

## SUPPLEMENTARY MATERIAL

**Table 1s.** Supplementary material- Baseline characteristics of the recruited infants (n=57)

<b>Mean age (at inclusion)</b>	0.6 months (range 0.2-1.17)		
<b>Sex</b>	Male	47.1%	
	Female	52.9%	
<b>Ethnicity</b>	Caucasian	84%	
	Hispanic	16%	
<b>Pregnancy</b>	Normal	86.3%	
	Pregnancy complications*	13.7%	
<b>Delivery</b>	Vaginal	80.4%	
	c-section	19.6%	
<b>Weight at the beginning of the intervention, mean (g)</b>	7759.04 (SD 1256.33)		
<b>Height at the beginning of the intervention, mean (cm)</b>	66.92 (SD 6.06)		
<b>Vaccination (per calendar)</b>	100%		
<b>Breastfeeding</b>	98% (mean duration 7 months)		
<b>Breastfeeding maintained at inclusion</b>	68.6%		
<b>Atopic dermatitis</b>	54.9%		
<b>Wheezing</b>	9.8% (confirmed bronchiolitis 7%)		
<b>Allergy to other foods</b>	15.5% has been diagnosed of other food allergies		
<b>Symptoms with milk intake (symptoms that led to diagnosis of milk allergy)</b>	<b>oFASS-3</b>	<b>oFASS-5</b>	<b>% of patients</b>
	<b>Mild</b>	<b>Grade 1</b>	4%
	<b>Moderate</b>	<b>Grade 2</b>	53%
		<b>Grade 3</b>	43%
	<b>Severe</b>	<b>Grade 4</b>	0
<b>Grade 5</b>		0	

\*Gestational diabetes (4 pregnancies), hypothyroidism (5 pregnancies), shortened cervix (1 pregnancy). Polyhydramnios (1 pregnancy).

SD, standard deviation

**Table 2s.** Describes the severity of the reaction graded by o-FASS-5 score, discriminating between the setting, either hospital or home, and treatment received. Reactions which happened on step 1 are highlighted in pink, step 2 in magenta, step 3 in blue and step 4 in green.

Patient	Step	oFASS-5	Setting	Treatment received	Current status
01011	2B	Grade 4	Hospital	OCS, b2	Tolerates milk.
	3A	Grade 4	Hospital	AH, OCS, b2, adrenaline	
01014	2A	Grade 1	Hospital	AH, OCS	Tolerates milk.
	2A	Grade 1	Hospital	AH	
	4A	Grade 1	Hospital	AH	
	4A	Grade 1	Home	Resolved without treatment	
02006	1A	Grade 2	Hospital	AH, OCS	Tolerates milk.
02011	1A	Grade 4	Hospital	AH, OCS	Study withdrawal. Reactive
	1B	Grade 4	Hospital	AH, OCS, adrenaline	
	2A	Grade 4	Hospital	AH, OCS	
	2B	Grade 4	Hospital	AH, OCS	
03002	2B	Grade 4	Hospital	AH, b2	Tolerates milk.
	4A	Grade 4	Hospital	AH, OCS, b2, adrenaline	
	4A	Grade 2	Home	AH	
	4A	Grade 4	Home	b2	
	4B	Grade 4	Hospital	AH	
	4B	Grade 1	Hospital	Resolved without treatment	
	4B	Grade 4	Hospital	AH, OCS, b2, adrenaline	
03004	3A	Grade 2	Hospital	AH	Tolerates milk.
	4A	Grade 4	Hospital	AH	
	4B	Grade 2	Hospital	Resolved without treatment	
	4B	Grade 1	Hospital	Resolved without treatment	

	4B	Grade 1	Hospital	AH	
03008	4A	Grade 4	Hospital	AH, OCS	Tolerates milk.
	4A	Grade 4	Hospital	AH, OCS	
	4A	Grade 4	Hospital	OCS, b2	
03010	2A	Grade 1	Home	Resolved without treatment	Tolerates milk.
	2B	Grade 4	Hospital	AH, OCS, b2	
	2B	Grade 4	Hospital	AH, b2	
	2B	Grade 4	Hospital	AH, OCS, b2	
	3A	Grade 4	Hospital	AH, OCS, b2	
	3A	Grade 4	Hospital	AH, OCS, b2, adrenaline	
	4B	Grade 2	Hospital	AH	
	4B	Grade 2	Hospital	AH	

