Atopic dermatitis

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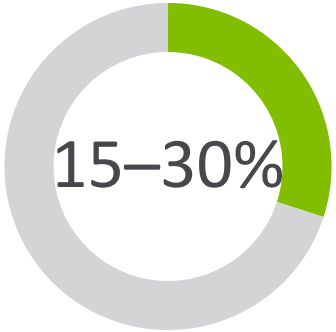
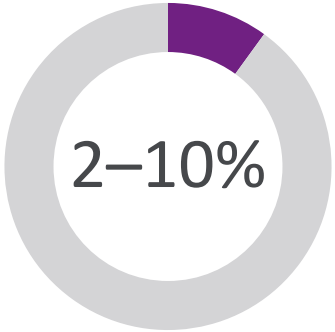
Introduction

- Atopic dermatitis (AD) is a chronically relapsing skin disease that occurs most commonly during early infancy and childhood.
- It is frequently associated with abnormalities in skin barrier function, allergen sensitization, and recurrent skin infections.
- There is no single distinguishing feature of AD or a diagnostic laboratory test.

AD is a common chronic inflammatory skin disease[1–3]



Lifetime prevalence in **children**[1,2]



Lifetime prevalence in **adults**[2,3]

Increase in **incidence** since the 1970s[4]

Dermatitis[a] accounts for the **largest skin disease** burden globally (Global burden of disease 2013 study)[5]

- [a]Including atopic, seborrheic, and contact dermatitis
AD, atopic dermatitis

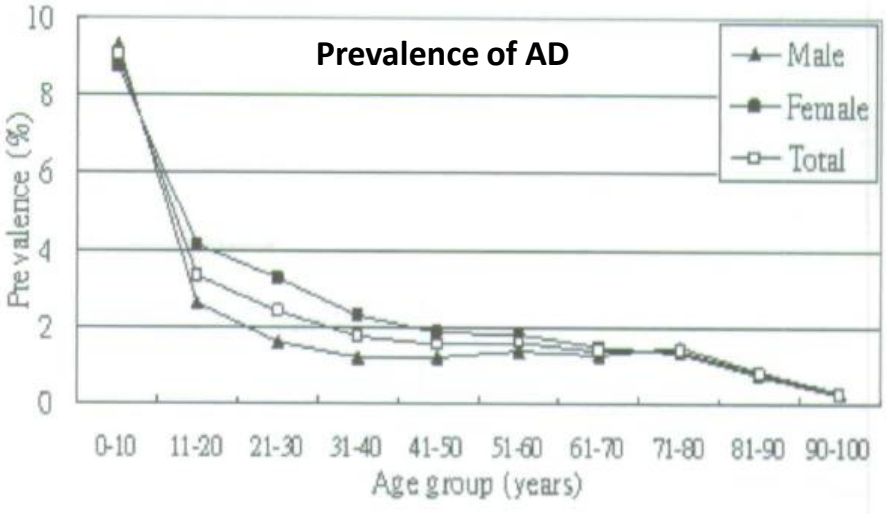
- 1. Bieber T. Ann Dermatol 2010;22:125–37; 2. Nutten S. Ann Nutr Metab 2015;66(Suppl. 1):8–16;
3. Abuabara K, et al. Ann Intern Med 2019;170:354–6; 4. Avena-Woods C. Am J Manag Care 2017;23:S115–S23;
5. Karimkhani C, et al. JAMA Dermatol 2017;153:406–12

THE OVERALL PREVALENCE OF AD IN TAIWAN IS 6.7%,

INVESTIGATIVE REPORT

Prevalence of Atopic Dermatitis, Allergic Rhinitis and Asthma in Taiwan: A National Study 2000 to 2007

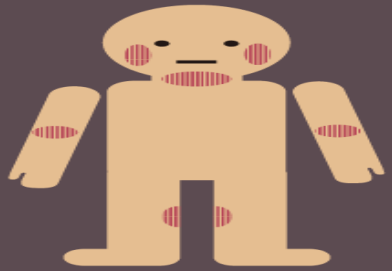
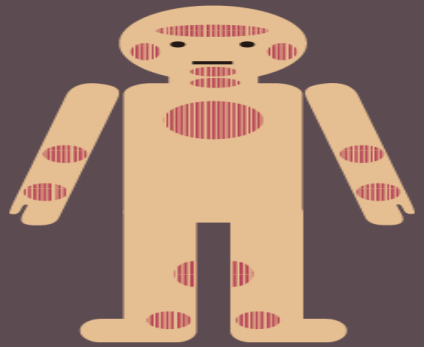
- National Health Insurance Research Database (NHIRD) nationally representative cohort from 2000 to 2007: **997,729** enrolled
- Overall, **66,446** patients were diagnosed with **atopic dermatitis with 6.7% prevalence (8 years)**
- The 8-years prevalence of AD in children (age < 20 years) was **9.6%**; in contrast, **4%** of adults were still affected by this disease

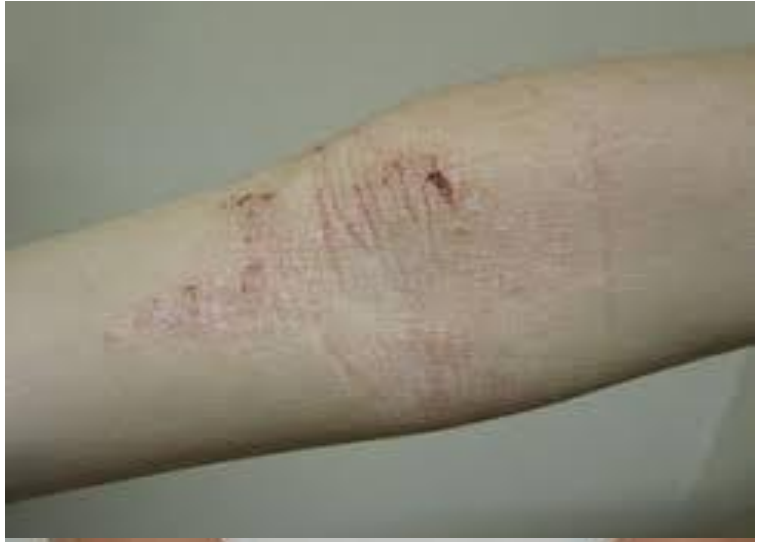


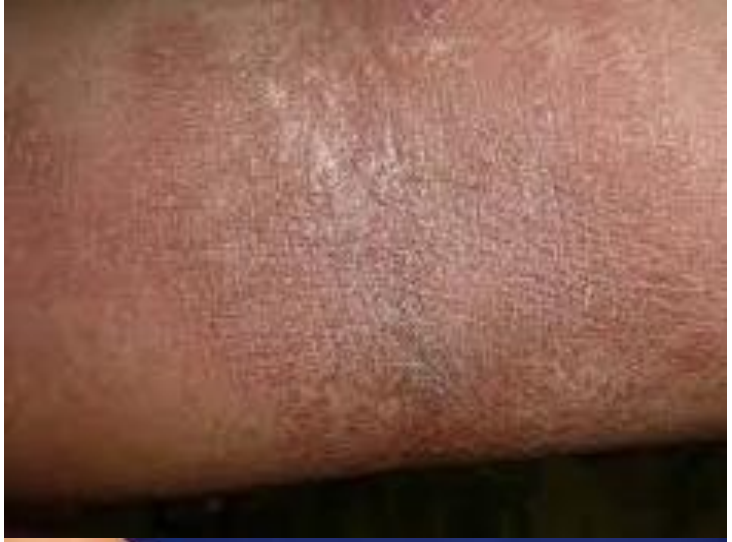
AD, atopic dermatitis; NHIRD, National Health Insurance Research Database

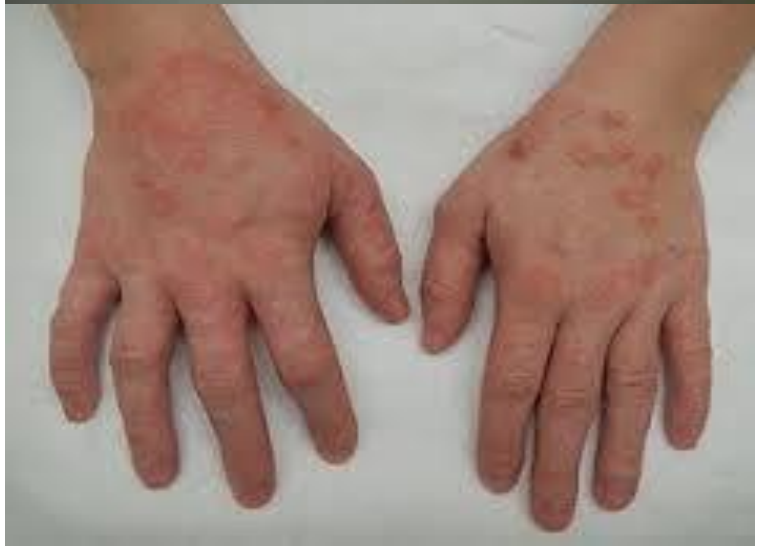
Hwang CY, et al. *Acta Derm Venereol* 2010; 90: 589–594.

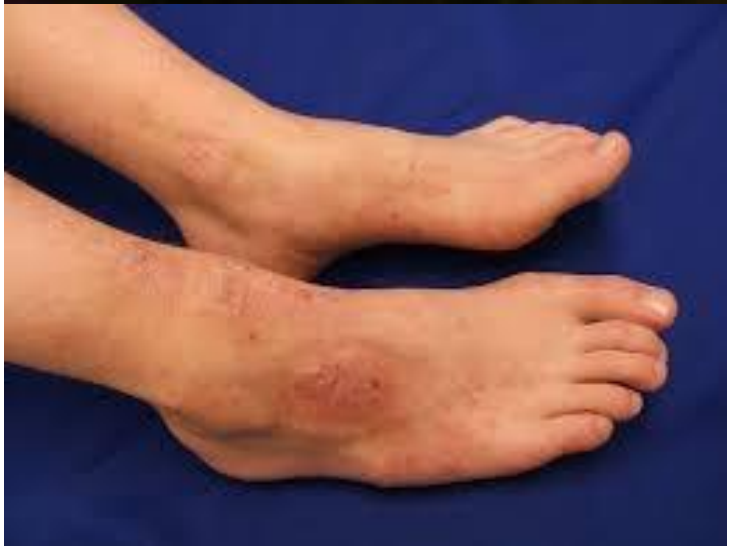
異位性皮膚炎病灶分佈

		常見位置	皮膚症狀
嬰兒時期		雙頰 前額 頭皮	紅疹、搔癢、 乾燥脫皮、 水泡
兒童時期		臉部 頸部 手肘窩 膝窩 手腳關節	皮膚乾裂、 苔癬樣皮膚、 慢性濕疹
青年及成人		臉部 頸部 前胸 手肘窩 手腕 膝窩 足關節	皮膚增厚、 膚色更深、 皮膚苔癬化嚴重

