



# Adjunctive vitamin d2 supplement improved clinical response and lung function in patients with allergen-specific immunotherapy; a randomized, double-blinded, placebo-controlled trial

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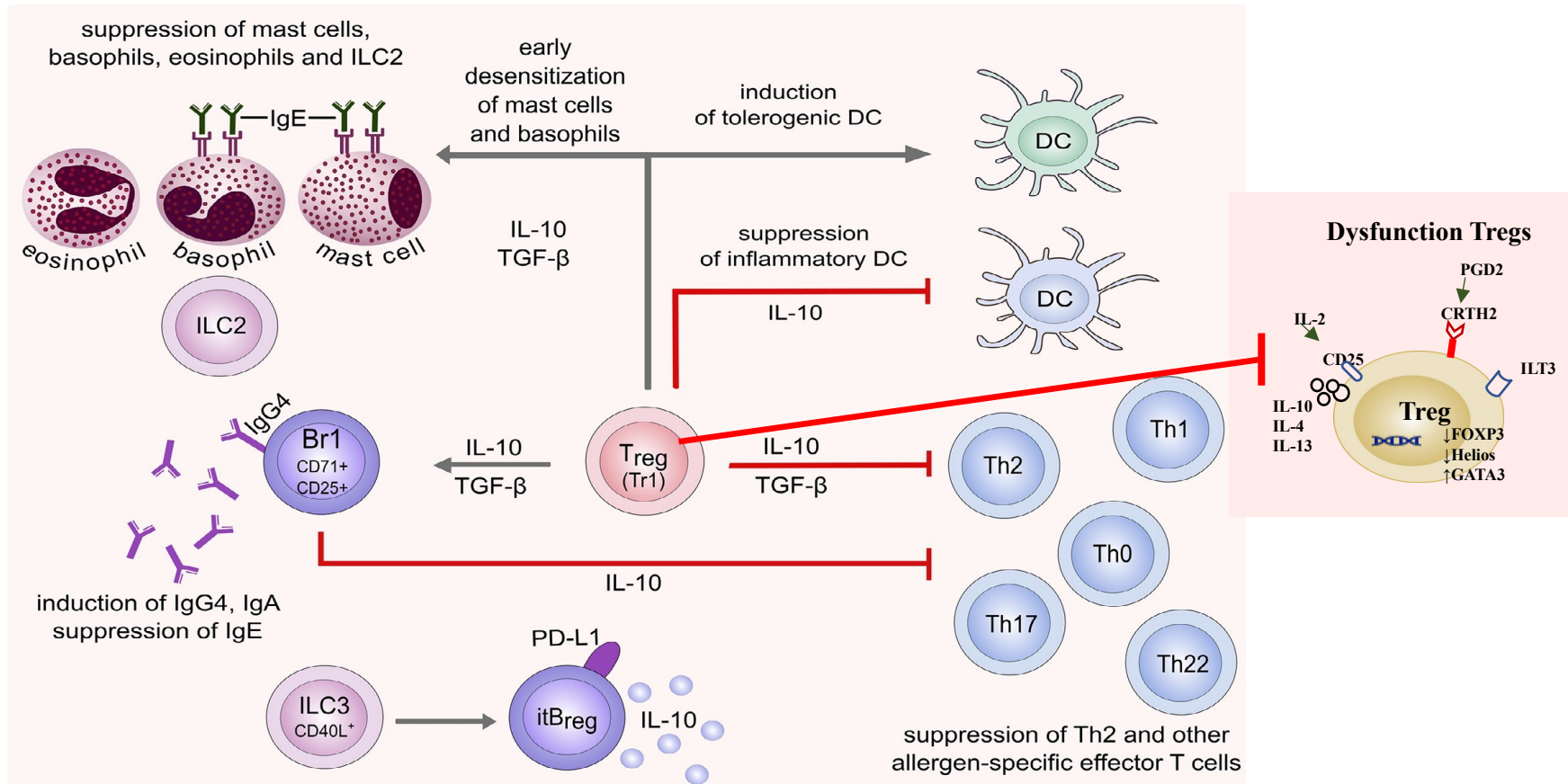
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Thai clinical trial registration number : 20190813001