Accepted

**Table 3s.** Supplementary material- Baseline (visit 1) allergological evaluation of the recruited babies (n=57)

<b>Determination</b>	<b>Median [P25, P75]</b>
<b>SPT milk</b> (mm)	4.5 [3.25, 6.5]
<b>SPT ALA</b> (mm)	5 [3.75, 7.25]
<b>SPT BLG</b> (mm)	5.5 [3.75, 7.25]
<b>SPT CAS</b> (mm)	4.25 [0, 6]
<b>SPT BSA</b> (mm)	0 [0, 4.13]
<b>SPT milk</b> (mm)	4.5 [3.25, 6.5]
<b>IgE total</b> (KU/l)	18.5 [7.75, 38.48]
<b>IgE milk</b> (KU/l)	1.64 [0.53, 4.47]
<b>IgE ALA</b> (KU/l)	0.29 [0.02, 1.12]
<b>IgE BLG</b> (KU/l)	0.53 [0.22, 1.79]
<b>IgE CAS</b> (KU/l)	0.28 [0.09, 1.54]

ALA:  $\alpha$ -lactalbumin, BLG:  $\beta$ -lactoglobulin, CAS: casein, BSA: bovine serum albumin.

Skin-prick test were performed with commercial extracts (Roxall Group, Hamburg, Germany). Total and specific IgE were determined using ImmunoCAP (Thermo Fisher Scientific, Waltham, MA, USA; manufactured: Phadia AB, Uppsala, Sweden)

**Table 4s.** Supplementary material- Allergological evaluation of the patients that received the intervention (N=26)

<b>Determination</b>	<b>1st VISIT</b>	<b>2nd VISIT</b>
	<b>Median [P25, P75]</b>	<b>Median [P25, P75]</b>
<b>SPT milk</b> (mm)	5 [3.5, 6.75]	7.5 [5.6, 9]
<b>SPT ALA</b> (mm)	5.5 [4, 8]	7.5 [6.1, 9.3]
<b>SPT BLG</b> (mm)	6 [4.25, 7.5]	6 [4.3, 7.8]
<b>SPT CAS</b> (mm)	4 [0, 7]	5.5 [4.5, 8]
<b>Total IgE</b> (KU/l)	32.9 [17.8, 53.3]	82.5 [29.8, 204.3]
<b>sIgE milk</b> (KU <sub>A</sub> /l)	2.9 [1.2, 7.1]	2.5 [1.3, 17.9]
<b>sIgE ALA</b> (KU <sub>A</sub> /l)	0.54 [0.02, 1.15]	0.9 [0.16, 4.9]
<b>sIgE (BLG)</b> (KU <sub>A</sub> /l)	0.75 [0.27, 2.3]	0.65 [0.3, 5.3]
<b>sIgE (CAS)</b> (KU <sub>A</sub> /l)	0.45 [0.09, 4.1]	1.7 [0.09, 6.45]

SPT, skin prick tests; ALA:  $\alpha$ -lactoalbumin, BLG:  $\beta$ -lactoglobulin, CAS: casein, BSA: bovine serum albumin; sIgE, specific IgE

**Table 5s.** Supplementary material-SPT, total IgE and sIgE values comparison between patients that did not experience reactions during the ML and those who had reactions in visit 1 and visit 2.