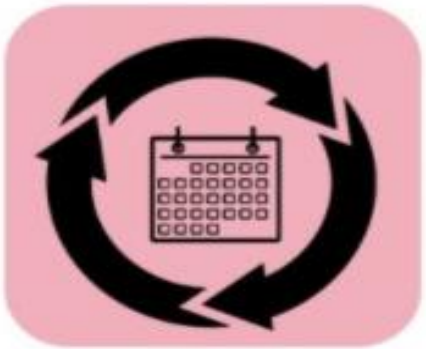








文/皮膚科 賴柏如 主任



慢性
反覆性

皮膚奇癢
反覆搔抓

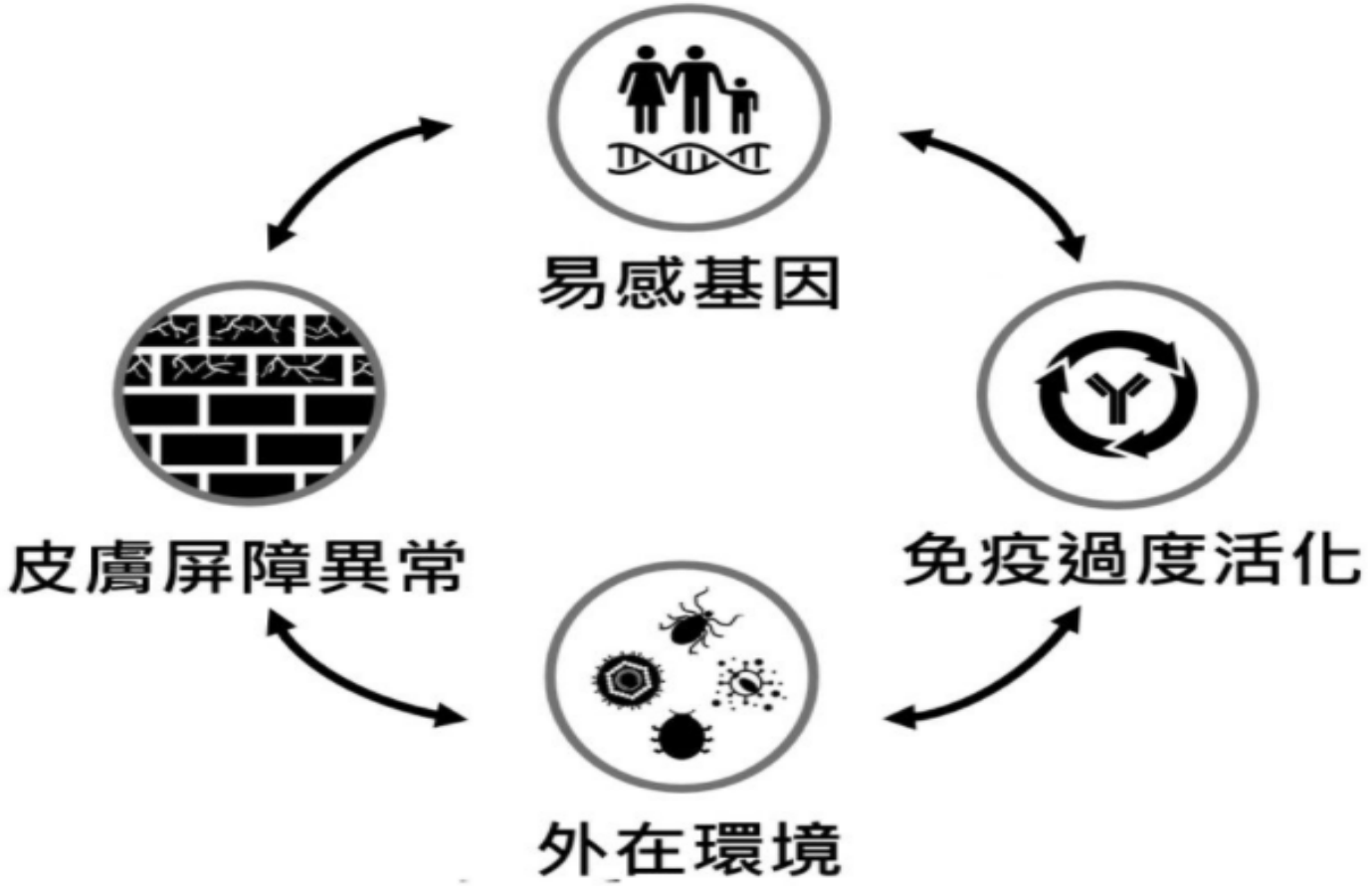
嬰兒
頭部/兩頰/四肢伸側
孩童(1~2歲後)
轉為四肢內側

個人/家族
具有過敏體質
(過敏性鼻炎/氣喘/
異位性皮膚炎)

(以上四項中有三項，即符合)

異位性皮膚炎診斷標準

Hanifin and Rajka Diagnostic Criteria for Atopic Dermatitis, 1980



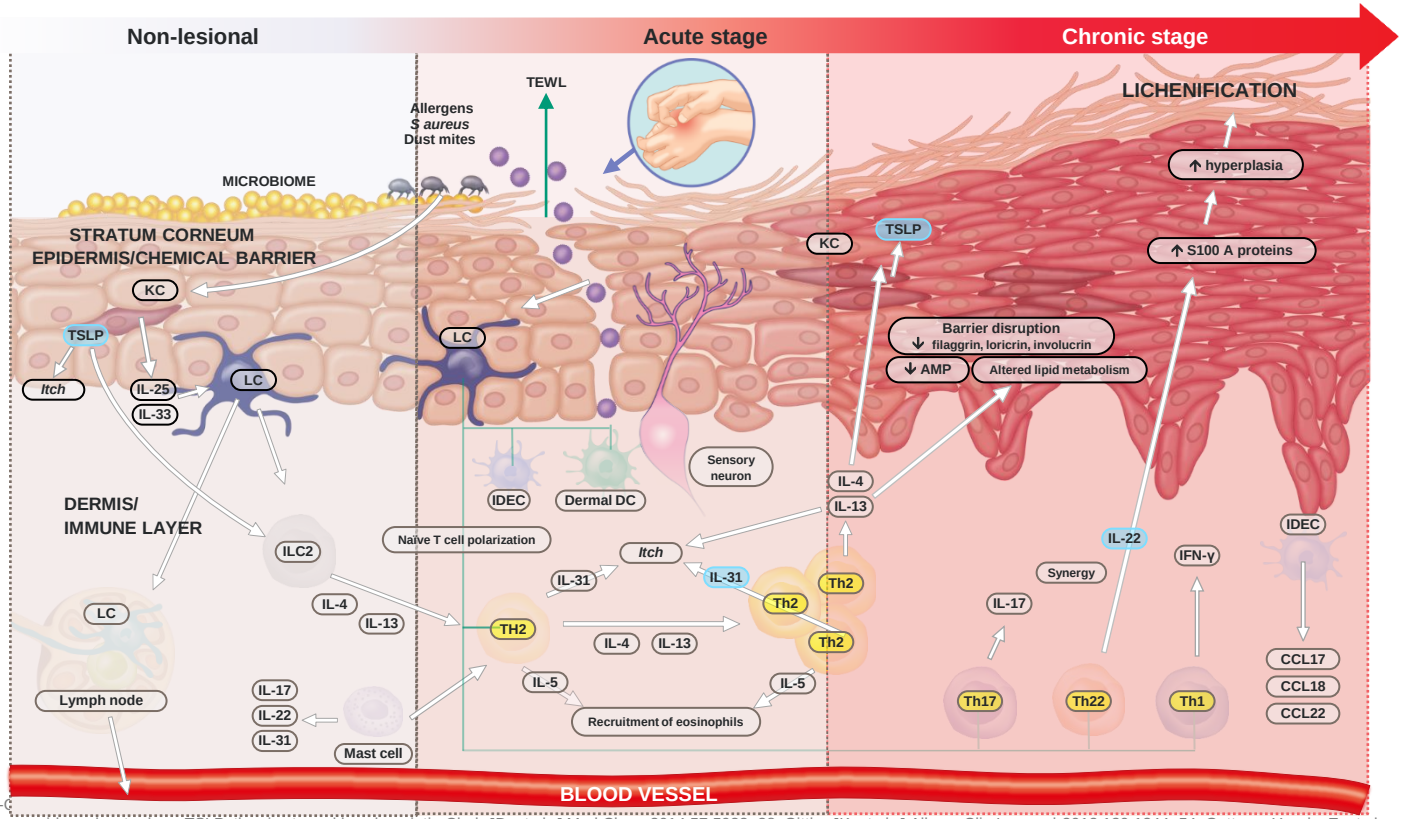
異位性皮膚炎致病機轉

The pathogenesis of AD is complex, involving multiple pathways

Skin barrier dysfunction

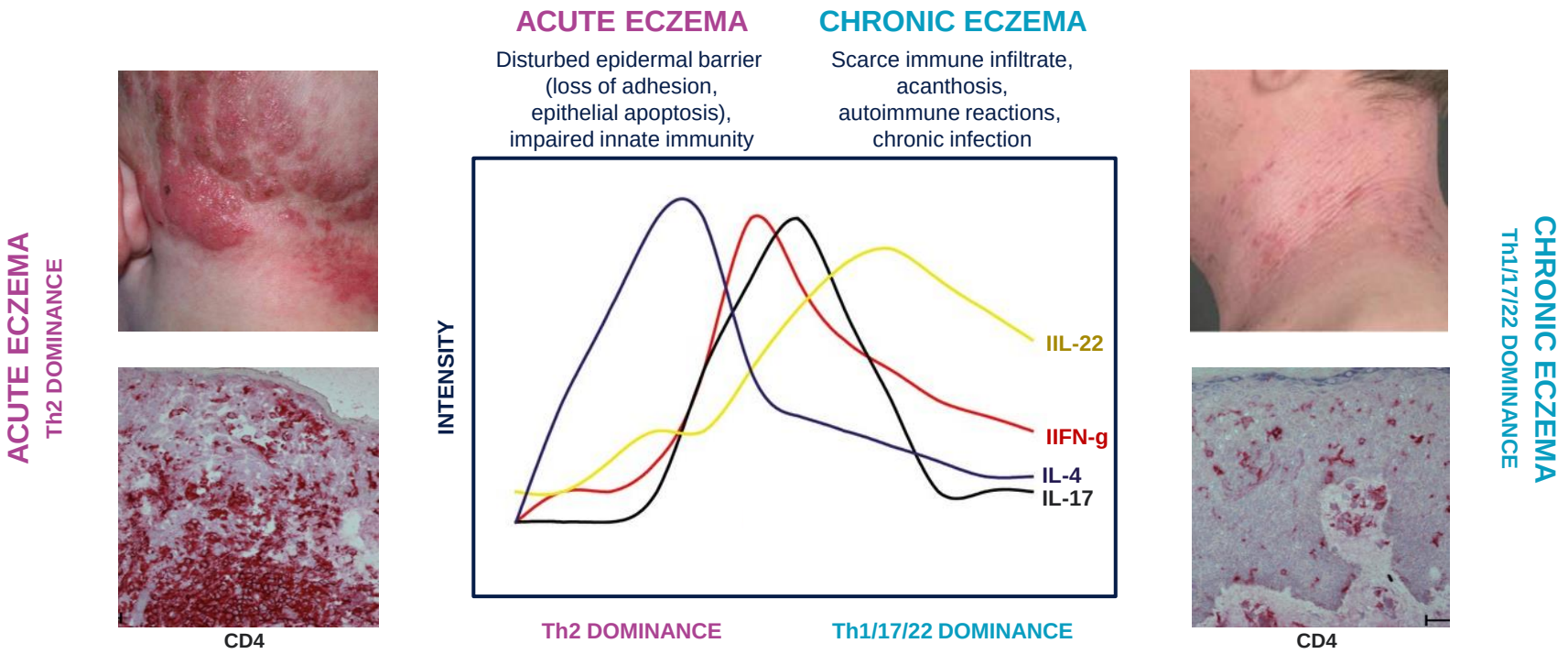
Sensory neuron activation

Immune dysregulation



AMP, antimicrobial protein; CCL, chemokine (C-C
KC, keratinocyte; LC, Langerhans cell; TEWL, transepidermal water loss; TSLP, thymic stromal lymphopoietin Clark JD, et al. J Med Chem 2014;57:5023–38; Gittler JK, et al. J Allergy Clin Immunol 2012;130:1344–54; Guttman-Yassky E, et al. Exp Dermatol 2018;27:409–17; Klonowska J, et al. Int J Mol Sci 2018;19:3086; Leung DY, et al. J Allergy Clin Immunol 2014;134:769–79; Virtanen A, et al. BioDrugs 2019;33:15–32; Winthrop KL. Nat Rev Rheumatol 2017;13:234–43

