

Organization of Care in AD 2021 meeting

Management of Atopic Dermatitis in Adults in Japan

Osaka Habikino Medical Center
Department of Dermatology and Allergology
YOKO KATAOKA, MD

Online ISAD Symposium Nov 26, 2021



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ORGANIZATION OF CARE
IN ATOPIC DERMATITIS
2021 MEETING

ONLINE SYMPOSIUM,
NOVEMBER 26, 2021

ISAD
INTERNATIONAL SYMPOSIUM ON ATOPIC DERMATITIS

COI Disclosure

Presenter: Yoko Kataoka

Companies with which the first author and co-presenters have a COI relationship that should be disclosed in relation to the content of the presentation

In the past three years,
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Sanofi K.K.
Sysmex Corporation

Funded research/Joint research:

Sanofi K.K.
Leo Pharma Corporation
Pfizer Japan Inc.
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Background in Japan

Health insurance system

- Universal health insurance coverage system
- Individual payment: mostly 30%

Atopic dermatitis is treated by

- Dermatologist, pediatrician, general physician
- Laboratory examination easily available :IgE, TARC etc.
- Atopic dermatitis is grasped as one of allergic diseases
- TCS, TCI, CyA(2008), Dupilumab(2018), Baricitinib(2020), Upadacitinib, Abrocitinib(2021)



Treatment goal

in Japanese guideline for atopic dermatitis 2018

“The goal of treatment is to reach **and maintain** a state in which symptoms are **absent or mild without being disturbed in daily activities by the disease** and drug therapy is scarcely required. Even when this level is not reached, the objective is to maintain a state in which symptoms are mild without rapid exacerbations that affect daily activities.”



Management of Atopic Dermatitis in Adults in Japan

1. Japanese disastrous history

2. Current status: Patients' perspective

Current status of atopic dermatitis in Japan (ADDRESS-J) 2017-2019
On-line survey in 2021

3. Ultimate proactive treatment “Tight control, T2T”

4. Dupilumab and New agent

5. Current status: Physicians' perspective

On-line survey for dermatologist in 2019-2020
On-line survey for patient-physician gap in 2017

6. What should we do next?



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Tragedy of steroid-phobia in 1990's



Absenteeism




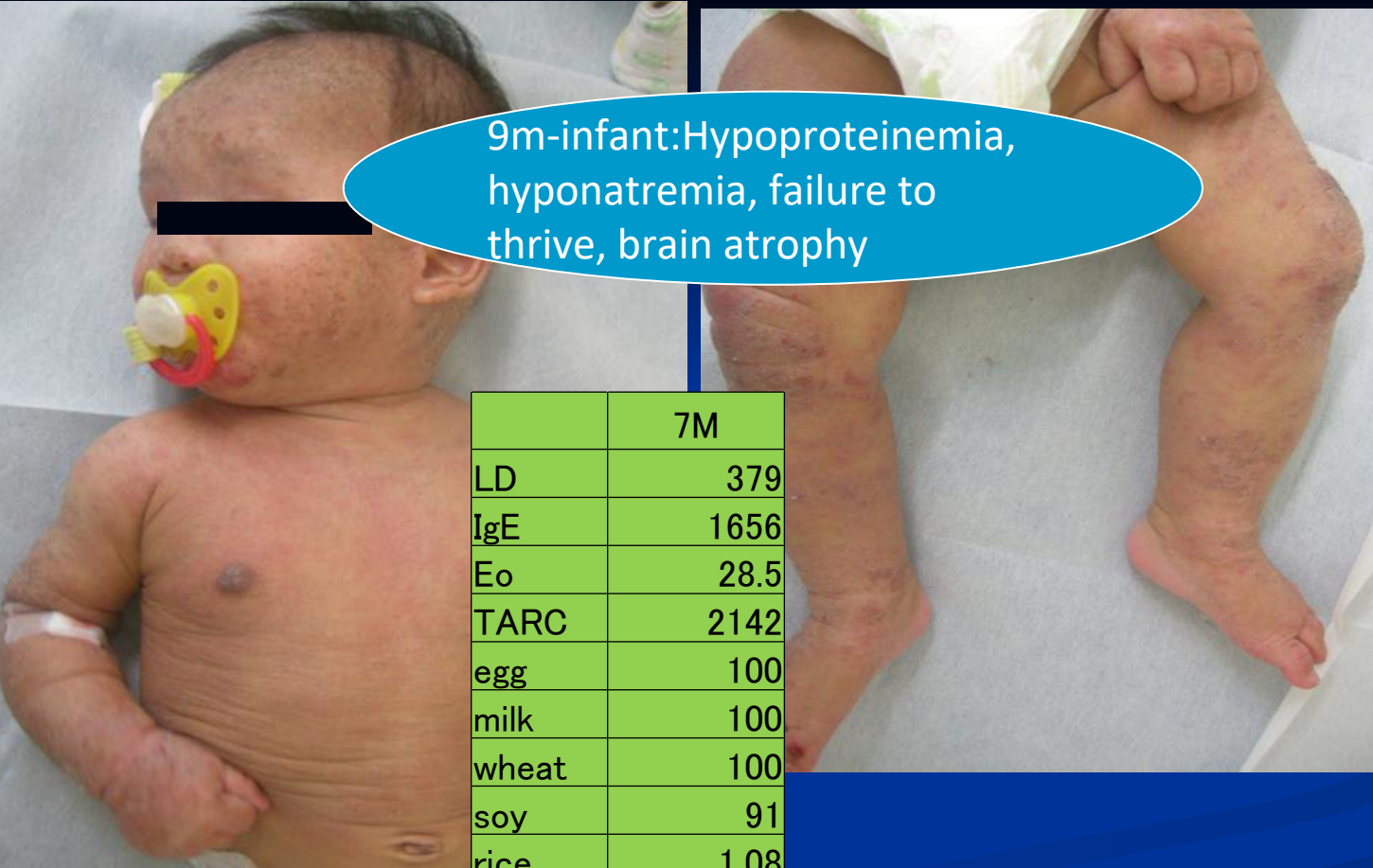
Depression



Disturbed quality of life

Eo	14.3
TARC	130679
LD	461
IgE	12355





9m-infant:Hypoproteinemia,
hyponatremia, failure to
thrive, brain atrophy

	7M
LD	379
IgE	1656
Eo	28.5
TARC	2142
egg	100
milk	100
wheat	100
soy	91
rice	1.08

Food allergy: anaphylaxis to milk, wheat

History of Atopic Dermatitis Treatment in Japan

		Allergen elimination	Inflammation control
1952	Topical hydrocortisone marketed		
1970	Period of abuse of topical steroids		
Early 1980s	First lawsuit case for steroid		
Late 1980s	The era of dietary restrictions		
1989	The beginning of steroid bashing media coverage		
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1990s	The era of glorifying de-steroids		
Late 1990s	The rise of the “atopy business”		
2000	The 1 st JDA guideline for management of atopic dermatitis		
2008	Proposal of the dual-allergen exposure hypothesis		
2008	The Emergence of Proactive Therapy		
2018	Dupilumab insurance coverage		
2020~	Baricitinib, Upadacitinib, Abrocitinib insurance coverage		



Treatment goal

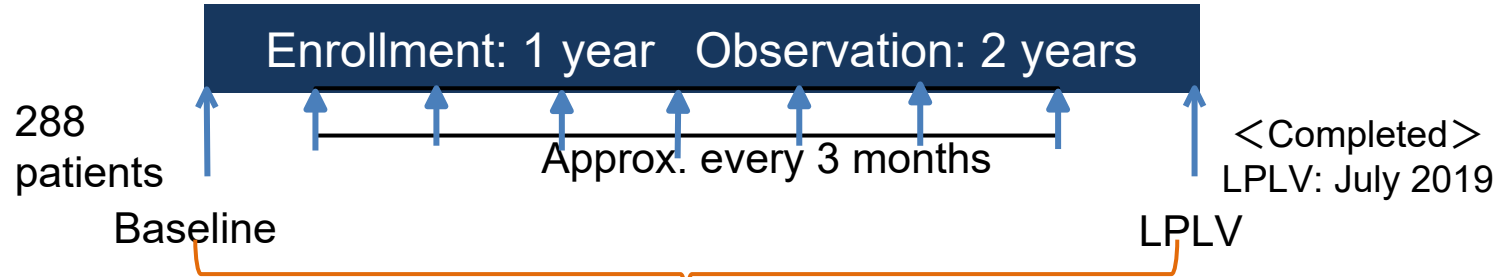
in Japanese guideline for atopic dermatitis 2018

“The goal of treatment is to reach **and maintain** a state in which symptoms are **absent or mild without being disturbed in daily activities by the disease** and drug therapy is scarcely required. Even when this level is not reached, the objective is to maintain a state in which symptoms are mild without rapid exacerbations that affect daily activities.”



