Randomized Trial of a Yogurt-type Amino Acid–based Formula in Infants and Children With Severe Cow’s Milk Allergy

*François Payot, †Alain Lachaux, ‡Florent Lalanne, and §Nicolas Kalach

ABSTRACT

Objectives: Evaluation of a spoon-fed amino acid–based formula (AAF) with a yogurt-type texture compared to the reference oral liquid formula (Neocate). Methods: Phase III/IV, prospective, randomized (1:1), open-label, multicenter study in infants/young children (6–36 months) with severe cow’s milk protein allergy (CMA) who had consumed AAF for ≥ 1 month before the study. Patients received reference + test formula (Neocate with a yogurt-type texture for spoon-feeding: group 1) or reference formula (group 2) for 28 days. The study formulae were integrated into the patients’ usual daily diet. Efficacy on Day 0, 14, and 28 was assessed primarily in terms of symptoms associated with CMA. The evolution of symptoms, amount of formula consumed, nutritional and energy intake, anthropometric data, and tolerability were also assessed.

Results: The incidence of CMA symptoms was similar in each group (P > 0.05) on day 0, 14, and 28. For specific symptoms, there was little change from day 0 and no significant difference between groups for incidence on day 0 or evolution at day 14 or 28. There was no difference in formula consumption (day 0–day 28) between groups (P = 0.90), but nutritional value was generally higher for group 1 and calcium intake was statistically higher for group 1 (P < 0.05). Weight-for-height, weight-for-age, and body mass index-for-age z-scores were higher for group 1 than group 2 (P < 0.05). Both formulae were well tolerated.

Conclusions: There was no difference in efficacy, formula consumption, and tolerability between the new spoon-fed yogurt-type AAF formula and the reference formula, whereas significantly higher calcium intake was achieved with the new formula.

Key Words: adherence, cow’s milk protein allergy, efficacy, nutritional therapy, symptoms

What Is Known

- Infant liquid formula consumption reduces with age, presenting a challenge for cow’s milk allergy management using exclusively liquid formulae.
- Cow’s milk allergy has an incidence of 2% to 3% in infants and young children.
- Hypoallergenic formulae are not tolerated by 10% of patients with cow’s milk protein allergy, that is, infants with severe cow’s milk protein allergy, for whom amino acid–based formulae are the only alternative.
- Commonly, amino acid–based formulae taste is a complaint that reduces compliance.

What Is New

- A new amino acid–based formulae with a yoghurt-type texture and improved taste had similar efficacy and tolerability compared to amino acid–based formulae alone.
- Consumption of the new amino acid–based formulae resulted in improved calcium intake.

Cow’s milk allergy (CMA) is characterized by a combination of dermatological, gastrointestinal, and respiratory clinical symptoms, which can lead to feeding difficulties (1,2). In infants and young children CMA is one of the most common food allergies with an incidence of 2% to 3% (3). Although it can be associated anaphylactic shock or even death, there is no medicinal treatment for CMA and its management is based on the elimination of cow’s milk protein from the diet and treatment of symptoms (4–6). For breast-fed infants with CMA, mothers should be encouraged to continue breast-feeding while avoiding milk proteins from their own diet (5). If breast-feeding is, however, not possible or cannot be maintained in patients with CMA, a hypoallergenic formula should be provided that contains <1% immune-reactive protein in relation to the total nitrogen content (extensive hydrolysate formula [eHF])
Methods

Study Design and Participants

This phase III/IV, prospective, randomized, open-label study was conducted in 8 centers in France. The protocol and 1 amendment were approved by an ethics committee (Comité de Protection des Personnes Sud-Est III, Lyon, France) and by the French National Health Authority (ANSM: reference number 131476B-32). The study conformed to Good Clinical Practice (ICH-E6) and the ethical principles of the Declaration of Helsinki (Fortaleza revision, 2013), and was conducted in accordance with applicable national regulatory requirements. Before enrolment, written informed consent was obtained from at least 1 parent/legal representative of each patient. The study took place from March 2014 to January 2016.