Immune pathway alterations over time in acute and chronic AD

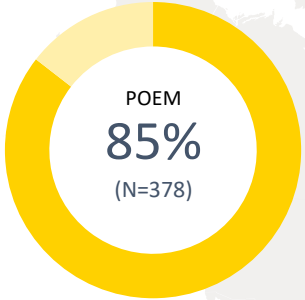


CD, cluster differentiation; IL, interleukin; IFN, interferon; Th, T-helper cell

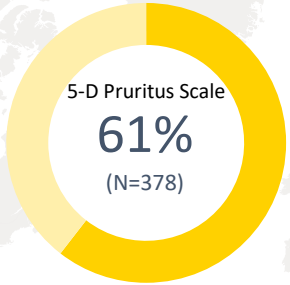
Eyerich K, Novak N. Allergy 2013;68:974–82

ITCH IS THE MOST BURDENSOME SYMPTOM OF ATOPIC DERMATITIS[1]

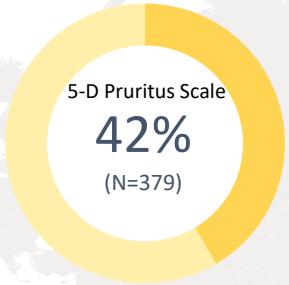
Patient-reported outcomes were collected at screening in a phase 2b clinical trial of dupilumab in adults with moderate-to-severe AD[2]



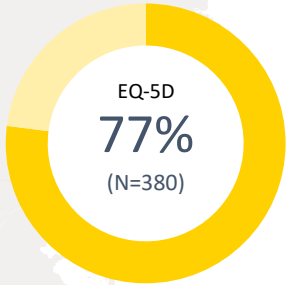
of patients with AD experience itch **on a daily basis**[2]



reported itching as **severe or unbearable**[2]



reported itching **≥18 hours per day**[2]



reported moderate or severe **pain or discomfort**[2]

Itch intensity: **6.5/10** on numerical rating scale[2]

AD, atopic dermatitis; POEM, Patient-Oriented Eczema Measure

1. Silverberg JI, et al. Ann Allergy Asthma Immunol 2018;121:340–7;
2. Simpson EL, et al. J Am Acad Dermatol 2016;74(3):491–8

THE SPANISH PSEDA STUDY SHOWED THAT THE BURDEN OF SLEEP DISTURBANCE INCREASES WITH DISEASE SEVERITY

A higher proportion of adults and children with moderate/ severe versus mild AD have **difficulty falling asleep***

	Mild N=97	Moderate N=179	Severe N=46
Adults:	76.2%	88.1%	100.0%
Children:	60.8%	90.1%	87.5%

A higher proportion of adults and children with moderate/ severe versus mild AD **wake up due to itching***

	Mild N=97	Moderate N=179	Severe N=46
Adults:	54.8%	76.2%	92.6%
Children:	36.0%	76.8%	87.5%

*Disease severity was assessed using the investigator's global assessment, which is based on six categories, with scores ranging from 0 (no disease, no inflammatory signs of AD) to 5 (very severe disease, with intense erythema and papules/intense infiltration with crusting/exudation)

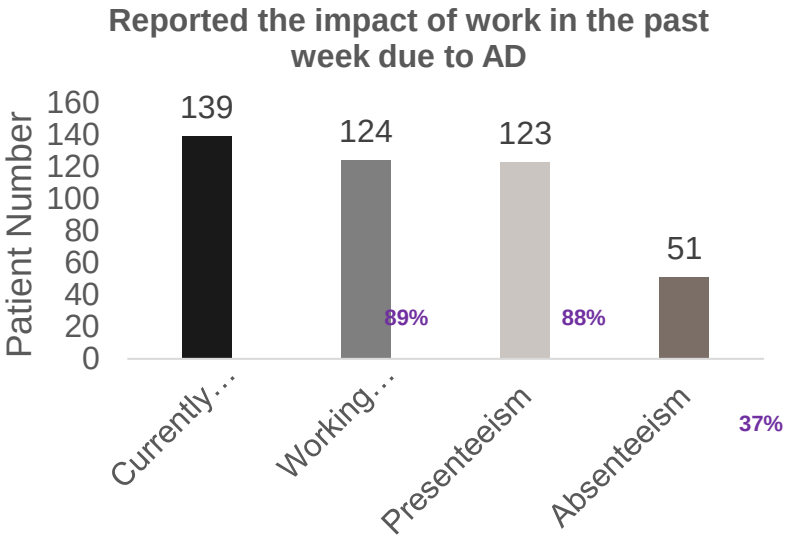
AD, atopic dermatitis

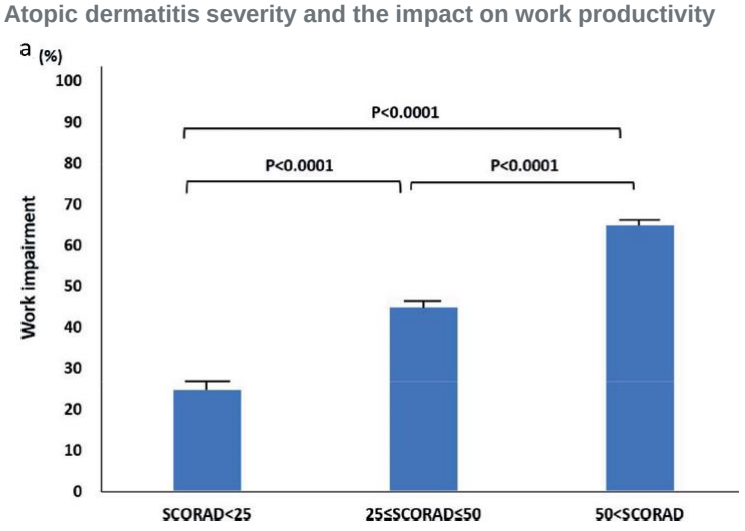
Sánchez-Pérez J, et al. *Actas Dermosifiliogr* 2013;104(1):44–52

NUMBER OF MISSED DAYS AT WORK INCREASES WITH INCREASING AD SEVERITY

Impact of Atopic Dermatitis on Work and Activity Impairment in Taiwan

A total of 200 patients with AD were recruited. Of these, 70 had mild AD, 72 had moderate AD, and 58 had severe AD.

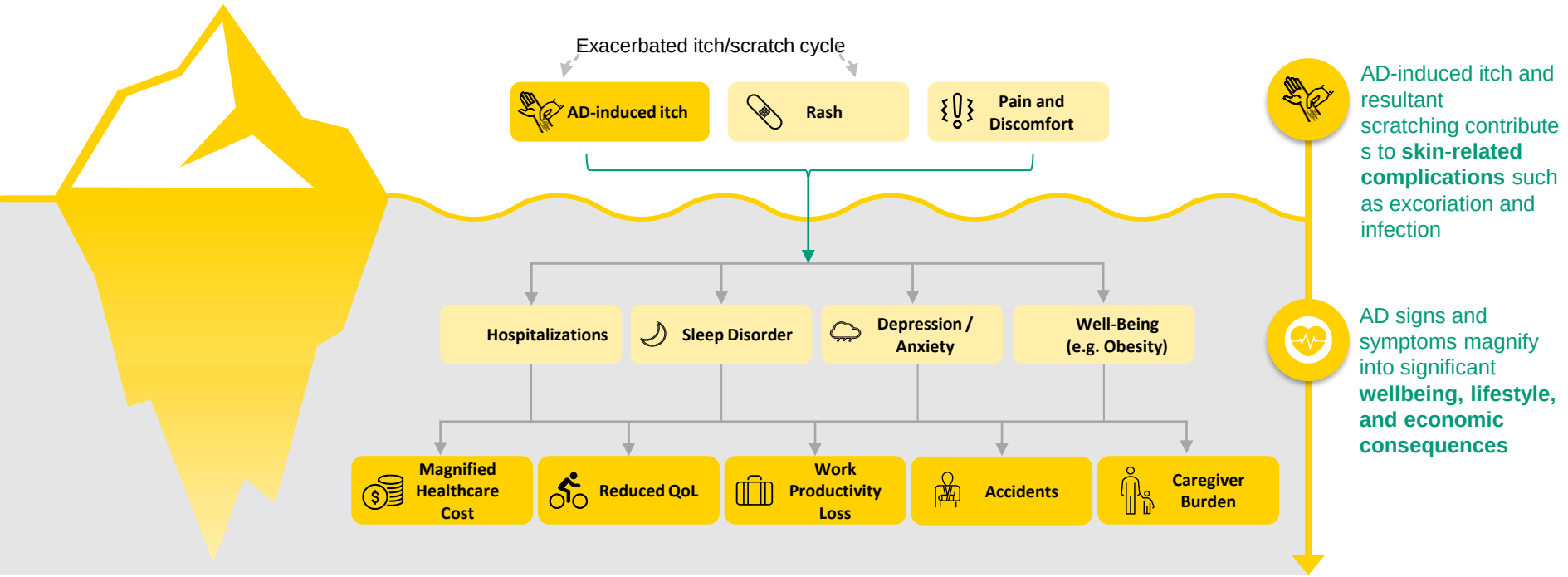




Median score of overall work impairment is 50.0

absenteeism (work time missed), presenteeism (impairment at work/reduced work-hour effectiveness), work productivity loss (overall work impairment from absenteeism plus presenteeism)

Chan, Tom C., et al. "Impact of atopic dermatitis on work and activity impairment in Taiwan." *Acta Dermato Venereologica* 101.9 (2021): adv00556-adv00556.