Current status of atopic dermatitis in Japan (ADDRESS-J)

ADDRESS-J*, a 2-year observational study to evaluate the characteristics and current treatment of Japanese adult[#] with moderate-to-severe atopic dermatitis (AD) was performed.(2017~2019)



Physicians

- EASI, IGA, BSA, prurigo status
- AD treatment
- **Flare**
- Treatment-related AEs
- Lab test (if any; include. TARC, blood eosinophil no. IgE, & LDH)

Patients (at visits)

- DLQI, EQ-5D
- AD-related hospital visit/admission, and work impairment

Patient (every week)

- Questionnaires: POEM, pruritus NRS, drug adherence



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AD treatment at baseline and by the indicated times

	N (%)	Baseline N (%)	– Month 12 N (%)	– Month 24 N (%)
Topical	Any TCS/TCI	287 (99.7)	288 (100.0)	288 (100.0)
	TCS: Strongest	120 (41.7)	167 (58.0)	177 (61.5)
	TCS: Very strong	249 (86.5)	270 (93.8)	277 (96.2)
	TCS: Strong	68 (23.6)	123 (42.7)	144 (50.0)
	TCS: Medium	145 (50.3)	186 (64.6)	194 (67.4)
	TCS: Weak	8 (2.8)	20 (6.9)	25 (8.7)
	TCI	108 (37.5)	186 (64.6)	197 (68.4)
	Topical only	231 (80.2)	182 (63.2)	172 (59.7)
Systemic anti-inflammatory	Any oral	42 (14.6)	78 (27.1)	86 (29.9)
	Oral corticosteroids	12 (4.2)	33 (11.5)	39 (13.5)
	Oral immunosuppressants	31 (10.8)	51 (17.7)	54 (18.8)
	Biologics	0	0	6 (2.1)
UV phototherapy		16 (5.6)	33 (11.5)	35 (12.2)
Adjunctive	Antihistamines/anti-allergy	236 (81.9)	264 (91.7)	267 (92.7)
	Chinese herbal medicine	6 (2.1)	16 (5.6)	21 (7.3)
	Psychotherapy	0	4 (1.4)	4 (1.4)

systemic anti-inflammatory therapies or UV phototherapies over the 2-year observational period TCS, Topical corticosteroids; TCI, Topical calcineurin inhibitors.

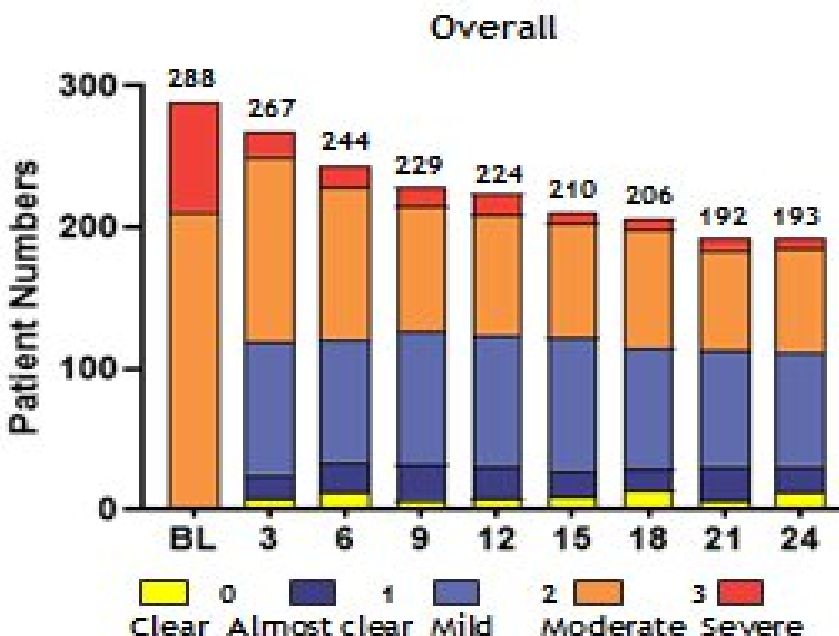


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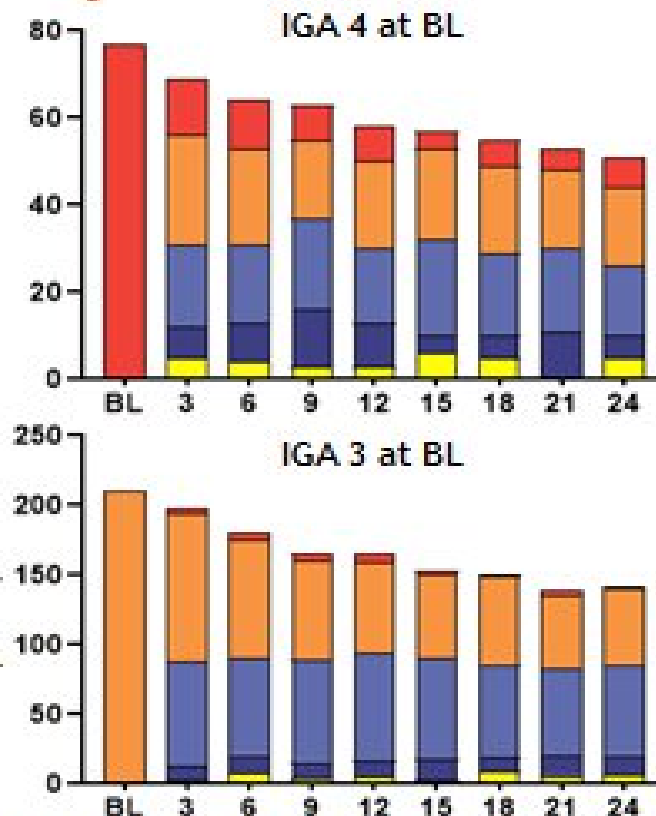
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AD severity over 2 years: IGA



IGA: Investigator's Global Assessment



- Starting from moderate or severe at BL, approximately half of the patients fell into mild or less severity at Month 3 that was maintained up to 2 years
- The proportion of patients achieved mild or less at Month 24 were 58% (51% for severe at BL and 60% for moderate at BL)