Infants and young children aged between 6 and 36 months, with a documented diagnosis of severe CMA, defined as persistence of symptoms with eHF, and who had consumed AAF for at least 1 month before the study with observed clinical efficacy were eligible. Those with a multiple food allergy were also eligible, and all were capable of consuming the minimum required quantity of test or reference formula for the duration of the study. The main exclusion criteria were birth weight <2500 g, prematurity (<37 weeks) with specific feeding requirements, history of potentially fatal severe acute reactions to ingestion of cow’s milk (stage III or IV anaphylaxis), one or more severe additional pathologies or congenital malformations, intolerance to lactose, or any component of the test or reference formulae, any indication that could compromise study completion, and participation in any other clinical study in the 2 weeks before the study and for the duration of the study.

After the inclusion visit (day-21 to d-7) patients were randomized by the investigator using an interactive Web response system on day 0 in a 1:1 ratio to a reference +test formula (Neocate with a yogurt type texture for spoon-feeding: group 1) or reference formula alone (group 2) for 4 weeks (28 ±2 days). The study formulae were integrated into the patients’ usual daily diet which was not otherwise affected by the study protocol. Patients were allocated a unique identification number during the randomization to ensure the confidentiality of personal data. Parents/legal representatives were contacted by telephone 2 weeks later (14 ±2 days) and visited the site for an end-of-study visit after 4 weeks (28 ±2 days).

Study Products

The reference formula was Neocate (infants aged <1 year) and Neocate Advance (young children aged 1–3 years). Both are oral liquid AAFs used in the treatment of severe CMA. Once reconstituted with water, the formulae contain a mixture of essential and nonessential amino acids, carbohydrates, lipids, vitamins, and minerals; they do not contain glucose, lactose, sucrose, fructose, galactose, or soya oil.

The test formula was Neocate with a yogurt-type texture for spoon-feeding obtained by the addition of highly purified rice starch as a texturing agent.

The nutrient composition of each study formula is presented in Supplementary Table 1 (Supplemental Digital Content, http://links.lww.com/MPG/B182).

Group 1 received the reference +test formula as needed, and ideally including 100 g/day (patients aged 6–12 months) or 200 g/day (patients aged 12–36 months) of test formula (ie, yogurt texture and spoon-fed). Group 2 received the reference formula but no test formula.

Study products were supplied in powdered form, stored <25°C, and reconstituted precisely with the volume of water specified in the manufacturer’s recommendations for both test and reference formulae within 1 hour of use.

Efficacy Assessments

Primary Criterion: Cow’s Milk Protein Allergy Symptoms

A clinical evaluation of symptoms associated with severe CMA was performed by the Investigator during the visits on day 0 and day 28 and during the telephone call on day 14 using evaluation scales (absence, mild, moderate, or severe) for cutaneous, gastrointestinal, and respiratory symptoms combined. Between evaluations, parents/legal representatives recorded symptoms daily and classified their severity using standard scales.

Secondary Criteria: Adherence to Nutritional Therapy and Evolution of Cow’s Milk Protein Allergy Symptoms

From day 0 to day 28, parents/legal representatives measured the total volume of AAF (groups 1 and 2) and the quantity of spoon-fed yogurt AAF (group 1) consumed daily. Two 3-day food diaries (1 in the week before day 0 and a second in the week before day 28) were completed by the parents/legal representatives. These served to monitor any major modifications in the feeding habits of the patients, which could have had an impact on the study results. The mean nutritional content (calcium, iron, vitamin D, and protein equivalent) for each group was calculated over 28 days based on the quantity consumed and the respective composition of each formula, and assessed for the overall population as well as for infants <12 months of age and >12 months of age.

The evolution of dermatological (angiodema, eczema, lip edema, urticaria, and other), gastrointestinal (constipation, diarrhea, gastroesophageal reflux, vomiting, and other), and respiratory (asthma, cough, laryngeal edema, rhinitis, and other) symptoms of CMA was evaluated on day 0, day 14, and day 28 by the investigators. The presence and severity of symptoms were recorded daily by parents/legal representatives.
Third Criterion: Anthropometric Data

Weight, height, and body mass index (BMI) were reported and z scores for weight-for-height, weight-for-age, height-for-age, and BMI-for-age were calculated for each group at enrollment and day 28 using WHO references (WHO Anthro) (26).

Safety Assessment

Adverse events (AEs) were recorded by the investigator during the visits on day 0 and day 28 and during the telephone call on day 14, and throughout the study by the parents/legal representatives.

