

Table EI: Baseline characteristics of the children

Characteristic	Overall (N=100)
Age (years)	11.25 (6 to 16.2)
Male	50 (50.0)
Overweight	9 (9.0)
Allergic comorbidities	
Allergic rhinitis	89 (89.0)
Atopic dermatitis	49 (49.0)
Food allergy	24 (24.0)
Food allergy + atopic dermatitis	11 (11.0)
Total IgE (kU.L ⁻¹)	742 (49 to 5000)
Eosinophil level (/mm ³)	500 (100 to 4000)
>2 allergic sensitizations	42 (42.0)
Asthma control	
Controlled	0
Partially controlled	10 (10.0)
Uncontrolled	90 (90.0)
Exacerbations	
Rate, previous year	3 (0 to 14)
> 2 exacerbations, previous year	63 (63.0)
History of hospitalization	31 (31.0)
Lung Function Tests	
FEV1 preB2 (% predictive value)	85.7 ± 20.9
FEV1/FVC preB2 (absolute value)	75.6 ± 11.7
FEV1 postB2 (% predictive value)	98.5 ± 22.6
FEV1/FVC post B2 (absolute value)	83.1 ± 9.6
Treatment of asthma	
ICS dose equivalent fluticasone (µg/day)	812 (335)
Dose of omalizumab/injection	325 (130)
Frequency of administration	
every 2 weeks	57 (57.0)
every 4 weeks	43 (43.0)
Patients with total IgE level higher than those in the dosing table*	33 (33%)

Values are presented as mean ± SD, median (range) or number (percentage).

* According to the omalizumab dosing table, the highest total IgE level was 700 kU/L up to January 2010 and 1500 kU/L after January 2010.

ICS: inhaled corticosteroid; FEV1: forced expiratory volume in one second; FVC: forced vital capacity

Table E2: Univariate associations between omalizumab discontinuation, baseline characteristics and asthma outcomes at 24 months of treatment[§]

	HR (CI95%)	P-value
<i>Baseline characteristics</i>		
Age	1.06 (0.95 to 1.18)	0.27
Male	0.59 (0.30 to 1.16)	0.13
BMI z-score	1.10 (0.87 to 1.38)	0.43
Rate of exacerbations over the previous year	1.11 (0.97 to 1.27)	0.12
Partially controlled	1.19 (0.42 to 3.38)	0.75
FEV1 preB2 (% predictive value)	1.01 (0.99 to 1.02)	0.64
ICS dose equivalent fluticasone	1.01 (0.92 to 1.11)	0.87
Allergic rhinitis	1.15 (0.56 to 2.37)	0.70
Atopic dermatitis	0.22 (0.08 to 0.57)	0.002
Food allergy	0.88 (0.40 to 1.91)	0.74
Total IgE ≥ 1500 (kU/L)	1.48 (0.71 to 3.09)	0.30
Eosinophil level ≥ 500 (/mm ³)	0.84 (0.41 to 1.72)	0.63
Polysensitization	0.98 (0.49 to 1.93)	0.95
Dose of Omalizumab/injection*	0.99 (0.88 to 1.12)	0.87
<i>Asthma outcomes at 24 months</i>		
Rate of exacerbations over the previous year	1.41 (0.85 to 2.34)	0.18
Controlled	1.23 (0.59 to 2.55)	0.57
FEV1 preB2 (% predictive value)	1.01 (0.99 to 1.04)	0.29
FEV1 postB2 (% predictive value)	1.02 (0.99 to 1.04)	0.15
FEV1/FVC preB2 (absolute value)	1.03 (0.98 to 1.07)	0.22
FEV1/FVC post B2 (absolute value)	1.02 (0.98 to 1.07)	0.28
ICS dose	1.02 (0.91 to 1.15)	0.72

[§] 24 months since treatment initiation; * Hazard ratio per 100 unit increase

HR: Hazard ratio; CI: confidence interval; FEV1: forced expiratory volume in one second;
ICS: inhaled corticosteroid; FVC: forced vital capacity

Table E3: Characteristics of the eight patients for whom omalizumab treatment was discontinued and restarted

