



Diagnostic Approaches for Food allergies

OIT: How to Use Laboratory Tools

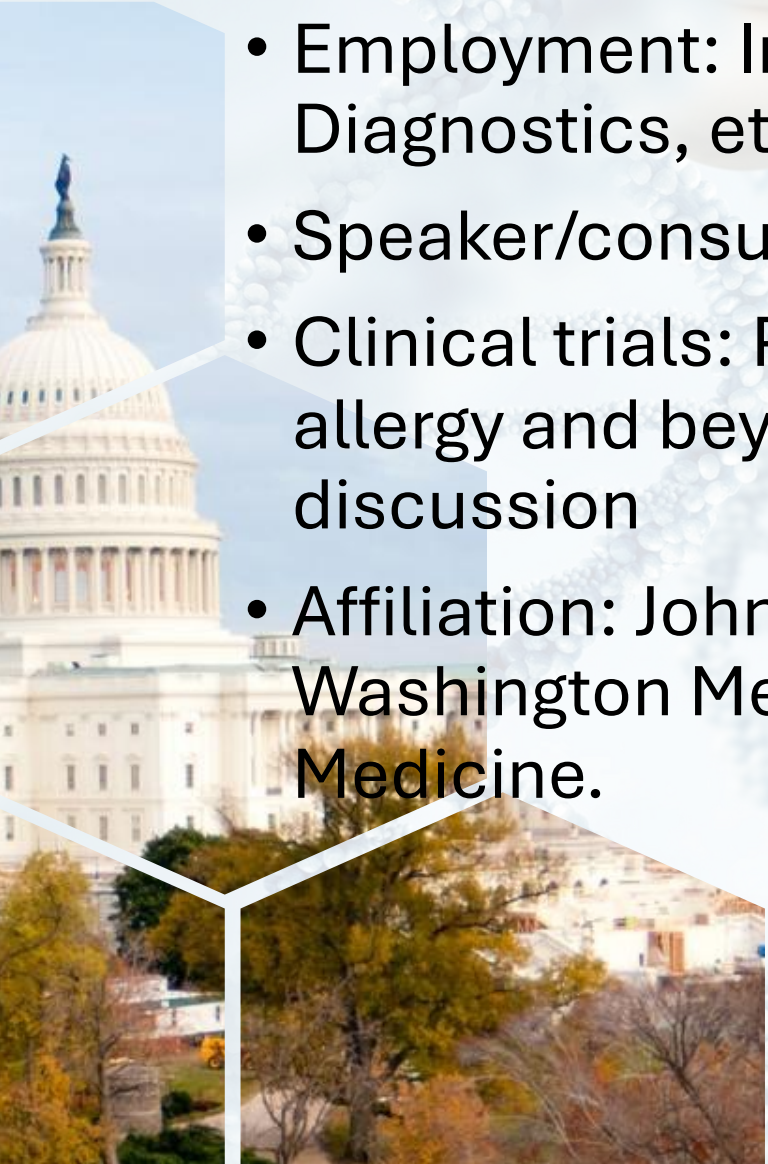
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Disclosure: H. Henry Li, MD, PhD

- Employment: Institute for Asthma and Allergy; Virant Diagnostics, etc.
- Speaker/consultation: None related to food allergies
- Clinical trials: PI or Sub-I in multiple clinical trials (food allergy and beyond), none related to the topic for this discussion
- Affiliation: Johns Hopkins University Hospital, George Washington Medical Center; Nankai University School of Medicine.

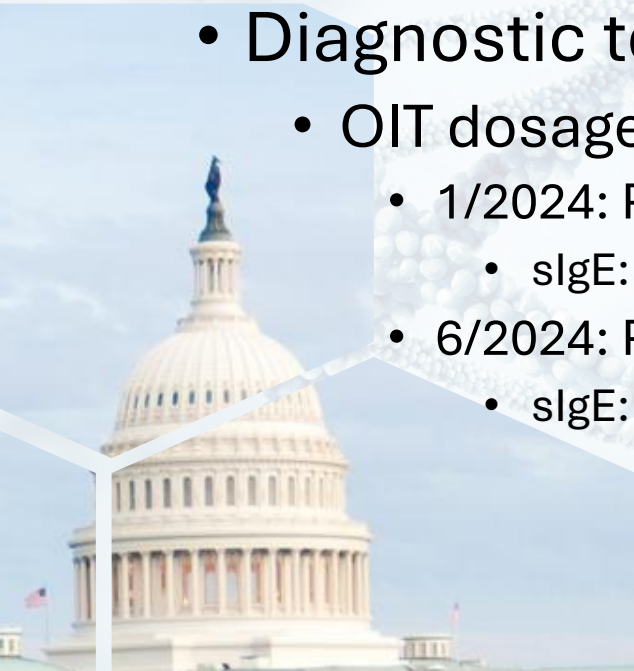


Learning Objectives

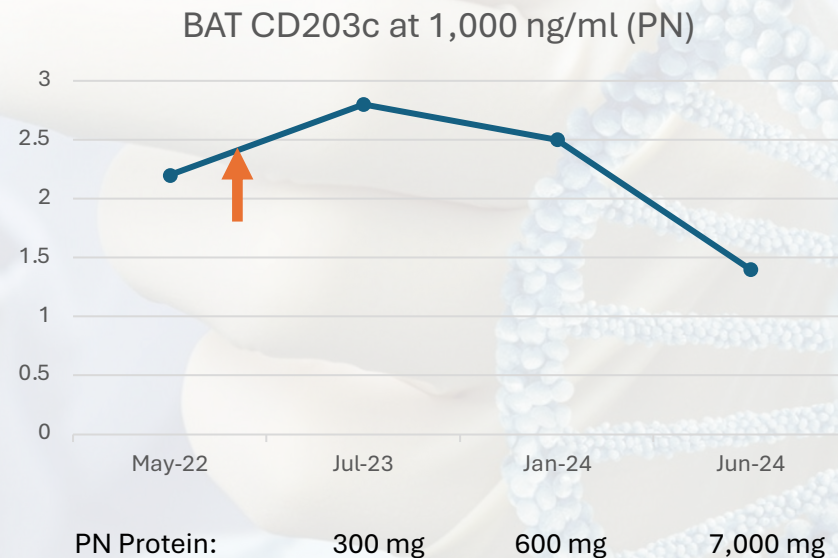
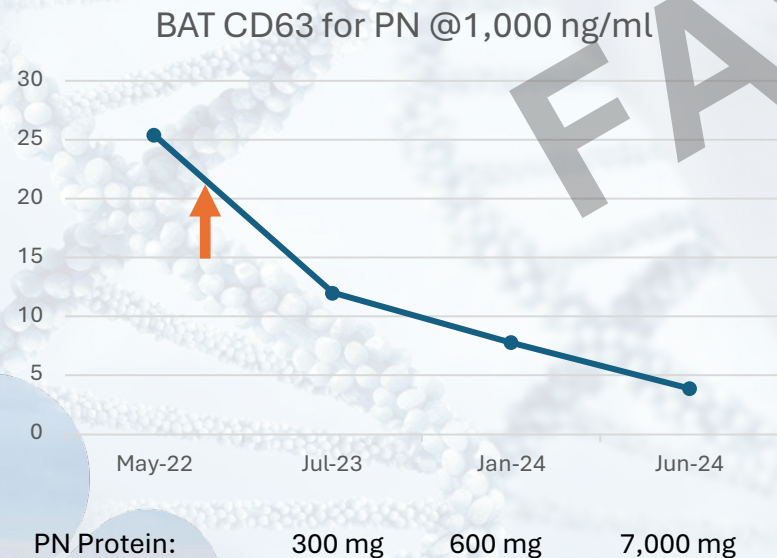
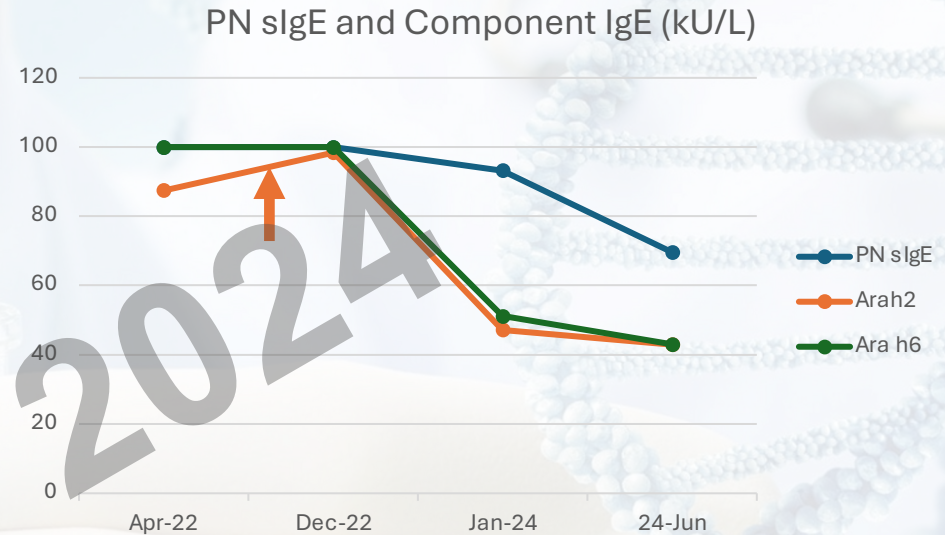
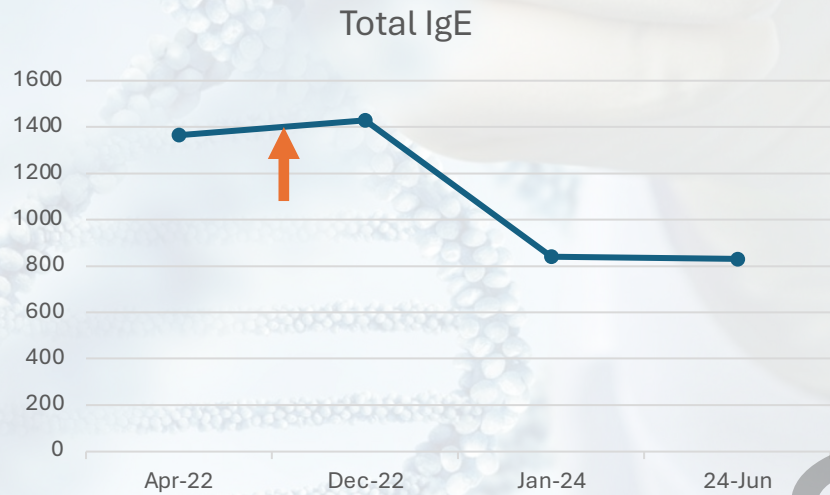
- To familiarize the common food allergy diagnostic tools
- To understand the timing and sequence for food allergy testing
- To use published data to assess clinical cases in terms testing sensitivity and specificity
- To monitor the progress of OIT/outcome measurement

