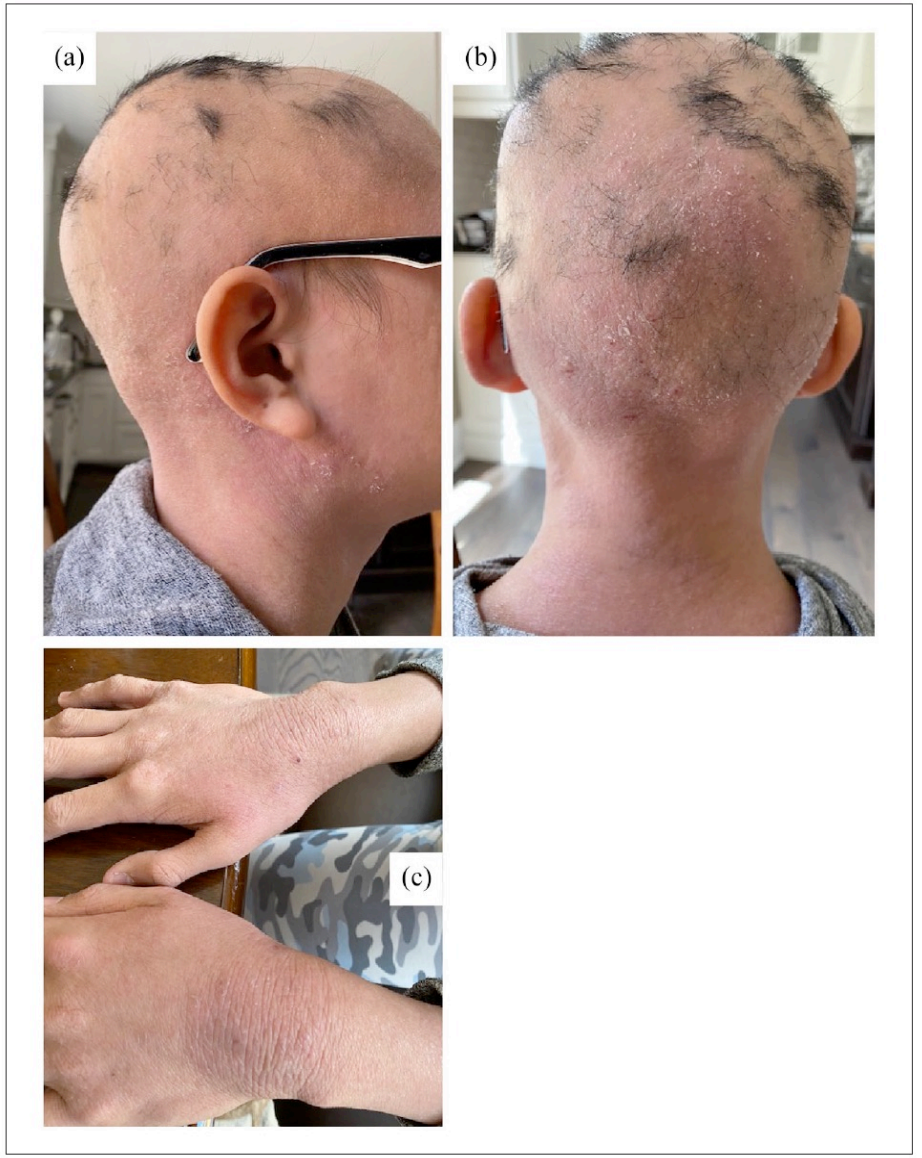


Figure 1. Clinical photographs of the patient at first appointment. Images were captured by the patient, which were reviewed. Photos of alopecia totalis of the scalp with a few scattered tufts of hair and erythematous dry skin. (a) Lateral view shows patches of hair in the parietal vertex. (b) Posterior view shows hair patches in the occipital vertex. (c) Picture of dorsal hands with severe and active dermatitis with xerosis, scaling and erythematous lichenification bilaterally.

Terapie precedenti: steroidi intralesionali, steroidi topici potenti e Protopic 0,1% unguento

Upadacitinib for the treatment of alopecia areata and severe atopic dermatitis in a paediatric patient: A case report

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After the initial visit, early treatment strategies discussed included systemic immunosuppressive treatment with methotrexate. In addition, topical application of stronger potency steroids and supplementation with folic acid, vitamin D and iron were administered concurrently. Due to concerns by the caregiver about the adverse events associated with methotrexate, administration was delayed for 16 months. In the meantime, the alopecia worsened with no improvement in hair growth. Five months after initial assessment, both the AA and AD worsened with frequent flare-ups, and cyclosporine 5 mg/kg/day was initiated for AD management. Treatment was well tolerated, with new hair growth in the frontal scalp and noticeable improvements in AD after just a month (Figure 2), as well as further improvements in the eyebrows after 5 months.

Unfortunately, after 7 months of cyclosporine, the patient reported new hair loss on the scalp and eyebrows in conjunction with a dermatitis flare-up. Low-dose systemic minoxidil (1.25 mg daily) was added to his regimen, but improvement in hair growth was minimal.

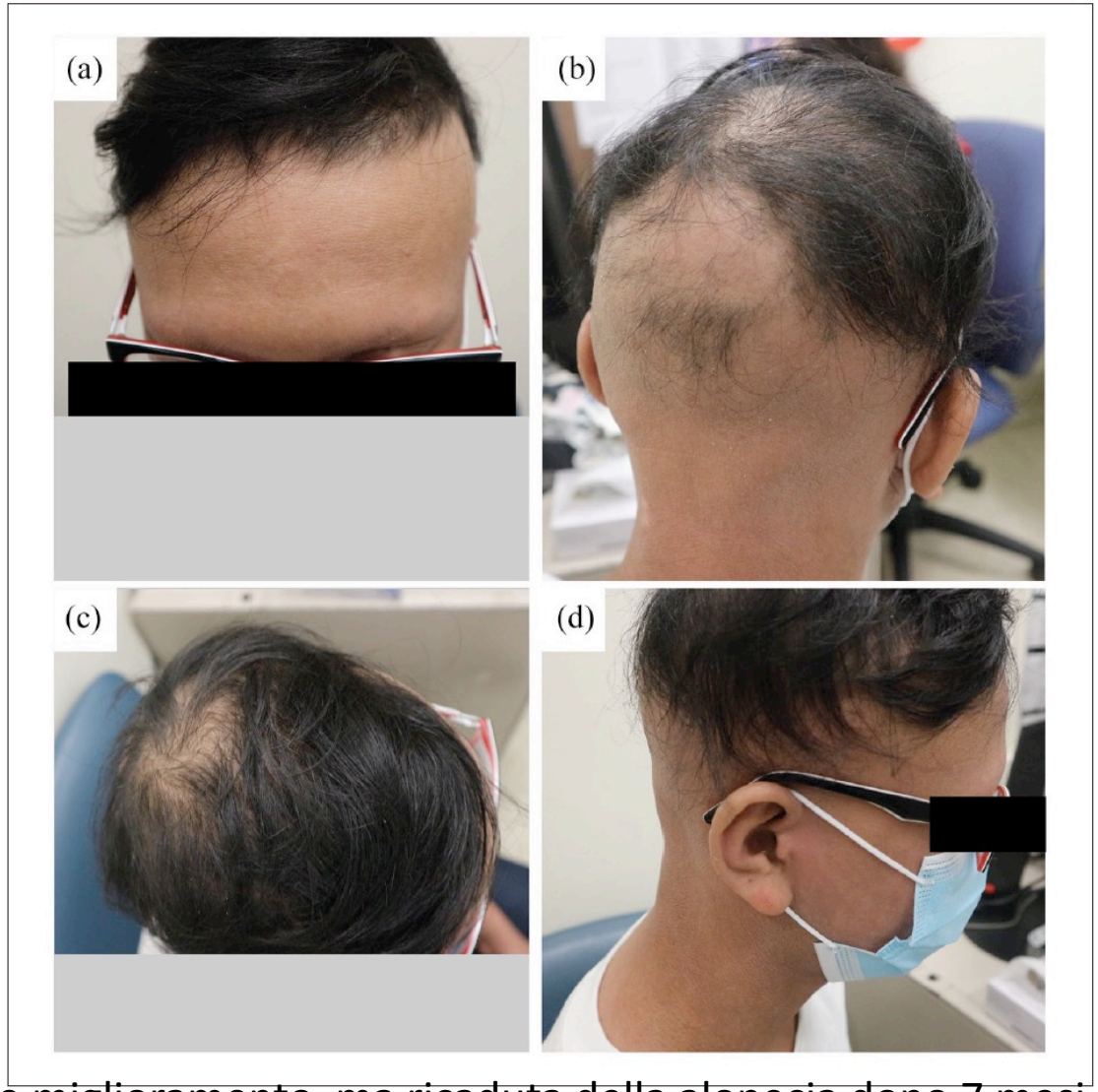

Figure 2. Clinical photographs of the patient after 1 month of treatment with cyclosporine. New hair growth in the frontal scalp. Confluent patches of smooth noon scarring alopecia in irregular areas of the occiput, vertex, parietal and temporal scalp. (a) Frontal, (b) posterior, (c) superior and (d) lateral view.

Terapie praticata per prima: Ciclosporina 5 mg/Kg/die con iniziale miglioramento, ma ricaduta della alopecia dopo 7 mesi, nonostante l'aggiunta di Minoxidil orale 1,25 mg/die .
La proposta iniziale era stata però Metotressato rinviata per timori familiari e topici steroidei potenti

Upadacitinib for the treatment of alopecia areata and severe atopic dermatitis in a paediatric patient: A case report

Adrienn N Bourkas[1,2] and Cathryn Sibbald[2,3]

SAGE Open Medical Case Reports
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Cyclosporin was discontinued and the family agreed to proceed with methotrexate, which was replaced with upadacitinib a month later. Improvements in both AA and AD were noted only 6 weeks after initiating upadacitinib, and by 5 months, the whole scalp was covered in hair (Figure 3). The patient continued to describe itching episodes, but his eczema also showed marked improvement.

La ciclosporina fu sospesa , si tentò metotressato che dopo un mese fu sostituito con Upadacitinib.
Miglioramento AA fu osservato dopo 6 settimane e dopo 5 mesi l'intero capo era coperto da capelli.
Meglio anche prurito e DA.