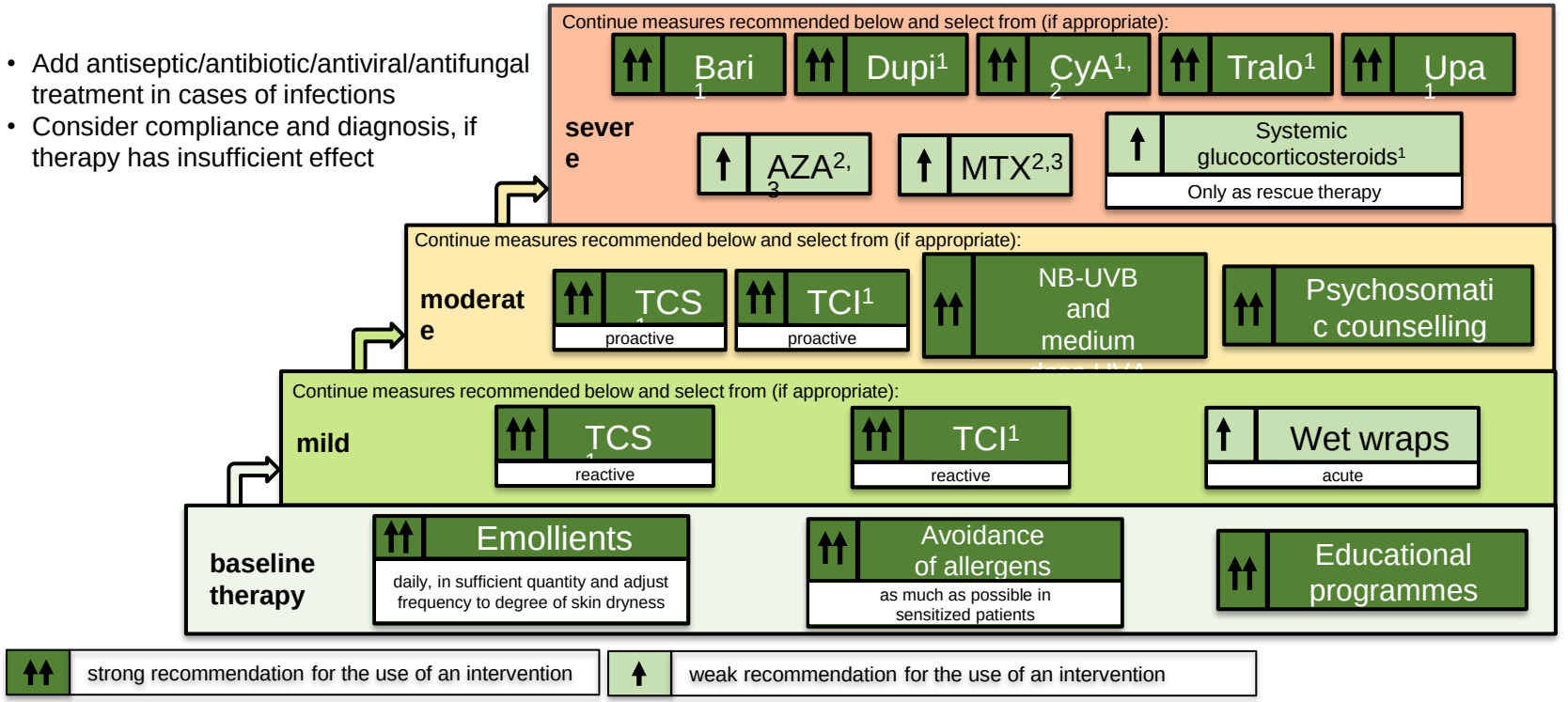
Whiteley J, et al. Curr Med Res Opin 2016:1–7Simpson EL, et al. J Am Acad Dermatol 2016;74:491–8; Drucker AM, et al. J Invest Dermatol 2017;137:26–30 . Silverberg JI. F1000Research 2018;7(F1000 Faculty Rev):303

AD, atopic dermatitis; QoL, quality of life

2022 EuroGuiDerm update

EuroGuiDerm 2022 Guidelines: Stepped-care Plan for Adults With Atopic Eczema

- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect



[1]Licensed indication; [2]refer to guideline text for restrictions.; [3]off-label treatment.

AZA=Azathioprine; Bari=Baricitinib; CyA=Ciclosporin; Dupi=Dupilumab; MTX=Methotrexate; TCI=Topical Calcineurin Inhibitors; TCS=Topical Corticosteroids; Tralo=Tralokinumab; Upa=Upadacitinib; UVA1 =Ultraviolet A1; NB-UVB=Narrow-band Ultraviolet B.

Wollenberg A, Kinberger M, Arents B, et al. European Dermatology Forum. EuroGuiDerm Guideline on Atopic Eczema - Version 1.0, June 2022: QC complete by Shoba Solomon, June 20, 2022.

2022 EUROGUIDERM GUIDELINE ON ATOPIC DERMATITIS
Candidates for systemic treatment

Candidates for systemic treatment may be *either* patients with a high composite score such as

- SCORAD above 50 (scale definition)
- Clinically failing to respond to an appropriately conducted topical therapy (functional definition)
- Unable to participate in normal daily life activities whilst following an adequate treatment regimen (social definition)

異位性皮膚炎的治療演進

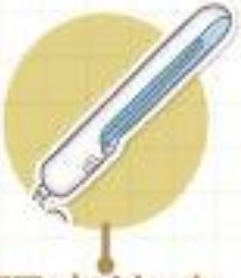
傳統治療

基礎保濕

口服免疫抑制劑與類固醇

外用藥膏

口服抗組織胺



照光治療

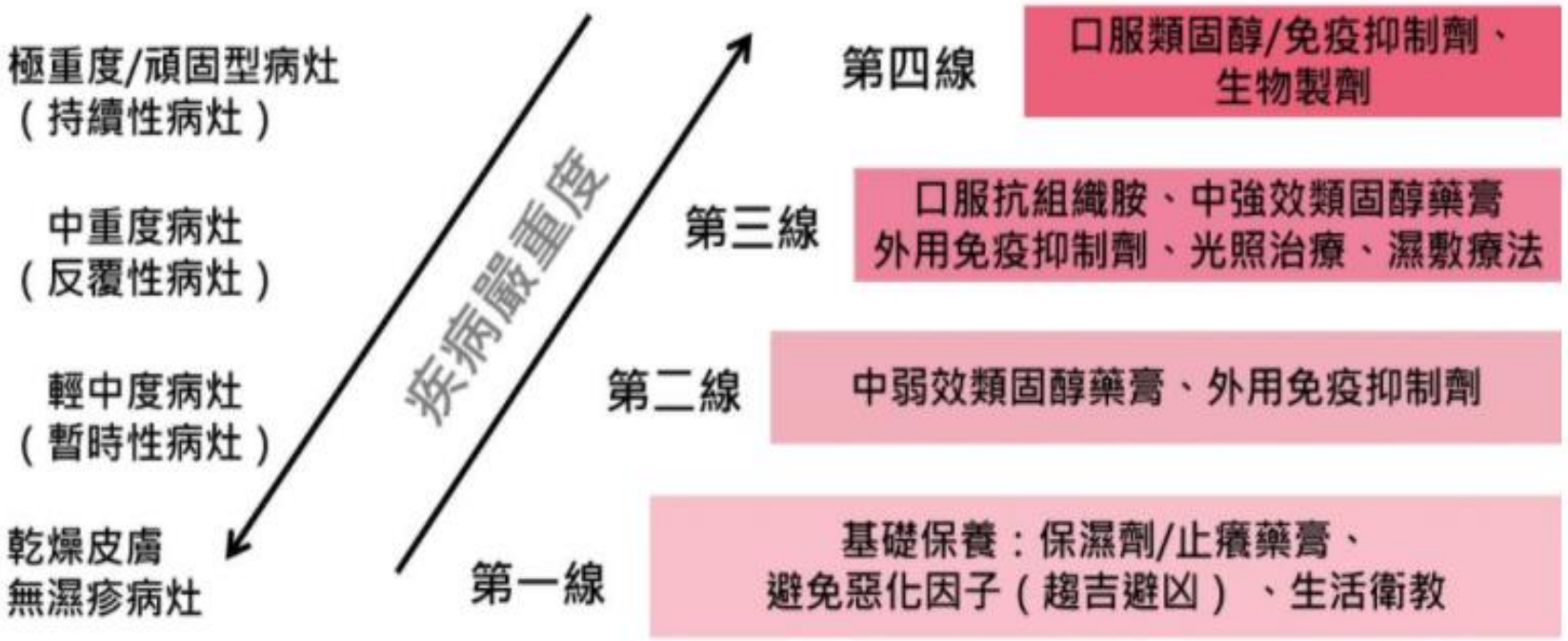
精準治療

生物製劑

口服標靶小分子新藥

針對中度至重度異位性皮膚炎

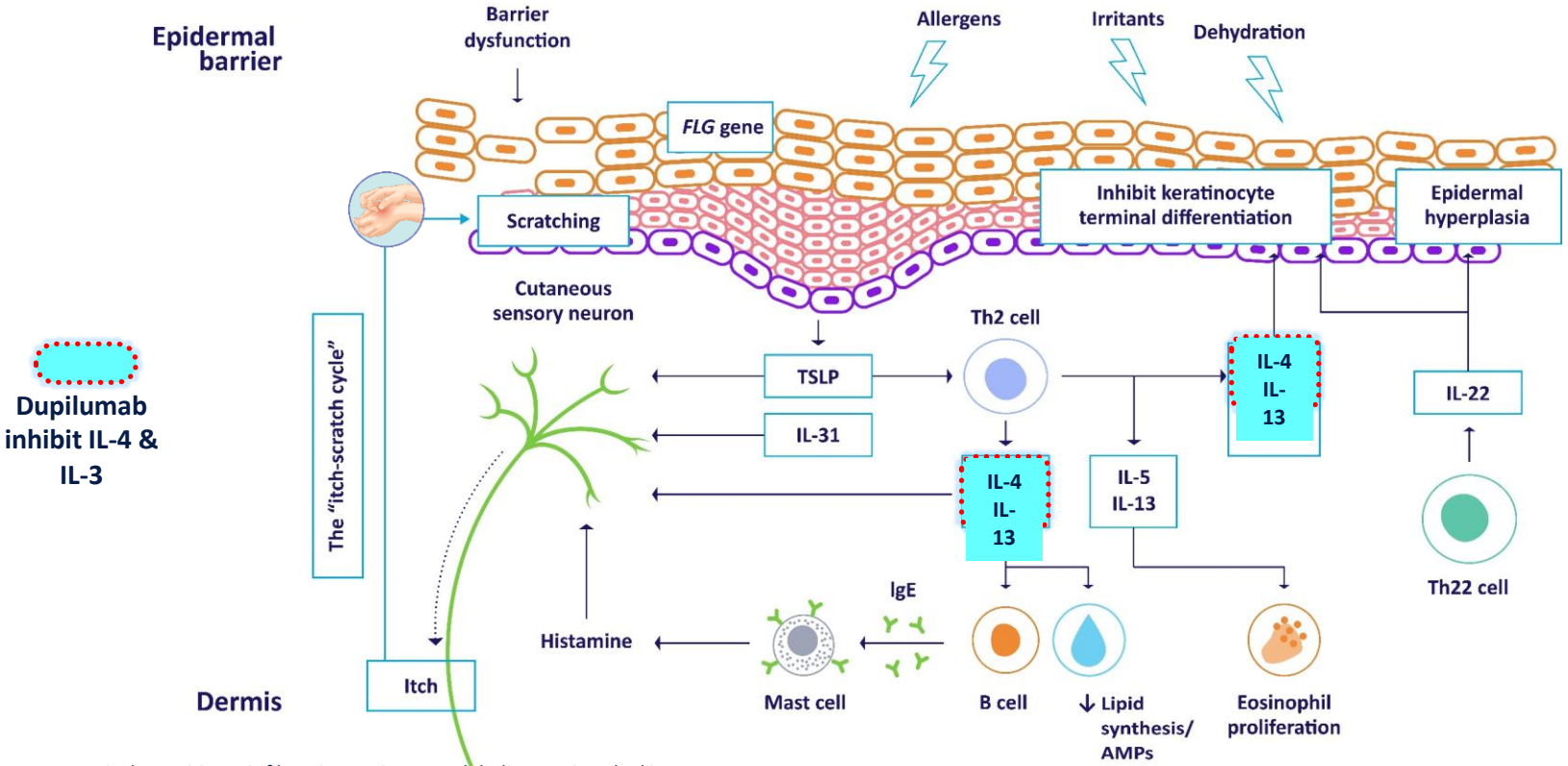
長庚醫訊 林口長庚皮膚部主治醫師　葛宗昀



異位性皮膚炎：治療階梯

J Eur Acad Dermatol Venereol. 2018 Jun;32(6):850-878.