Case #1

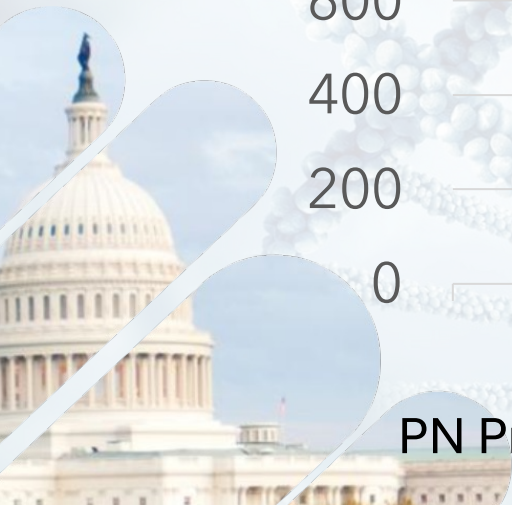
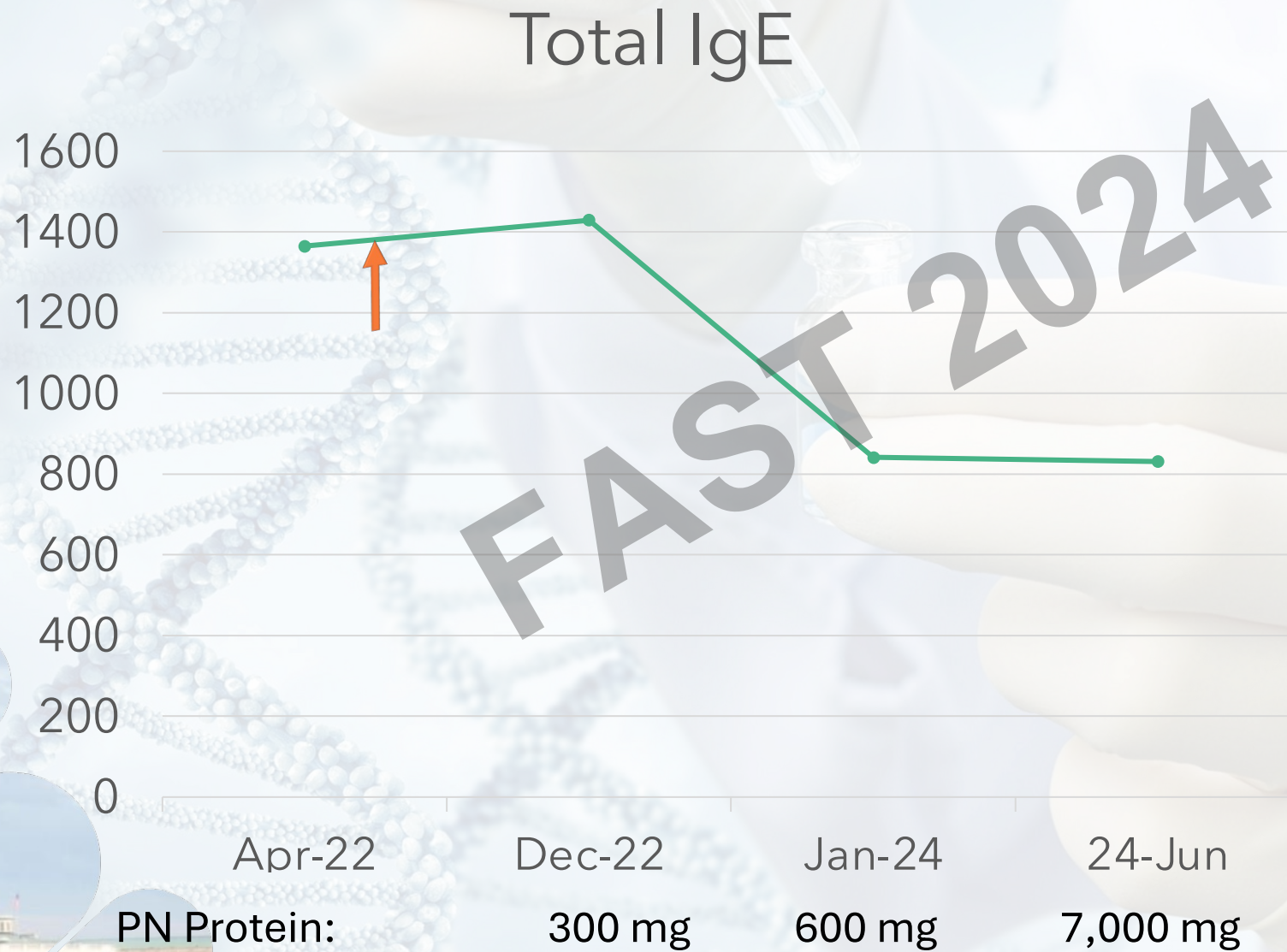
- 13 y/o boy, started mixed nut OIT in 9/2022
- Last visit on 6/8/2024, reached a maintenance dose of 7 gm of peanut protein; 5 gm of walnut and pecan protein (each) without reactions
- Diagnostic tests had performed before and after the OIT
 - OIT dosage at the time of the tests
 - 1/2024: Peanut ~1.0 gram (protein)
 - sIgE: 93.2; Ara h2: 47.2; Ara h6: 57.2
 - 6/2024: Peanut ~ 7.0 gram (protein)
 - sIgE: 69.6 ; Ara h2: 42.9 ; Ara h6: 43.0



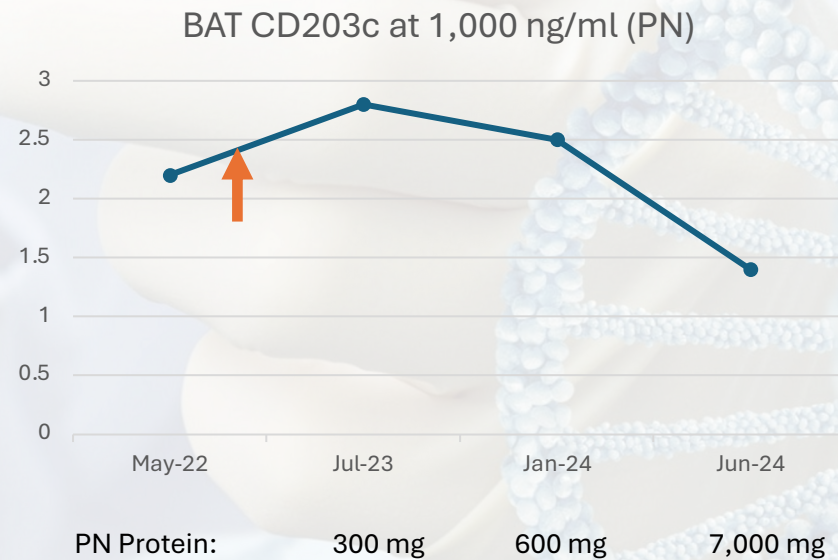
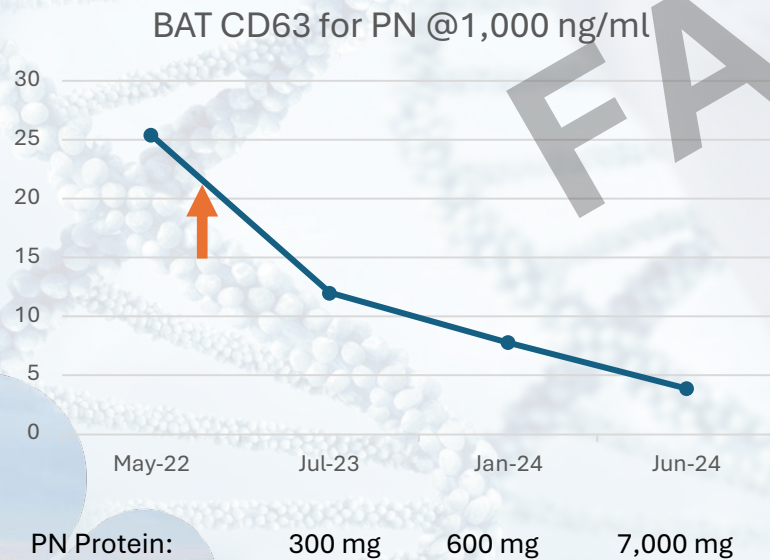
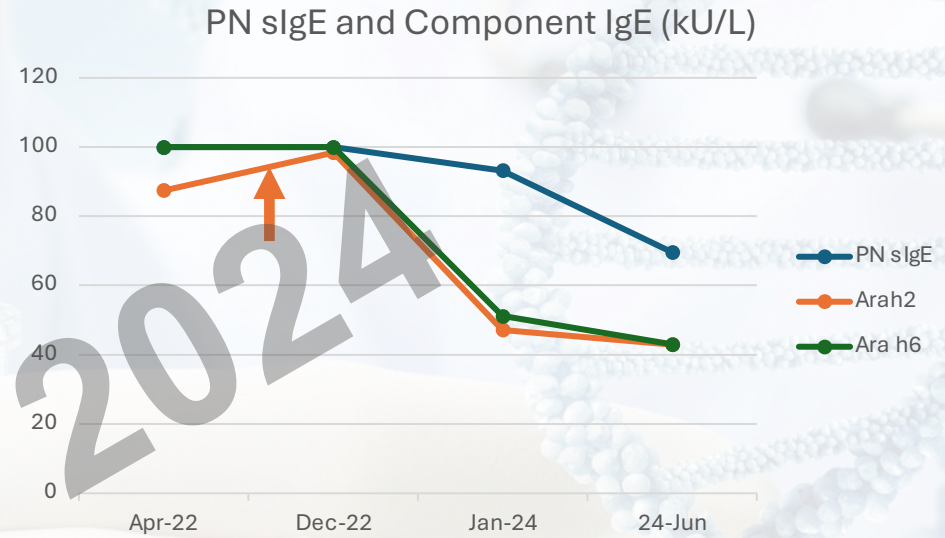
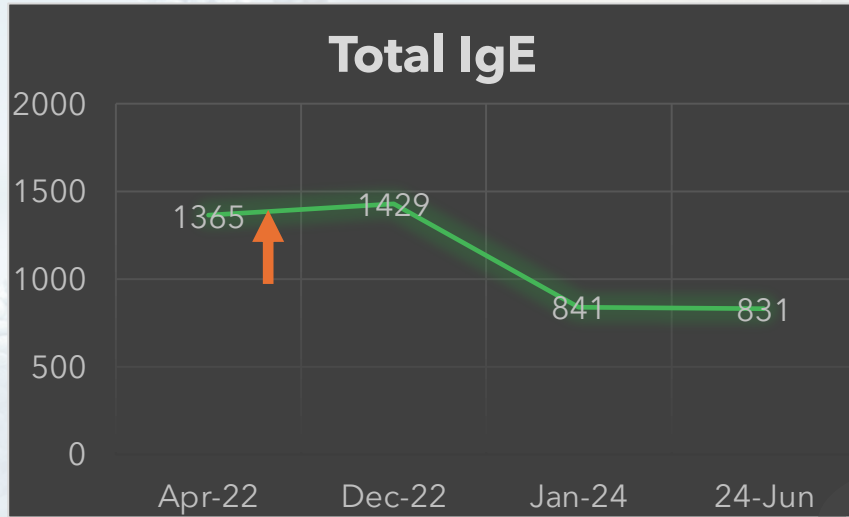
Case #1: Laboratory Value Changes Over Time