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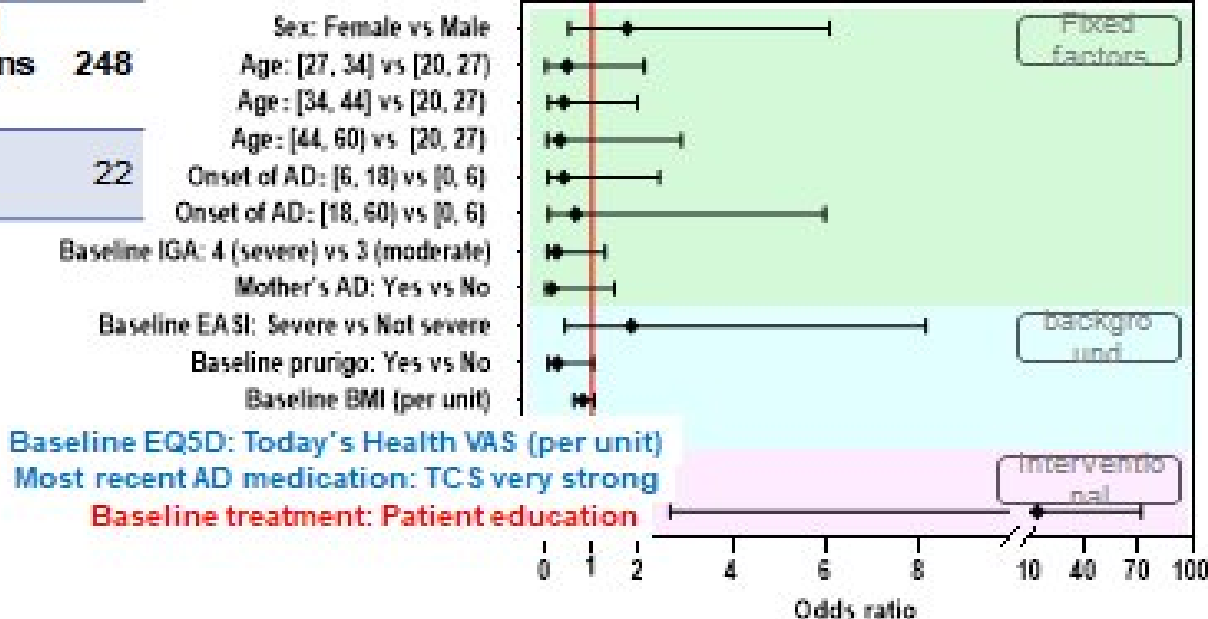
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Identified associating factors with Achievement of IGA ≤ 1 at month 3

Number of observations used 248

Outcome achieved 22



Positively related factors, Odds ratio [95% C.I.]

Baseline treatment of Patient education, 13.8 [2.67, 71.7] vs No

Negatively related factors, Odds ratio [95% C.I.]

Most recent treatment of TC S very strong, 0.27 [0.08, 0.92] vs No

Baseline EQ5D Today's Health VAS, 0.95 [0.92, 0.98] per unit

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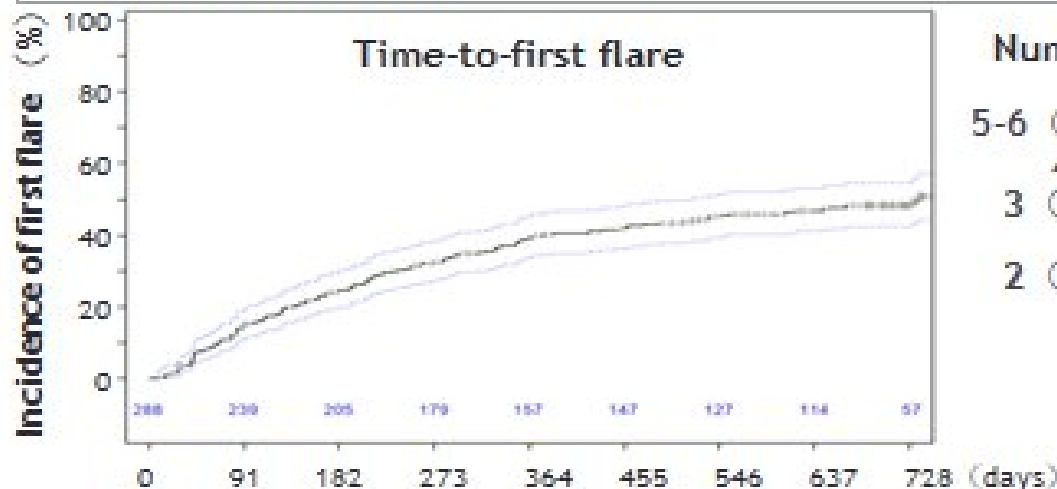


Occurrence of pre-specified AD flare

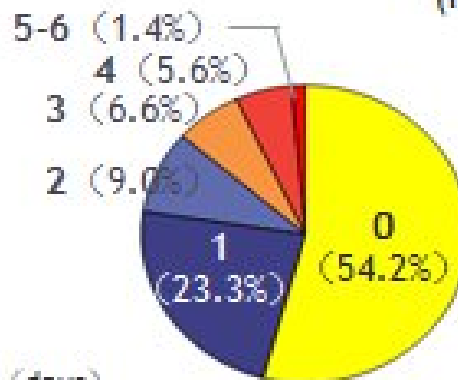
Definition of a flare:

worsening of AD symptoms with IGA score ≥ 3 requiring intensification of AD treatment per the Investigator's judgment*

*optimization of the standard care for AD, addition/dose increase of AD medication, or change to a higher potency class of TCS



Number of flares in 2 years (N=288)



- At least 1 flare occurred in 132/288 patients (45.8%) in this 2-year observation
- Incidence of flares was 0.53 (95%CI 0.47-0.60) /person-year (PY) based on entire observation period (2 years)
- Incidence of flares was 0.97 (95%CI 0.75-1.22) /PY based on the initial 3 months



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Attitude Survey on the Impact of Atopic Dermatitis on Patients' Lives

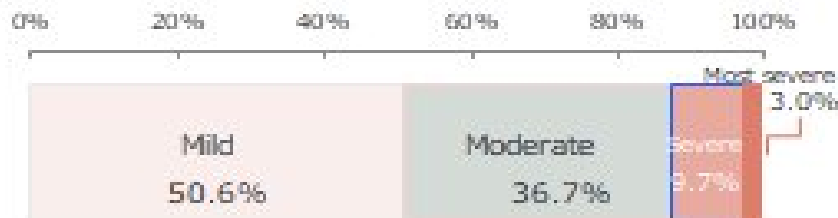
Courtesy of AbbVie GK

Survey period	Thursday, February 18, 2021 to Wednesday, February 24, 2021
Survey method	Internet survey
Target	<p>[Patients with atopic dermatitis] Persons who fall under all of the following categories.</p> <ul style="list-style-type: none">- Men and women aged 20 years old or older- Currently employed (persons who gave their occupation as a company employee, public officer/public organization staff member, specialist, self-employed, freelance professional, or part-time worker)- Currently affected by atopic dermatitis (Diagnosed with atopic dermatitis by a doctor.)- Having worked when suffering in atopic dermatitis.
Number of valid responses	1,000 persons (Men: 50%, Women: 50%) *Without equal assignment by age.
Supervisor of the survey	Yoko Kataoka, Deputy Director and Principal General Manager and Director of Atopic Dermatitis Center, Osaka Habikino Medical Center



Survey respondents: Details: Severity and disease record of atopic dermatitis

Severity (N= 1,000)	
Color Category	%
Mild	50.6
Moderate	36.7
Severe	9.7
Most severe	3.0



All patients (N= 1,000)

Disease record (N= 1,000)	
Category	%
Less than 1 month	1.9
1 month to less than 2 months	1.6
2 months to less than 6 months	2.6
6 months to less than 1 year	2.9
1 year or longer	91.0

Q. In which category was your diagnosis by your doctor for your symptoms when you were diagnosed with atopic dermatitis?

Mild: Guide (the same applied below): Only a mild skin rash seen regardless of the area.

Moderate: Skin rash with strong inflammation seen over less than 10% of body surface.

Severe: Skin rash with strong inflammation seen over 10% to less than 30% of body surface.

Most severe: Skin rash with strong inflammation seen over 30% or more of body surface.

Distribution by severity: Mild: 54%, Moderate: 32%, Severe to Most severe: 14%
90% of respondents have a record of atopic dermatitis of 1 year or more.