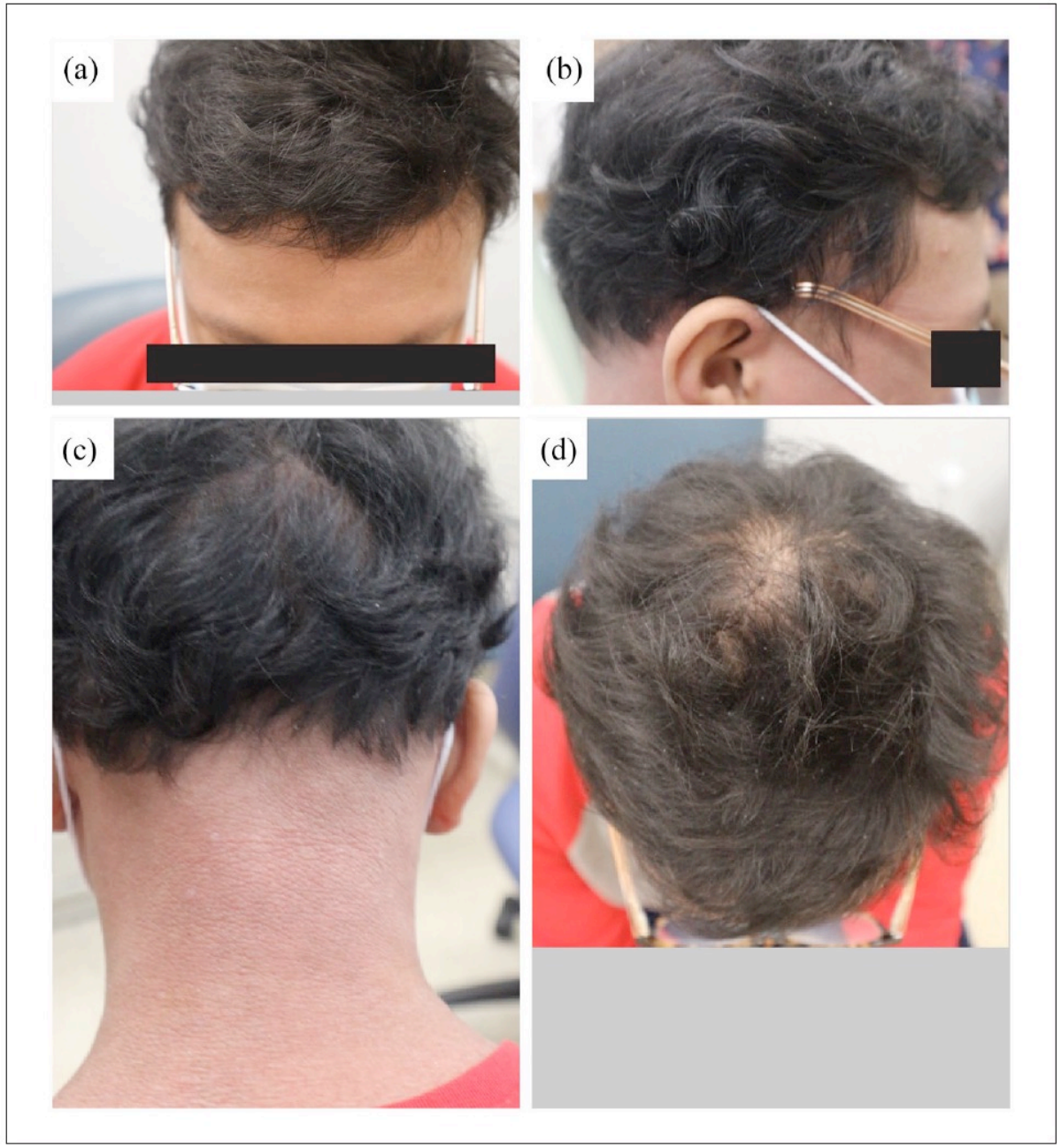


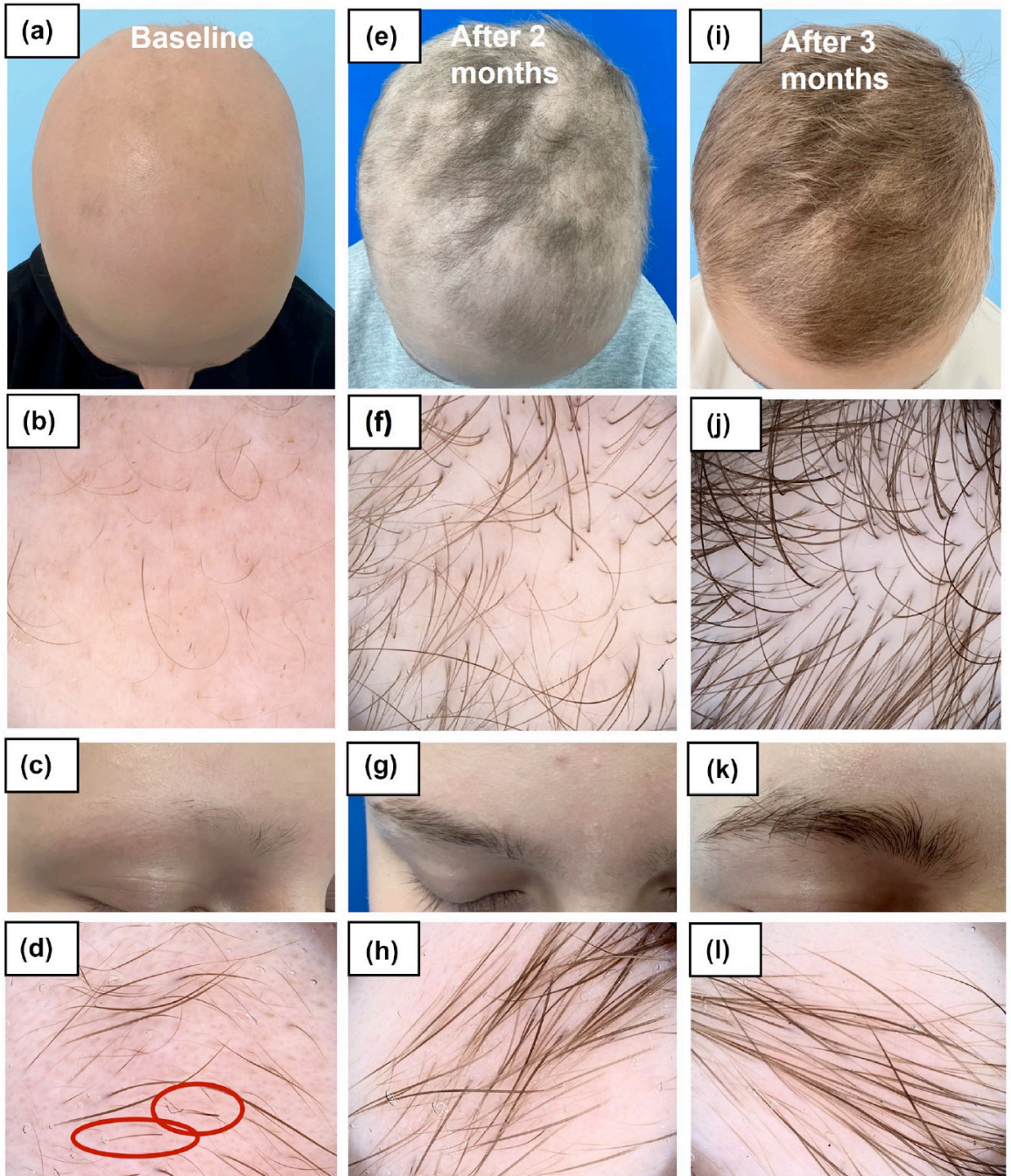
Figure 3. Clinical photographs of the patient after 5 months of treatment with upadacitinib. Significant hair growth in the entire scalp. (a) Frontal, (b) lateral, (c) posterior and (d) superior view of the scalp.

Alopecia Universalis in an Adolescent Successfully Treated with Upadacitinib—A Case Report and Review of the Literature on the Use of JAK Inhibitors in Pediatric Alopecia Areata

Dermatol Ther (Heidelb) (2023) 13:843–856

Kinga Kołcz · Magdalena Żychowska · Edyta Sawińska · Adam Reich

◀**Fig. 1** Clinical and trichoscopic presentation at **a**–**d** baseline; **e**–**h** after 2 months of therapy with upadacitinib; **i**–**l** after 3 months of therapy with upadacitinib. **a** Nearly complete hair loss on the scalp; **b** trichoscopy showing yellow dots, single black dots, and several regrowing hair; **c** over 50% hair loss of the eyebrows; **d** trichoscopy showing broken hairs and exclamation mark hairs (red circles); **e** significant regrowth of hair on the scalp after 2 months of therapy; **f** trichoscopy showing numerous terminal hair and thin regrowing hair. Single yellow dots were present; **g** complete regrowth of the eyebrows after 2 months of therapy; **h** trichoscopy of the eyebrows showing terminal hair, no broken hairs or exclamation mark hairs were present; **i** complete hair regrowth on the scalp after 3 months of therapy; **j** trichoscopy showing normal terminal hair; **k** complete regrowth of the eyebrows after 3 months of therapy; **h** trichoscopy of the eyebrows showing normal terminal hair



Bambina caucasica di 14 anni con AU. Diverse terapie precedenti: minoxidil 5% e mometasone fluorato senza esito. Un anno prima difenciprone e UVB con esito parziale. Presentava moderata dermatite atopica. Inizia Upadacitinib 15 mg/die.

Alopecia Universalis in an Adolescent Successfully Treated with Upadacitinib—A Case Report and Review of the Literature on the Use of JAK Inhibitors in Pediatric Alopecia Areata

Baricitinib e ruxolitinib sono entrambi anti JAK1/2
Tofacitinib è un anti JAK1/3

Kinga Kołcz · Magdalena Żychowska · Edyta Sawińska · Adam Reich

Dermatol Ther (Heidelb) (2023) 13:843–856

ABSTRACT

Alopecia areata (AA) is a cell-mediated autoimmune disease in which a cytotoxic T-cell response against hair follicles occurs. AA has been demonstrated to frequently co-exist with atopic dermatitis (AD), and the coincidence of atopy predisposes to a more severe course of the disease. To date, therapeutic options in AA, especially in the pediatric population, are mainly limited to corticosteroids, irritants, sensitizers, and immunosuppressive agents. Recently, innovative therapies have emerged, among which Janus kinase (JAK) inhibitors, effective in both AD and AA, appear to be the most promising. Here, a 14-year-old girl with alopecia universalis (AU) and mild AD is demonstrated, who was successfully treated with a selective JAK1 inhibitor, upadacitinib, which has been approved for the treatment of AD in adults and children aged 12 years and older. Resolution of eczema and complete hair regrowth was achieved after 3 months of therapy. Apart from transient mild leukopenia at weeks 4 and 8, no adverse events were noted. Data in the literature on the efficacy and safety of JAK inhibitors in the treatment of AA in the pediatric population is based on single case reports and case series. So far, topical tofacitinib and ruxolitinib, as well as systemic tofacitinib, ruxolitinib, and baricitinib have been used off-label in this indication in children. Upadacitinib is another effective treatment option with a good benefit–risk ratio for patients with AA, including cases coexisting with AD.

Putterman, Elana; Castelo-Soccio, Leslie (2018). *Topical 2% tofacitinib for children with alopecia areata, alopecia totalis, and alopecia universalis. Journal of the American Academy of Dermatology, 78(6), 1207–1209.e1.*

It is presumed that topical JAK inhibitors have minimal adverse effects, the main one being irritation in the area of application. Considering these small molecules are poorly soluble in water, JAK inhibitors might be most effective when delivered in a liposomal base, which often consist of phospholipids mixed with water.[3] Clinical trials investigating the efficacy of topical formulations for adults are underway, but data regarding pediatric patients are limited to case reports.[3-5]

We report the characteristics and outcomes of 11 pediatric patients ages 4-16 years with AA, AT, or AU, treated with nonpatented formulations of 2% topical tofacitinib prepared by Chemistry Rx (Philadelphia, PA) (Table I).

All patients tolerated treatment without adverse effects, which were recorded at each visit on the basis of a standard review of systems screening for new fatigue, infection, headache, rash, and gastrointestinal symptoms. One individual reported application-site irritation. Blood levels of tofacitinib were not obtained.