# Mechanism of Allergen Specific Immunotherapy (AIT)

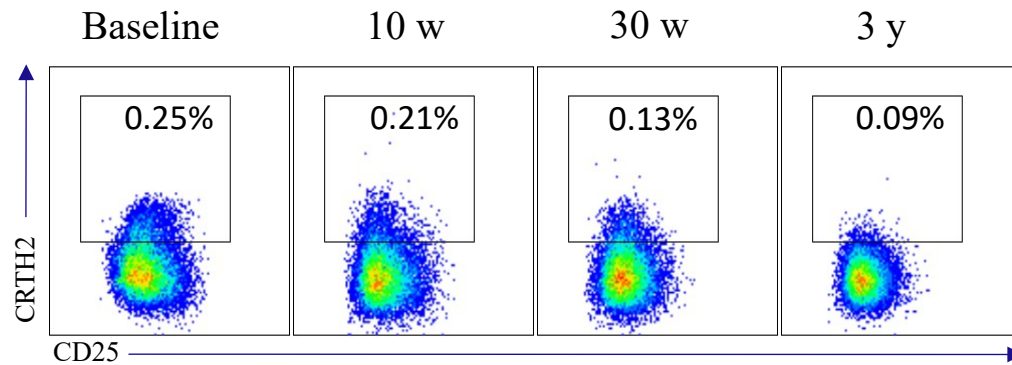


Globinska A, Boonpiyathad T, Satitsuksanoa P, Kleuskens M, van de Veen W, So- kolowska M, et al. Mechanisms of allergen-specific immunotherapy: diverse mechanisms of immune tolerance to allergens. *Ann Allergy Asthma Immunol* 2018;121:306-12.

Boonpiyathad T, et al. The role of Treg cell subsets in allergic disease  
Boonpiyathad T. et al. IL-10 producing T and B cells in allergy. *Semin Immunol*. 2019;44:101326



# CRTH2<sup>+</sup> Treg ( Dysfunctional Treg) Cells During HDM AIT

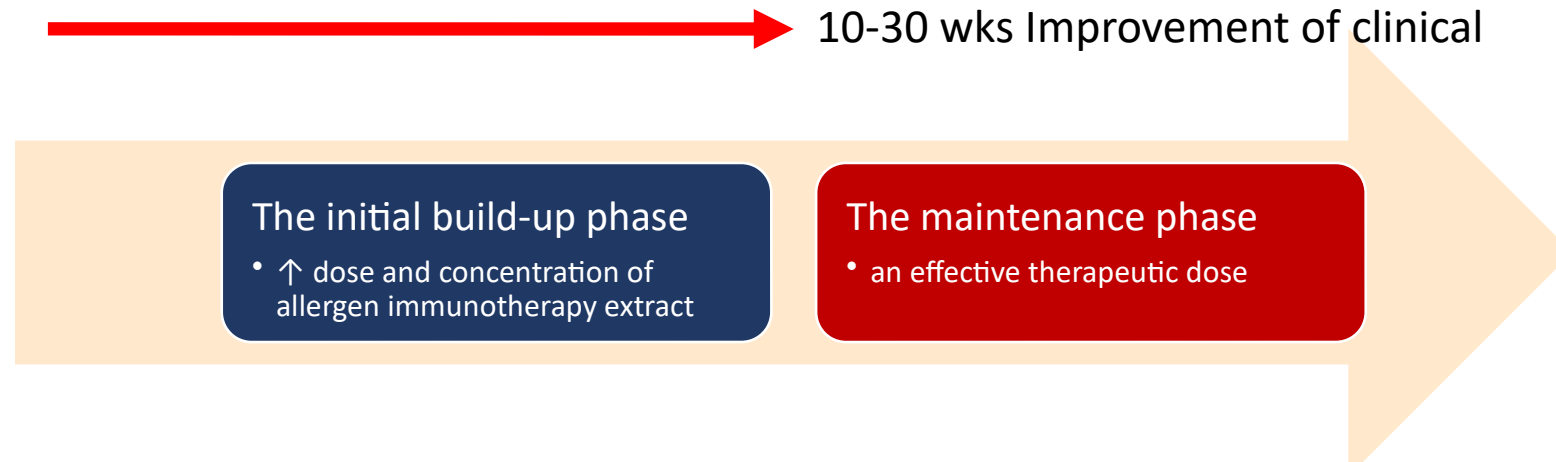


Boonpiyathad T, Sokolowska M, Morita H, et al. Der p 1-specific regulatory T-cell response during house dust mite allergen immunotherapy. *Allergy*. 2019;74(5):976-985.