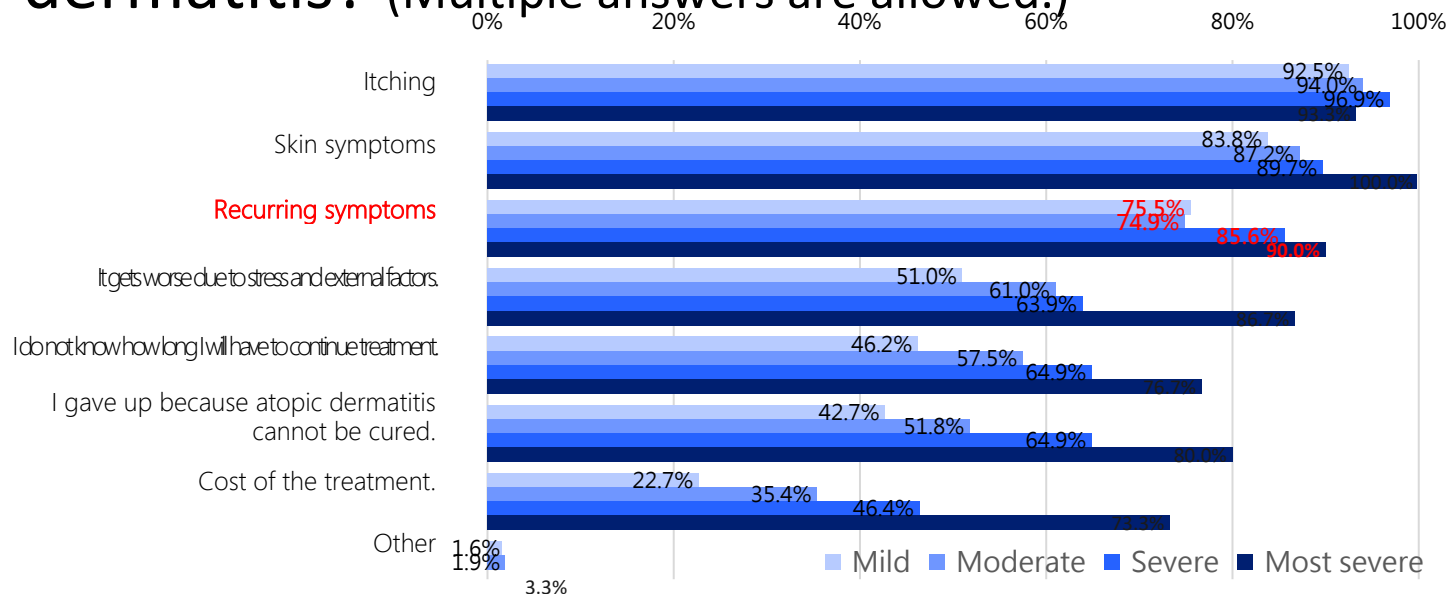


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Q. What anxiety and suffering do you have related to the symptoms of atopic dermatitis? (Multiple answers are allowed.)



All patients (N=1,000)
By severity: Mild: N=506, moderate: N=367, severe: N=97, Most severe: N=30.

Regardless of severity, a common suffering is that the "symptoms" of atopic dermatitis "are recurring."

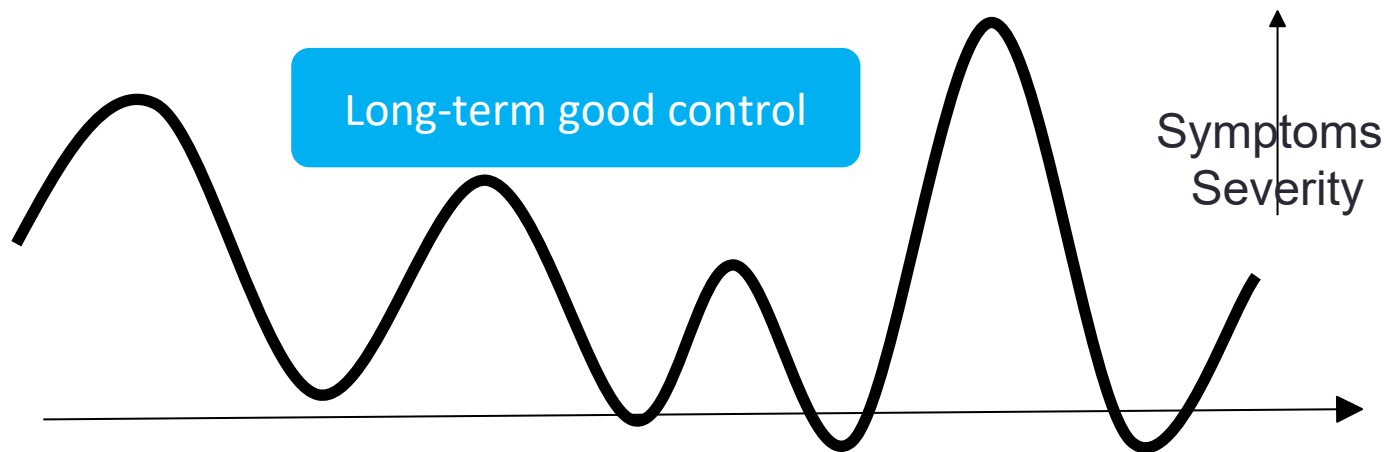


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The definition of AD is chronic eczema with frequent remissions and flares, But what is the goal of treatment?



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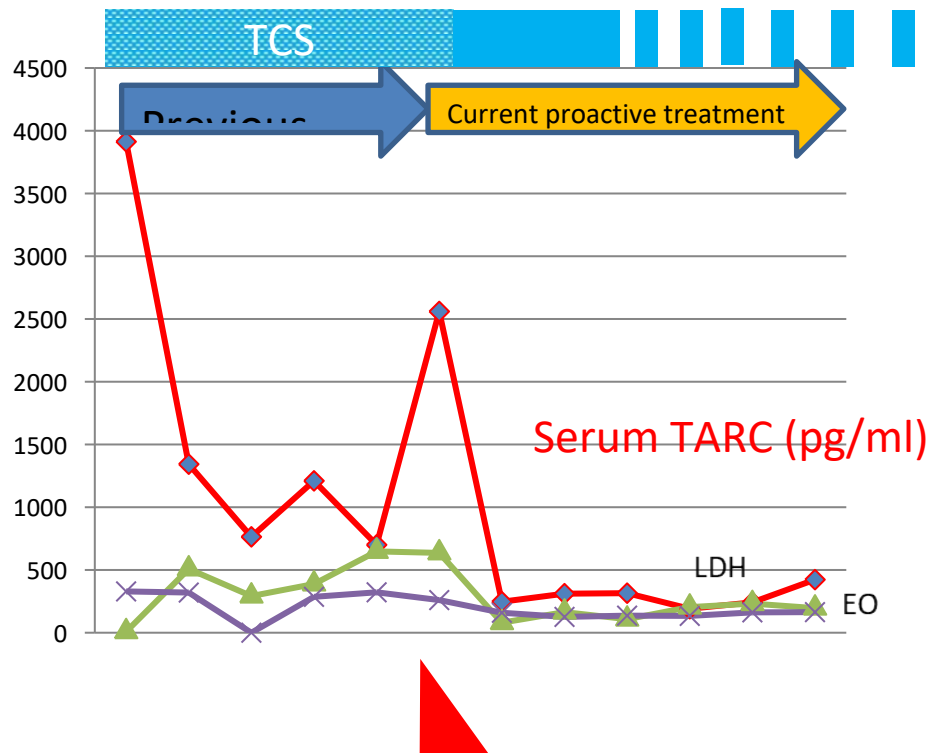
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The truth of waning and waxing



education

Remission

Induction

1

Maintain
everyday
2

Procedure of T2T
(accurate proactive therapy)