Table I. Patient characteristics, treatments, and outcomes

Patient no.	Age, y	Age at onset, y	Sex	Dx	Most recent failed topical regimen	At initiation, time since maximal hair loss	Treatment regimen*	Labs performed	Lab results	Treatment duration, wk	Initial SALT	SALT after therapy	Change in SALT	Cosmetic improvement
1	7	4	F	AU	Fluocinonide 0.05% ointment daily M-F × 10 wk	15 mo	Tofacitinib 2% in liposomal base BID for scalp	CBC and CMP at initiation and 12 wk	WNL	29	100	83	−17	Appreciable but not cosmetically acceptable
2	15	13	F	AT	Anthralin 1% cream M-F, mometasone furoate 0.1% ointment daily on weekends × 5 wk	<1 mo	Tofacitinib 2% in liposomal base BID for scalp	CBC and CMP at 4, 10, and 18 wk, then q3-4 mo thereafter	WNL	12	70	80	+10	Not appreciable
3	16	8	F	AU	Clobetasol propionate 0.05% ointment daily × 8 wk	4 mo	Tofacitinib 2% in liposomal base BID for scalp	None		12	100	100	0	Not appreciable
4	14	5	M	AU	Fluocinonide 0.05% ointment daily M-F × 8 mo	8 mo	Tofacitinib 2% in liposomal base BID for scalp	None		72	100	10.5	−89.5	Cosmetically acceptable
5	12	9.5	F	AA	Clobetasol propionate 0.05% ointment daily M-F × 6 wk	13 mo	Tofacitinib 2% in liposomal base BID for scalp	None		40	15	10	−5	Appreciable but not cosmetically acceptable
6	6	3	F	AU	Fluocinonide 0.05% ointment daily M-F × 6 mo	3 mo	Tofacitinib 2% in liposomal base BID for scalp	CBC, CMP, and lipids at 6 mo	WNL	54	100	10	−90	Cosmetically acceptable
7	15	11	F	AU	Clobetasol proprionate 0.05% ointment BID × 6 wk	3 mo	Tofacitinib 2% in verabase BID for scalp, methotrexate, triamcinolone acetonide injectable suspension	CBC and CMP at start, 6 wk, q3 mo thereafter	WNL	28	87	61	−26	Appreciable but not cosmetically acceptable
8	11	1	F	AT	Fluocinonide 0.05% ointment daily × 3 mo	Within 1 mo before initiation	Tofacitinib 2% in liposomal base once daily for scalp	None		25	96	4	−92	Cosmetically acceptable
9	11	5	F	AU	Mometasone furoate 0.1% ointment daily M-F × 5 mo	6 y	Tofacitinib 2% in liposomal base once daily for scalp, mometasone, methotrexate	CBC and CMP at initiation and q3 mo thereafter	WNL	24	77	53	−24	Appreciable but not cosmetically acceptable
10	15	12	F	AT	Clobetasol propionate 0.05% ointment daily M-F × 6 mo, then 2X/wk × 5 mo	Unable to obtain	Tofacitinib 2% in liposomal base BID for scalp	None		8	80	80	0	Not appreciable
11	4	1	M	AT	Clobetasol propionate 0.05% ointment daily × 8 wk	6 mo	Tofacitinib 2% in liposomal base once daily for 56 w; increased to BID wk 57-76	None		76	100	78.5	−21.5	Appreciable but not cosmetically acceptable

Auricular leishmaniasis in a child successfully treated with intralesional amphotericin B

Andrea Diociaiuti MD, PhD[1] | Simona Giancristoforo MD[1] | Francesca Ippolita Calò Carducci MD[2] | Claudia Bracaglia MD[3] | Alessandra Boni MD[3] | Stefania Pane PhD[4] | Andrea Onetti Muda MD[5] | Fabrizio De Benedetti MD, PhD[3] | Lorenza Putignani PhD[6] | May El Hachem MD[1]

Bambino di 9 anni con lesione presente da 4 mesi.
Biopsia: Giemsa presenza di *Leishmania* spp. confermata da PCR.
Presenza anche di anticorpi ematici.

Treatment was initiated with intravenous liposomal amphotericin B (L-AmB) 3 mg/kg/day for 7 days, plus an infusion on the 14th day and 21st day, combined with 15% paromomycin ointment twice daily. No drug toxicity occurred but despite initial improvement, he had evidence of persistent infection after 3 months of therapy. Therefore, we treated with intralesional L-AmB (2 mg/ml), injecting 0.4 ml/cm^2 into the lesion. The auricular lesion rapidly healed 1 month after the first treatment session (Figure 1B) and no relapse has occurred after 1 year of follow-up. No other intralesional L-AmB sessions were required.

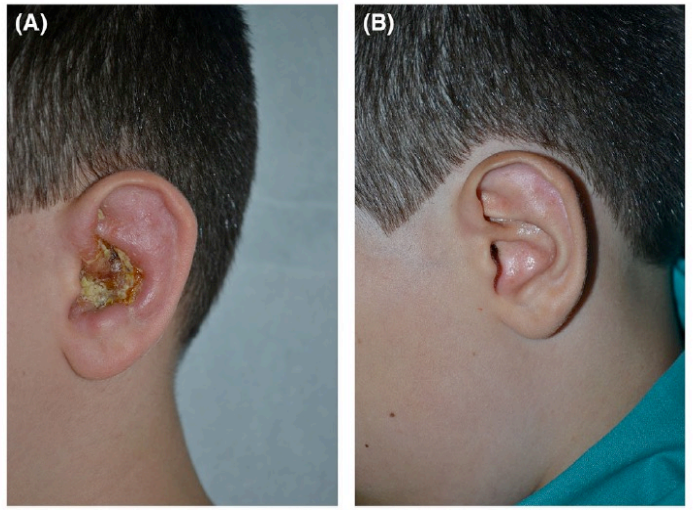


FIGURE 1 (A) Erythematous, edematous, ulcerated lesion covered by a thick crust on left auricle. (B) The auricular lesion rapidly healed 1 month after the first treatment with intralesional L-AmB multiple injections. L-AmB, liposomal amphotericin B.

Pediatric Dermatology. 2022;39:832–833.

Triple-combination clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel for moderate-to-severe acne in children and adolescents: Randomized phase 2 study

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Abstract

Background/Objectives: Topical clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel (IDP-126) is the first fixed-dose triple-combination formulation in development for acne. This post hoc analysis investigated efficacy and safety of IDP-126 in children and adolescents with moderate-to-severe acne.

Pediatric Dermatology. 2023;1–8.

Triple-combination clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel for moderate-to-severe acne in children and adolescents: Randomized phase 2 study

Lo studio includeva 394 pazienti pediatrici con età media 14,9 anni. Il 50% erano femmine e il 75% bianchi. Una applicazione al giorno.

La compliance fu superiore al 92%.

TABLE 1 Evaluator's Global Severity Score. IGA

Score	Grade	Description
0	Clear	Normal, clear skin with no evidence of acne vulgaris
1	Almost clear	Rare noninflammatory lesions present, with rare noninflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)
2	Mild	Some noninflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
3	Moderate	Noninflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may be 1 nodulocystic lesion
4	Severe	Inflammatory lesions are more apparent, many comedones and papules/pustules, there may be up to 2 nodulocystic lesions

TABLE 2 Participant demographics, baseline characteristics, and compliance (ITT population).

	IDP-126 ($n = 76$)	BPO/ADAP ($n = 87$)	CLIN/BPO ($n = 77$)	CLIN/ADAP ($n = 78$)	Vehicle ($n = 76$)
Age, mean (SD), years	14.8 (1.4)	14.7 (1.6)	14.8 (1.8)	15.0 (1.8)	15.0 (1.5)
Age, median (range), years	15.0 (11–17)	15.0 (10–17)	15.0 (10–17)	15.0 (11–17)	15.0 (11–17)
Female, *n* (%)	38 (50.0)	43 (49.4)	40 (51.9)	38 (48.7)	40 (52.6)
Ethnicity, Hispanic/Latino, *n* (%)	12 (15.8)	14 (16.1)	16 (20.8)	12 (15.4)	18 (23.7)
Race, *n* (%)					
White	60 (78.9)	70 (80.5)	62 (80.5)	60 (76.9)	62 (81.6)
Black/African American	10 (13.2)	10 (11.5)	8 (10.4)	10 (12.8)	5 (6.6)
Asian	3 (3.9)	1 (1.1)	5 (6.5)	0	3 (3.9)
Other[a]	3 (3.9)	6 (6.8)	2 (2.6)	8 (10.3)	6 (7.9)
Inflammatory lesion count, mean (SD)	41.9 (14.2)	39.9 (10.9)	43.0 (14.6)	39.7 (9.1)	40.4 (10.7)
Noninflammatory lesion count, mean (SD)	58.0 (23.2)	50.2 (16.6)	53.7 (21.6)	53.8 (20.6)	54.6 (20.1)
Evaluator's Global Severity Score, *n* (%)					
3—Moderate	64 (84.2)	69 (79.3)	62 (80.5)	67 (85.9)	62 (81.6)
4—Severe	12 (15.8)	18 (20.7)	15 (19.5)	11 (14.1)	14 (18.4)
Compliance, %[b]	69 (94.5)	74 (92.5)	72 (97.3)	70 (94.6)	68 (94.4)

Abbreviations: ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat; SD, standard deviation.

Pediatric Dermatology. 2023;1–8.

Triple-combination clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel for moderate-to-severe acne in children and adolescents: Randomized phase 2 study

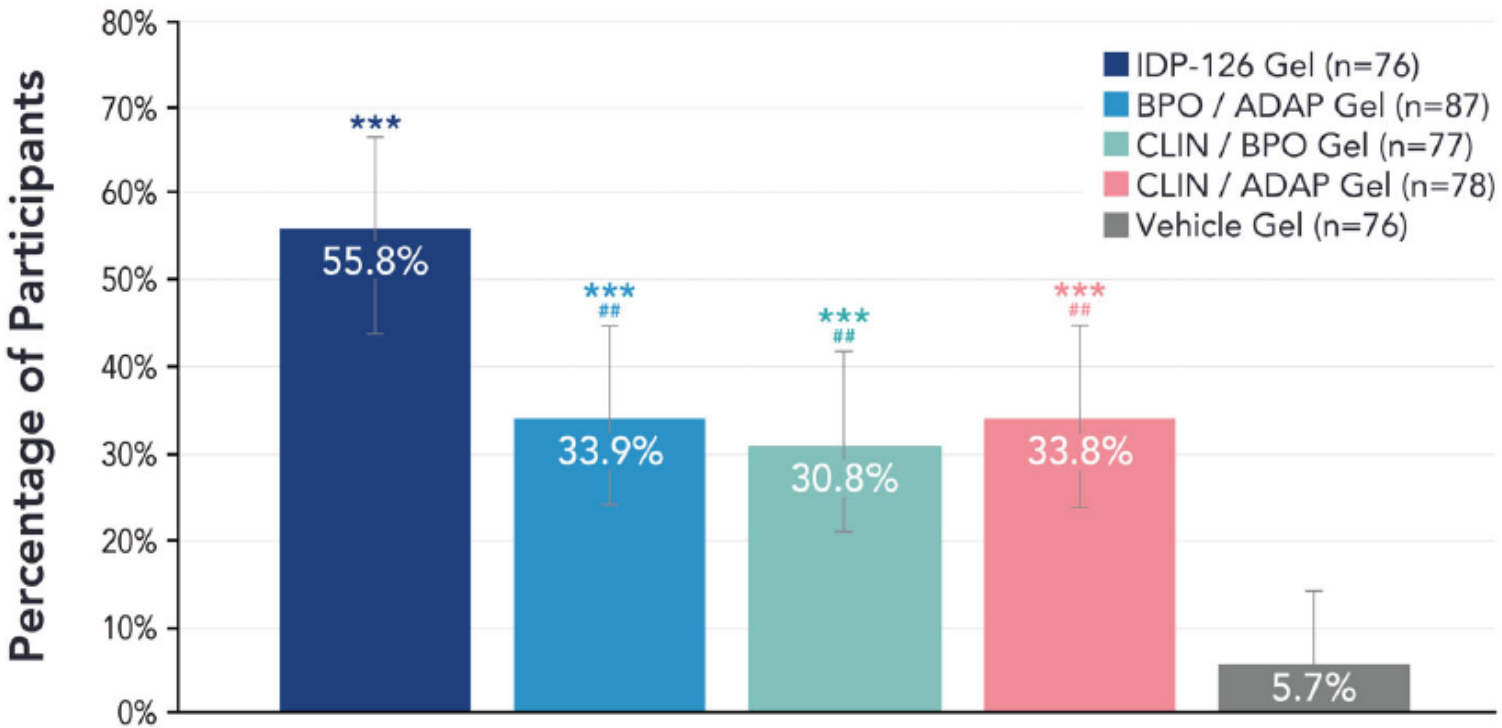

FIGURE 1 Treatment success at Week 12 (intent-to-treat population). Treatment success was defined as at least a two-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear). ***p < .001 versus vehicle; ##p < .01 versus IDP-126. Error bars represent 95% confidence intervals. ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%.

Pediatric Dermatology. 2023;1–8.

Triple-combination clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel for moderate-to-severe acne in children and adolescents: Randomized phase 2 study

TABLE 3 Summary of adverse events through Week 12 (safety population).