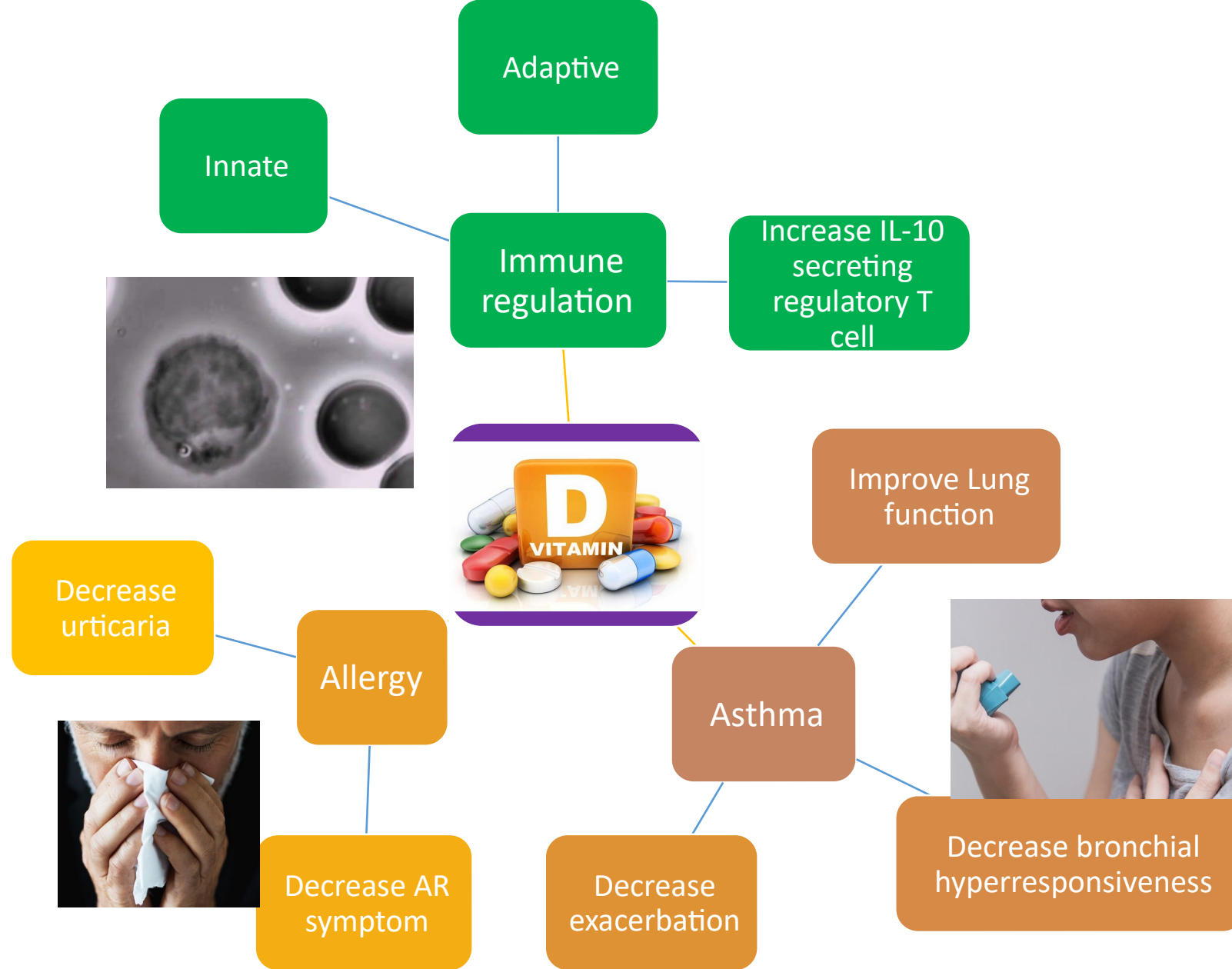
# AIT Administration

- After 30 weeks of AIT, TNSS score significantly decreased
- During the first 10 weeks of AIT, TNSS score slightly decreased



Cox L, et al. Practice parameter 3<sup>rd</sup> update. JACI 2011;127,s1-55.