Statistical Analyses

The primary efficacy objective of the present study was to evaluate the clinical efficacy of the test formula in terms of the number of patients with combined CMA symptoms at day 14 and day 28. Secondary objectives included an evaluation of adherence to the nutritional therapy in each group in terms of the volume of AAF consumed daily, and further description of specific CMA symptoms on days 0, 14, and 28 and their evolution (appearance, no change, or disappearance of symptoms). For anthropometric data, z scores were calculated based on WHO growth data (27). The change from baseline (day 0) was compared between groups by analysis of covariance using age at baseline as a covariate. AEs were also assessed as a secondary safety objective.

The normality of quantitative data was assessed using the Shapiro-Wilk test and comparisons performed using the Student t test if the distribution for each group was normal and using the Wilcoxon Mann-Whitney test if at least one of the distributions was not normal. Qualitative comparisons were performed using the Chi² or Fisher exact test. In addition, a generalized estimating equations model was used to compare the evolution of qualitative data taking into account covariates of formula, time, and formula*time, and the nature of the parameter (binary or ordinal) and other factors including age, treatment duration, and nature of the CMA. All statistical comparisons used a 5% significance threshold (P = 0.05).

The evaluation of CMA symptoms, adherence to treatment, nutritional intake, and anthropometric data was performed using the per protocol (PP) set (all included patients who were randomized and completed the study with no major protocol deviation). The assessment of AEs was performed using the safety set (SS) (all included patients who had at least one administration of the test or reference formula). The intent-to-treat (ITT) set was used to evaluate patient characteristics and demography (all included patients who were randomized).

Based on previous clinical studies (11,13,17,20,28–30), for an alpha level of 0.05 for statistical significance and a power of 80%, a sample size of 48 patients (24 patients per group) was considered sufficient to detect a significant difference in the number of patients presenting CMA symptoms between groups. Assuming an attrition rate of 10%, an overall sample size of 54 patients was appropriate to meet the primary objective of the study.

The statistical analyses were done using SAS Version 9.3 (SAS Institute, Cary, NC).

RESULTS

Patients Studied

Thirty-four patients were enrolled in the study and randomized to group 1 (N = 17) or group 2 (N = 17) (Fig. 1). All patients had CMA, with the incidence of symptoms at baseline being 42.9% and 50.0% in group 1 and group 2, respectively, which was mainly non–IgE-mediated (76.5% of patients in each group). The median (range) time since the start of AAF treatment was similar in each group (21.5 [5–52] weeks in group 1 and 26.0 [5–100] weeks in group 2). In group 1, 2 patients discontinued the study (1 due to an AE and 1 due to an SAE), and 15 patients in group 1 and all patients in group 2 completed the study as planned. In groups 1 and 2, respectively, 14 and 16 patients were included in the PP set (Fig. 1) of whom CMA was still symptomatic for 6 and 8 patients in groups 1 and 2, respectively, at baseline. Overall in group 1 (PP set) patients consumed 60.05 ± 38.45 g of the test product per day.

Baseline demographic and anthropometric characteristics were similar in each group—for the ITT set in group 1 and group 2, respectively, the median (range) age at inclusion was 13.0 (6–25) months and 13.0 (5–35) months, gestation was 39.0 (35–41) weeks and 38.0 (35–40) weeks, weight was 3.50 (1.7–4.2) kg and 3.10 (1.8–3.6) kg, height was 0.495 (0.43–0.52) m and 0.490 (0.43–0.53) m, and head circumference was 35.0 (30–36) cm and 34.0 (29–36) cm. In each group there were more boys than girls (76.5% and 58.8% boys in group 1 and group 2) and most were born by vaginal delivery (76.5% in each group). The demographic data were similar for the PP and ITT sets.

Efficacy Assessments

Primary Criterion: Cow’s Milk Protein Allergy Symptoms

The incidence of patients with CMA symptoms (PP set) was similar in group 1 and group 2 at day 0 (6/14 patients [42.9%] and 8/16 patients [50.0%]), day 14 (7/14 patients [50.0%] and 7/16 patients [43.8%]), and day 28 (6/14 patients [42.9%] and 9/16 patients [53.3%]). Statistical comparison (Fisher exact test) confirmed no difference (P > 0.05) between groups on any occasion (Fig. 2).