Participants, *n* (%)	IDP-126 (*n* = 75)	BPO/ADAP (*n* = 84)	CLIN/BPO (*n* = 77)	CLIN/ADAP (*n* = 76)	Vehicle (*n* = 76)
Reporting any TEAE	32 (42.7)	30 (35.7)	17 (22.1)	21 (27.6)	14 (18.4)
Reporting any SAE	1 (1.3)[a]	0	0	0	0
Discontinued study drug due to TEAE	1 (1.3)	4 (4.8)	0	0	1 (1.3)
Related TEAEs	13 (17.3)	19 (22.6)	3 (3.9)	8 (10.5)	1 (1.3)
Treatment-related TEAEs[b]					
AS pain	5 (6.7)	10 (11.9)	1 (1.3)	1 (1.3)	0
AS dryness	5 (6.7)	4 (4.8)	2 (2.6)	4 (5.3)	0
AS irritation	0	3 (3.6)	1 (1.3)	2 (2.6)	0
AS dermatitis	2 (2.7)	1 (1.2)	0	2 (2.6)	0
AS exfoliation	2 (2.7)	1 (1.2)	0	0	1 (1.3)
Sunburn	0	1 (1.2)	0	2 (2.6)	0

Abbreviations: ADAP, adapalene 0.15%; AS, application site; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

[a]SAE of sickle cell anemia with crisis, considered by the investigator to be unrelated to the study drug; the participant experiencing this event completed the study.

[b]Reported by >2% of participants in any treatment group.

Efficacy and Safety of 1% Clascoterone Cream in Patients Aged ≥12 Years With Acne Vulgaris

Adelaide A. Hebert MD,[a] Lawrence F. Eichenfield MD,[b] Diane Thiboutot MD,[c] Linda Stein Gold MD,[d] Snejina Vassileva MD PhD,[e] Yanita Mihaylova MD,[f] Martina Cartwright PhD,[g*h] Luigi Moro PhD,[i] Enrico Fragasso MS,[i*] Jenny Han MS,[j] Nicholas Squittieri PhD,[k] Alessandro Mazzetti MD[i]

Studio in doppio cieco contro veicolo (712 pz) di una crema al clascoterone 1% (un inibitore androgenico topico) applicato 2 volte al dì (709 pz) in bambini di età maggiore o uguale a 12 anni con acne moderata/grave del volto trattati per 12 settimane.

Per la valutazione si usa IGA (Investigator Global Score)

Valutazione efficacia in base al successo ottenuto: 19,9% dei pz in terapia contro 7,7% del veicolo. Inoltre il calo delle lesioni infiammatorie, non infiammatorie e totali mostrò differenza statisticamente significativa (-40% vs-26,1% con P<0,0001).

Clascoterone is the first topical androgen receptor inhibitor to be approved by the FDA.[18] Topical 1% clascoterone represents a novel mechanism of action for the treatment of acne and is the first topical agent targeting the hormonal pathway that may be used safely in males.[19] Clascoterone cream is applied topically, and serious drug-related systemic side effects were not observed in this analysis or in previous studies.[2,20,21] Clascoterone is metabolized quickly, and the primary metabolite, cortexolone, is inactive. These properties support local action with minimal systemic exposure and side effects.[20] Antiandrogenic effects such as reduced libido or feminization in male participants were not observed.[19] Currently, 1% clascoterone cream is the only approved topical antiandrogen treatment for acne.

Il Clascoterone è il primo anti recettore androgenico topico Approvato dalla FDA. La terapia in crema all'1% rappresenta un trattamento per l'acne con un meccanismo di azione innovativo che può essere utilizzato con sicurezza anche nei maschi in cui studi precedenti **non** avevano mostrato effetti antiandrogenici quali femminilizzazione o calo della libido.

J Drugs Dermatol. 2023;22(2):174-181

Efficacy and Safety of 1% Clascoterone Cream in Patients Aged ≥12 Years With Acne Vulgaris

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LSRs through week 12 (Table 3). The majority of LSRs observed were minimal or mild in severity, and the most frequent were erythema, scaling/dryness, and skin atrophy. The most frequent LSRs considered moderate in severity were pruritus and erythema, in 1.7% and 1.5% of vehicle-treated patients and in 1.1% and 0.8% clascoterone-treated patients, respectively. Pruritus was considered severe in only 0.4% of vehicle-treated and 0.3% of clascoterone-treated patients (Table 3).

Gli effetti collaterali locali furono minimi o lievi e rari (eritema, secchezza, desquamazione) e pressoché sovrapponibili rispetto al veicolo. Prurito grave fu riportato solo nello 0,4% dei pazienti trattati col veicolo e nello 0,3% dei pazienti trattati con clascoterone.

Gli effetti collaterali generali osservati in corso dello studio (mal di testa, naso-faringiti e dolore orofaringeo) si osservarono in quantità sovrapponibile o inferiore al veicolo.

LSRs: local skin reactions

Analysis of current data on the use of topical mTOR inhibitors in the treatment of facial angiofibromas in tuberous sclerosis complex—An update

J Eur Acad Dermatol Venereol. 2022;00:1–14.

Riccardo Balestri[1] | Laura Rizzoli[1] | Annalisa Pedrolli[2] | Silvana Anna Maria Urru[3]
Giulia Rech[1] | Iria Neri[4] | Carlo R. Girardelli[1] | Michela Magnano[1]

Abstract

Tuberous sclerosis complex (TSC) is an autosomal dominant neurocutaneous syndrome causing hamartomatous growths in multiple organs. Facial angiofibromas occur in up to 80% of patients and can be highly disfiguring. Treatment for these lesions is challenging. Recently, topical rapamycin has been proposed as an effective option to treat angiofibromas but a commercially available compound has not yet been developed in Europe. We conducted a retrospective review with the aim to update the current data on the use of topical rapamycin in the treatment of angiofibromas in TSC, focusing on the optimal concentration and trying to establish which vehicle should be preferred. Thirty-nine reports describing the use of topical rapamycin in the treatment of angiofibromas in TSC were considered, involving a total of 483 patients.

La sclerosi tuberosa presenta angiofibromi in oltre l'80% dei casi ed essi possono essere assai sfiguranti. Di recente la rapamicina è stata proposta come terapia locale e si è mostrata efficace per tali lesioni, ma un composto commerciale manca ancora in Europa.
Questa review valuta i risultati ottenuti in 39 studi riguardanti 483 pazienti.

Il Sirolimus è un antibiotico macrolide scoperto come prodotto di un batterio (*Streptomyces hygroscopicus*) in un campione di terreno proveniente da *Rapa Nui* (isola di Pasqua), e per questo motivo è anche chiamato Rapamicina.
La rapamicina nei mammiferi ha come bersaglio una serina treonina chinasi (mTOR, mechanistic Target Of Rapamycin) che regola la crescita, la proliferazione, la motilità e la sopravvivenza delle cellule.

Wikipedia

Analysis of current data on the use of topical mTOR inhibitors in the treatment of facial angiofibromas in tuberous sclerosis complex—An update

Riccardo Balestri[1] | Laura Rizzoli[1] | Annalisa Pedrolli[2] | Silvana Anna Maria Urru[3]
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An improvement of the lesions has been shown in over 90% of subjects, particularly if the treatment was started at early stages. Several different formulations (ointment, gel, solution and cream) with a wide range of concentrations (0.003%–1%) were proposed, of which a pharmacological analysis has also been performed. Topical rapamycin can be considered an effective and safe option for the treatment and the prevention of facial angiofibromas in younger patients, but the best formulation has yet to be established. Our review demonstrates that ointment and gel should be preferred, but it is not clear which concentration is optimal. However, according to this study, the 0.1% concentration represents the first choice. Long-term and comparative studies between topical rapamycin formulations are required in order to establish which treatment has a better outcome and lower recurrence rate.

Un miglioramento si era ottenuto nel 90% dei casi ed oltre, soprattutto se la terapia era iniziata precocemente.
Molte le diverse concentrazioni utilizzate (dallo 0,003 all' 1%) e tuttora manca una concentrazione e veicolazione ottimale del farmaco anche se lo 0,1% appare la concentrazione ottimale e il veicolo può essere gel o unguento.

J Eur Acad Dermatol Venereol. 2022;00:1–14.

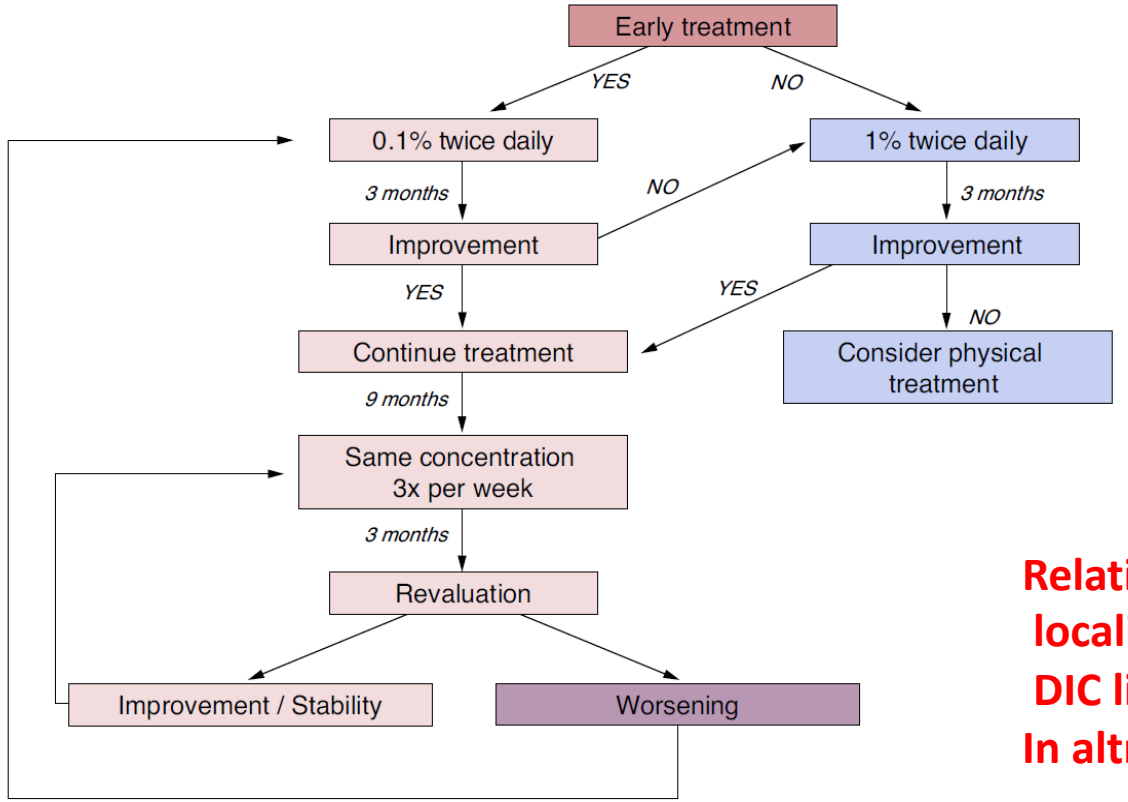
TABLE 2 Vehicles

Formulation	N. of Pt.	Preparation methods	References
Cream	140		
	113	Vehicle not specified	30
	25	Sirolimus powder compounded with Dexeryl®	13,27
	2	Rapamycin 1 mg/mL solution compounded with Eucerin®	2
Gel	104		
	61	Powder in gel	11,22,32
	33	Raparimus® gel;	38
	10	Not reported	9,36
Ointment	214		
	84	Crushed tablets mixed in petrolatum/Vaseline/paraffin	1,3,8,11,16,17,19–21,23–26
	50	Rapamycin powder mixed in calcitriol	35
	44	Rapamycin powder mixed in petrolatum	15,29
	9	Powder mixed in hydrophilic ointment	34
	9	Rapamune® mixed in 0.03% tacrolimus ointment.[a]	7
	2	Crushed tablets mixed in hydrophilic ointment	14
	2	Rapamicyn (non specified) in petrolatum	28,33
	14	Not reported	4,9,18,31,37
Solution	4		
		Commercially available oral rapamycin solution	5,8
Other	18		
		Skincerity®	10
Not reported	3		
			6,12,39

Abbreviation: N. of Pt., Number of patients.

[a]Rapamune, Pfizer Inc, New York, New York

Analysis of current data on the use of topical mTOR inhibitors in the treatment of facial angiofibromas in tuberous sclerosis complex—An update



Adverse events (AE)

Concerning non-RCT studies, local adverse side effects (LASE) were reported in 34 patients.[5,15,17,20,24,25,27,36,38]

LASE included acne, mild irritant contact dermatitis, tingling, transient stinging, dry skin, increased sebum, skin redness and pruritus. Worsening of acne was reported in 8 patients.[27,36,38]

In the 39 articles evaluated, there were no deaths or drug-related serious AE (SAE).