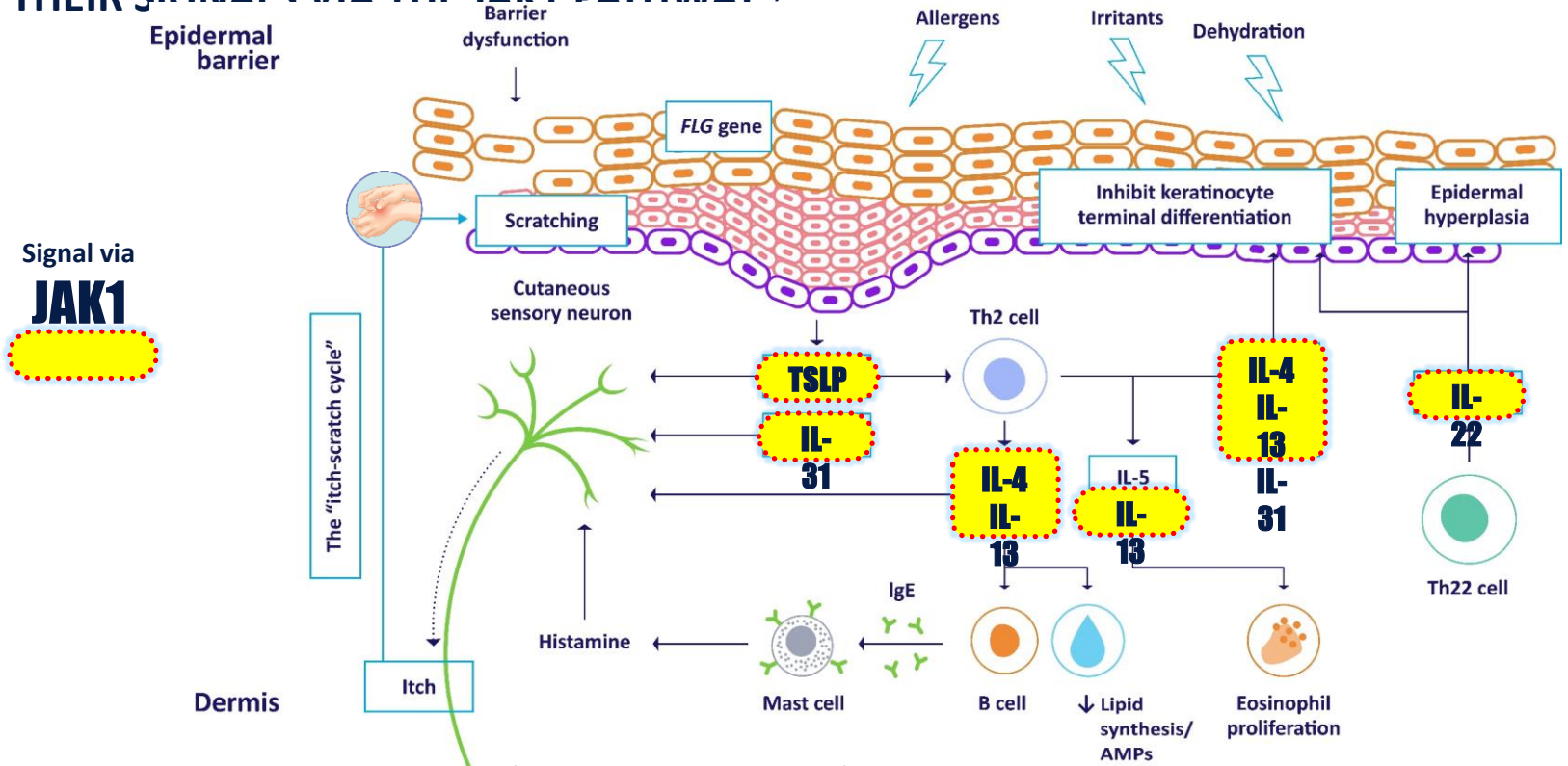
AD PATHOLOGY INVOLVES A DIVERSE NETWORK OF IMMUNE PATHWAYS[1,2]



AD, atopic dermatitis; FLG, filaggrin; IgE, immunoglobulin E; IL, interleukin; Th, T helper; TSLP, thymic stromal lymphopoietin

Figure adapted from Furue M, et al. Allergol Int 2017;66:398–403: 1. Furue M, et al. Allergol Int 2017;66:398–403; 2. Bao L, et al. JAK-STAT 2013;2:e24137 3. Dupixent prescription information TWPI-2020Dec May-2020, USPI

MANY OF THE PRO-INFLAMMATORY CYTOKINES THAT DRIVE AD PATHOLOGY TRANSDUCE THEIR SIGNALS VIA THE JAK1 PATHWAY[1,2]

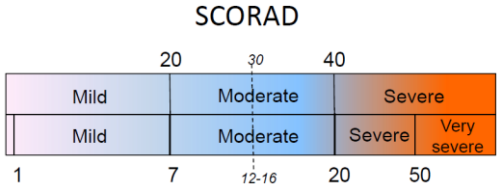


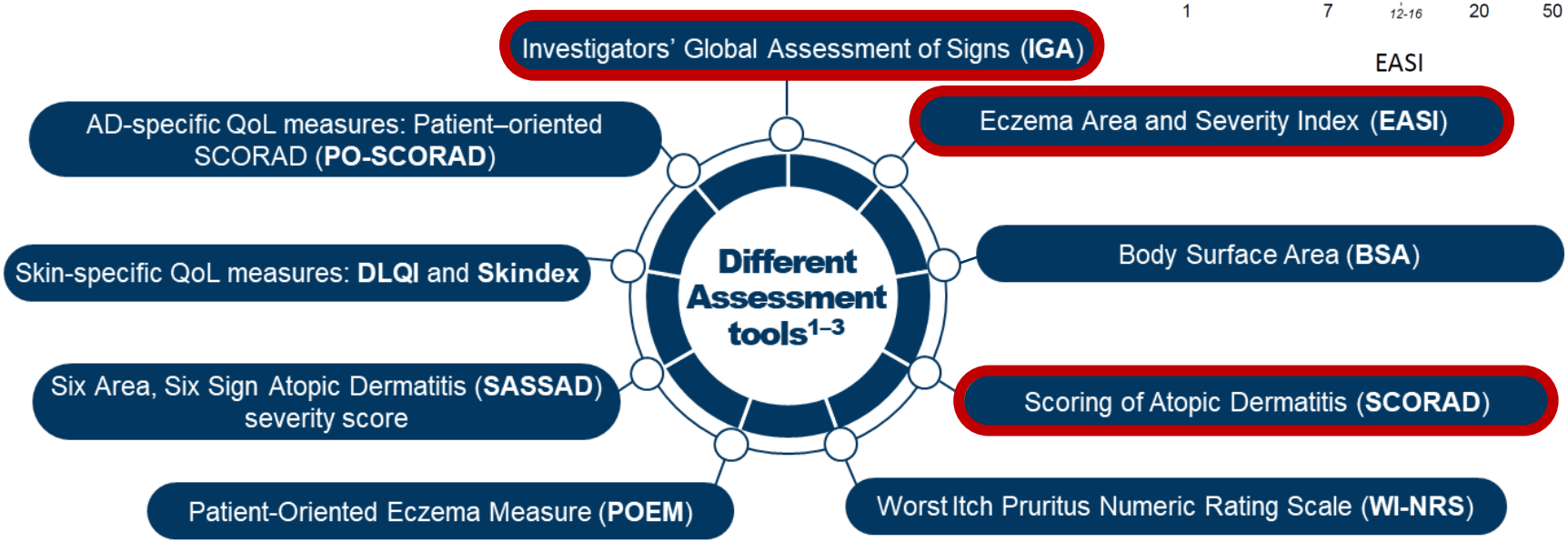
AD, atopic dermatitis; AMP, antimicrobial peptide; FLG, filaggrin; IgE, immunoglobulin E; IL, interleukin; Th, T helper cell; TSLP, thymic stromal lymphopoietin

Figure Adapted from Furue M, et al. Allergol Int 2017;66:398–403: 1. Furue M, et al. Allergol Int 2017;66:398–403; 2. Bao L. et al. JAK-STAT 2013:2:e24137

Scoring system for AD severity assessment

IGA, EASI and SCORAD are often used as outcome measures in clinical trials





AD, atopic dermatitis; DLQI, Dermatology life Quality Index; QoL, quality of life.