Boonpiyathad T, Sokolowska M, Morita H, et al. Der p 1-specific regulatory T-cell response during house dust mite allergen immunotherapy. *Allergy*. 2019;74(5):976-985.





# Objectives

Efficiency of adjunctive vitamin D2 supplement in AR and AR with asthma patients with AIT

- Primary Objective

- Study Clinical score (Symptom medication score(SMS), ACT score) and PEFR in patients

- Secondary Objective

- Study blood level of dysfunctional regulatory T cell (CRTH2+ Treg) in patients
- Study serum IL-10 and Der p2-specific IgG4 in patients

## Total medication score (TMS)

- 1 point : Use Beta-2 agonist, antihistamine, pseudoephedrine, Montelukast
- 2 points : Use inhaled/intranasal corticosteroid
- 3 points : Use Systemic steroid

Symptom medication score (SMS)  
= Total nasal symptom score(TNSS) +  
Total medication score (TMS)



# Inclusion Criteria

1. Age 18 to 70 years
2. Allergic rhinitis with or without asthma patients
3. Never get allergen specific immunotherapy or last allergen specific immunotherapy 6 months
4. Want to treatment with AIT build-up phase
5. 25-OH vitamin D level  $< 100$  ng/mL
6. Serum calcium  $< 10.5$  mg/dL
7. No History of Calciferol allergy