Relativamente agli studi non-RCT effetti collaterali locali avversi osservati in 34/483 pazienti furono acne, seborrea, DIC lieve, pizzicore, bruciore, cute secca, rossore e prurito. In altri 8 pazienti si osservò aggravamento di acne preesistente

FIGURE 1 Flow-chart suggesting how to use topical rapamycin. It is advisable to start with the minimum effective concentration (e.g.: 0.1%), then revaluating the response after 3 months. (i) In responder patients, treatment should be continued maintaining the effective dosage for at least a further 9 months, then a reduction in posology can be proposed. At this point the patient should be revaluated every 3 months, returning to the initial posology in case of worsening. (ii) In patients non-responder to the initial concentration, the latter should be increased (e.g. to 1%). If after 3 further months, an improvement is not observed, a physical treatment (e.g.: surgery, laser and cryotherapy) should be considered. Please note that concentrations reported in this flow-chart are an example based on our experience and on the literature review, but the algorithm remains valid with any other concentration.

New Developing Treatments for Molluscum Contagiosum

Francesco Lacarrubba · Giuseppe Micali · Andrea Calogero Trecarichi · Enrica Quattrocchi · Giuseppe Monfrecola · Anna Elisa Verzì

ABSTRACT

A large variety of treatments for molluscum contagiosum (MC) are available, but none are Food and Drug Administration (FDA) approved and there is no consensus on the optimal approach, mainly owing to a lack of high-level data. Physical modalities are widely used, but require repeated outpatient visits for administration, are painful and difficult to perform in children, and are associated with the possibility of residual scarring and post-inflammatory hypo- or hyperpigmentation. Two experimental topical drugs, a new standardized preparation of topical cantharidin, called VP-102, and a topical nitric oxide (NO)-releasing product containing berdazimer, called SB206, represent promising products that have been designed to overcome the limitations of current treatments. They have recently shown good results in terms of safety and efficacy in large cohorts of patients in phase III studies and have the potential to be the first FDA-approved therapies for the treatment of MC.

Due topici sperimentali sono studiati: una nuova formulazione standardizzata di cantaridina in soluzione locale filmogena (VP-102) e Berdazimer cioè un prodotto che rilascia monossido di azoto (SB206).

Entrambi hanno dimostrato buoni risultati in termini di efficacia e sicurezza e hanno il potenziale per essere i primi approvati dalla FDA per il trattamento dei molluschi contagiosi.

Dermatol Ther (Heidelb) (2022) 12:2669–2678

New Developing Treatments for Molluscum Contagiosum

Escluse lesioni vicino ad orifizi mucosi

Robust phase III trials are available for both drugs, showing complete clearance in 50% of patients treated with VP-102 and 32% of patients treated with SB206, with mild to moderate local skin reactions.

It is still unclear whether VP-102 and SB206 are superior or not in terms of efficacy to the currently adopted MC treatments as in the clinical trials they were compared with vehicle.

Based on good results in terms of safety and efficacy, VP-102 and SB2016 have the potential to be the first FDA-approved MC therapies.

Dermatol Ther (Heidelb) (2022) 12:2669–2678

Table 2 New developing drugs with phase III study for molluscum contagiosum

Drug name	VP-102	SB206
Formulation	Topical solution	Topical gel
Schedule	Single application to be repeated every 3 weeks until complete lesion clearance (up to four treatments)	Once daily for up to 12 weeks
Modality of administration	Physician administered	Self or caregiver administered
Number of subjects enrolled in the study	528 aged 2 years or older	891 aged 6 months or older
Complete clearance	50% at day 84 (versus 20% vehicle)	32.4% at day 84 (versus 19.7% vehicle)
Common adverse events	Application site pain, pruritus, erythema, and blistering, mild or moderate in severity	Application site pain and erythema, mild in severity
AE-related discontinuation rates	1.9% (versus 0.5% vehicle)	4% (versus 0.7% vehicle)

New Developing Treatments for Molluscum Contagiosum

Francesco Lacarrubba · Giuseppe Micali · Andrea Calogero Trecarichi · Enrica Quattrocchi · Giuseppe Monfrecola · Anna Elisa Verzì

MC is a self-limiting condition that usually resolves spontaneously within 6–9 months in immunocompetent individuals [14]. In a retrospective study [15] on treated and untreated MC lesions, a 12-month resolution rate of 45.6% and 48.8%, respectively, was observed. After 18 months, the resolution rate was 69.5% in the treated versus 72.6% in the untreated group [15]. For this reason, the decision to treat or not is made on a case-by-case basis, and some clinicians suggest a wait-and-see approach to avoid painful, time-consuming, and costly therapies that may result in skin discoloration and/or scarring [16]. However, in some cases, the lesions can spread and persist for several months to years. In a study on 306 children affected by MC, 30% of the cases persisted at 1.5 years, and 13% at 2 years [17].

I molluschi contagiosi di solito guariscono spontaneamente in 6/9 mesi negli immunocompetenti. Dopo 12 mesi e 18 mesi i tassi di risoluzione spontanea arrivano rispettivamente al 48,8% e 72,6% e sono superiori a quelli dei pazienti trattati. Pertanto la decisione di trattare o meno va presa caso per caso.
Tuttavia, in taluni casi, le lesioni possono ampiamente diffondersi e persistere per molti mesi o anni. In uno studio su 306 bambini il 30% dei casi presentava molluschi persistenti dopo 1,5 anni e il 13% dopo 2 anni

Update on the Management of Pediatric Psoriasis: An Italian Consensus

Dermatol Ther (Heidelb) (2022) 12:1753–1775

Ketty Peris · Anna Belloni Fortina · Luca Bianchi · Gabriella Fabbrocini · Paolo Gisondi · Anna Balato · Federico Bardazzi · Nicoletta Bernardini · Domenico Bonamonte · Maria Rita Bongiorno · Cinzia Buligan · Francesco Cusano · Maria Beatrice De Felici Del Giudice · May El Hachem · Maria Concetta Fargnoli · Giulio Gualdi · Claudio Guarneri · Katharina Hansel · Giovanna Malara · Carlo Mazzatenta · Giuseppe Micali · Alessandra Narcisi · Iria Neri · Teresa Oranges · Michele Panzone · Aurora Parodi · Lucia Restano · Oriana Simonetti · Marina Venturini · Vito Di Lernia

Table 4 Practical recommendations for topical therapy

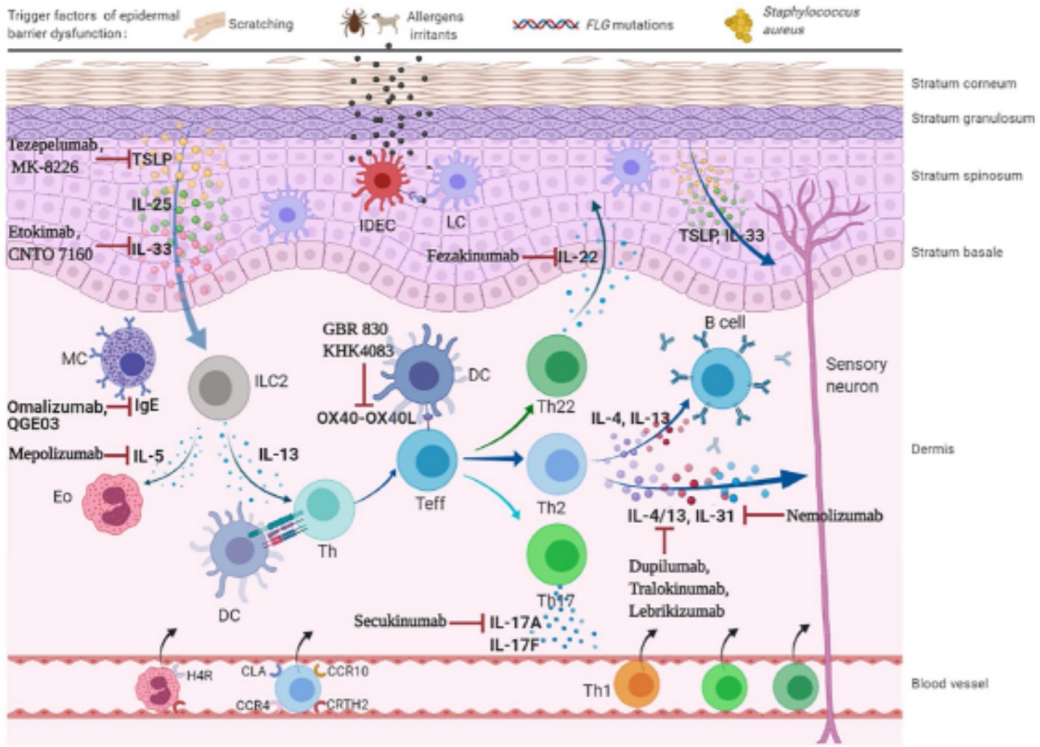
Topical therapy [8, 21, 72]	
Corticosteroids	Class II and Class III
	Apply once daily and avoid prolonged or repeated treatment
	In sensitive areas, 1–2 week-treatment duration
	Class IV only for certain areas (scalp) and very short periods
	Discontinue treatment gradually
Calcipotriol-betamethasone dipropionate (off-label)	Fixed-dose combination of 50 mcg/g calcipotriene and 0.643 mg/g betamethasone dipropionate (foam, gel, ointment)
	Apply once daily for up to 4 weeks
	Approved by FDA in patients aged ≥ 12 years
Vitamin D analogues (off-label)	Calcipotriene, tacalcitol
	Apply once daily
	Do not apply to large skin areas (< 30% BSA for calcipotriene; < 15% BSA for tacalcitol)
	Treatment duration ≥ 2 weeks for full efficacy
Calcineurin inhibitors (off-label)	Tacrolimus 0.1%, pimecrolimus
	Use preferentially for sensitive areas (face, body folds, genitals)
	Recommended twice day for a short term use and intermittent use in long term

Systemic therapy—biologics [73–77]	
Adalimumab	Children aged 4–17 years
	Patient weight ≥ 15 kg and < 30 kg: initial dose of 20 mg SC, followed by 20 mg SC every other week
	Patient weight ≥ 30 kg: initial dose of 40 mg SC, followed by 40 mg SC every other week
	In non-responders, treatment beyond 16 weeks should be carefully considered
Ixekizumab	Children aged ≥ 6 years, with body weight ≥ 25 kg and for adolescents
	Patient weight 25–50 kg: start with 80 mg SC, followed by 40 mg SC every 4 weeks
	Patient weight > 50 kg: start with 160 mg SC (two 80 mg-injections), followed by 80 mg SC every 4 weeks
Secukinumab	Children aged ≥ 6 years
	Weekly dosing for 5 weeks, followed by monthly dosing for maintenance
	Body weight < 25 kg: 75 mg SC
	Body weight ≥ 25 kg and < 50 kg: 75 mg SC
	Body weight ≥ 50 kg: 150 mg SC (may be increased to 300 mg SC)
Etanercept	Children aged ≥ 6 years
	25 mg twice weekly or 50 mg SC once weekly
	Alternatively: 50 mg SC twice weekly for up to 12 weeks, followed by 25 mg SC twice weekly, or 50 mg SC once weekly, if needed
	Treatment should be continued until remission, for up to 24 weeks
	Discontinue treatment if no response after 12 weeks
Ustekinumab	Children aged ≥ 6 years
	Administer at week 0 and 4, and then every 12 weeks
	Body weight < 60 kg: 0.75 mg/kg SC (table with injection volumes available in EMA label)
	Body weight ≥ 60 kg SC and ≤ 100 kg: 45 mg SC
	Body weight > 100 kg: 90 mg SC
	Discontinue treatment if no response after up to 28 weeks of treatment