1. Rehal B, et al. *PLoS One.* 2011;6:e17520; 2. Gooderham MJ, et al. *J Cutan Med Surg*. 2018;22(1_suppl):10S-16S; 3. Naegeli AN, et al. *Int J Dermatol*. 2015 Jun;54(6):715-722

Systemic immunosuppressants

For patients with moderate to severe or refractory AD that substantially impacts their QoL and social activities

- Non-biologic systemic immunosuppressants include[1] :

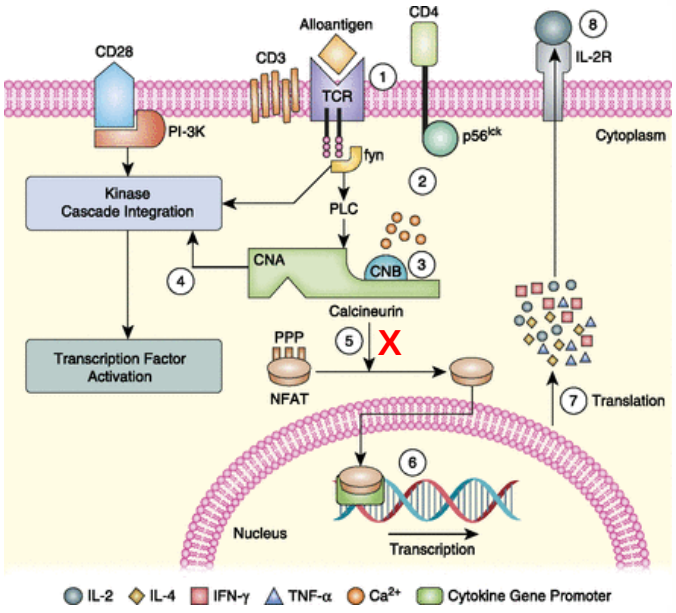
* Cyclosporine (Neoral®) is the only reimbursed non-biologic immunosuppressant with TFDA approved AD indication

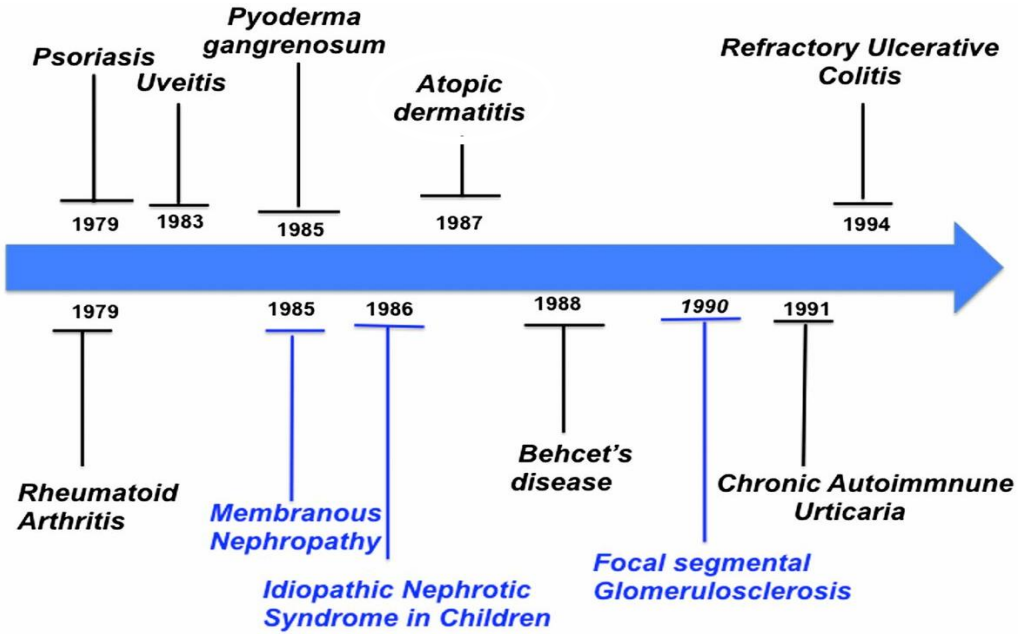
- Immunosuppressants are prescribed for moderate to severe AD in children and adults[2]
- Immunosuppressants help to stop the itch-scratch cycle of eczema; allow the skin to heal; and reduce the risk of skin infection[2]
- Current guidelines do not provide suggestions for the order of use of the different oral immunosuppressive drugs. Therefore, the prescribing mode will vary between countries and individual physicians, based on preferences, experiences, costs and the drug availability[3]

AD, atopic dermatitis

1. Chu CY et al. J Formos Med Assoc. 2021 Jan;120(1 Pt 2):429-442; 2. National eczema association. Accessed on November 22, 2019; 3. Garritsen FM, et al. J Eur Acad Dermatol Venereol. 2018 Aug;32(8):1336-1342;

Cyclosporine remain the standard of care in different autoimmune diseases over past 40 years

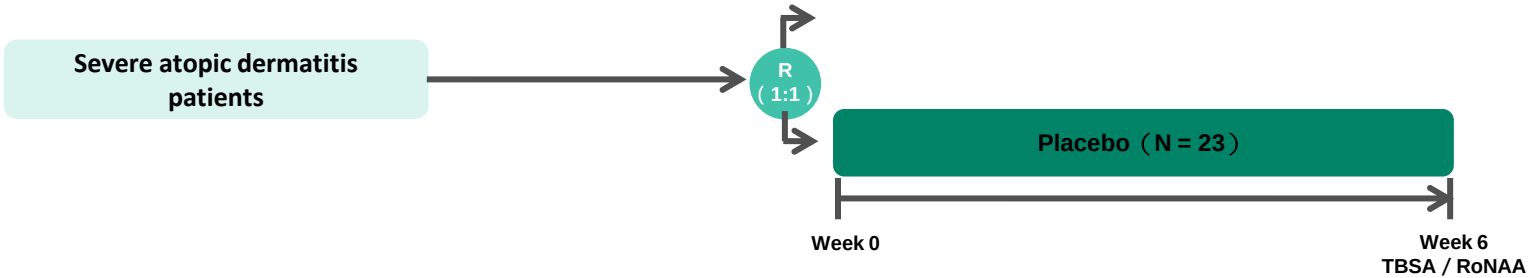


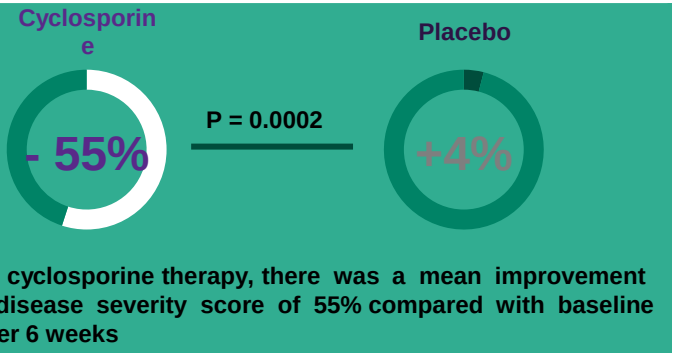


J Immunol. 2013 Dec 15;191(12):5785-91

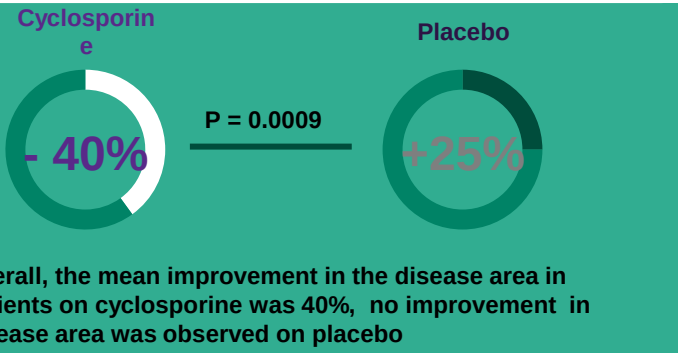
Cyclosporine is an effective treatment that can significantly improve the disease severity and the extent of the disease for atopic dermatitis in adults

A multicenter placebo-controlled study: cyclosporine in atopic dermatitis





◆ On cyclosporine therapy, there was a mean improvement in disease severity score of 55% compared with baseline after 6 weeks



◆ Overall, the mean improvement in the disease area in patients on cyclosporine was 40%, no improvement in disease area was observed on placebo

In all studies analyzed, cyclosporine consistently decreased the severity of atopic eczema and the efficacy is similar in adults and children

A systematic review and meta-analysis of controlled and uncontrolled trials

Articles evaluated for inclusion in the systematic review

27 articles identified and reviewed (Medline, Cochrane Library, hand search)

→ **11 articles excluded (did not meet eligibility criteria)**

16 full-text articles reviewed

→ **1 articles excluded (double publication on identical study)**

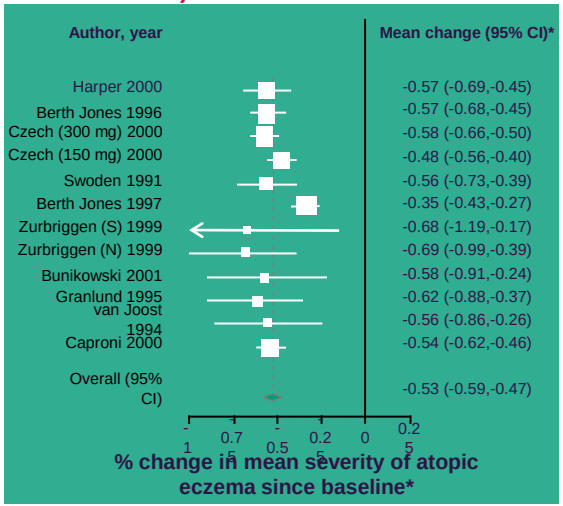
- 12 studies appeared homogeneous enough to be pooled
- Age range of participants: 1-80 years

- **Dose-related response with a pooled mean decrease in disease severity after 2 weeks of treatment**

low-dose cyclosporine (≤ 3 mg/kg)

high-dose cyclosporine (≥ 4 mg/kg)

- **Meta-analysis of mean relative change in severity of atopic eczema compared to baseline after 6-8 weeks of continuous treatment with cyclosporine**
  - **The mean benefit was 55% (95%-CI, 48-62%)**



* negative change in severity indicates clinical improvement

In all studies analyzed, children might have better tolerability of cyclosporine than adult

A systematic review and meta-analysis of controlled and uncontrolled trials (continued)

Articles evaluated for inclusion in the systematic review

27 articles identified and reviewed (Medline, Cochrane Library, hand search)

11 articles excluded (did not meet eligibility criteria)

16 full-text articles reviewed

1 articles excluded (double publication on identical study)

- As surrogate variables for drug safety, frequencies of typical adverse events of cyclosporine were abstracted from the 15 articles included

- **Adverse events and withdraws due to adverse events were observed more frequently in adults than in children and were also more likely in patients treated with higher dosages (n/percent per month of cyclosporine treatment)**

	Creatinine increases	Hypertension	Infection	Gastrointestinal symptom
Low-dose	2.0	0.6	1.8	4.6
High-dose	2.8	1.2	5.9	15.4
Children	2.5	0.0	3.9	17.5
Adult	3.2	1.6	9.1	18.1

	Paraesthesia	Headache	Withdraws due to adverse event
Low-dose	0.7	5.4	0.4
High-dose	9.6	7.0	1.5
Children	3.1	9.1	0.8
Adult	12.9	5.8	1.6

Efficacy and safety of long-term treatment with cyclosporin A for atopic dermatitis

2007 Retrospective study

Unmet needs

- **Cyclosporin A (CsA) is being increasingly used in the treatment of severe refractory atopic dermatitis**
- **Clinical efficacy and safety of short-term CsA treatment in atopic dermatitis patients has been proven**
- **However, data on long-term treatment are limited**

To investigate the efficacy and safety of long-term treatment (≥ 6 months) with CsA for atopic dermatitis

- **73** patients with severe atopic dermatitis
- Mean age of **33.8** years

- Refractory to conventional therapy that was treated with CsA

- Average treatment duration time: **1.3** years

CsA long-term treatment results

Serum creatinine levels increases > 30% (7/73)

Arterial hypertension appeared during treatment (11/73)

Relapse after discontinuation of treatment (40/73)