Gradually weaning

3

TCS / TCI

Systemic Medication

Eczema
Skin
inflam

Remission
induction

Neither visible nor palpable &
Serum TARC less than 600pg/ml

Maintaining disease-free with
medicine

Disease-free
with minimum
medicine



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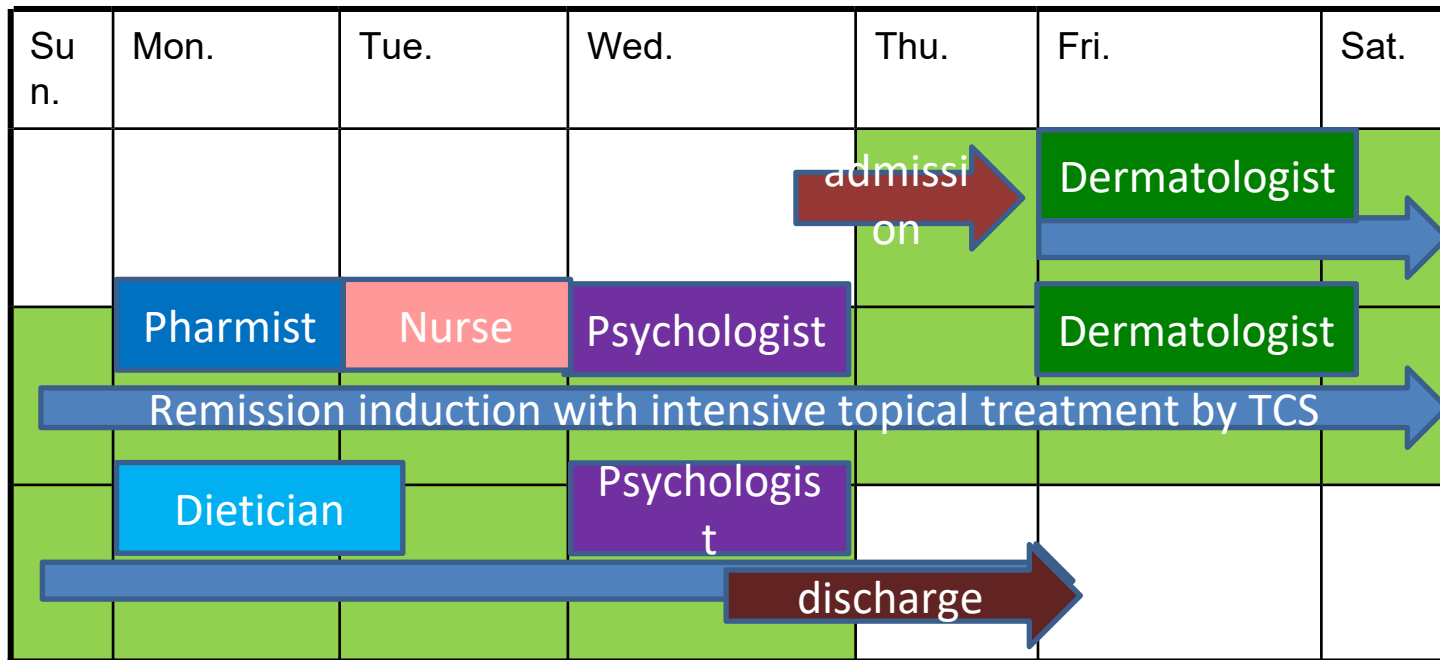
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“Atopic dermatitis college”

Remission induction combined with
multidisciplinary education



Data-driven educational program during two-weeks hospitalization



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ISAD 2008 Kyoto

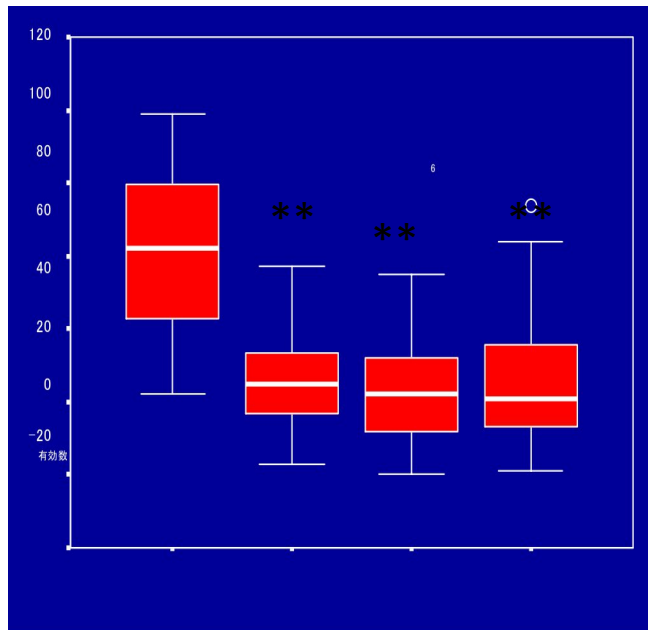


Too many atopic dermatitis
patients are
insufficiently treated!!

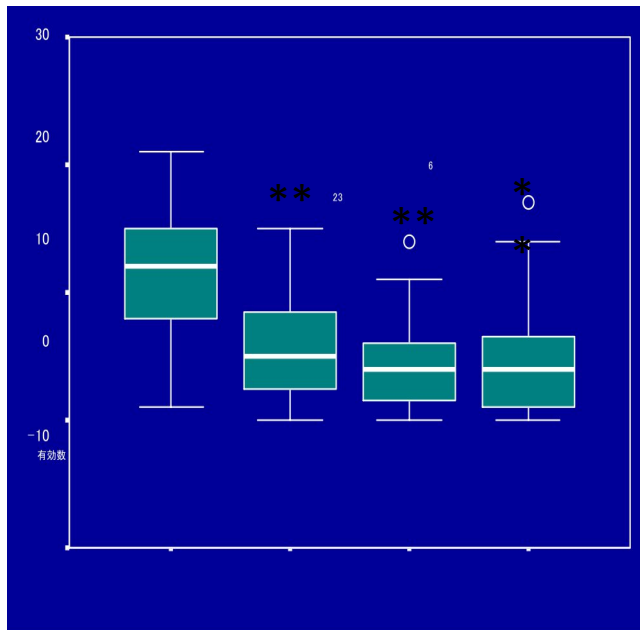


Quality of Life (ADQOL-J)

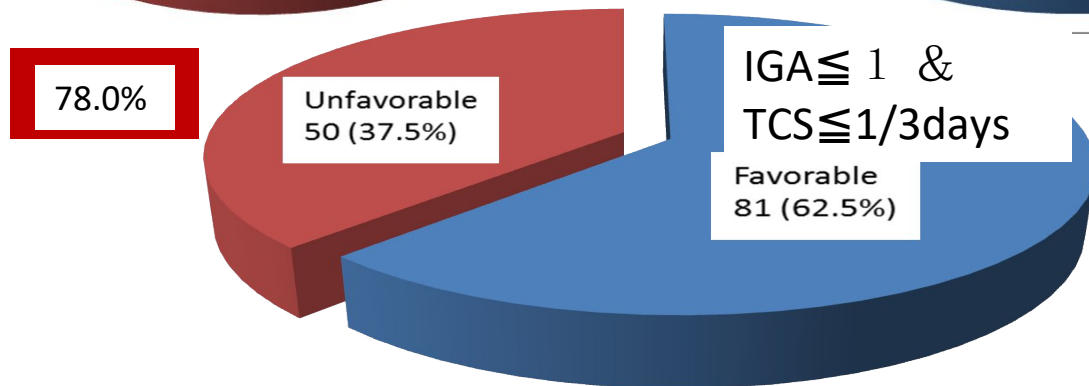
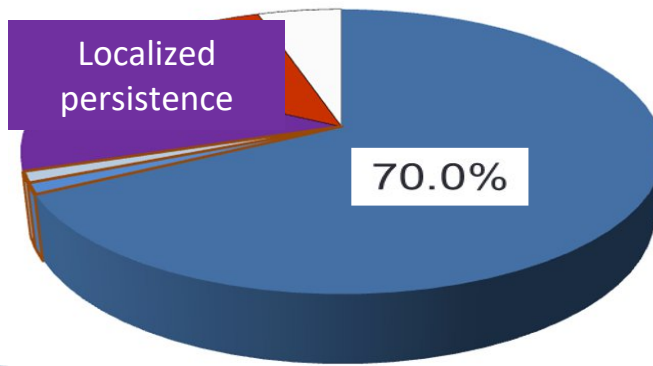
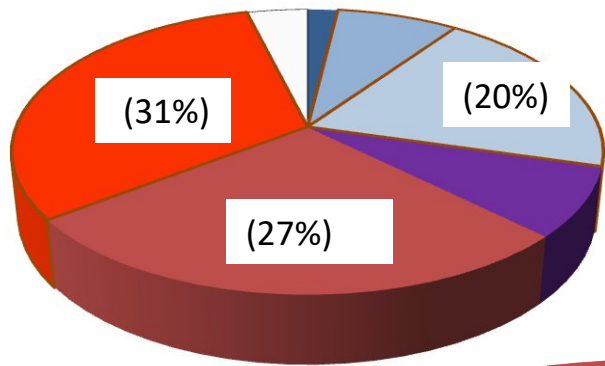
Total score