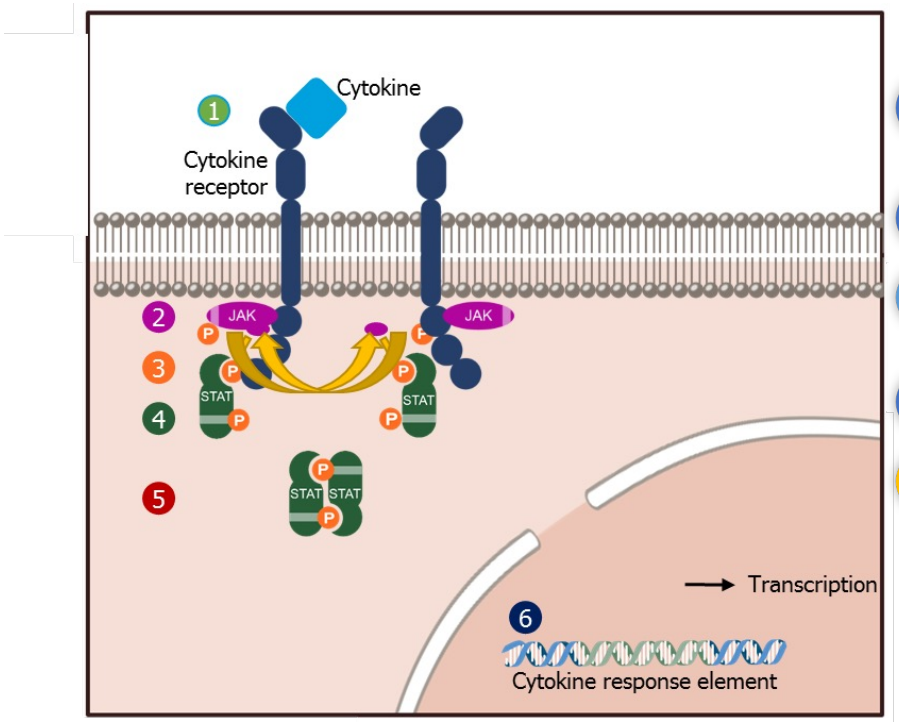
SC subcutaneously

Nuove terapie per la Dermatite Atopica (DA)

Biologici (fl sc)



Piccole molecole (cp)



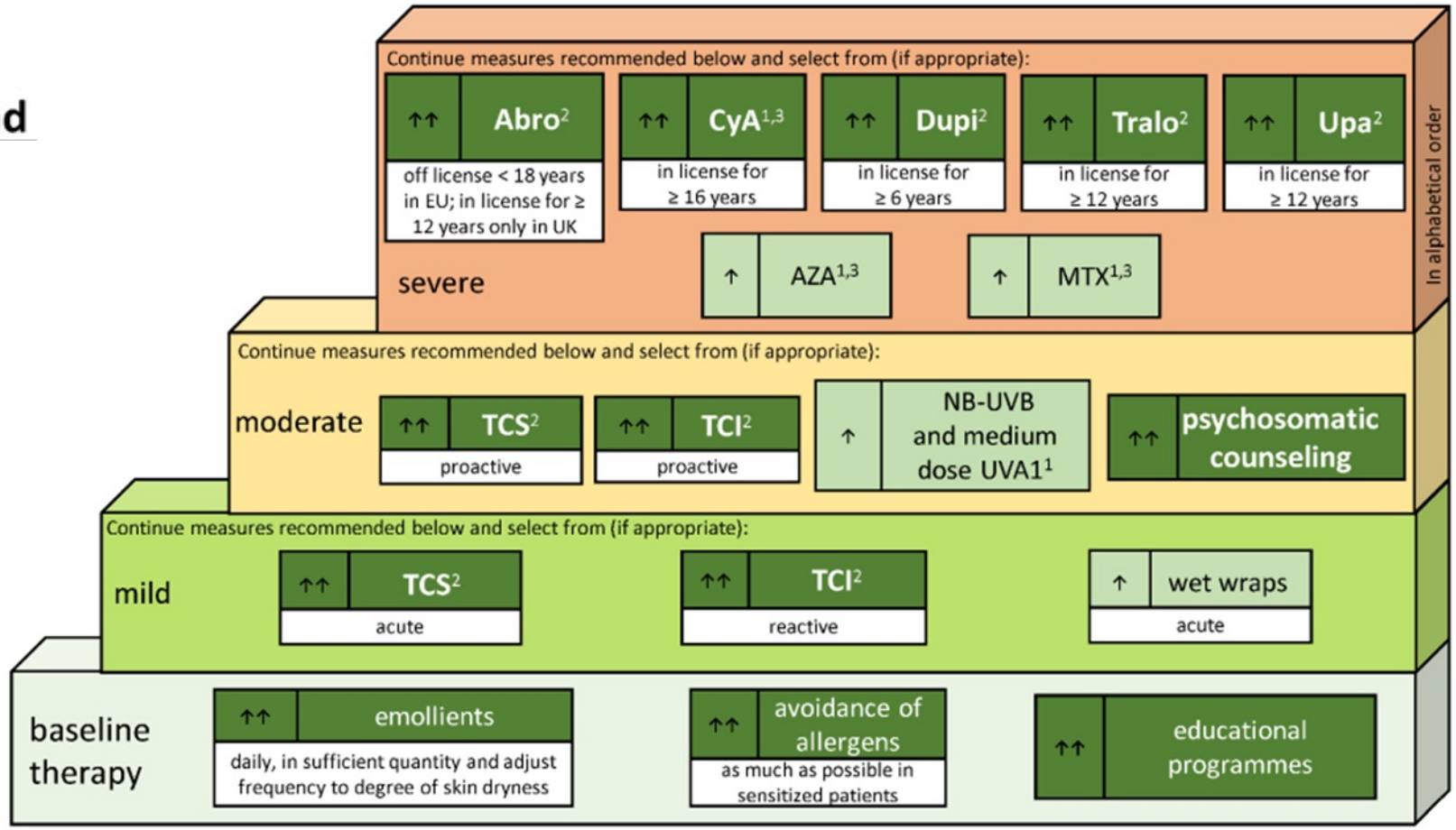
- JAK1: Upadacitinib[2], Abrocitinib[2]
- JAK1: Baricitinib[2]
- JAK2
- JAK1: *Delgocitinib*[2,3]
- JAK3: *Tofacitinib*[2]

EuroGuiDerm Atopic Eczema guideline

European Dermatology Forum

Stepped-care plan for children and adolescents with atopic eczema

- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to table 3 for TCS classes recommended



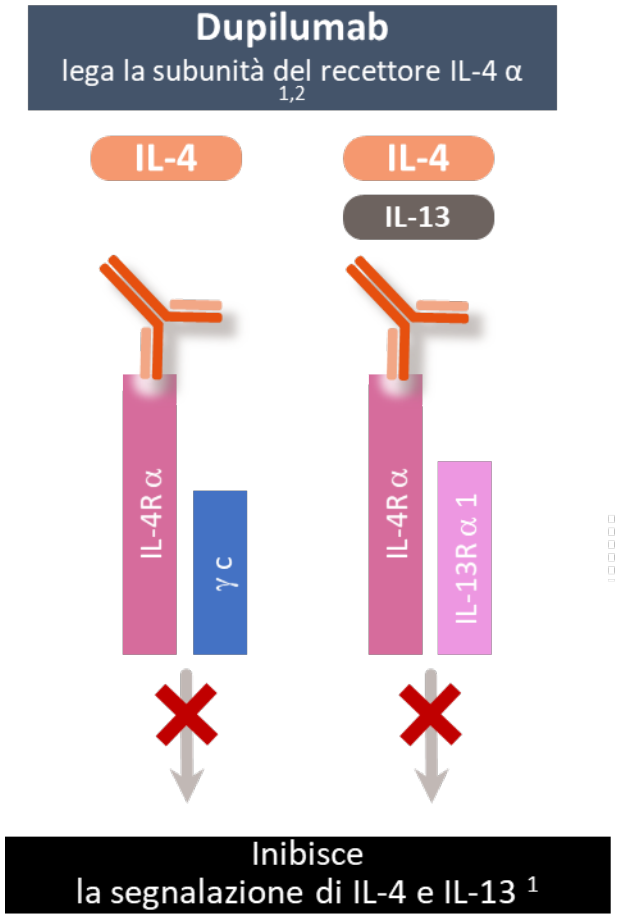
>75%
12/15

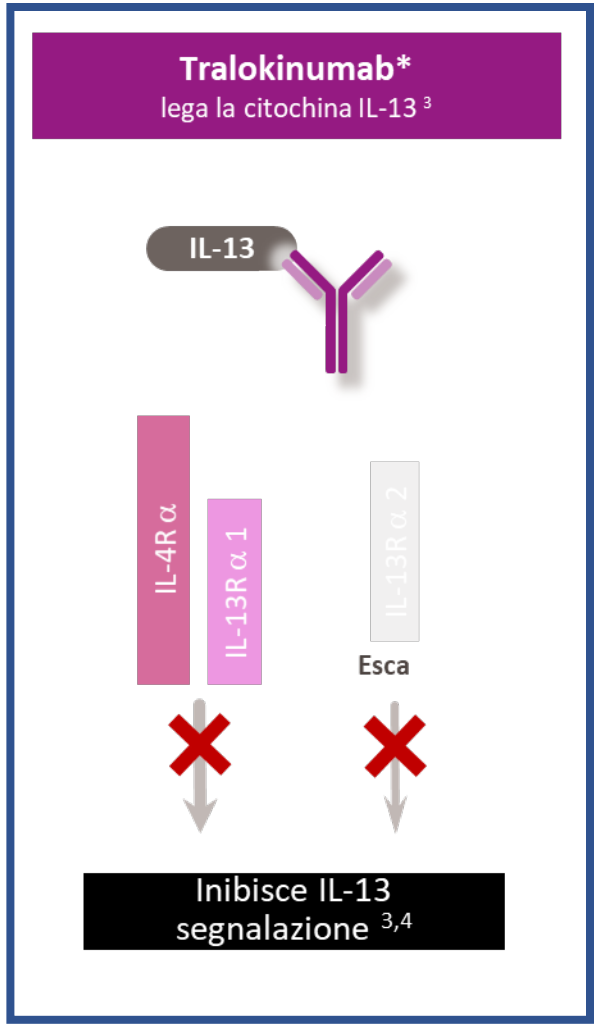
[1] refer to guideline text for restrictions, [2] licensed indication, [3] off-label treatment
↑↑ (dark green) strong recommendation for the use of an intervention / ↑ (light green) weak recommendation for the use of an intervention
For definitions of disease severity, acute, reactive, proactive see section 'VII' and section 'Introduction to systemic treatment' of the EuroGuiDerm Atopic Eczema Guideline

Wollenberg A, et al. J Eur Acad Dermatol Venereol. 2022. EUROGUIDERM GUIDELINE ON ATOPIC ECZEMA Version 2.1, December 2022