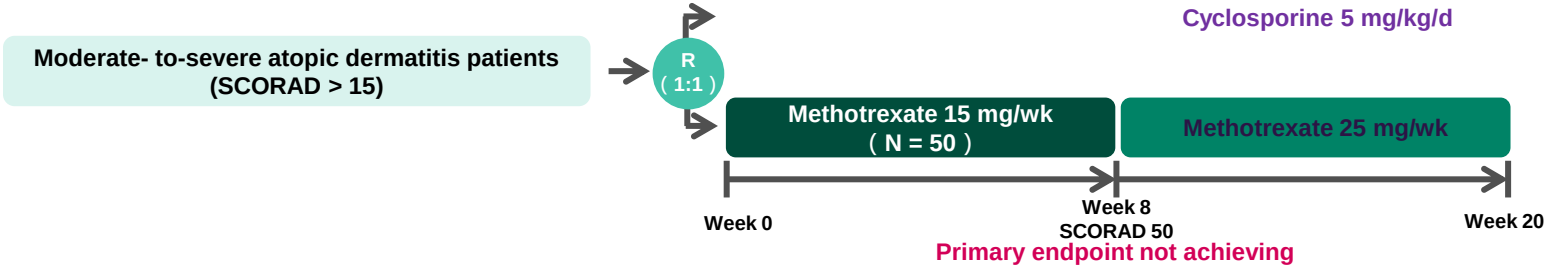
Experienced clinical remission for at least 3 months (33/73)

Experienced a rebound phenomenon (6/73)

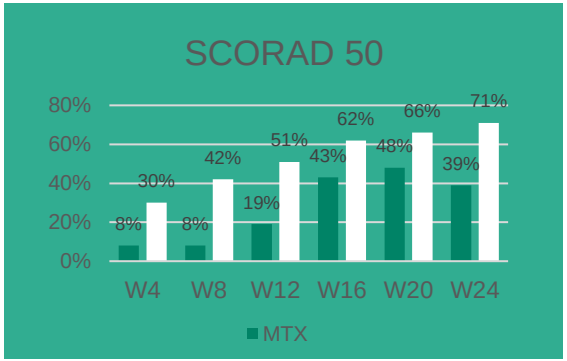
➢ No correlation between treatment duration and nephrotoxicity or hypertension was found

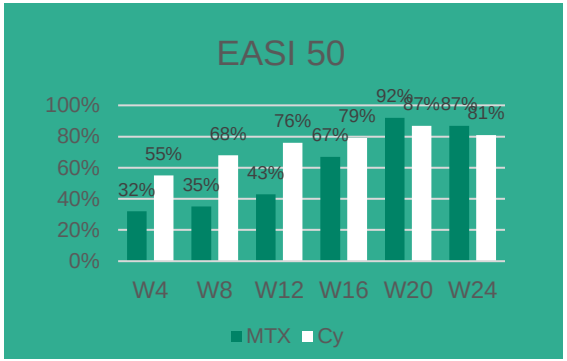
CsA has higher efficacy than MTX in adults with moderate-to-severe atopic dermatitis

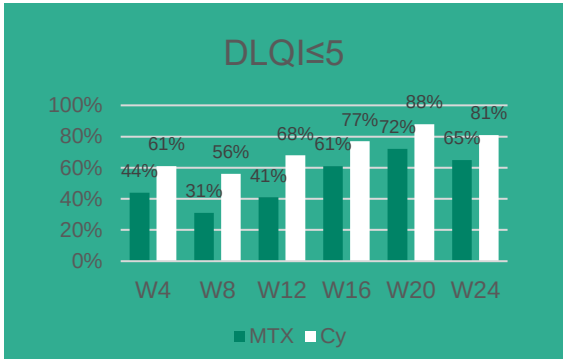
A phase III randomized trial



- The efficacy of cyclosporine was superior to methotrexate from week 4 to week 24







Administration Information of Neoral

For AD treatment the recommended dose range is 2.5 to 5 mg/kg/day given in 2 divided oral doses

- Oral 25 mg and 100 mg soft gelatin capsules:
  - A micro-emulsion form which reduces the variability of pharmacokinetic parameters and provides dose linearity of cyclosporin exposure
  - Less influenced by concomitant food intake
- Daily doses
  - 2 divided doses are recommended
  - Swallow whole
  - Should be left in the blister pack until required for use

Atopic dermatitis

Sandimmun Neoral treatment should be initiated by physicians with experience in the diagnosis and treatment of atopic dermatitis. Due to the variability of this condition, treatment must be individualised. The recommended dose range is **2.5 to 5 mg/kg/day** given in 2 divided oral doses. If a starting dose of 2.5 mg/kg/day does not achieve a satisfactory response within 2 weeks, the daily dose may be rapidly increased to a maximum of 5 mg/kg. In very severe cases, rapid and adequate control of the disease is more likely to occur with a starting dose of 5 mg/kg/day. Once satisfactory response is achieved, the dose should be reduced gradually and, if possible, Sandimmun Neoral should be discontinued. Subsequent relapse may be managed with a further course of Sandimmun Neoral.

AD, atopic dermatitis

Sandimmun Neoral Prescribing Information, TWI-310720

Summary of the safety profile

In the various indications the overall spectrum of side effects is essentially the same

- The principal adverse reactions observed in clinical trials and associated with the administration of cyclosporine include renal dysfunction, tremor, hirsutism, hypertension, diarrhea, anorexia, nausea and vomiting.

- Many side effects associated with ciclosporin therapy are dose-dependent and responsive to dose reduction.

Patients with renal or hepatic impairment
Reduce initial dose. Concentration monitoring is recommended.

Pediatric population
Clinical studies have included children from 1 year of age. In several studies, pediatric patients required and tolerated higher doses of cyclosporine per kg body weight than those used in adults.

Elderly population (age 65 years and above)
Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

Sandimmun Neoral Prescribing Information, TWI-310720

Immunosuppressives and biologics during pregnancy and lactation

Cyclosporine A may be a relatively safer choice for pregnancy and lactation

	Substance	Pre-conception	Pregnancy	Lactation	EL	RG
Immunosuppressives	Antimalarials				2	B
	Apremilast				5	D
	Azathioprine / 6-mercaptopurine				2	B
	Cyclophosphamide	3 months			2	C
	Cyclosporine A				2	B
	Leflunomide	24 months*			2	C
	Methotrexate	3 months			2	B
	Mycophenolate	1.5 months			2	B
	Sulfasalazine				2	B
	Tacrolimus				2	B
	Tofacitinib	1.5 months*			4	C

Biologics	Adalimumab				2	B
	Certolizumab				2	B
	Etanercept				2	B
	Golimumab				4	C
	Infliximab				2	B
	Abatacept				4	D
	Anakinra				4	D
	Belimumab				4	D
	Rituximab				4	D
	Secukinumab				5	D
	Tocilizumab				4	D
	Ustekinumab				4	D
	Vedolizumab				4	C

A consensus report issued by the Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation

green, substance may be applied; yellow, data is insufficient for substance recommendation; red, substance application is not recommended.

*Shown to be teratogenic in animal models, insufficient or unavailable data in humans

ıtion

Wien Klin Wochenschr. 2019; 131(1): 29–44.

表一　生物製劑與小分子標靶藥物的差別

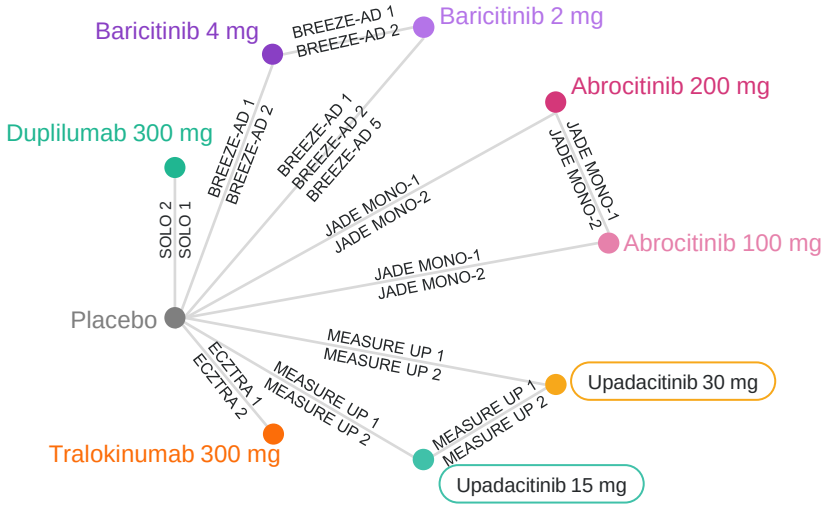
	生物製劑	小分子標靶藥物
藥品名稱	杜避炎	銳虎、喜續果、愛滅炎
服用方式	皮下注射	口服
作用方式	抑制體內特定發炎介白素 4 和 13	抑制體內多種發炎細胞激素
特性	熱不穩定需冷藏、人工合成單株抗體、有限度的毒性、無法穿透細胞	室溫保存、可藉由肝臟酵素代謝和腎臟排除、有潛在毒性
藥物半衰期	長（數天到數週）	短（6 到 12 小時）
常見副作用	注射部位反應、結膜炎、鼻咽炎	痤瘡、噁心、感染、頭痛等
肝腎功能	無影響	需依照肝腎功能調整劑量
藥物交互作用	無影響	有潛在藥物交互作用
定期抽血檢查	不需要	需要
安全性	有潛在過敏反應 immunogenicity	需定期監測血液數值，如全血球、肝腎功能、病毒性肝炎 (B 肝、C 肝)、肺結核，需要做風險管理

Dermatol Ther (Heidelb) (2022) 12:1181–1196
https://doi.org/10.1007/s13555-022-00721-1

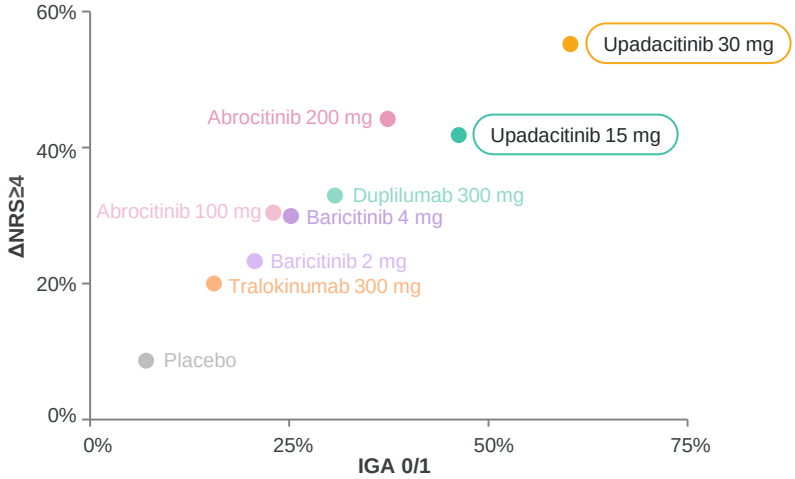
ORIGINAL RESEARCH

Comparative Efficacy of Targeted Systemic Therapies for Moderate to Severe Atopic Dermatitis without Topical Corticosteroids: Systematic Review and Network Meta-analysis