	Patients (number/gender)							
Characteristics	1, M	2, F	3, F	4, F	5, M	6, M	7, F	8, M
Age (baseline)	7Y 10Mo	10Y 2Mo	11Y 1Mo	7Y 4Mo	11Y 8Mo	10Y 4Mo	15Y 7Mo	11Y 4Mo
Total IgE (kU/L)	226	399	1556	1627	950	465	897	2715
Eosinophils (/mm ³)	700	800	660	1000	850	600	600	800
Allergic rhinitis	+	+	-	+	-	+	+	+
Atopic Dermatitis	+	+	+	-	-	-	-	+
Food allergy	+	0	0	+	0	0	+	+
Rate of exacerbations over the previous year (baseline)	2	3	4	2	2	4	6	3
FEV1 % PV preB2 (baseline)	95	82	79	80	93	75	70	83
FEV1/CV preB2 (baseline)	78	81	75	73	76	80	83	77
Omalizumab dose (mg)	150/4weeks	225/2weeks	225/2weeks	300/2weeks	450/2weeks	300/4weeks	375/2weeks	375/2weeks
Duration of treatment (months)	41	26	28	37	24	44	24	72
Duration before restarting (months)	3	17	7	5	7	9	17	4
Reason for restarting	LAC /3ex	LAC/2ex	LAC/2ex	LAC/3ex	LAC/2ex	LAC/4ex	LAC/6ex	LAC/2ex
Response to restarting (last visit)	C	C	C	C	C	C	PC	C

M= male; F= female; Y = year; Mo = month; FEV1 = forced expiratory volume in one second; PV = predicted value; LAC: loss of asthma control; C = controlled; PC= partially controlled; ex = exacerbation

Table E4: Adverse events recorded during treatment with omalizumab

Number of patients with at least one adverse event	38
Painful injection	17
Headache	11
Fatigue	10
Local reaction at injection site	10
Rash	3
Abdominal pain	2

Table E5: Baseline characteristics and asthma outcomes at 24 months after treatment with omalizumab in children with treatment maintenance and children with treatment discontinuation (2 groups, each of 30 children matched for length of follow-up).

	Maintenance (N=30)	Discontinuation (N=30)	P-value
Follow-up duration (months)	46.2 (31.5 to 90.3)	55.8 (31.5 to 90.3)	-
Treatment duration (months)	-	41 (25 to 72)	-
Age (years)	10.3 ± 3.9	10.8 ± 2.7	0.52
Male	11 (36.7)	19 (63.3)	0.03
Overweight	4 (15.4)	3 (11.5)	0.66
Allergic comorbidities			
Allergic rhinitis	26 (86.7)	20 (66.7)	0.067
Atopic dermatitis	20 (66.7)	4 (13.3)	<0.0001
Food allergy	6 (20.0)	7 (23.3)	0.76
Food allergy + atopic dermatitis	3 (10.0)	5 (16.7)	0.48
Total IgE (kU.L ⁻¹)	786 (100 to 4116)	704 (80 to 3762)	0.76
Eosinophil level (/mm ³)	600 (100 to 4000)	500 (100 to 1300)	0.77
>2 allergic sensitizations	12 (40.0)	18 (60.0)	1.00
Baseline			
Asthma control			
Controlled	0	0	0.32
Partially controlled	1 (3.3)	3 (10.0)	
Uncontrolled	29 (96.7)	27 (90.0)	
Exacerbations			
Rate, previous year	3 (0 to 8)	3 (0 to 12)	0.28
History of hospitalization	9 (30)	10 (33.3)	0.78
Respiratory Function Tests			
FEV1 preB2 (% predictive value)	74.0 ± 18.8	87.3 ± 20.4	0.01
FEV1/FVC preB2 (%)	69.6 ± 13.6	76.4 ± 10.2	0.02
FEV1 postB2 (% predictive value)	92.5 ± 21.9	100.9 ± 21.0	0.13
FEV1/FVC post B2 (%)	79.5 ± 10.1	84.2 ± 9.8	0.04
Treatment of asthma			
ICS dose equivalent fluticasone (µg/j)	1000 (250 to 1250)	850 (320 to 1600)	0.52
Asthma outcomes at 24 months			
Asthma control			
Controlled	15 (51.7)	20 (69.0)	0.72
Partially controlled	13 (44.9)	8 (27.6)	
Uncontrolled	1 (3.4)	1 (3.4)	
Exacerbations			
Rate, previous year	0 (0 to 3)	0 (0 to 2)	0.68
Respiratory Function Tests			
FEV1 preB2 (% predictive value)	93.1 ± 16.4	92.9 ± 12.2	0.91
FEV1/FVC preB2 (%)	75.6 ± 8.2	78.8 ± 6.8	0.04
FEV1 postB2 (% predictive value)	100.0 ± 14.3	100.6 ± 14.3	0.92
FEV1/FVC post B2 (%)	81.0 ± 9.8	82.5 ± 6.3	0.34
Treatment of asthma			
ICS dose equivalent fluticasone (µg/j)	450 (200 to 1000)	500 (100 to 1000)	0.45
Decrease ≥ 50% from baseline ICS dose (%)	16 (53%)	14 (47%)	0.60