Terapie biotecnologiche per la DA adulto approvate

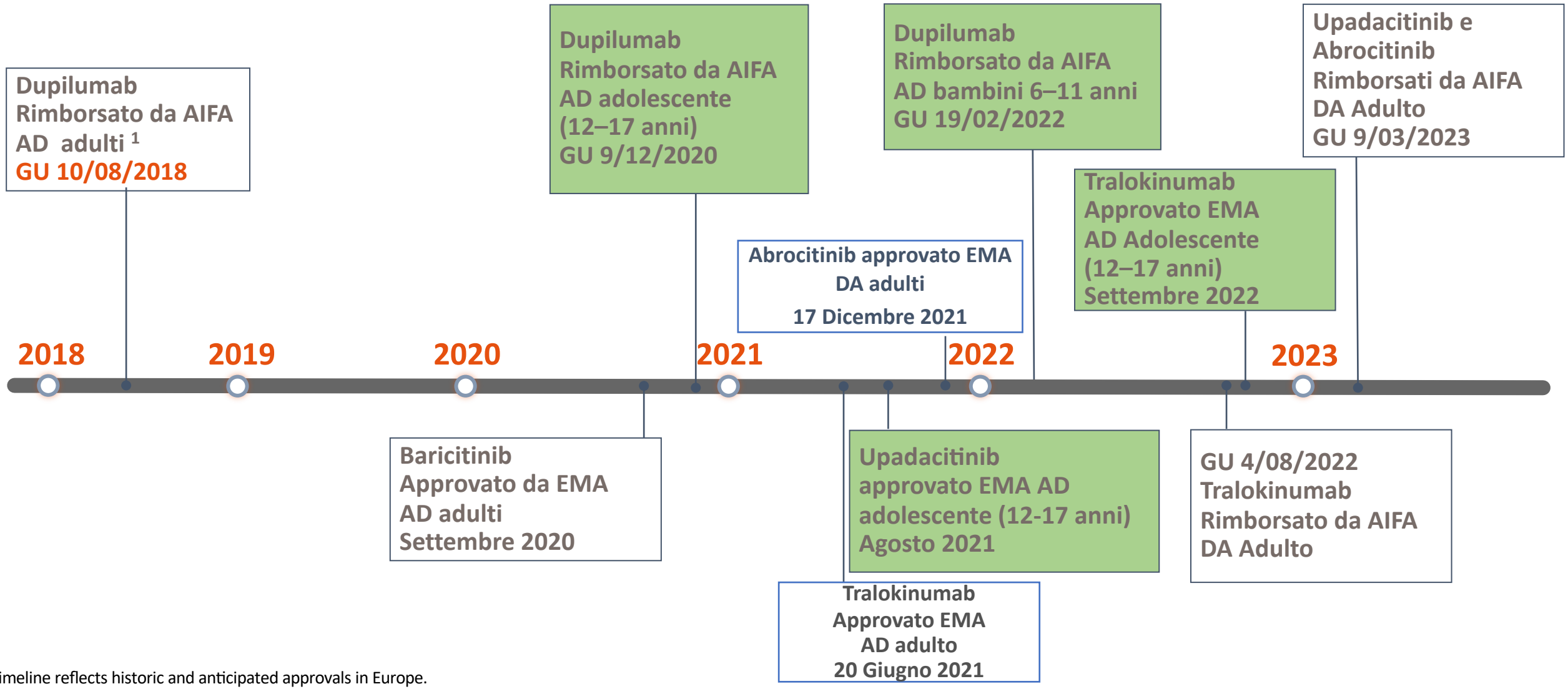
- Tralokinumab è un Ab monoclonale IgG4 completamente umano che specificamente lega l'IL-13 con alta affinità
- Previene l'interazione dell'IL-13 con il suo rececettore





1. Simpson EL, et al. *N inglese J Med.* 2016;375(24):2335-2348. 2. Gandhi NA, et al. *Nat Rev Drug Discov* . 2016;15:35-50. 3. Popovic B, et al. *J Mol Biol.* 2017;429(2):208-219.
4. McCormick SM, et al. *citochina* . 2015;75(1):38–50. 5. Kabashima K, et al. *N inglese J Med.* 2020;383(2):141-150.

Nuove terapie per la DA < 18 anni



Timeline reflects historic and anticipated approvals in Europe.

1. https://www.ema.europa.eu/en/medicines/human/EPAR

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Dupilumab indicazione rimborsabilità di AIFA: ADOLESCENTE 12-17 anni e BAMBINO 6-11 ANNI

INNOVATIVITÀ TERAPEUTICA

L'Agenzia Italiana del Farmaco (AIFA) ha concesso la rimborsabilità di **dupilumab al trattamento della dermatite atopica grave in pazienti dai 6 anni di età** eleggibili per la terapia sistemica.

La DA grave viene definita da:

EASI (Eczema Area and Severity Index) ≥24

OPPURE

EASI <24 in presenza di almeno una delle seguenti:

- **localizzazione in aree visibili e/o sensibili (viso, collo, mani genitali)**
- **NRS Prurito ≥7,**
- **compromissione della qualità della vita: DLQI (Dermatology Life Quality Index) e cDLQI (children DLQI) ≥ 10.**


SERIE GENERALE

Anno 161° - Numero 305

GAZZETTA UFFICIALE

DELLA REPUBBLICA ITALIANA

PARTE PRIMA — Roma - Mercoledì, 9 dicembre 2020 — SI PUBBLICA TUTTI I GIORNI NON FESTIVI


SERIE GENERALE

Anno 163° - Numero 42

GAZZETTA UFFICIALE

DELLA REPUBBLICA ITALIANA

PARTE PRIMA — Roma - Sabato, 19 febbraio 2022 — SI PUBBLICA TUTTI I GIORNI NON FESTIVI

Posologia di dupilumab ADOLESCENTI 12 e 17 anni

	Dose iniziale	Dopo 2 settimane	Dosaggio ogni 2 settimane
Meno di 60 Kg	400 mg SC (2 x 200 mg)		200 mg SC q2w
Più di 60 Kg	600 mg SC (2 x 300 mg)		300 mg SC q2w

Trattamenti concomitanti

Dupilumab può essere usato con o senza corticosteroidi topici
Gli inibitori topici della calcineurina possono essere usati, ma dovrebbero essere riservati solo alle aree problematiche, come le aree del viso, del collo e genitali

16 Sett.

Risposta al trattamento

Deve essere presa in considerazione la sospensione del trattamento nei pazienti che non hanno mostrato risposta dopo 16 settimane di trattamento
Alcuni pazienti con risposta parziale iniziale possono successivamente migliorare con il trattamento continuato oltre le 16 settimane

Posologia di dupilumab BAMBINI 6 e 11 anni

	Dose iniziale	Dopo 4 settimane dalla 2° SC	Dosaggio ogni 4 settimane
Dai 15 Kg a < 60 kg	300mg il giorno 1 seguita da 300 mg il giorno 15		300 mg SC q4w

* La dose può essere aumentata a 200 mg ogni 2 settimane in pazienti con peso corporeo da 15 kg a meno di 60 kg in base alla valutazione del medico.

	Dose iniziale	2 settimane dopo	Dosaggio per le altre settimane
> 60 kg	600 mg SC (2 x 300 mg)		300 mg SC q2w

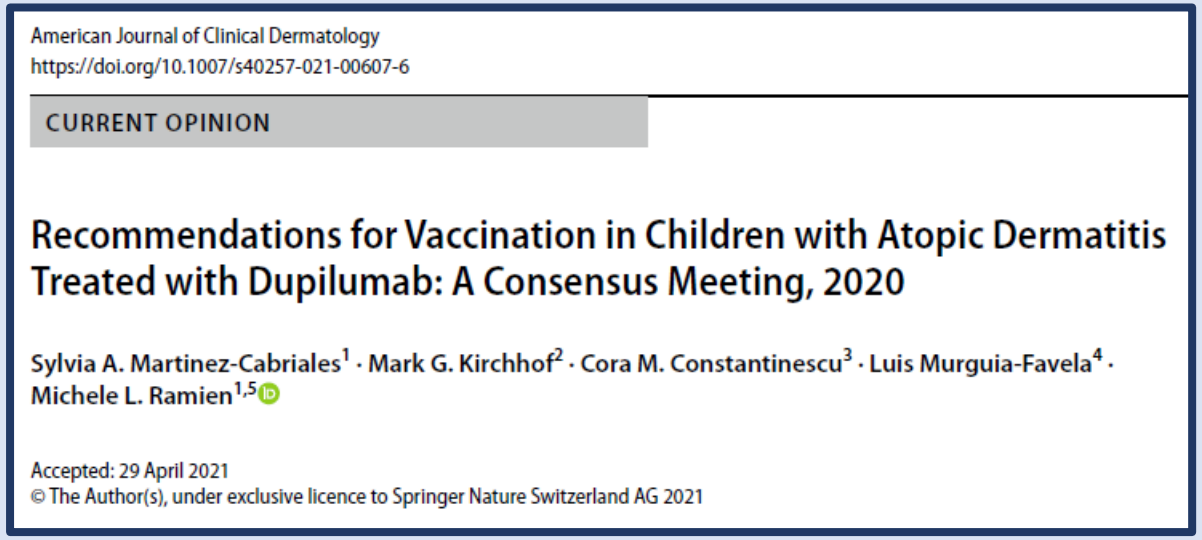
Trattamenti concomitanti

Dupilumab può essere usato con o senza corticosteroidi topici. È consentito l'utilizzo di inibitori topici della calcineurina, ma deve essere limitato solo alle aree problematiche come viso, collo e zone intertriginose e genitali

Terapia con dupilumab e vaccinazione

- VACCINI INATTIVATI O NON VIVI: AUTORIZZATI in concomitanza con D (1), ma distanziare di una settimana le somministrazione di dupilumab rispetto al vaccino[2].
- VACCINI VIVI E VIVI ATTENUATI: NON AUTORIZZATI* in concomitanza con D (1,2).

  Vaccinazioni dovrebbero precedere il trattamento con dupilumab di almeno 4 settimane



American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-021-00607-6

CURRENT OPINION

Recommendations for Vaccination in Children with Atopic Dermatitis Treated with Dupilumab: A Consensus Meeting, 2020

Sylvia A. Martinez-Cabriales[1] · Mark G. Kirchhof[2] · Cora M. Constantinescu[3] · Luis Murguia-Favela[4] · Michele L. Ramien[1,5]

Accepted: 29 April 2021
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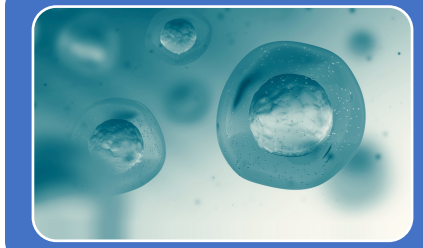
*poiché la sicurezza e l'efficacia clinica non sono state stabilite (1).

1)Riassunto della Caratteristiche del Prodotto, Dupixent; 2) Dupixent, European Public Assessment Report, accessed via https://www.ema.europa.eu/en/documents/variation-report/dupixent-h-c-4390-x-0004-geparassessment- report-variation_en.pdf 3) Blauvelt A et al. J Am Acad Dermatol. 2019 Jan;80(1):158-167.e1. https://doi.org/10.1016/j.jaad.2018.07.048. 4) Michael E. et al. Journal of Allergy and Clinical Immunology: Global, Volume 1, Issue 1, 2022, Pages 9-15, https://doi.org/10.1016/j.jacig.2021.12.003

Dupilumab agisce come un immunomodulatore, non come un immunosoppressore



Dupilumab è classificato come immunomodulatore dal Center for Drug Evaluation and Research della FDA statunitense: un anticorpo monoclonale di natura proteica che tratta una malattia inibendo o modificando una risposta immunitaria preesistente [1]

Un'analisi dei dati della Real Word Evidence ha dimostrato una minore incidenza di infezioni gravi con la terapia con dupilumab rispetto ad altri farmaci sistemici non biologici [2] - **in linea con i dati raccolti da 7 studi clinici** nell'DA [3]

In un'analisi aggregata dei dati di tre studi randomizzati controllati con placebo con dupilumab in pazienti adulti e pediatrici con DA da moderata a severa **NON sono state riscontrate variazioni clinicamente significative nei parametri di laboratorio di routine**

- FDA degli Stati Uniti, Food and Drug Administration degli Stati Uniti.

- 1. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/761055Orig1s000RiskR.pdf . Consultato novembre 2022. 2. Schneeweiss MC, et al. *J Am Acad Dermatol* . 2021;85 : 321-329 . 3. Eichenfield LE, et al. *Sono J Clin Dermatol* . 2019;20(3):443–456. 4. Wollenberg A, et al. *Br J Dermatol* . 2020;182(5):1120–1135. 5. Castro M., et al. *N Inglese J Med* . 2018;378(26):2486–2496. 6.RabeKF, et al. *N Inglese J Med* . 2018;378(26):2475–2485. 7. Bachert C, et al. *Lancetta.* 2019;394:1638–1650.