Determination	1st VISIT			2nd VISIT		
	NO REACTIONS	REACTIONS	p-value	NO REACTIONS	REACTIONS	p-value
	Median [P25, P75]			Median [P25, P75]		
<b>SPT milk</b> (mm)	5 [4, 7]	5 [3, 6.37]	0.726	6.75 [4.75, 7.87]	9 [6.62, 10.12]	<b>0.024</b>
<b>SPT ALA</b> (mm)	5.5 [2, 8.25]	5.5 [4.12, 7.5]	0.953	7 [5.12, 8]	8.25 [7.12, 9.87]	0.131
<b>SPT BLG</b> (mm)	6.5 [3.5, 7.25]	5.5 [4.62, 8.25]	0.683	6.25 [3.62, 6.87]	6 [5.12, 9.5]	0.816
<b>SPT CAS</b> (mm)	4 [0, 7]	3 [0, 7.75]	0.760	5.25 [4, 7.5]	7 [5.12, 8.37]	0.152
<b>Total IgE</b> (KU/l)	37 [19, 49]	30 [17.3, 79]	0.916	54 [6, 102]	188 [80, 284]	<b>0.041</b>
<b>sIgE milk</b> (KU <sub>A</sub> /l)	1.69 [1.03, 4.47]	10.25 [1.94, 16.3]	<b>0.035</b>	1.54 [0.64, 4.23]	18.4 [8.76, 42.90]	<b>&lt;0.01</b>
<b>sIgE ALA</b> (KU <sub>A</sub> /l)	0.28 [0, 1.11]	1.03 [0.15, 7.6]	0.140	0.44 [0, 1.01]	4.91 [1.20, 18.55]	<b>&lt;0.01</b>
<b>sIgE (BLG)</b> (KU <sub>A</sub> /l)	0.5 [0.23, 2.29]	1.57 [0.88, 2.93]	0.201	0.42 [0.22, 0.91]	5.29 [0.80, 16.27]	<b>0.011</b>
<b>sIgE (CAS)</b> (KU <sub>A</sub> /l)	0.32 [0.08, 1.53]	2.67 [0.18, 12.50]	0.127	0.16 [0.03, 1.54]	6.16 [3.35, 48.20]	<b>&lt;0.01</b>

ALA:  $\alpha$ -lactoalbumin, BLG:  $\beta$ -lactoglobulin, CAS: casein, BSA: bovine serum albumin; sIgE, specific IgE. Comparisons were calculated by using Mann-Whitney U test. P-values below 0.05 were considered statistically significant.

There were no statistically significant differences regarding severity of the initial reaction with milk, age, sex, atopic dermatitis or occurrence of wheezing.

**Table 6s.** Supplementary material- Description of the symptoms experienced during reactions. Reactions that happened at home are highlighted in light blue.

PATIENT	STEP	SETTING	GRADE	SYMPTOMS
1011	2B	Hospital	Grade 4	Cough
	3A	Hospital	Grade 4	Cough, urticaria, angioedema, rhinitis and conjunctivitis
1014	2A	Hospital	Grade 1	Peri-labial erythema and two isolated hives
	2A	Hospital	Grade 1	Peri-labial erythema and pruritus
	4A	Hospital	Grade 1	Peri-labial erythema
	4A	Home	Grade 1	Peri-labial erythema and peri-labial hives
2006	1A	Hospital	Grade 2	Urticaria
2011	1A	Hospital	Grade 4	Cough, urticaria and flushing
	1B	Hospital	Grade 4	Cough, rhinitis
	2A	Hospital	Grade 4	Cough, urticaria and rhinitis
	2B	Hospital	Grade 4	Cough, rhinitis
3002	2B	Hospital	Grade 4	Cough, rhinitis and urticaria
	4A	Hospital	Grade 4	Cough, rhinitis and urticaria
	4A	Home	Grade 2	Facial erythema and pruritus
	4A	Home	Grade 4	Cough
	4B	Hospital	Grade 4	Cough and flushing

	4B	Hospital	Grade 1	Peri-labial erythema
	4B	Hospital	Grade 4	Cough, urticaria and vomits
<b>3004</b>	3A	Hospital	Grade 2	Urticaria
	4A	Hospital	Grade 4	Cough, wheezing and urticaria
	4B	Hospital	Grade 2	Abdominal pain
	4B	Hospital	Grade 1	Peri-labial erythema
	4B	Hospital	Grade 1	Oral itching and peri-labial erythema
<b>3008</b>	4A	Hospital	Grade 4	Cough and rhinitis
	4A	Hospital	Grade 4	Cough and rhinitis
	4A	Hospital	Grade 4	Cough
<b>3010</b>	2A	Home	Grade 1	peri-labial erythema
	2B	Hospital	Grade 4	Cough, rhinitis and conjunctivitis
	2B	Hospital	Grade 4	Cough urticaria and vomits
	2B	Hospital	Grade 4	Cough and rhinitis
	3A	Hospital	Grade 4	Cough
	3A	Hospital	Grade 4	Vomits, diarrhea, rhinitis and conjunctivitis
	4B	Hospital	Grade 2	Flushing
	4B	Hospital	Grade 2	Flushing