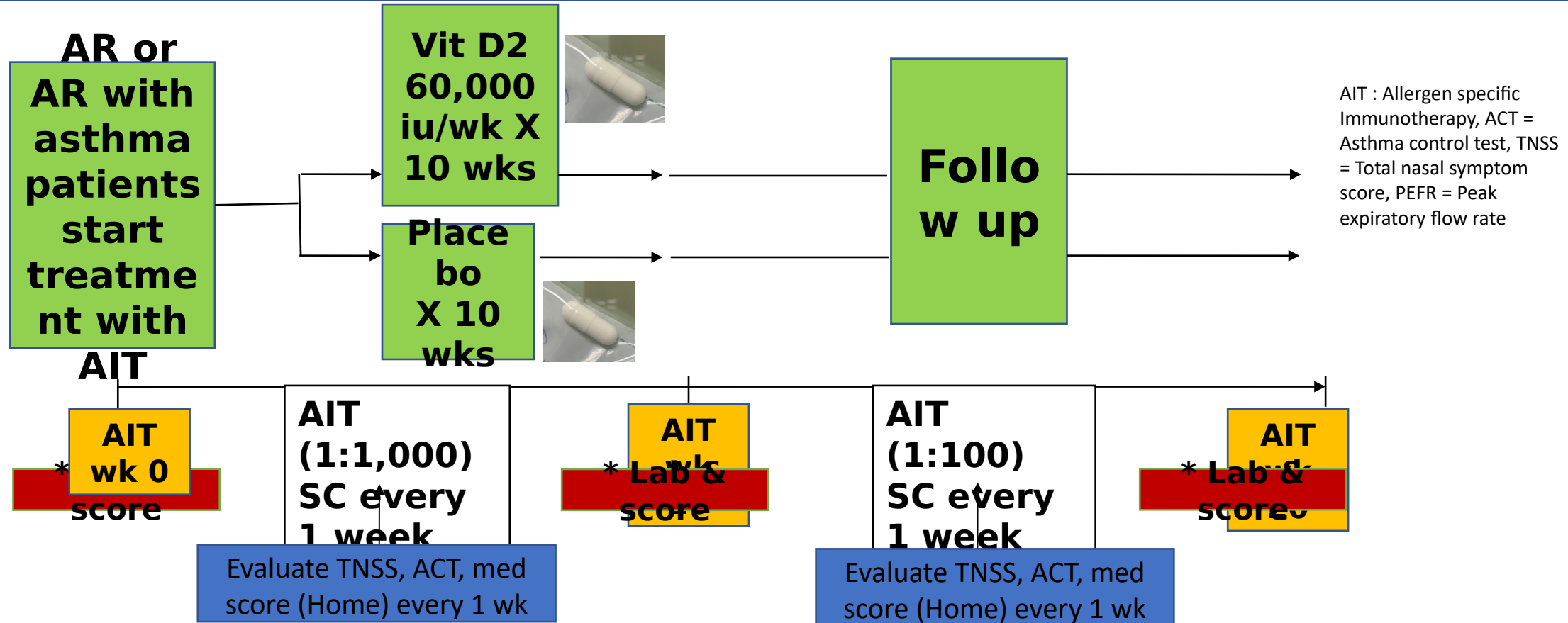
# Exclusion Criteria

1. Previous vitamin D uses
2. Suspected severe allergy to AIT or Calciferol
3. Uncontrolled or severe asthma
4. Active heart disease e.g. ischemic heart less than 4 weeks
5. On immunosuppressive drugs e.g. corticosteroid, cyclosporin, chemotherapy in 30 days
6. Primary and secondary Immunodeficiency
7. Participants in other research less than 30 days
8. Pregnancy