31 MARZO 2023:
Dupilumab è on label ma non rimborsato dal SSN

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Press Release

(dupilumab) approved by European Commission as first and only targeted medicine for children as young as six months old with severe atopic dermatitis

- Approximately seven times as many patients aged 6 months to 5 years with severe atopic dermatitis treated with Dupixent experienced clear or almost clear skin and reduced overall disease severity compared to placebo
- Patients treated with Dupixent achieved rapid itch reduction as early as three weeks after start of therapy, with significant improvements at 16 weeks sustained through o year
- Dupixent is now a treatment option for the approximately 80,000 infants and young children living with uncontrolled severe atopic dermatitis in Europe

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PARTE PRIMA

Roma - Venerdì, 28 aprile 2023

Condizioni cliniche e criteri di rimborsabilità (il/la Paziente soddisfa tutte le condizioni sottostanti)

Farmaci prescrivibili: abrocitinib, upadacitinib.
☐ è stata diagnosticata dermatite atopica grave definita con punteggio EASI ≥24,
☐ è eleggibile alla terapia sistemica
☐ età maggiore/uguale a 18 anni

PAZIENTI **SENZA** I FATTORI DI RISCHIO INDICATI DA EMA	PAZIENTI **CON** I FATTORI DI RISCHIO INDICATI DA EMA
Il/la Paziente soddisfa tutte le condizioni sottostanti:	*Il/la Paziente soddisfa tutte le condizioni sottostanti:*
☐ ha fallito* il trattamento con ciclosporina	☐ ha fallito* i precedenti trattamenti con farmaci appartenenti alle seguenti classi: ☐ ciclosporina ☐ anti-IL-4/13 ☐ anti-IL-13

La prescrizione deve essere effettuata in accordo con il Riassunto delle Caratteristiche del Prodotto (RCP).
*il fallimento comprende: l'inefficacia/perdita di efficacia, la comparsa di eventi avversi o la presenza di fattori che a giudizio clinico del medico prescrittore controindichino/rendano inappropriato il trattamento nel singolo paziente.

Data

Timbro e firma del medico prescrittore

fattori di rischio indicati da EMA (età pari o superiore a 65 anni, a rischio aumentato di gravi problemi cardiovascolari - come infarto del miocardio o ictus -, fumatori o ex-fumatori di lunga durata e a maggior rischio di cancro): in caso di fallimento* del trattamento con ciclosporina.

J Eur Acad Dermatol Venereol. 2023 Mar 8. doi: 10.1111/jdv.19011. Online ahead of print.

Real-life efficacy and safety of upadacitinib in adolescents with moderate-to-severe atopic dermatitis unresponsive to dupilumab: A case series

Cataldo Patruno [1], Gabriella Fabbrocini [2], Luca Potestio [2], Lucia Genco [2], Maddalena Napolitano [3]

Dermatol Ther (Heidelb). 2023 Feb;13(2):651-660. doi: 10.1007/s13555-022-00882-z. Epub 2023 Jan 9.

Real-Life Effectiveness and Safety of Upadacitinib in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: A Single-Center 16-Week Study

Luigi Gargiulo [1] [2], Luciano Ibba [3] [4], Andrea Cortese [1] [2], Jessica Avagliano [1], Mario Valenti [1] [2], Antonio Costanzo [1] [2], Alessandra Narcisi [1]

Adv Ther. 2023 Mar 21. doi: 10.1007/s12325-023-02490-5. Online ahead of print.

Real-Life Effectiveness and Tolerance of Upadacitinib for Severe Atopic Dermatitis in Adolescents and Adults

Axel De Greef [1], Pierre-Dominique Ghislain [2], Laurence de Montjoye [2], Marie Baeck [2]

Nuove terapie per la DA

mAb

- Efficaci nelle forme moderato gravi
- No interazioni con altri farmaci
- No esami di screening/monitoraggio
- Maneggevoli nei pz con alto carico di malattia
- **Azione comorbidità atopiche**
- Sicuri ed efficaci nel lungo termine
- Sicuri anche nell'anziano

- Ago-fobia
- Dose non modulabile
- Effetti collaterali: congiuntivite, red face, dermatiti psoriasiformi

JAKi

- Efficaci nelle forme moderato gravi (anche con localizzazione importante al volto)
- Rapidità d'azione
- Possibilità di modulare la dose
- **Somministrazione orale/topica più maneggevole**
- **Più adatti ai pazienti giovani con basso carico di malattia**

- Esami di screening e monitoraggio
- Interazioni con altri farmaci
- Controindicazioni nei pazienti:
  - Insufficienza epatica/renale
  - Rischio cardiovascolare alto
  - Neoplasie
- Effetti collaterali: acne, infezioni alte vie respiratorie, anemia, cefalea, dislipidemia

Optimizing topical management of atopic dermatitis

Sneha Butala, MD; Amy S. Paller, MD

Ann Allergy Asthma Immunol 128 (2022) 488–504

Table 1 (*Continued*)

Name	Target	Dosing and Indication	Advantages	Disadvantages	Comments
Crisaborole	PDE4 inhibitor; increases cyclic AMP and inhibits proinflammatory cytokine release	2% ointment; mild-to-moderate AD for ≥ 3 mo and older	1. Nonsteroidal agent 2. Safe and effective for delicate areas (eg, face), given does not cause atrophy 3. No known ocular toxicity	1. A sensation of skin burning and stinging at sites of application, especially the face, is common.	1. EMA approval is for ≥ 2 y of age with mild-to-moderate AD
Topical Ruxolitinib	Selective inhibitor of JAK1 and JAK2 signaling pathways, implicated in AD pathogenesis	1.5% cream; approved for mild-to-moderate AD for ages ≥ 12 y old	1. Nonsteroidal agent 2. Rapid improvement in itch and inflammation 3. Safe and effective for delicate areas (eg, face), given does not cause atrophy 4. No known ocular toxicity	1. Only approved for ages ≥ 12 y 2. May decrease pruritus	1. Currently being studied in ages ≥ 2 to 11 y (NCT04921969)
Emerging therapy, currently in phase 3 trials and potentially available in the United States in 2022					
Topical Roflumilast	PDE4 inhibitor; increases cyclic AMP and inhibits proinflammatory cytokine release	0.15% cream for mild-to-moderate AD in trials	1. Nonsteroidal agent 2. Improvement in itch and inflammation 3. Safe and effective for delicate areas (eg, face), given does not cause atrophy 4. No known ocular toxicity	1. Local irritation (and stinging/burning) uncommon 2. Adverse effects to suggest systemic absorption of PDE4 inhibitor (nausea and diarrhea) are rare (< 1%)	1. Currently being studied in ages ≥2 y old (NCT04773587, NCT00746382, NCT04773600, NCT04845620)
Topical Tapinarof	TAMA; agonizes keratinocyte aryl hydrocarbon receptor and also inhibits artemin and its stimulation of TRPV1 receptors on neurons	1% cream for moderate-to-severe AD in trials	1. Nonsteroidal agent 2. Reported improvement in inflammation and itch	1. Only known associated adverse event is local folliculitis	1. Currently being studied in ages ≥ 2 y old (NCT05142774, NCT05014568, NCT05032859)

Abbreviations: AD, atopic dermatitis; AMP, adenosine monophosphate; EMA, European Medicines Agency; FDA, Food and Drug Administration; IL, interleukin; JAK, Janus kinase; NFAT, nuclear factor of activated T cells; PDE4, phosphodiesterase 4; TAMA, therapeutic aryl hydrocarbon modulating agent; TCI, topical calcineurin inhibitors; TCS, topical calcineurin inhibitors; TRPV1, transient receptor potential vanilloid subtype 1.

Nuovi studi in corso per la terapia della idrosadenite suppurativa negli adolescenti

- Adalimimab approvato da EMA e rimborsato da AIFA per adulti ed adolescenti sopra i 12 anni di età con patologia attiva di grado da moderato a severo e con risposta inadeguata alla terapia sistemica convenzionale. Adalimumab può essere continuato se si attuano terapie chirurgiche.

- Secukinumab autorizzato da EMA, ma ancora non rimborsato da AIFA

2021


MEDICAL DERMATOLOGY

BJD British Journal of Dermatology

Evidence for a 'window of opportunity' in hidradenitis suppurativa treated with adalimumab: a retrospective, real-life multicentre cohort study*

A.V. Marzano, G. Genovese, G. Casazza, C. Moltrasio, P. Dapavo, G. Micali, R. Sirna, P. Gisondi, A. Patrizi, V. Dini, D. Bianchini, L. Bianchi, L. Fania, F. Prignano, A. Offidani, L. Atzori, V. Bettoli, S.P. Cannavo, M. Venturini, M. R. Bongiorno, A. Costanzo, G. Fabbrocini and K. Peris


JAMA Surgery | Original Investigation

Efficacy and Safety of Adalimumab in Conjunction With Surgery in Moderate to Severe Hidradenitis Suppurativa
The SHARPS Randomized Clinical Trial

Falk G. Bechara, MD; Maurizio Podda, MD; Errol P. Prens, MD, PhD; Barbara Horváth, MD, PhD; Evangelos J. Giamarellos-Bourboulis, MD, PhD; Afsaneh Alavi, MSc, MD; Jacek C. Szepietowski, MD, PhD; Joslyn Kirby, MD, MS, MEd; Ziqian Geng, PhD; Christine Jean, PhD; Gregor B. E. Jemec, MD, DMSc; Christos C. Zouboulis, MD, PhD


JEADV Journal of The European Academy of Dermatology and Venereology

EADV

Letter to the Editor | Full Access

Effectiveness of Secukinumab in the treatment of moderate-severe hidradenitis suppurativa: results from an Italian multicentric retrospective study in a real-life setting

S. Ribero, A. Ramondetta, G. Fabbrocini, V. Bettoli, C. Potenza, A. Chiricozzi, M. Licciardello, A.V. Marzano, L. Bianchi, G. Rozzo, L. Fania, C. Marasca, G. Odorici, A. Mambrin ... See all authors

Table 4. Anti-IL-17 agents for HS treatment.

Biologic Drug	Structure	Studies	Dosage Regimen	Efficacy
SECUKINUMAB	Human IgG1κ monoclonal antibody	Open-label trial (*n* = 9) [100]	weeks 0, 1, 2, 3, 4–300 sc mg from week 8–300 mg sc every 4 weeks	78% of patients achieved HiSCR at week 24
		Open-label trial (*n* = 20) [101]	weeks 0, 1, 2, 3, 4–300 mg sc from week 6/8–300 mg sc every 2/4 weeks	70% of patients achieved HiSCR at week 24
		Retrospective cohort study (*n* = 20) [102]	weeks 0, 1, 2, 3, 4–300 mg sc from week 8–300 mg sc every 4 weeks	75% of patients achieved HiSCR by week 16
		Phase III RCTs (NCT03713619, NCT03713632, NCT04179175) [107–109]	Ongoing	
BRODALUMAB	Human IgG2 monoclonal antibody	Open-label trial (*n* = 10) [111]	weeks 0, 1, 2–210 mg sc from week 4–210 mg sc every 2 weeks	100% of patients achieved HiSCR
		Open-label trial (*n* = 10) [112]	every week–210 mg sc	100% of patients achieved HiSCR
BIMEKIZUMAB	Humanized IgG1κ monoclonal antibody	Phase II RCT (*n* = 90) [115]	week 0–640 mg sc from week 2–320 mg sc every 2 weeks	57.3% of patients achieved HiSCR at week 12 vs. 26.1% of patients treated with placebo
		Phase III RCTs (NCT04242446, NCT04242498, NCT04901195) [116–118]	Ongoing	
IXEKIZUMAB	Humanized IgG4κ monoclonal antibody	Case reports (*n* = 3) [120–122]	week 0–160 mg sc weeks 2, 4, 6, 8, 10, 12–80 mg sc from week 16–80 mg sc every 4 weeks	Good disease control
CJM112	Human IgG1κ monoclonal antibody	Phase II RCT (NCT02421172) (*n* = 66) [124]	weeks 0, 1, 2, 3, 4–300 sc mg from week 6–300 mg sc every 2 weeks	HS-PGA response rate with CJM112 32.5% vs. 12.5% with placebo

Abbreviations: HiSCR: Hidradenitis Suppurativa Clinical Response; HS-PGA: Hidradenitis Suppurativa–Physician Global Assessment; RCT: Randomized Controlled Trial; sc: subcutaneously.

Nuovi studi in corso per la terapia della vitiligine

- Terapia per os :
- Baricitinib JAK1/2: studio fase 2 associato a fototerapia
- Ritlecitinib JAKi3: trial in corso di definizione in Italia
- Brepocitinib TYK2/JAKi1: trial ongoing associato a fototerapia
- Ifidancitinib JAK1/3: in uso per areata e trial in atto fase 2 per vitiligine

- Terapia locale:
- Cerdulatinib SYK/JAK: trial in gel allo0,37%
- Delgocitinib anti JAK1,2,3 ed anti TYK2: trial in fase 3 nell'eczema cronico delle mani

Front Immunol. 2021; 12: 790125.

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