Anxiety score



Outcome of tight control with conventional therapy After 6 months→After 2 years



Follow up data from 113 educated inpatients in 2015 in Osaka Habikino Medical center

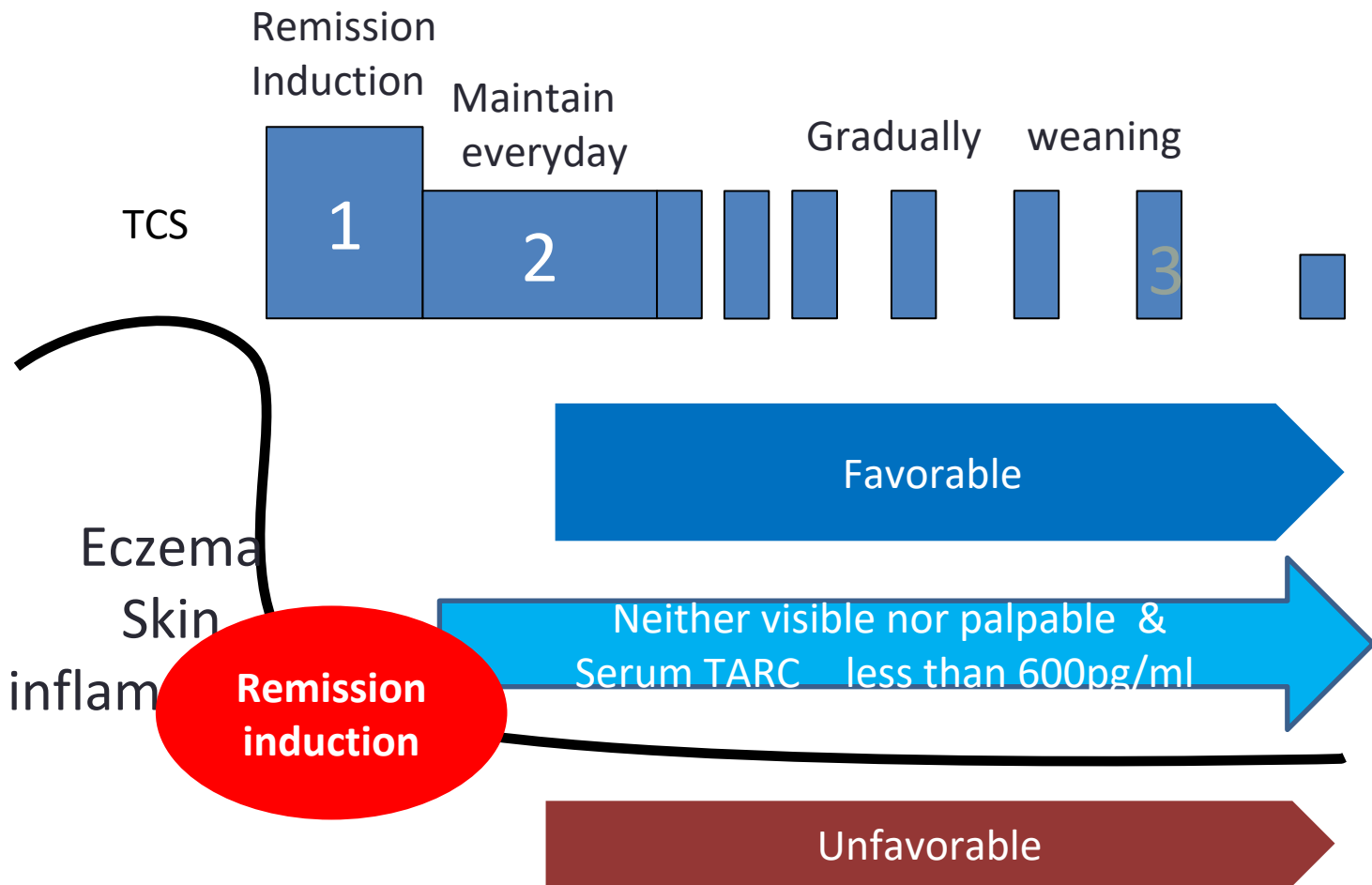


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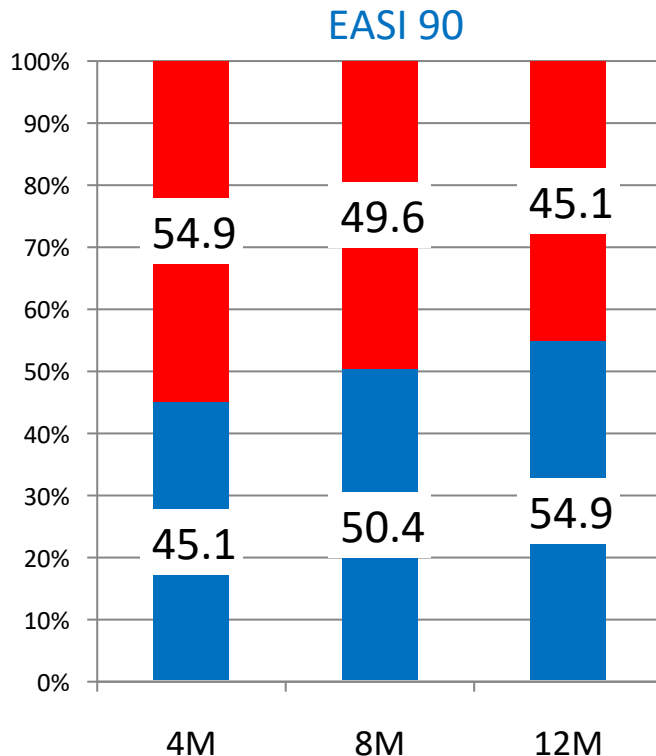
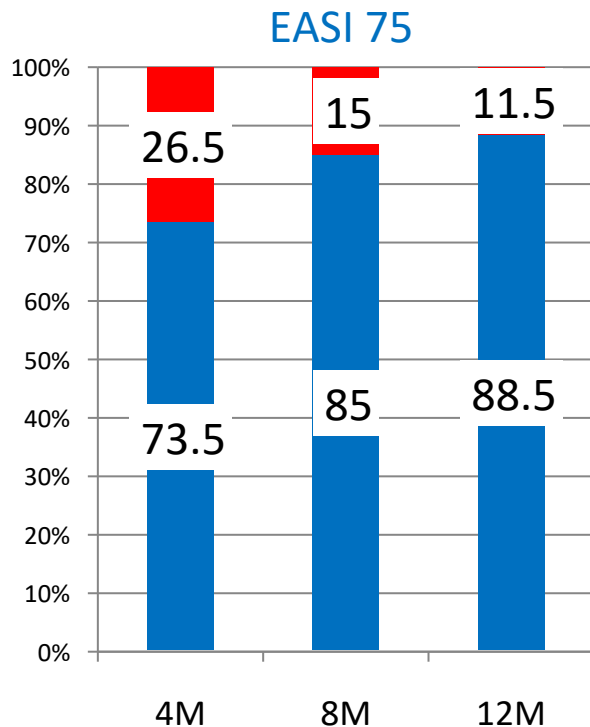