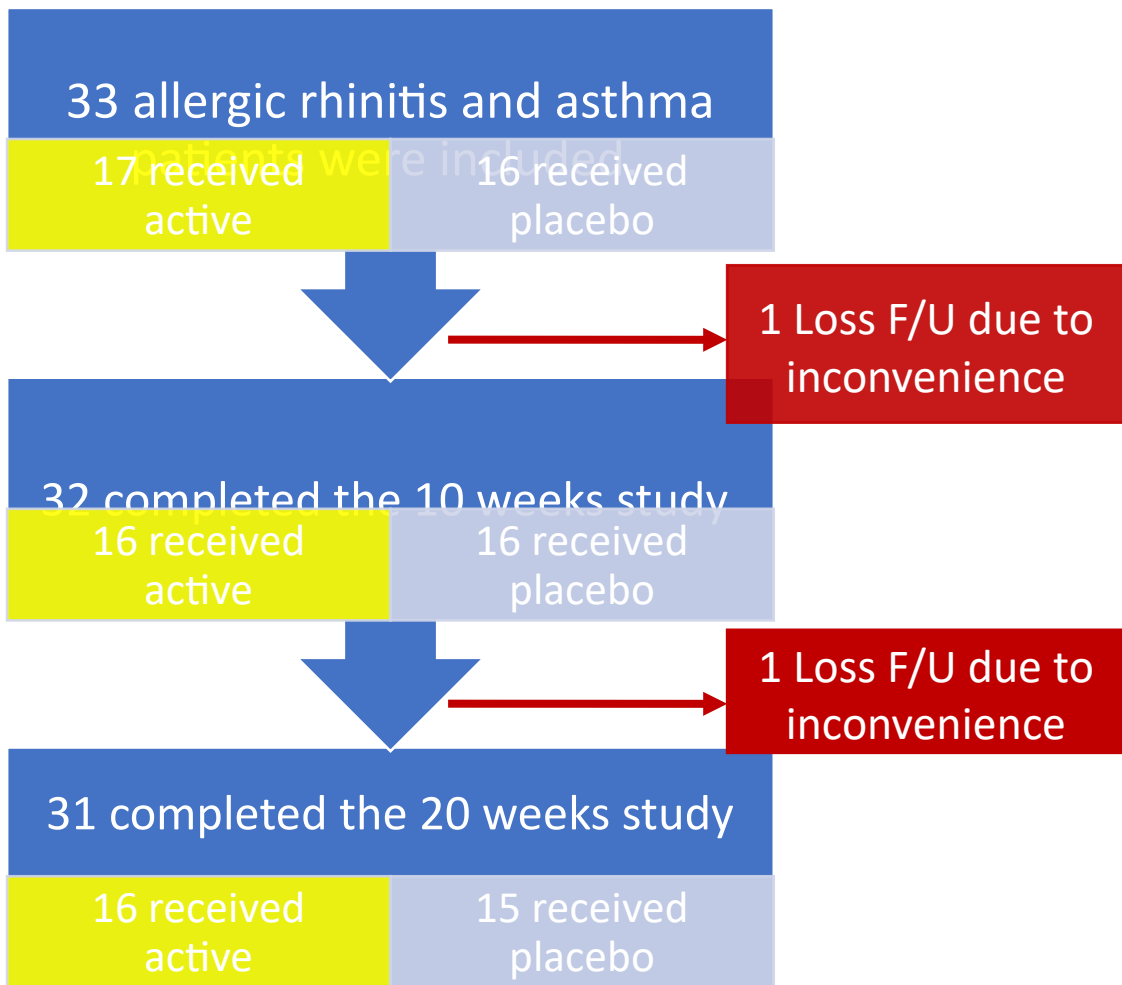
# Methods



**\* Lab = Blood for Serum 25-OH Vit D level, dysfunctional regulatory T cell (CRTH2+ Treg), IL-10, Der p2-specific IgG4 Calcium Score = Evaluate ACT score, TNSS, Total Med score, SMS, PEFr**



# Consort chart & Baseline Characteristics



	Active	Placebo
	n = 16	n = 15
Sex (Female)	11	10
Age	41.40±16.15.04	38.73±12.44
Allergic disease		
Allergic rhinitis (%)	16 (100%)	15 (100%)
Allergic asthma (%)	5 (31.25)	6 (40)
Atopic dermatitis (%)	1 (6.25)	0 (0)
Allergic conjunctivitis (%)	0 (0)	2 (13.3)
Allergen sensitization (%)		
Mite	16 (100)	13 (86.7)
Pollen	1 (6.25)	3 (20)
Fungus	9 (56.25)	4 (26.7)
Weed	0 (0)	3 (20)
Pet (dog, cat)	1 (6.25)	4 (26.7)
Cockroach	4 (25)	4 (26.7)
Absolute Eosinophil (cells/ $\mu$ l)	274.61±217	211.56±162
TNSS	8.13±2.75	6.73±3.77
Total medication score	1.77 ± 0.64	2 ± 0
SMS	9.87±2.9	8.77±3.7
Vitamin D (ng/ml)	19.75±5.99	18.41±5.58
Vitamin D insufficiency	6 (37.5)	5 (33.3)
Vitamin D deficiency	9 (56.25)	10 (66.6)