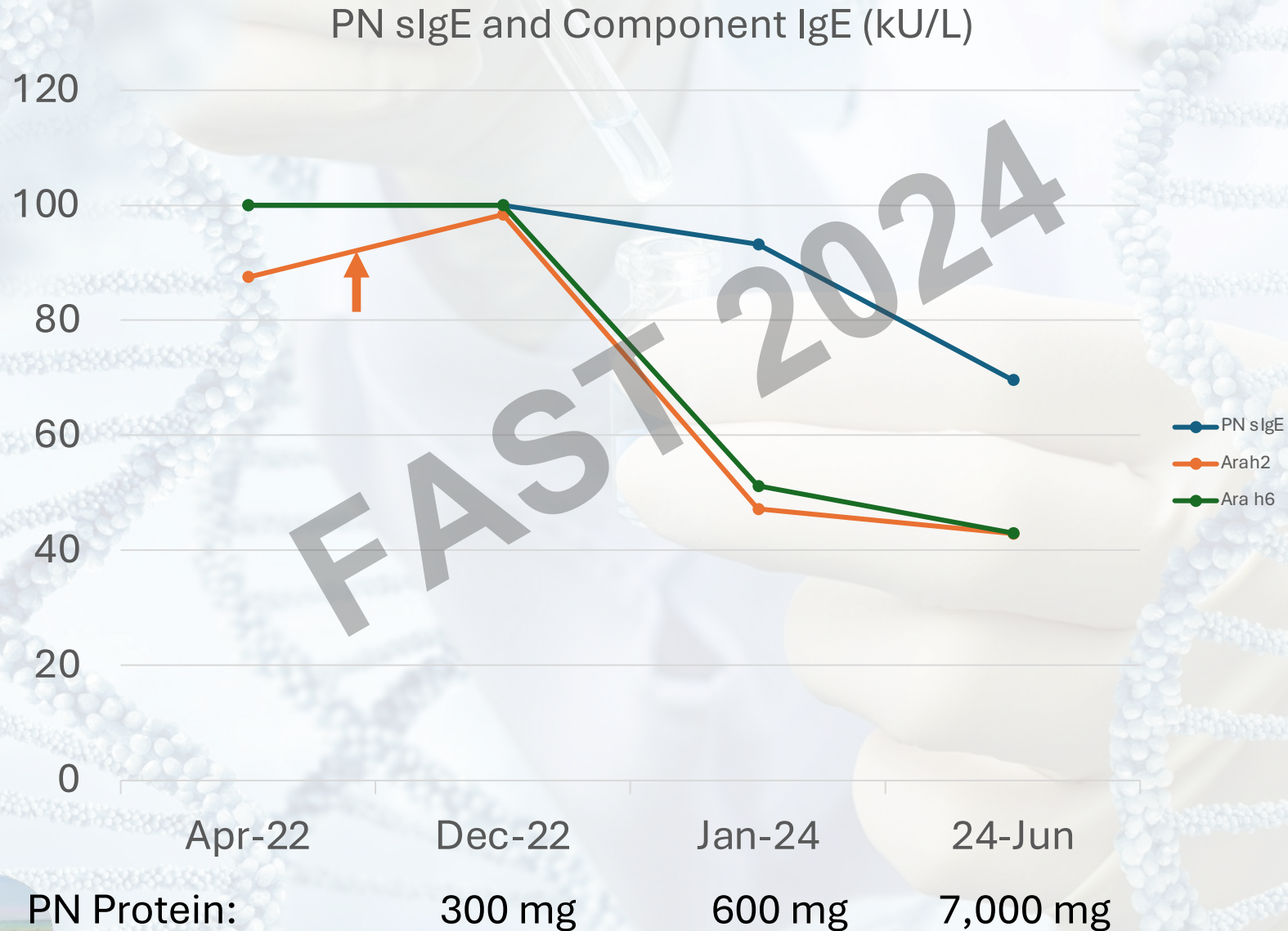
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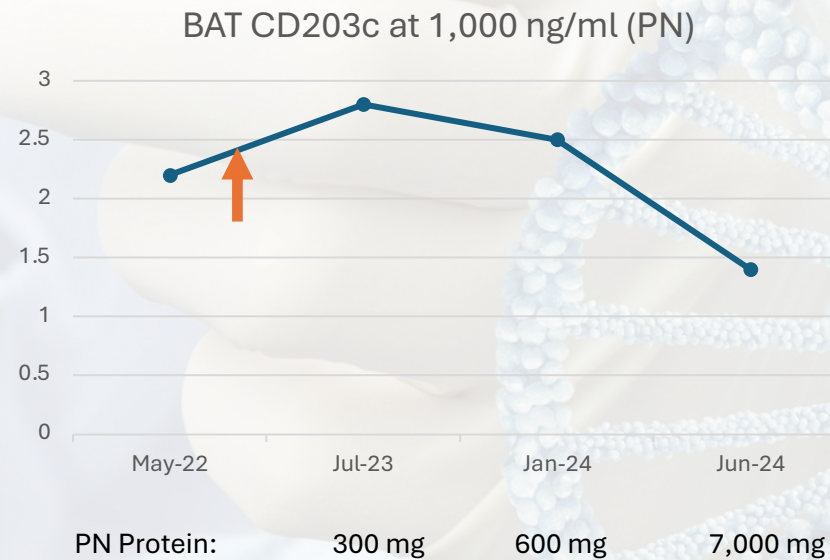
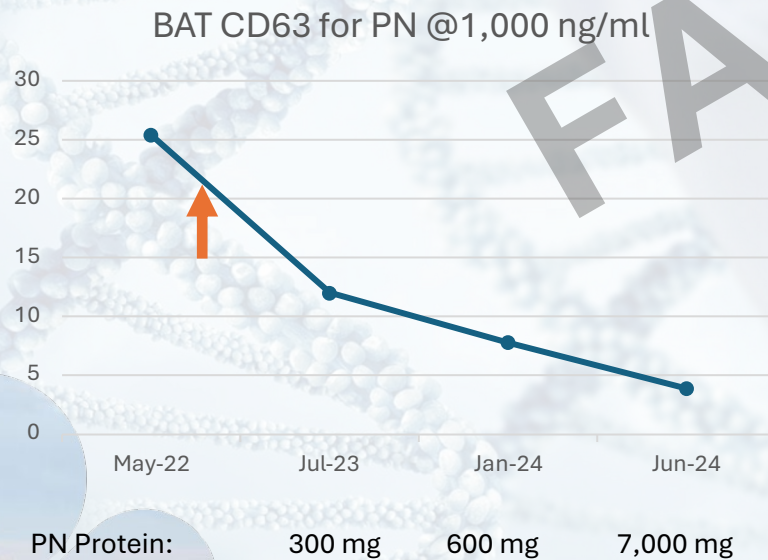
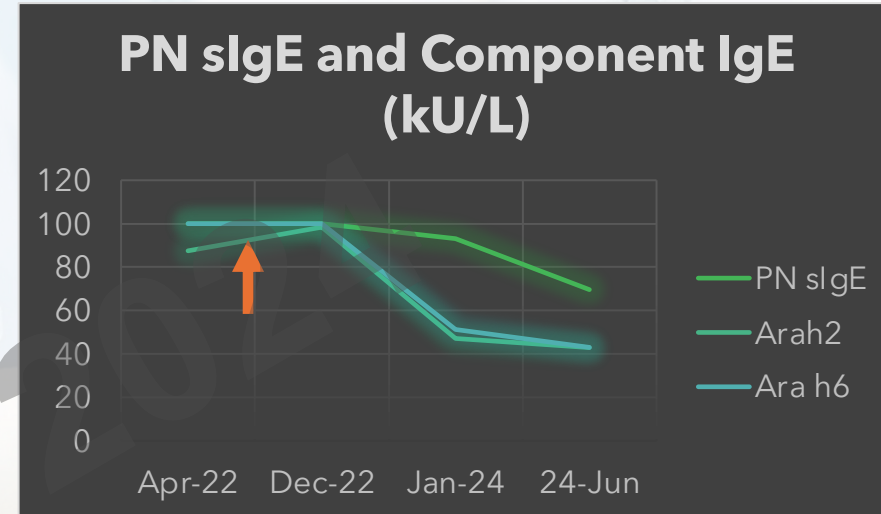
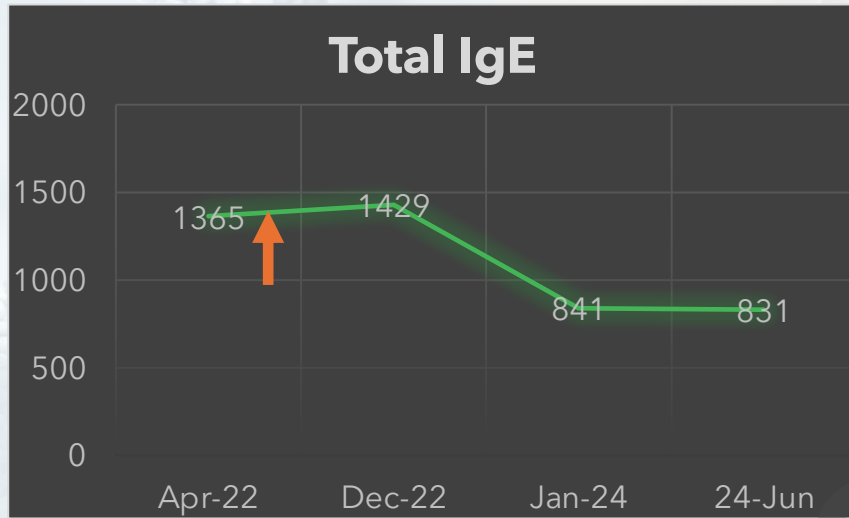
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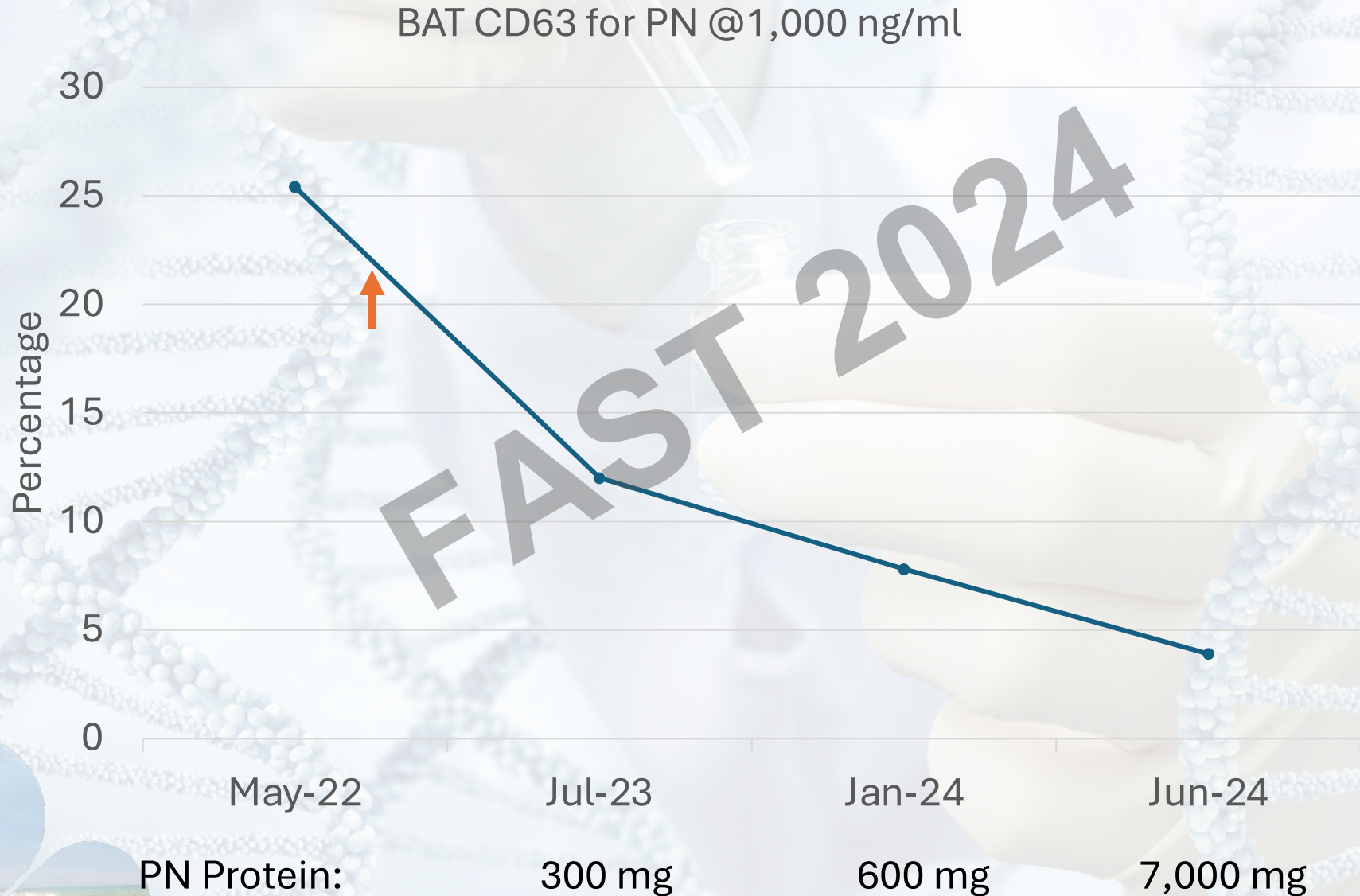