Dupilumab introduction since 2018

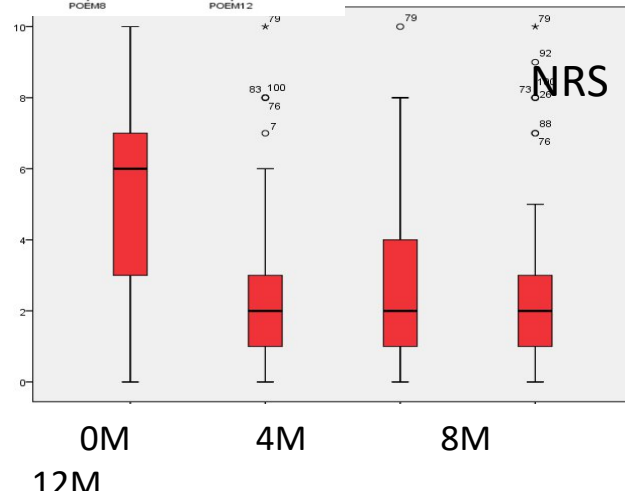
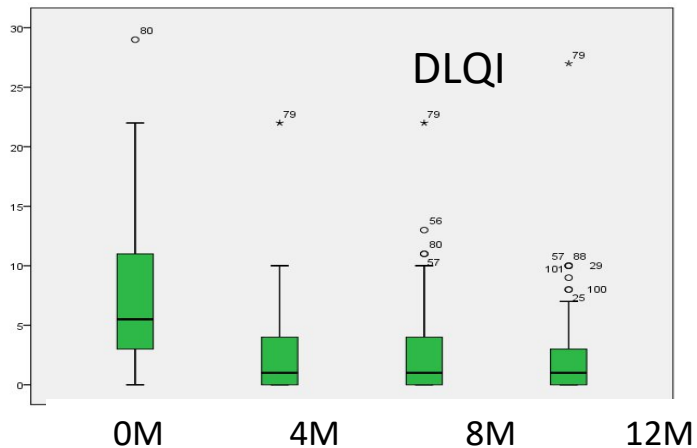
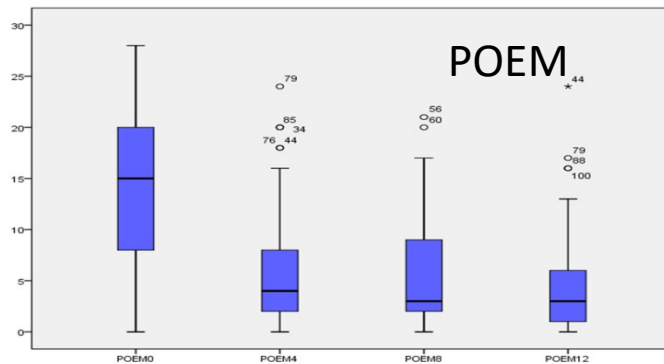
Response summary of 118 cases with moderate or severe adults

Follow up data from 118 cases in Osaka Habikino Medical center



Patient Reported Outcomes

Follow up data from 118 cases in Osaka Habikino Medical center



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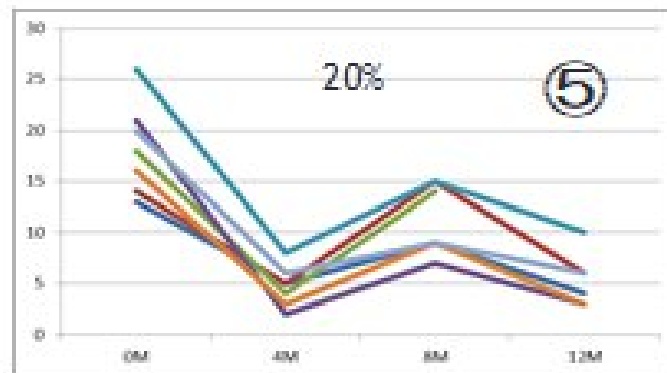
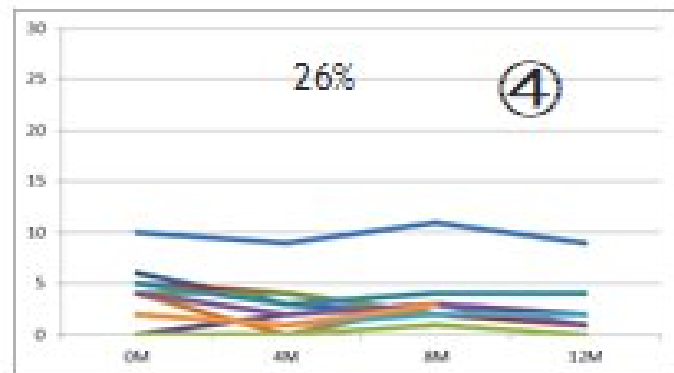
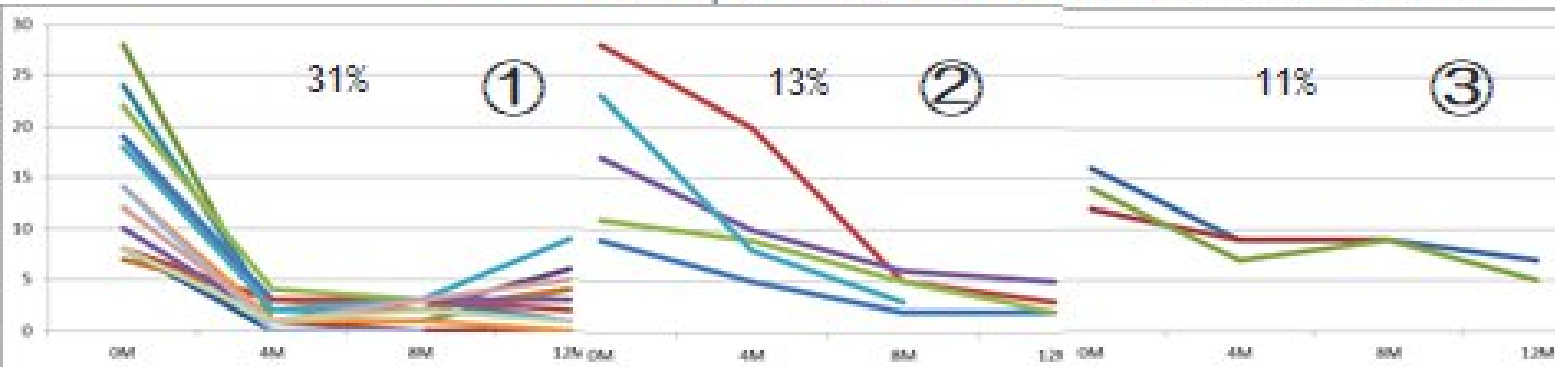
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Subtypes of response to Dupilumab according to POEM change