# 25-OH Vitamin D level and Symptom Medication Score(SMS)

Active group = 16 , Placebo group = 15

**A** Vitamin D levels

**B** Symptom-medication score



# Subgroup Analysis AR With Asthma

Active group = 5 , Placebo group = 6

**A** Asthma control test

**B** Peak expiratory flow rate (PEFR)



# Subgroup Analysis Vitamin D Deficiency

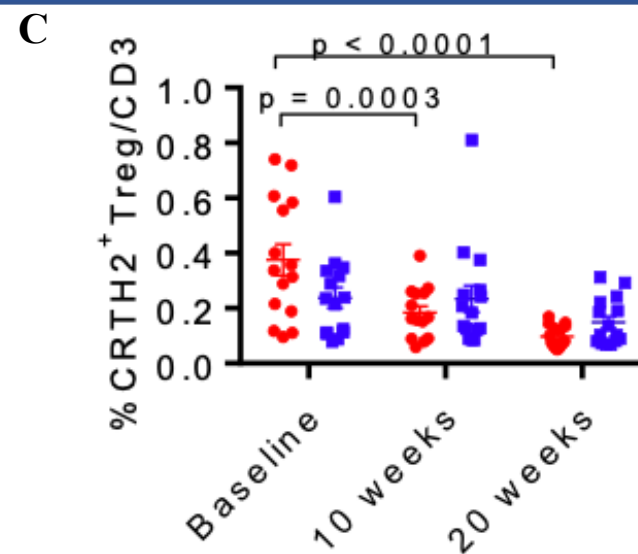
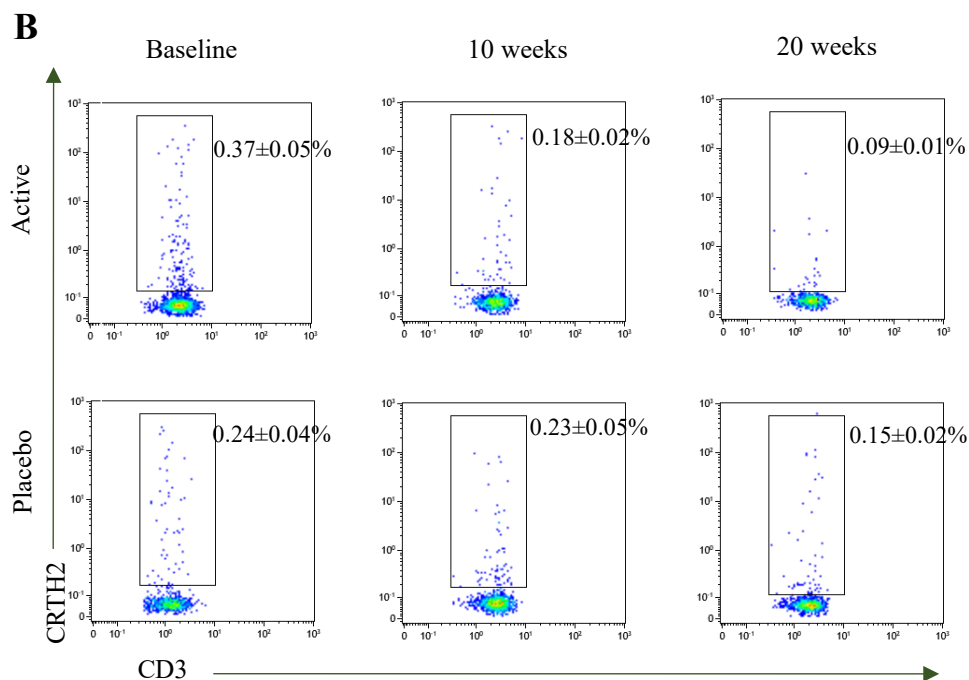
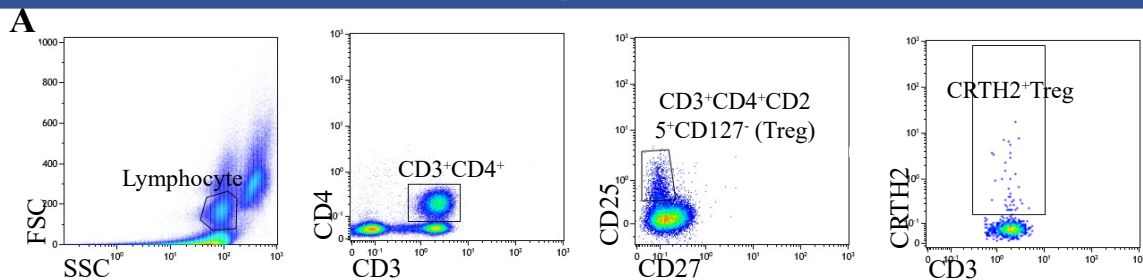
Active group = 9 , Placebo group = 10

Symptom-medication score



# Flow Cytometry Evaluate CRTH2+ Treg(Dysfunctional Treg)

## Active group = 16 , Placebo group = 15



**D**



# Absolute Eosinophil and Plasma IL-10 levels

Active group = 16 , Placebo group = 15

**A** Absolute eosinophils

**B** Plasma IL-10 levels



Plasma Der p2-specific IgG4  
Active group = 16 , Placebo group = 15





# Discussion

- **The first** study that study efficiency of vitamin D2 supplementation in early phase AIT patients
- Adjunctive vitamin D2 supplement during booster phase of AIT did **not significantly improvement** in symptom medication score(**SMS**)
- In subgroup analysis
  - **Vitamin D deficiency** : Significantly improve in SMS
  - **AR with asthma** : Significantly improve in PEFr
  - Help improve patient clinical in initial phase of AIT
- Vitamin D2 could help AIT patients :
  - Significantly decreasing CRTH2+ Treg
  - Trend to increase Der p2-specific IgG4



# Acknowledgements



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