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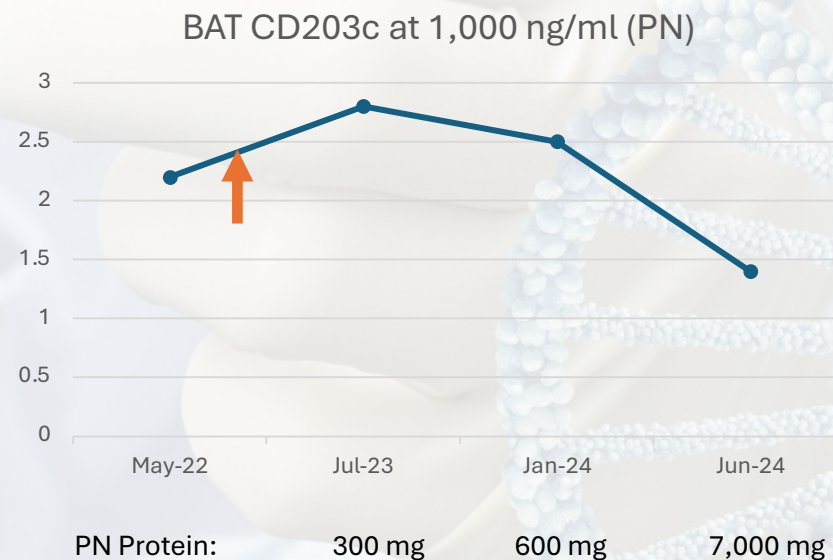
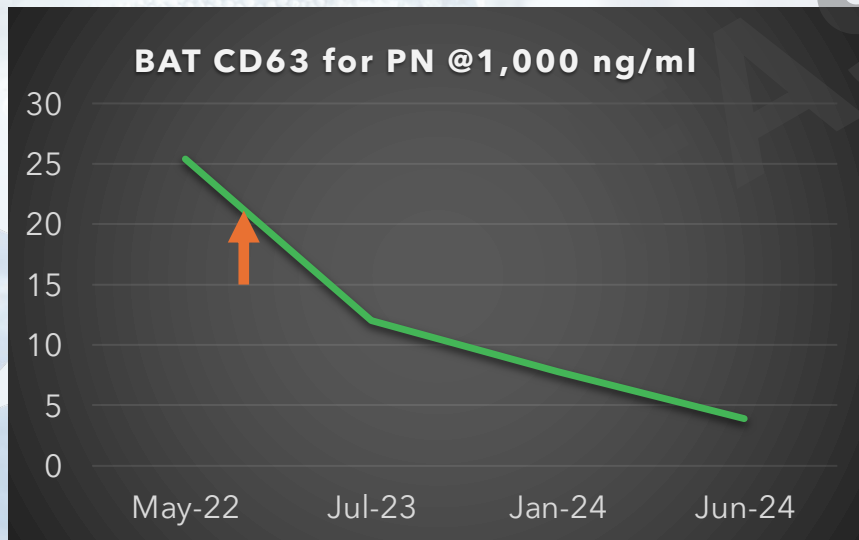
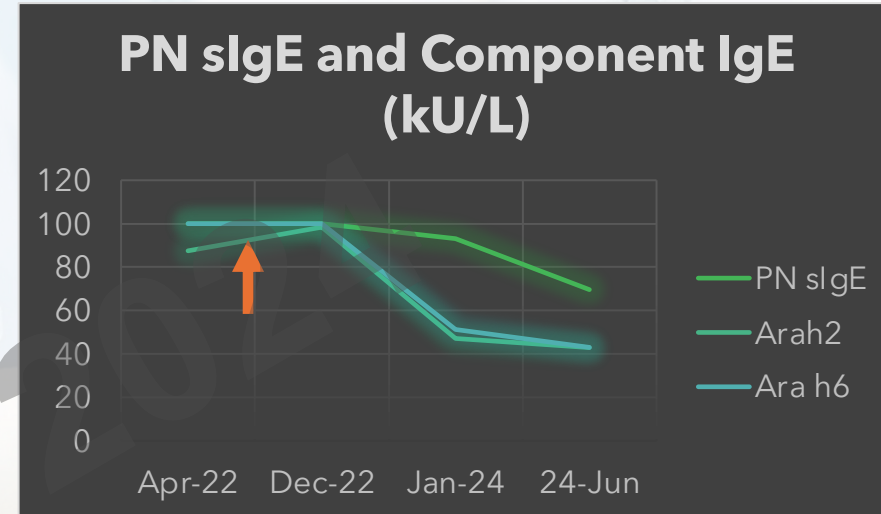
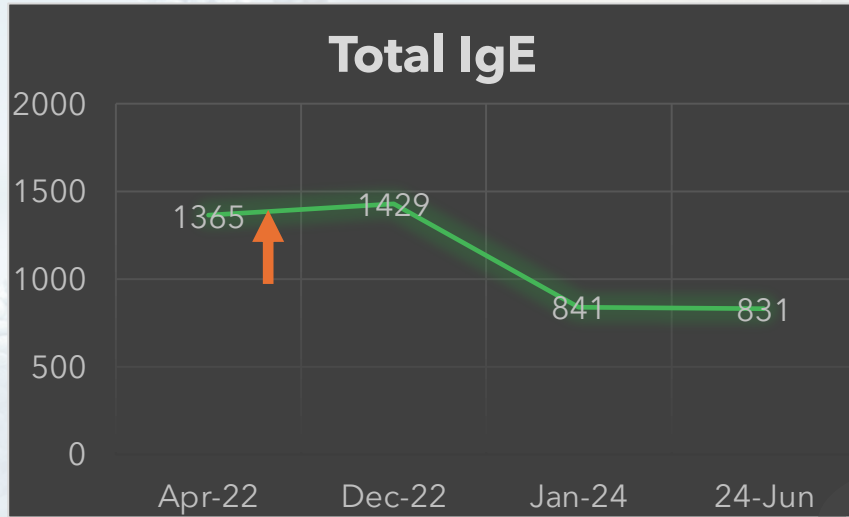
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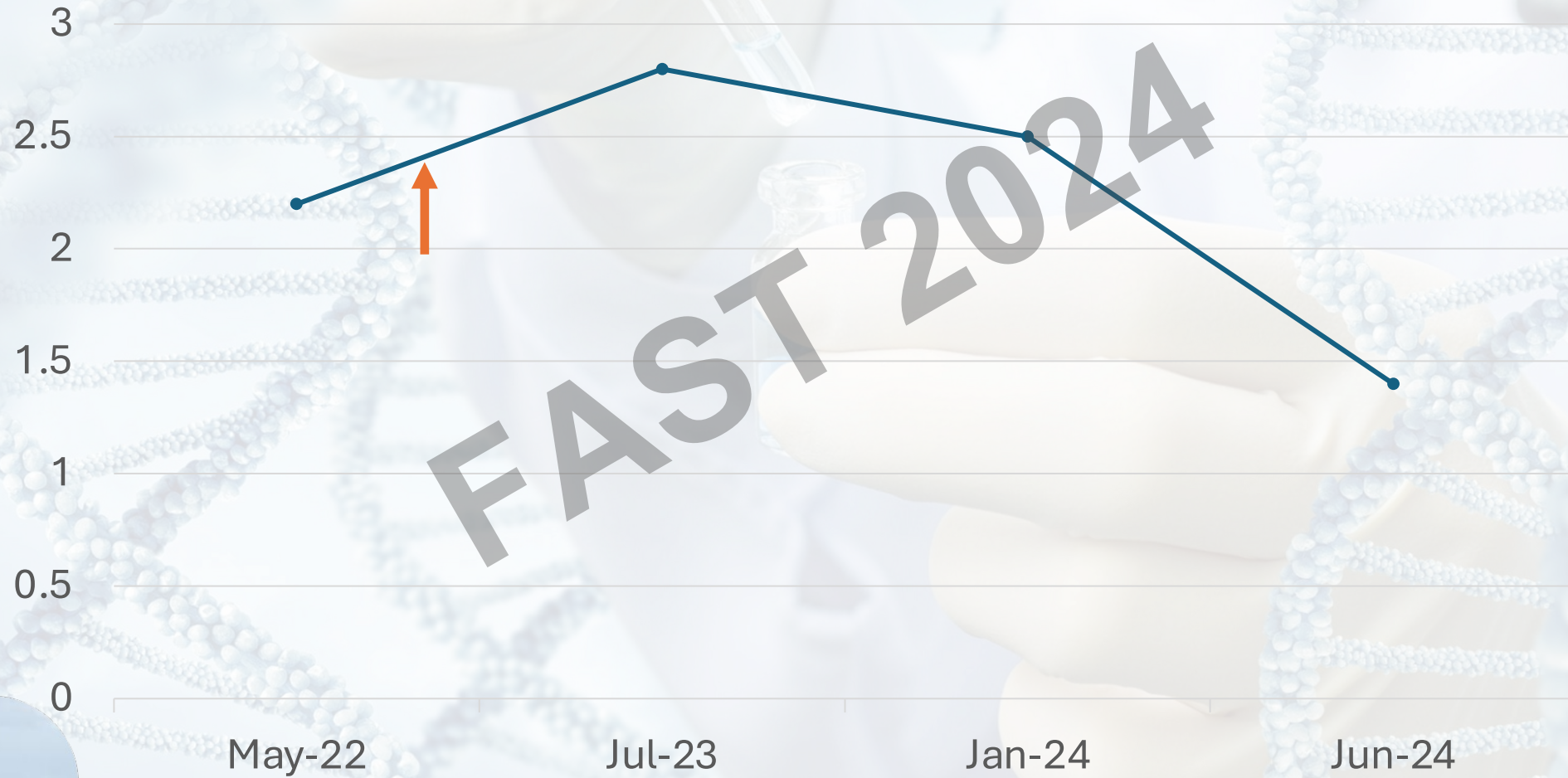