Values are presented as mean ± SD, median (range) or count (percentage). ICS: inhaled corticosteroid; FEV1: forced expiratory volume in one second; FVC: forced vital capacity

Table E6: Baseline characteristics and asthma outcomes at 24 months after treatment with omalizumab in the 65 children with omalizumab maintenance according to their inclusion status in the nested-case-control study.

	Not included (N=35)	Included (N=30)	p-value
Follow-up duration (months)	25.4 (24.3 to 36.5)	46.2 (31.5 to 90.3)	<0.0001
Age (years)	10.8 ± 3.6	10.3 ± 3.9	0.58
Male	18 (51.4)	11 (36.7)	0.23
Overweight	2 (5.9)	4 (15.4)	NA
Allergic comorbidities			
Allergic rhinitis	31 (88.6)	26 (86.7)	1.00
Atopic dermatitis	26 (74.3)	20 (66.7)	0.50
Food allergy	9 (25.7)	6 (20.0)	0.59
Food allergy + atopic dermatitis	3 (8.6)	3 (10.0)	NA
Total IgE (kU.L ⁻¹)	823 (49 to 5000)	786 (100 to 4116)	0.87
Eosinophil level (/mm ³)	500 (100 to 1100)	600 (100 to 4000)	0.41
>2 allergic sensitization	16 (45.7)	12 (40.0)	0.64
Baseline			
Asthma control			
Controlled	0	0	0.21
Partially controlled	5 (14.3)	1 (3.3)	
Uncontrolled	30 (85.7)	29 (96.7)	
Exacerbations			
Rate, previous year	3 (0 to 14)	3 (0 to 8)	0.77
History of hospitalization	33 (97.1)	30 (100.0)	NA
Respiratory Function Tests			
FEV1 preB2 (% predictive value)	92.3 ± 21.0	74.0 ± 18.8	0.002
FEV1/FVC preB2 (%)	79.4 ± 10.4	69.6 ± 13.6	0.004
FEV1 postB2 (% predictive value)	99.8 ± 25.1	92.5 ± 21.9	0.23
FEV1/FVC post B2 (%)	85.4 ± 8.7	79.5 ± 10.1	0.021
Treatment of asthma			
ICS dose equivalent fluticasone (µg/j)	800 (250 to 1250)	1000 (250 to 1250)	0.69
Asthma outcomes at 24 months			
Asthma control			
Controlled	19 (54.3)	15 (51.7)	0.91
Partially controlled	14 (40.0)	13 (44.9)	
Uncontrolled	2 (5.7)	1 (3.4)	
Exacerbations			
Rate , previous year	0 (0 to 2)	0 (0 to 3)	0.58
Respiratory Function Tests			
FEV1 preB2 (% predictive value)	95.2 ± 23.4	93.1 ± 16.4	0.70
FEV1/FVC preB2 (%)	80.3 ± 10.2	75.6 ± 8.2	0.07
FEV1 postB2 (% predictive value)	101.8 ± 20.4	100.0 ± 14.3	0.69
FEV1/FVC post B2 (%)	84.1 ± 9.6	81.0 ± 9.8	0.24
Treatment of asthma			
ICS dose equivalent fluticasone (µg/day)	400 (0 to 1000)	450 (200 to 1000)	0.69

Values are presented as mean ± SD, median (range) or count (percentage). ICS: inhaled corticosteroid; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; NA: not applicable