Follow up data from 118 cases in Osaka Habikino Medical center



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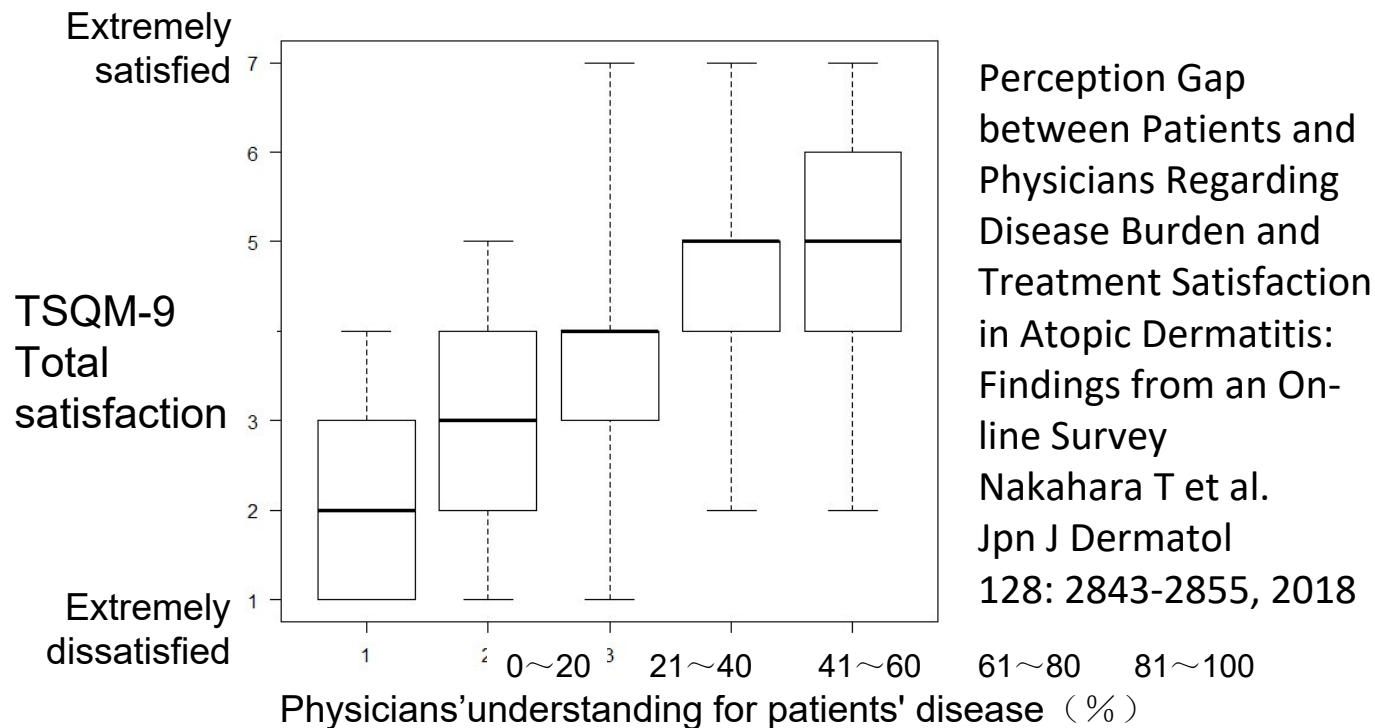
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Patients' total satisfaction and their sense of physician's comprehension of their disease



**** $p < 0.0001$

Spearman: $r = 0.584^{****}$

Perception Gap
between Patients and
Physicians Regarding
Disease Burden and
Treatment Satisfaction
in Atopic Dermatitis:
Findings from an On-
line Survey
Nakahara T et al.
Jpn J Dermatol
128: 2843-2855, 2018



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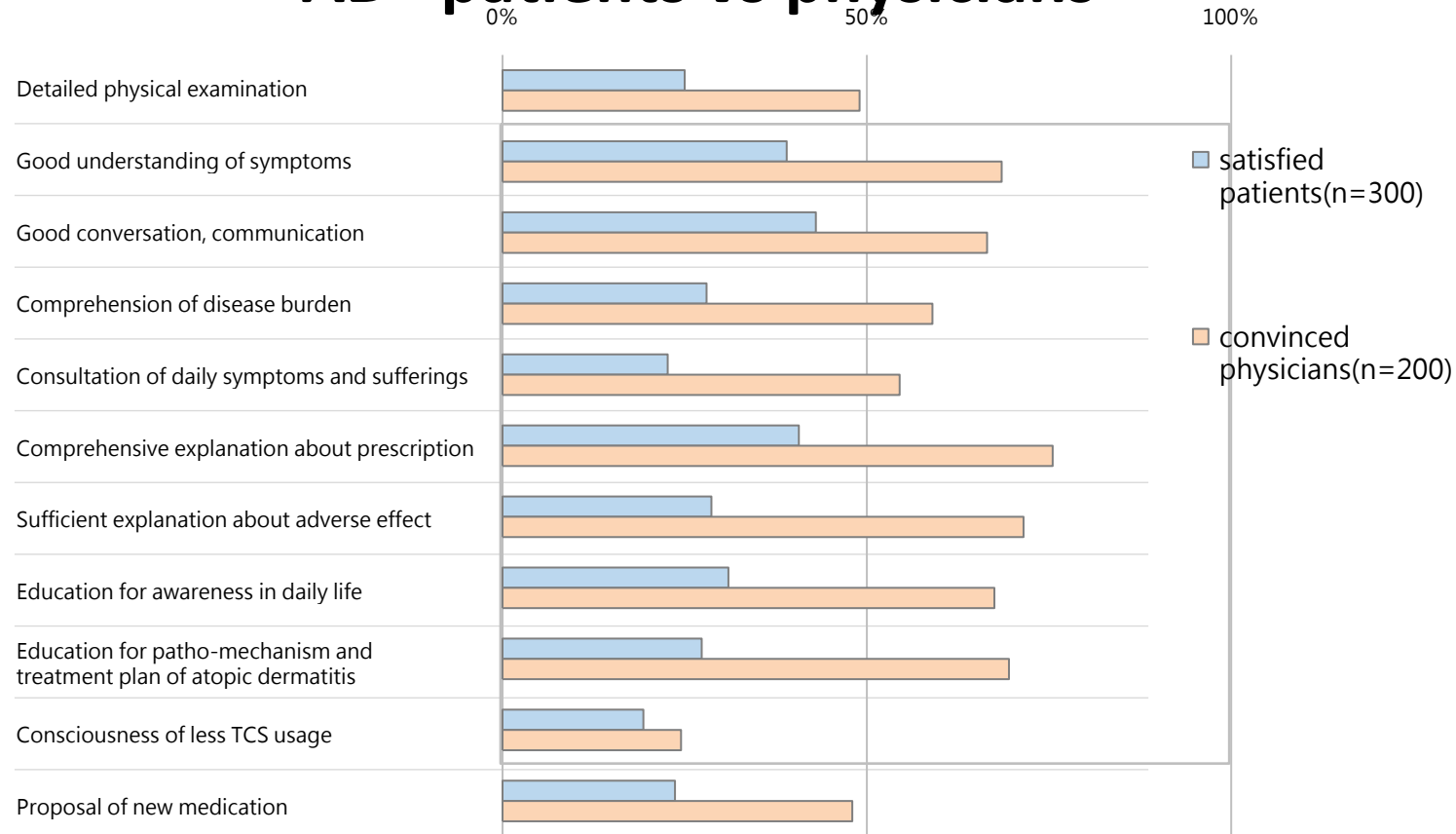
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Gaps of satisfaction with management of AD patients vs physicians



Nakahara T et al. Jpn J Dermatol 128: 2843-2855, 2018



Physician's perspective and practices in atopic dermatitis management “ A cross-sectional online survey in Japan”

A Survey for JSCIA members

		Difficulty in AD treatment			p-value
		Low (n=53)	Moderate (n=99)	High (n=91)	
Age		55 (45.0-60)	57 (41.5-58)	49 (41.0-58)	0.075 [†]
Japanese Guideline for AD 2018	Read	7 (5-10)	8 (6-10)	7 (5-9.5)	0.140
	Refer	7 (5-9)	8 (6-9)	8 (6-10)	0.269
	Possibility of AD cure (Good long-term control)	8 (7-10)	7 (5-9)	8 (5-8)	0.018 [*]
Self-assesment of physician's own practice	Satisfaction with treatment outcome	8 (7-9)	7 (6-8)	6 (5-7)	<0.001 ^{**}
	Motivation to AD treatment	8 (7-10)	8 (7-8)	7 (6-8)	0.019 [*]
	Outpatients number / week	50 (20-100)	40 (20-100)	50 (20-120)	0.430
	Patients treated with cyclosporine	5 (2-20)	5 (2-20)	5 (1-17.5)	0.475

Kruskal-Wallis rank sum test , [†]non-parametric version of one-way analysis of variance



History of Atopic Dermatitis Treatment in Japan

		Allergen elimination	Inflammation control
1952	Topical hydrocortisone marketed		
1970	Period of abuse of topical steroids		
Early 1980s	First lawsuit case for steroid		
Late 1980s	The era of dietary restrictions		
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treatment goal,
education for patients, education for physicians
including good communication
maximize the effect of conventional/new medication