PN Protein: 300 mg 600 mg 7,000 mg

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Case #1: Laboratory Value Changes Over Time

BAT CD203c at 1,000 ng/ml (PN)

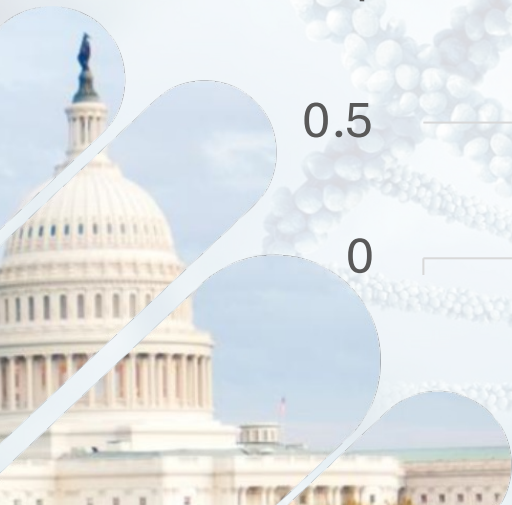


PN Protein:

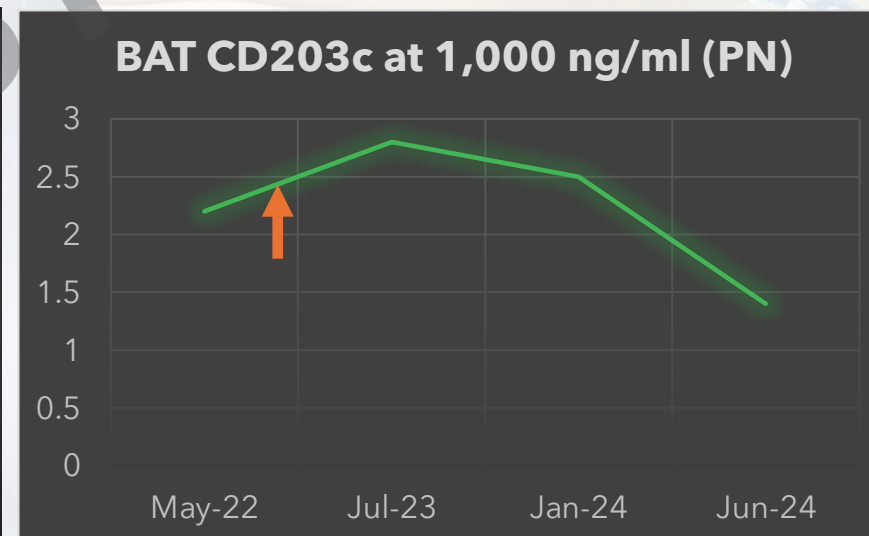
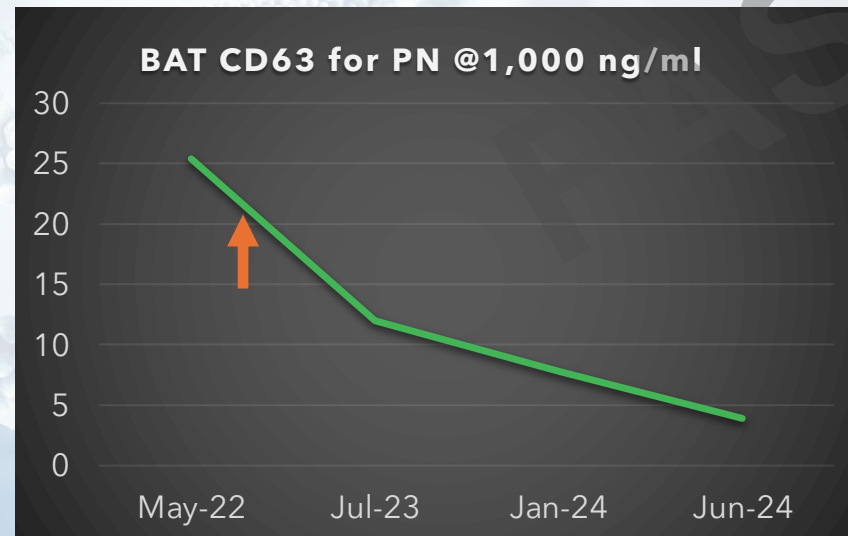
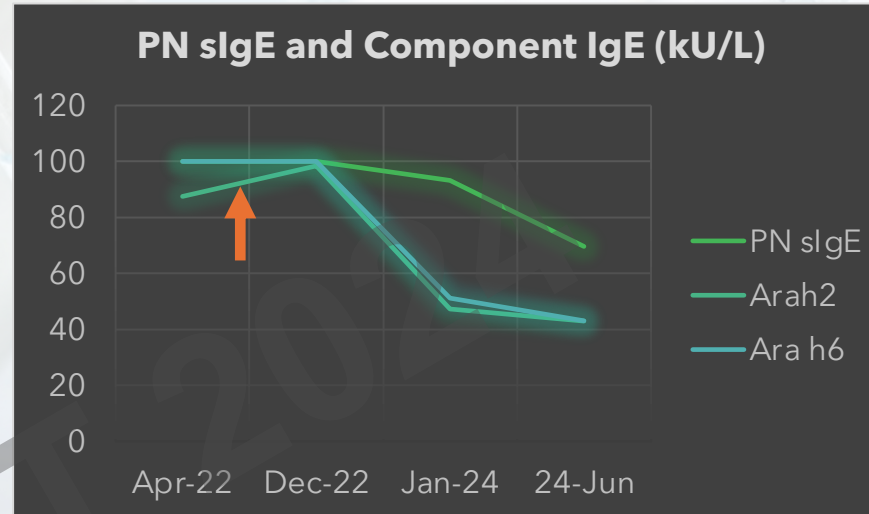
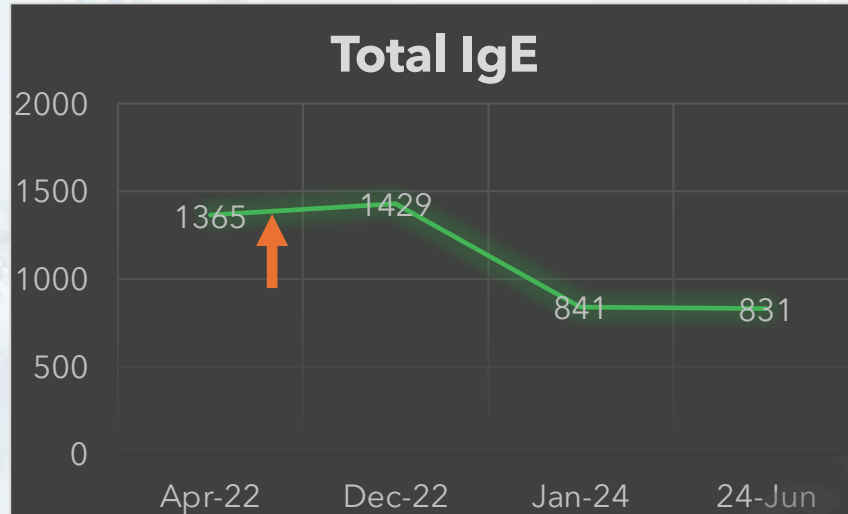
300 mg

600 mg

7,000 mg



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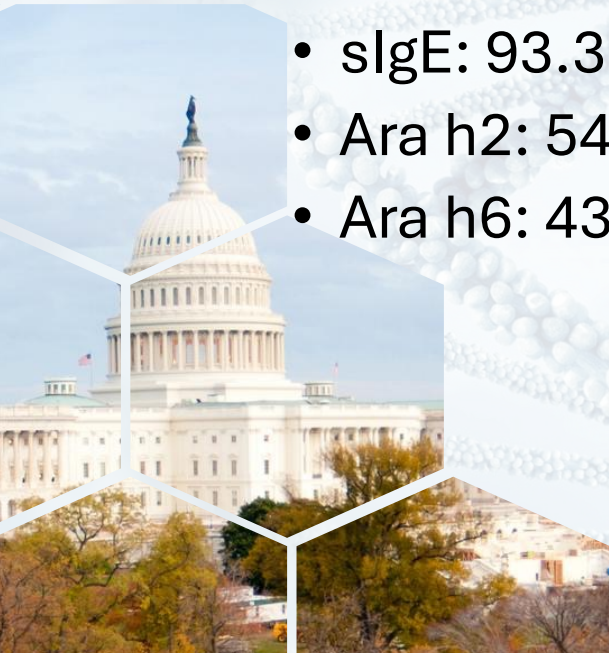