Network meta-analysis diagram



IGA 0/1 versus ΔNRS ≥ 4 absolute response rate estimates for moderate to severe atopic dermatitis

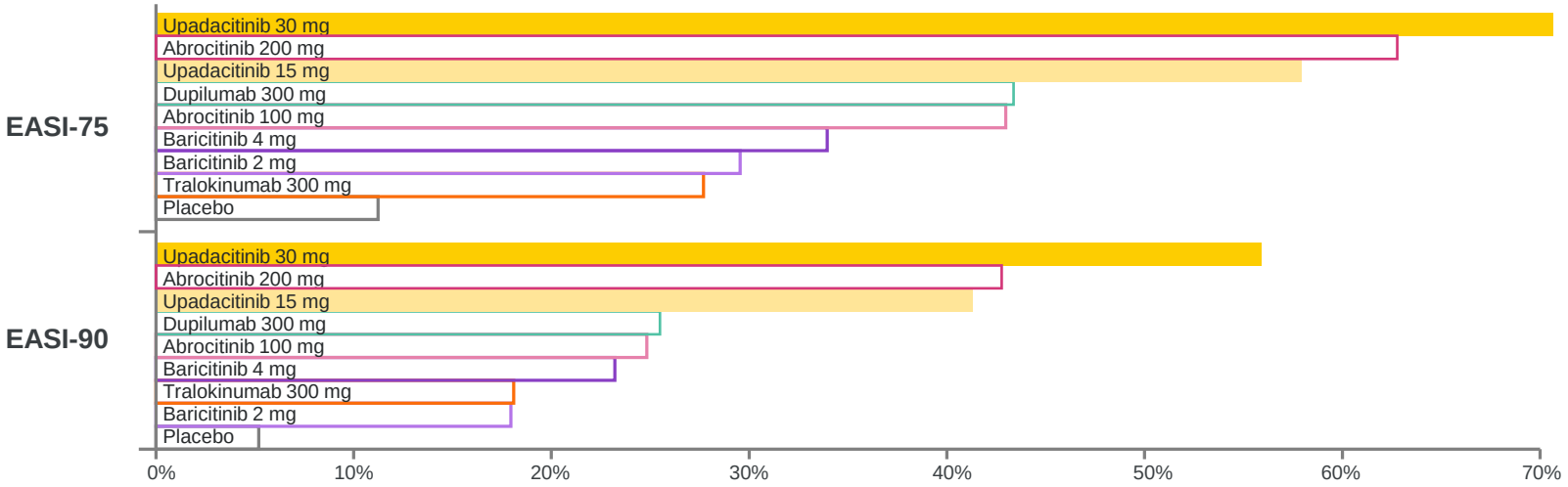


- Network meta-analysis (NMA) included 6 records representing 9 unique studies + 2 upadacitinib trials
- Primary endpoint (week 12 or 16)

6,254 patients

* Tralokinumab is not approved in Taiwan.

EASI-75 and EASI-90 absolute response rate estimates for moderate to severe atopic dermatitis

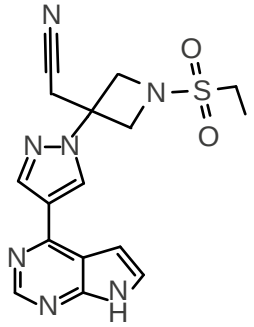


Upadacitinib 30 mg daily, **upadacitinib 15 mg daily**, and **abrocitinib 200 mg daily** may be the most efficacious targeted systemic therapies over 12-16 weeks of therapy in AD.

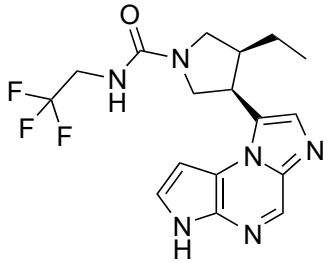
* Tralokinumab is not approved in Taiwan.

JAKis Offer an Alternative Mechanism of Action That May Address Unmet Needs in Patients

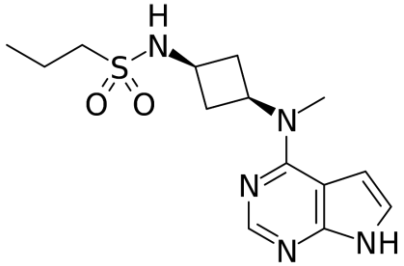
- **JAKis represent an emerging oral treatment option in AD with a different mechanism of action compared to current SOC therapies[1,2]**
- **Current approved JAKis[3-7]:**



Baricitinib



Upadacitinib



Abrocitinib

- bDMARD: biologic disease-modifying antirheumatic drug; JAKi: Janus kinase inhibitor; RA: rheumatoid arthritis; SOC: standard of care; tsDMARD: targeted synthetic disease-modifying antirheumatic drug.

1. Aletaha D, Smolen JS. *JAMA*. 2018;320:1360-1372. 2. Taylor PC, et al. *Rheumatol (Oxford)*. 2019;58(Suppl 1):i17-i26. 3. Serhal L, Edwards CJ. *Expert Rev Immunol*. 2019;15:13-25. 4. Markham A, Keam SJ. *Drugs*. 2019;79:887-891. 5. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/211675Orig1s000ltr.pdf

SIMPLE

JAKi		Baricitinib[1]	Abrocitinib [2]	Upadacitinib[3]
Recommended dose		**4 mg QD**	200 mg QD	30 mg QD (XR)
Formulation		**Immediate-Release**	Not mentioned in label	Extended-Release
Half life	T_{max}	1h (0.5-3.0)	2h	2-4h
	Elim. $T_{1/2}$	12.9h	5h	8-14h
Method of administration		With or without food If unable to swallow whole table, alternate administration may be considered through oral dispersion, gastrostomy tube or nasogastric tube**	With or without food Should not be split, crushed, or chewed	With or without food Should not be split, crushed, or chewed

This table show the summary from TFDA label and is not meant for products direct comparison.

**Pharmacokinetics: The pharmacokinetics in patients with COVID-19 who are intubated and have baricitinib administered via NG tube is similar to that in healthy subjects. The half-life of baricitinib in healthy subjects is approximately 10 hours.[5]

1. Baricitinib TFDA label 2. Abrocitinib TFDA label 3. Upadactinib TFDA label 4. Baricitinib FDA EUA factsheet

仿單

JAKi		Baricitinib[1] (Olumiant®)	Upadacitinib[2] (Rinvoq® ER)	Abrocitinib[3] (Cibinqo®)
Indication		RA, AD, COVID19	RA, AD, PsA, AS	AD
Age		≥ 18 years	≥ 12 years	≥ 18 years
Recommended dose in AD		4 mg QD	15 mg or 30 mg QD	200 mg or 100 mg QD 對大多數病人建議起始劑量200 mg QD
Half life	T_{max}	1 h	2-4 h	1 h
	Elim. $T_{1/2}$	12.9 h	8-14 h	5 h
Administration		口服溶散、NG tube	整粒吞服，不應剝半、攪碎或咀嚼	整粒吞服，不得切割、壓碎或嚼碎
Renal impairment	Mild	No dose adjustment	No dose adjustment	eGFR 60-<90 ml/min: No dose adjustment
	Moderate (Ccr or eGFR 30-60 ml/min)	2 mg	No dose adjustment	half dose
	Severe (Ccr or eGFR <30 ml/min)	Not recommended	15 mg	starting: 50 mg，max: 100 mg
Hepatic impairment	Mild (Child Pugh A)	No dose adjustment	No dose adjustment	No dose adjustment
	Moderate (Child Pugh B)			
	Severe (Child Pugh C)	Not recommended	Not recommended	Not recommended
Elderly		≥75 years: 2 mg	≥65 years: 15 mg	≥65 years: 100 mg
Note		治療8周後仍無治療益處證據的病人應考慮中止治療	NA	對於經過24周治療沒有顯示治療效益證據的病人，應考慮停止治療

SIMPLE

JAKi	Baricitinib[1] (Olumiant®)	Upadacitinib[2]	Abrocitinib[3]
Metabolism	**Kidney** **Substrate of OAT3**	**Liver** Substrate of **CYP3A4** Substrate for P-gp	**Liver** **CYP2C19** (~53%), **CYP2C9** (~30%) **CYP3A4** (~11%) , CYP2B6 (~6%), OAT3
DDI	• **Coadministration with OAT3 inhibitors: 2mg**	• Use with strong CYP3A4 inhibitor: **Use with caution** • Use with strong CYP3A4 inducers: **not recommended**	• Use with CYP2C19 inhibitor: **half dose** • Use with strong CYP inducers: **not recommended**
Cyclosporine (CYP3A4-, Pgp-)	No adjustment	**Coadministration not recommended**	No data
Ketoconazole (CYP3A4-)	No adjustment	**Dose adjustment**	No data
Fluconazole (CYP2C19-, CYP2C9-, CYP3A-)	No adjustment	No data	**Abro 增加 155%**
Fluvoxamine 抗憂鬱 (CYP2C19-, CYP3A-)	No data	No data	**Abro 增加 91%**
Rifampin (CYP3A4+, CYP2C) not available in Taiwan	No adjustment	**Coadministration not recommended**	**Abro 減少 56%**
Probenecid (OAT3-)	~~Dose adjustment~~	~~No data~~	~~**Abro 增加 66%**~~

09Nov2017_20Sep2018_21Jul2020_21Jan2021-5Feb2021 v3

2. Upadacitinib PRESCRIBING INFORMATION. Reference ID: 4478363
3. Abrocitinib TFDA label

Cytochrome P450 enzymes metabolize 90% of drugs[2]

CYP3A inducers

↑ metabolism of substrates

↓ plasma concentration

Potentially decrease effect of substrates

CYP3A4/2D6/2C9/2C19 inhibitors

↓ metabolism of substrates

↑ plasma concentration

Potentially increase AE of substrates

健保審字第1120670519號 (自112年4月1日生效)

健保規範

處方科別

12 歲以上至未滿 18 歲患者：限皮膚科專科醫師，或具兒童過敏免疫風濕專長之兒科專科醫師處方。

18 歲以上患者：限皮膚科及風濕免疫科專科醫師處方。

經照光治療及其他系統性(全身性)治療無效

足量PUVA、nb-UVB治療達12週，每週至少2次。

至少使用兩種其他系統性(全身性)治療，分別達12週

	12-17 歲	18 歲以上
Methotrexate	每週 10 mg	每週 15 mg
Cyclosporin	2.5 mg/kg/d	5 mg/kg/d
Azathioprine	1 mg/kg/d	2 mg/kg/d

慢性中重度之異位性皮膚炎患者

1. 病灶持續至少 6 個月
2. Eczema area severity index (EASI) ≧16
3. 異位性皮膚炎皮膚紅腫體表面積 (BSA)需≧30%
4. Investigator's Global Assessment (IGA):3~4。

Rinvoq給付劑量

EASI 16-20: 限用15mg
EASI 20以上，且18歲以上: 每日得使用30mg

續用條件

治療6個月後達EASI 50 可續用

重新申請條件

疾病再復發達50%，或EASI ≧16

abbvie