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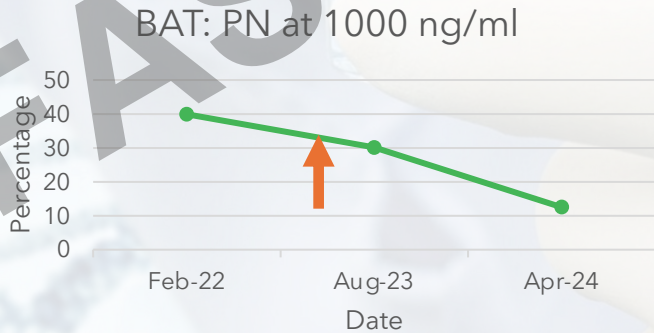
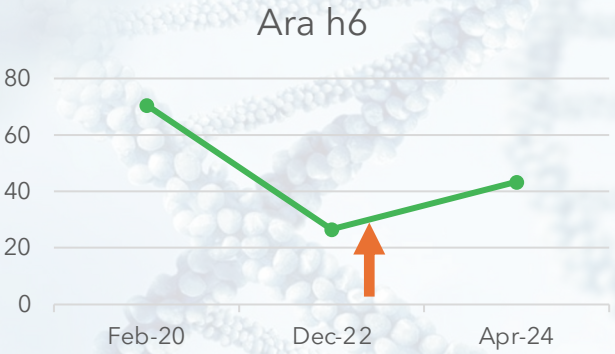
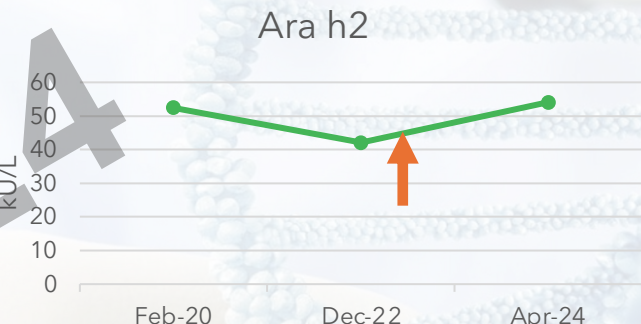
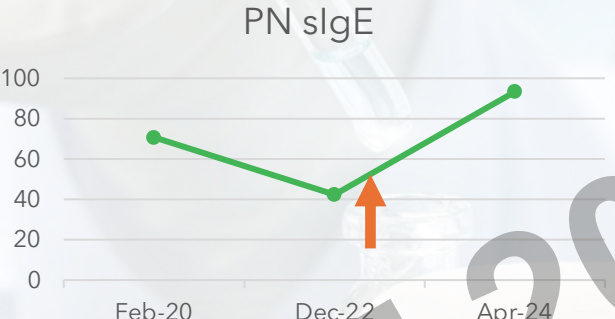
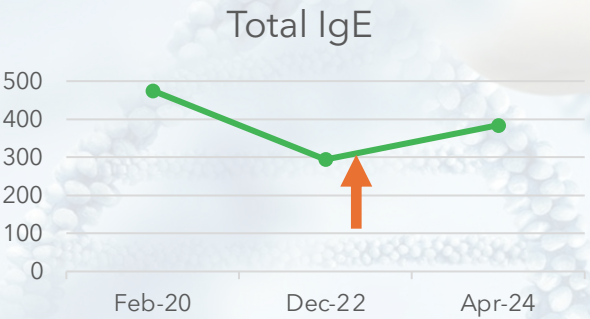
PN Protein: 300 mg 600 mg 7,000 mg

Case #2

- Started OIT at age of 14 y/o
- History of multiple nut allergies, with anaphylaxis and Epipen use
- Before OIT: peanut sIgE: 42.3 kU/L; Ara h2: 42.1; Ara h6: 26.6
- On OIT, at a dose of 516 mg peanut protein:
 - sIgE: 93.3 kU/L
 - Ara h2: 54.1 kU/L
 - Ara h6: 43.4 kU/L

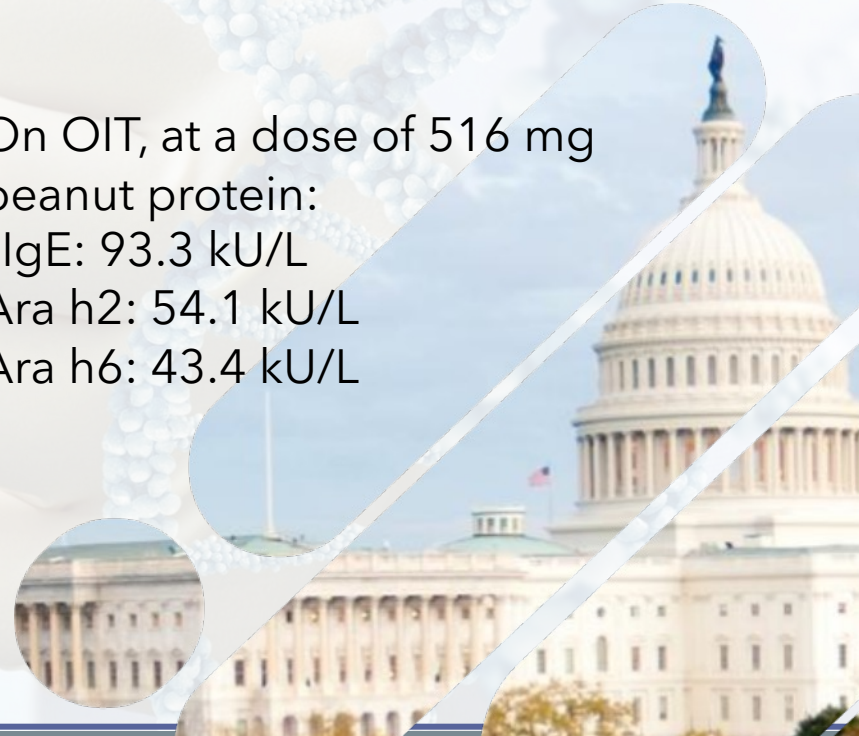


Total IgE, sIgE, cIgE, and BAT: Correlation with OIT



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sIgE: 93.3 kU/L
Ara h2: 54.1 kU/L
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EAST 2024



Diagnostic Tests in OIT

- Skin Prick Tests (SPT)
- Specific IgE to extracts (sIgE)
- Specific IgE to components (cIgE)
- Specific IgE to allergen peptides (sIgE-ap)
- Basophil activation test (BAT)
- Mast cell activation test (MAT)
- Specific IgG4 to extracts (sIgG4)
- T cell activation tests or T cell transformation tests (TAT or TTT)
- Food Patch Tests

Skin Prick Tests (SPT) and sIgE

- Detect the presence of specific IgE
- Positive cut-off point
 - $\geq 3\text{mm}$ (neg control) and $\geq 0.35\text{ kU/L}$
 - High sensitivity and NPV; Low specificity and PPV
- Food specific cut off point with high PPV
- Very useful tools for initial diagnosis
- Not ideal for follow up OIT progress



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Skin Prick Tests vs Specific IgE

	95% PPV			
	SPT (mm)		sIgE (kU/L)	
	≤2 y/o	>2 y/o	≤2 y/o	>2 y/o
Peanut	≥6	≥8		15-34
Tree nuts		≥8		20
Egg	≥4	≥7	2	7
Milk	≥6	≥8	5	15
Sesame		≥8		50 (86)

Du Toit G, et al, *Pediatr Allergy Immunol.* 2009, 20(4):309-19.

Foong RX, et al. *J Allergy Clin Immunol Pract.* 2021 Jan;9(1):71-80.

Specific IgE to Allergen Components (cIgE)

- Component-resolved diagnostics (CRD): measures IgE to specific proteins within a food (cIgE)
- Clinically significant sensitization (risk for systemic reaction) compared with clinically irrelevant crossreactivity (oral allergy syndrome)
- Storage protein vs Profilin and Lipid Transfer Protein

Specific IgE to Allergen Components (cIgE)

	Food Allergies	IgE (kU/L)	PPV	Specificity
Casein	Baked Milk	20.2	69%	
OvoMucoid	Baked egg	50	95%	
	Cooked egg	26.6	95%	
	Raw egg	5.21	95%	
Ara h2	Peanut	0.35 – 42.2	90 – 95%	
Ana o3	Cashew	0.16	98%	95%
Cor a9	Hazelnut	1 - 2	79%	100%
Cor a14		0.72 – 47.8	87%	90%
Gly m8	Soy	13.55	89%	74%
Tri a 19	Wheat	0.04 - 41	100%	81%

Foong RX, et al. *J Allergy Clin Immunol Pract.* 2021 Jan;9(1):71-80.

Specific IgE to allergen peptides (Epitope mapping)

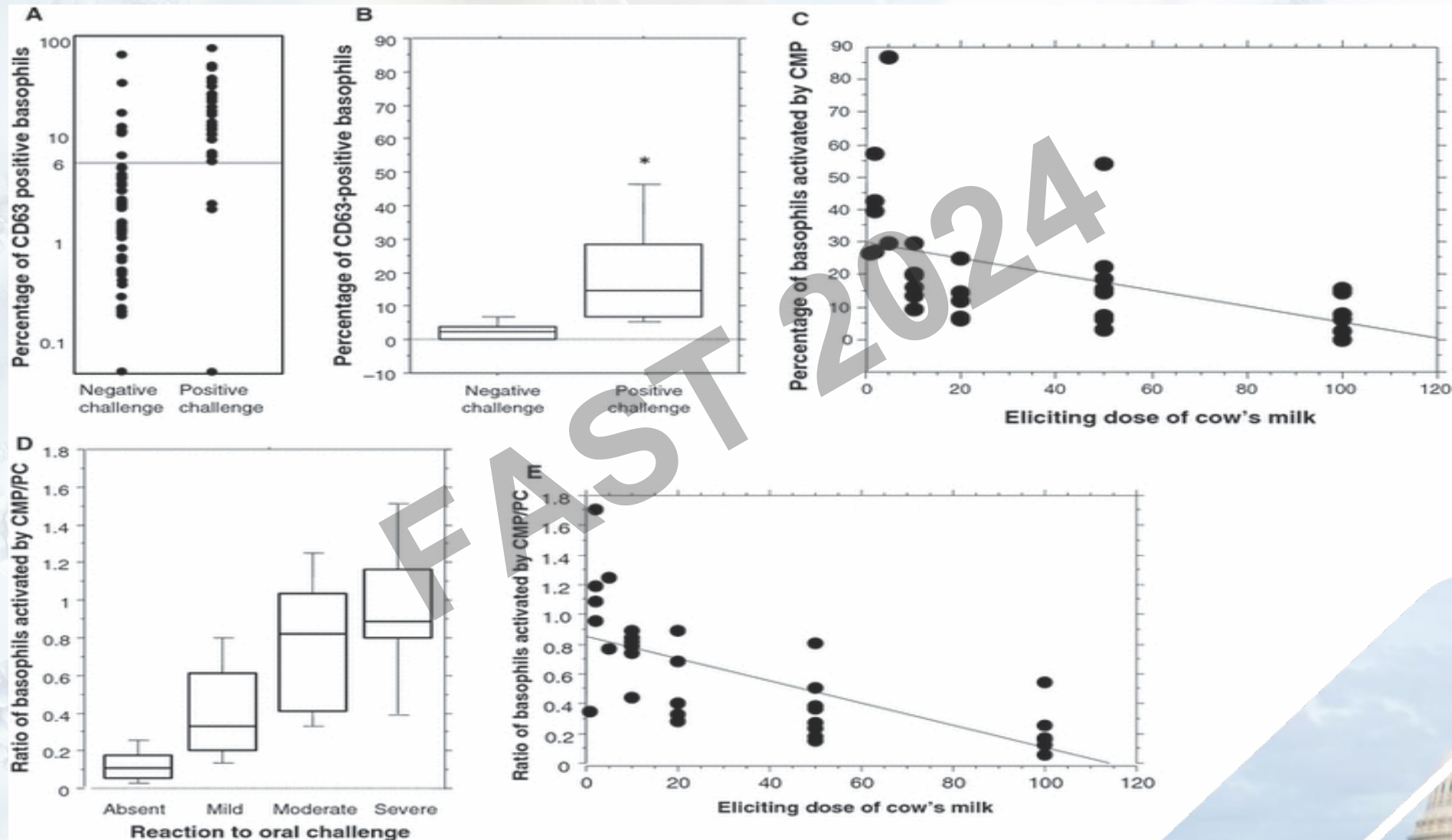
- Identify specific epitopes that IgE binds within individual allergens
- Clinical relevance and prognosis
- Methodology: Spot Membranes; Microarrays, Luminex-based, etc.
- Peanut >> Milk >> Shellfish > Legumes
 - Predict the likelihood of successful OIT, milk and peanut
 - More useful when interpreted in combination with other assays, sIgE, cIgE, and BAT, etc.
- Not widely used, more studies are needed

Basophil Activation Tests (BAT)

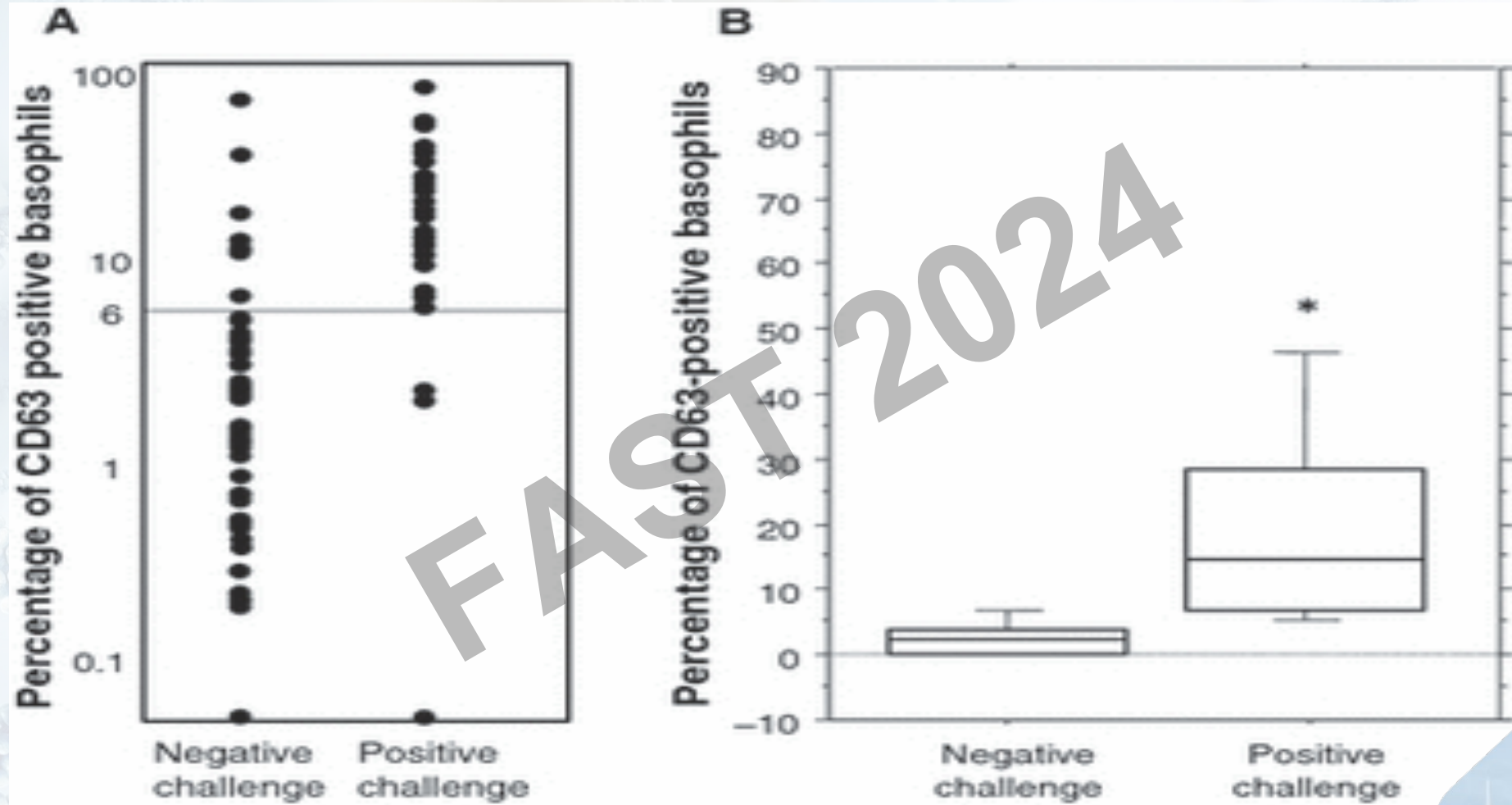
- Functional Assay, virtual challenge test for individual allergens
- CD63 and/or CD203c upregulation upon stimulation
- High Specificity (98.5%, LEAP, LEAP-On, and PAS)
- In a CMA studies:
 - Sensitivity of BAT: 91%
 - Specificity of BAT: 90%
 - Sensitivity of sIgE for milk: 41%



Benefit of BAT in deciding when to reintroduce cow's milk in allergic children

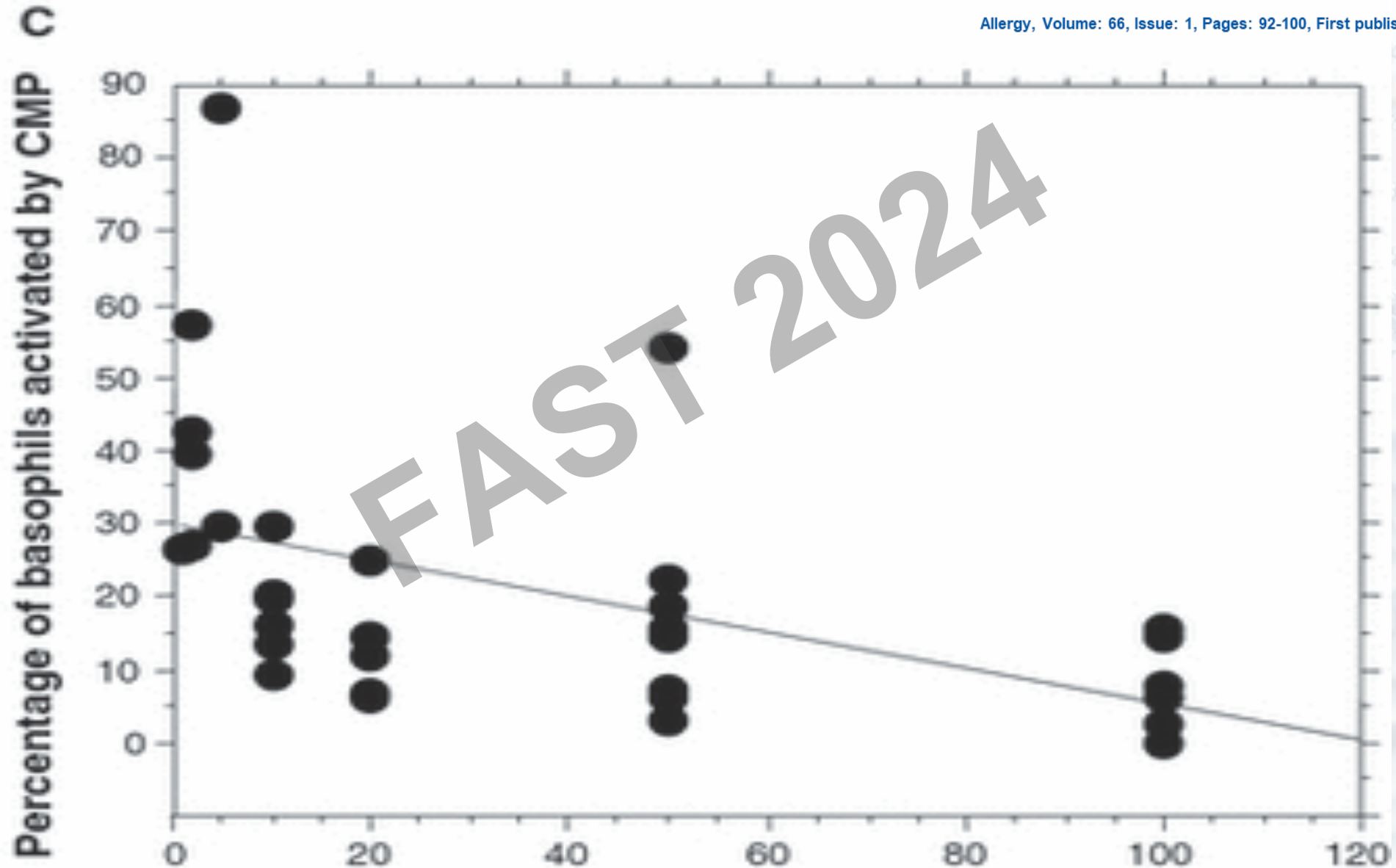


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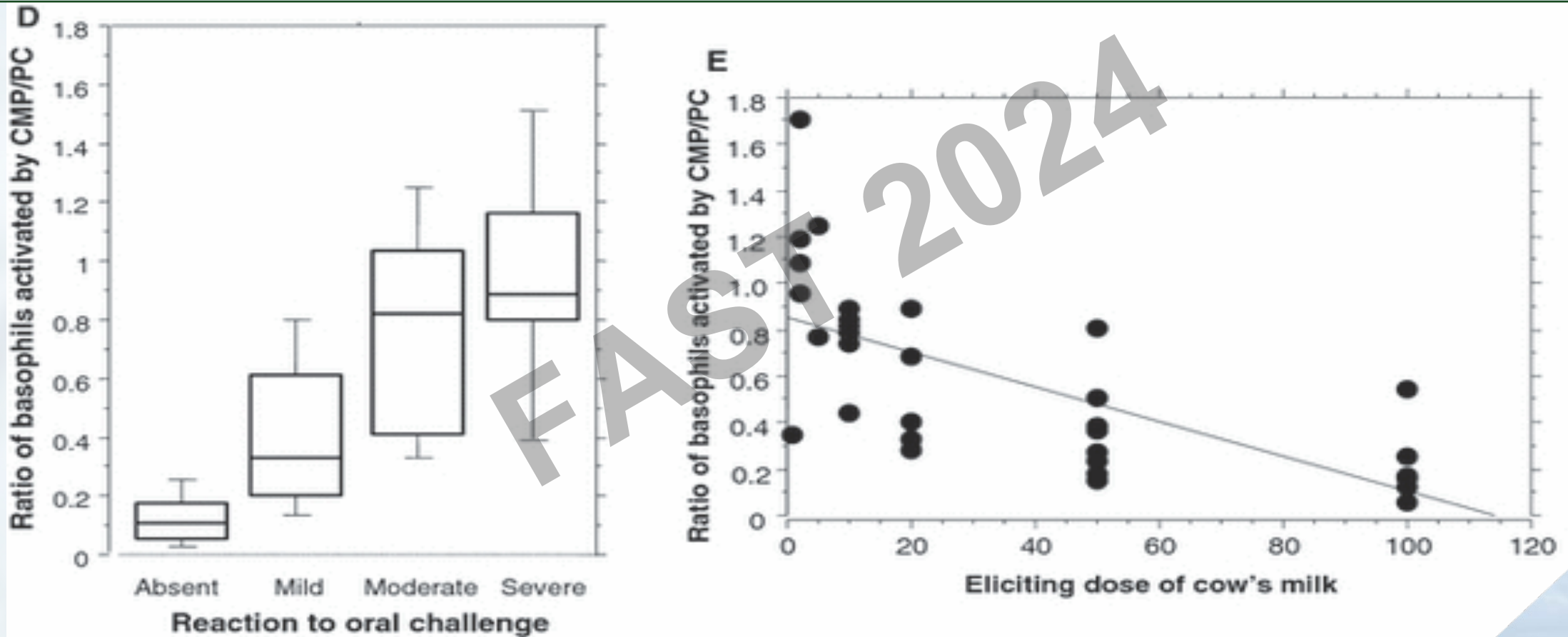


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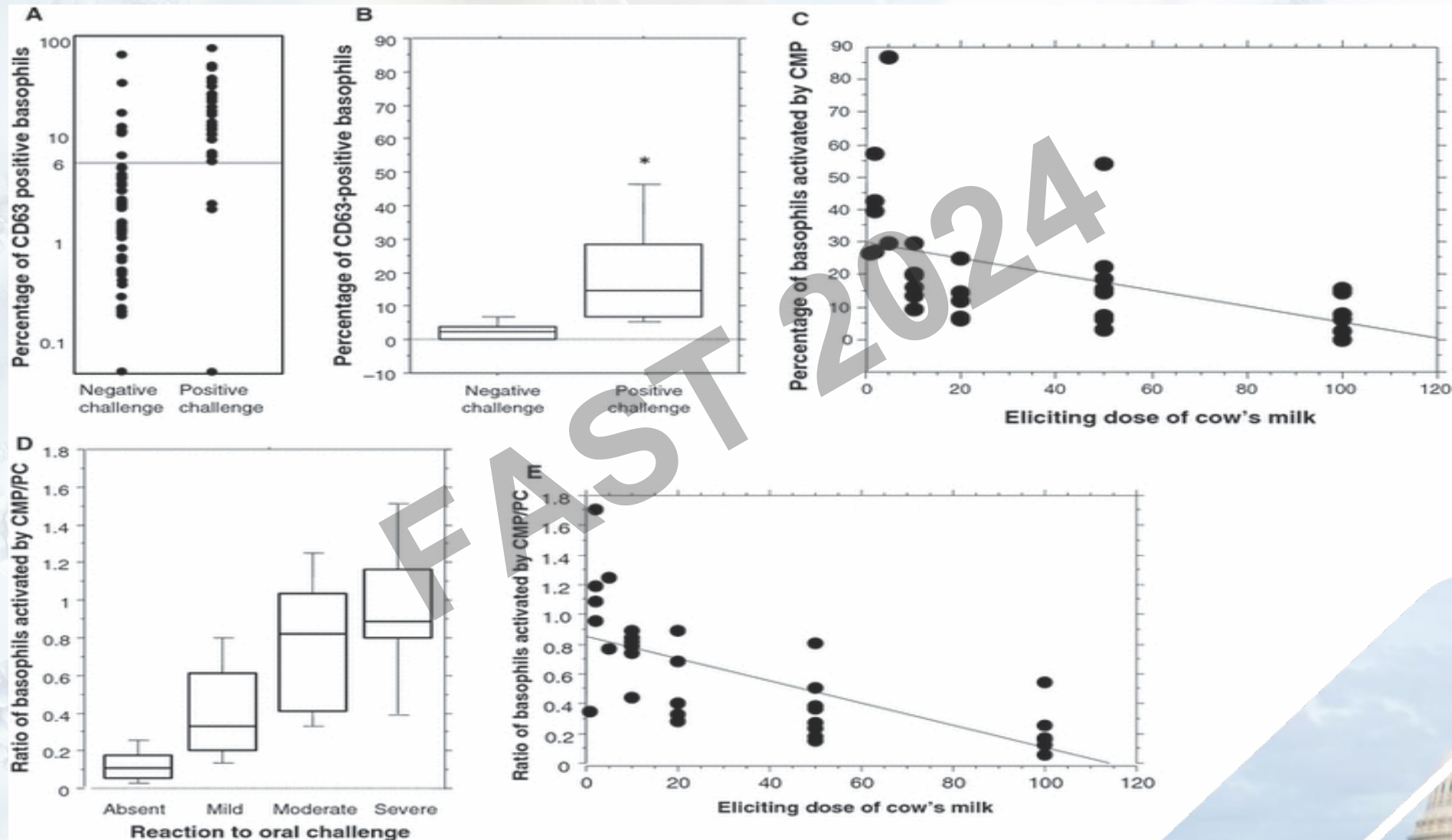
Allergy, Volume: 66, Issue: 1, Pages: 92-100, First published: 03 December 2010,



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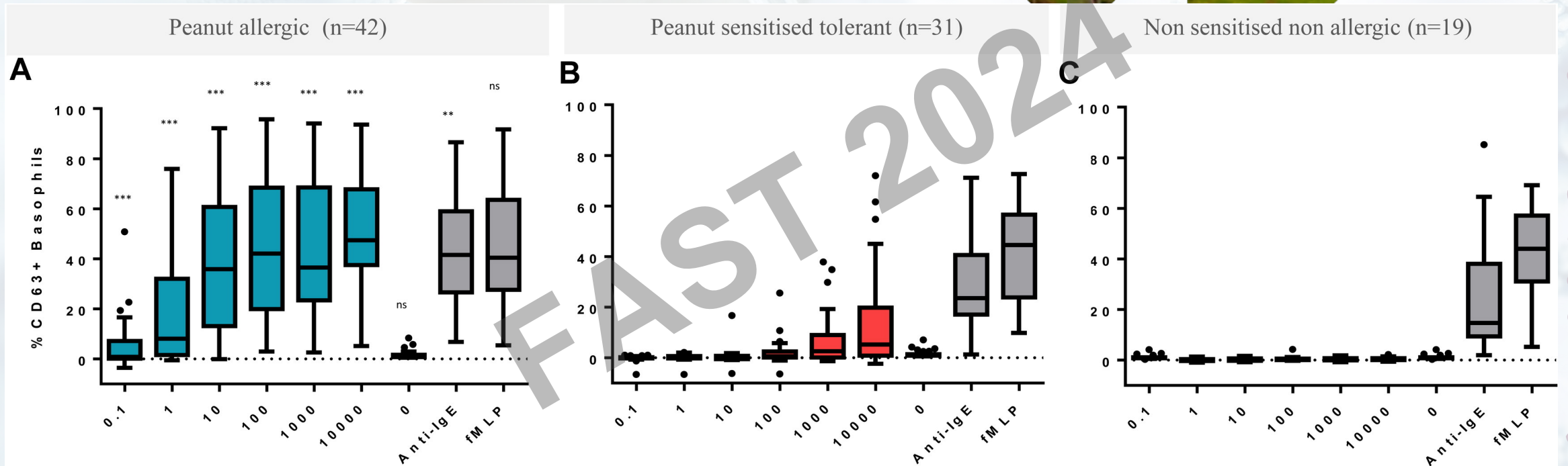
Correlation between OFC (CMA) and BATs

BAT cut-off: percentage of basophils activated by CMP	Se (%)	Spe (%)	PPV (%)	NPV (%)	Efficiency (%)	Correlation factor ϕ with oral challenge	P (χ^2)
2%	97	51	48	97	65	0.463	<0.0001
4%	91	75	63	95	80	0.612	<0.0001
5%	91	82	70	95	85	0.686	<0.0001
6%	91	90	81	96	90	0.752	<0.0001
8%	70	89	74	86	83	0.595	<0.0001
12%	64	92	78	84	83	0.586	<0.0001
15%	45	94	79	79	79	0.480	<0.0001

Comparing OFC and Different PN Tests

Tests	PPV (%)	False Positives	False Negative
SPT	75	1	1
slgE	55	3	3
Ara h2	79	1	2
BAT	86	2	1

BAT for PN Allergy Assessment



Comparison of Different Food Allergy Tests

	Advantages	Disadvantages
SPT	<ul style="list-style-type: none"> Quick result High sensitivity and NPV Allow testing with fresh food 	<ul style="list-style-type: none"> Low specificity; low PPV Risk for systemic Rx (Rare) Need to stop AH Clear skin (i.e. no active eczema)
slgE	<ul style="list-style-type: none"> More quantitative Standardized methodology High Sensitivity and NPV Not affected by AH use Sample can be stored 	<ul style="list-style-type: none"> Low specificity; low PPV More expensive than SPT Limited allergens available
clgE	<ul style="list-style-type: none"> High specificity Differentiate sensitization vs Systemic reactions 	<ul style="list-style-type: none"> Not more informative except for PN, HN Limited allergens available Sensitization profile: pt specific
slgE-AP	<ul style="list-style-type: none"> May increase dx accuracy 	<ul style="list-style-type: none"> Only detects sequential epitopes Tested in isolation (not the whole allergen)
BAT	<ul style="list-style-type: none"> High Sensitivity and specificity High PPV and NPV No risk for allergic reaction No need to stop AH 	<ul style="list-style-type: none"> Ideally <24 hr after collection 10 – 15% nonresponders More expensive than SPT, slgE and clgE per test
MAT	<ul style="list-style-type: none"> High specificity and PPV Can be stored No risk for allergic reaction No need to stop AH 	<ul style="list-style-type: none"> Lower sensitivity and NPV than BAT More expensive than BAT.

Conclusion: Food allergy testing

- Clinical history: Very important
- Initial screening, establishing diagnosis
 - SPT, sIgE, and cIgE should be considered as first and second line tests
 - Understand the pros and cons of each test methods
- BAT is a very important tool particularly in OIT patients
- sIgE-ap (Epitope mapping): limited clinical use, high cost, limited studies, and not ready for wide clinical application
- MAT: insurance coverage is a major challenge in US. More in clinical studies and in Europe.

Thankyou.

FAJST 2024