Regarding the evolution of overall CMA symptoms during the study in patients who had symptoms, at day 14 most patients in each group had no change in symptoms (4/7 patients [57.1%] and 6/7 patients [85.7%] in group 1 and group 2); 1/7 patients (14.3%) in group 2 showed an improvement and 3/7 patients (42.9%) in group 2 showed worsening. At day 28, of those who had symptoms, most patients in each group had no change in symptoms (4/6 patients [66.7%] in group 1 and 5/9 patients [55.6%] in group 2) or an improvement (1/6 patients [16.7%] in group 1 and 4/9 patients [44.4%] in group 2); 1 patient [16.7%] in group 1 showed worsening of symptoms at day 28.

Statistical analysis using the generalized estimating equations model showed a visit effect with more symptom improvement of symptoms at day 28.

Secondary Criteria: Adherence to Nutritional Therapy, Nutritional Value, Evolution of Cow’s Milk Protein Allergy Symptoms

The mean ± SD consumption of AAF powder from day 0 to day 28 was 2834 ± 532.4 g in group 1 and 2801 ± 805.6 g in group 2, with no statistical difference (P = 0.90, Student t test) between groups. The mean nutritional daily intake for calcium overall (P = 0.012) and for patients <12 months of age (P = 0.006) was statistically higher in group 1 than group 2. There were no significant differences for iron, vitamin D, protein intake, and energy for any age group (Table 1). From the food diary data there were no major modifications to the usual feeding habit for any patient.

Dermatological, gastrointestinal, and respiratory symptoms were absent in most patients on day 0 and there was little change at day 28.
Anthropometric Data

Compared with baseline (day 0), z score at day 28 was significantly higher for group 1 than group 2 for weight-for-height ($P = 0.021$), weight-for-age ($P = 0.022$), and BMI for age ($P = 0.023$), and was similar between groups for height-for-age ($P = 0.487$) (Fig. 3).

Safety Assessment

The incidence of treatment-emergent AEs (TEAEs) was slightly higher in group 1 (14/17 patients [82.4%] experienced 29 TEAEs) and group 2 (10/17 patients [58.8%] experienced 16 TEAEs). In group 1, 7 TEAEs were considered to be related to the study formula (2 episodes of vomiting [2 patients], 2 episodes of diarrhea [2 patients], and single episodes of gastroenteritis with abdominal pain and anorexia); no TEAE in group 2 was considered to be related to the reference formula. Most lasted 1 to 7 days, were mild or moderate in severity, and resolved after treatment.

Episodes of severe diarrhea (1 patient) and severe vomiting (1 patient), which occurred 1 day and 8 days after the first intake of study formula and lasted 27 days and 8 days, respectively, led to the discontinuation of 2 patients in group 1.

There were 2 SAEs (diarrhea in group 1 and gastroenteritis in group 2). The diarrhea necessitated discontinuation of treatment, and the gastroenteritis resulted in hospitalization and treatment with Motilium (domperidone) and Gaviscon (alginate).

DISCUSSION

In children with severe CMA, the therapeutic objective of the spoon-fed yogurt-type AAF is not to provide a superior clinical efficacy to that of the reference liquid version, but to facilitate and to ensure the consumption of an AAF, which can be problematic in infants and young children due to its taste and/or texture. In the present study, there was no reduction in consumption between...
groups, indicating that the introduction of the spoon-fed yogurt-type formula did not adversely affect the amount of AAF consumed. In infants aged 6 to 12 months, the higher nutritional content of the test formula meant that for an equivalent overall consumption over the 28 days of the study, those who received the test formula (group 1) received a greater calcium intake than those fed the reference formula (group 2). The intake of calcium was statistically higher in group 1 than group 2 for the overall population and patients <12 months of age. No other statistically significant differences were observed for nutrients or energy. It is important to note that these data present the nutrient intake provided by the formulae alone, and therefore do not represent the total daily nutrient intake which was otherwise unaffected. Interestingly, there were significant differences in increases of some anthropometric data—z scores for weight-for-height, weight-for-age, and BMI-for-age were higher at day 28 for patients consuming Neocate with a yogurt-type texture. We can speculate that these differences in z score could be explained by the higher energy content of the Neocate with a yogurt-type texture compared to the liquid formulae, although no differences in energy intake and protein intake were observed between the 2 groups as changes in total intakes were not investigated. A further possible explanation could be that the consumption of Neocate with a yogurt-type texture improves the use and/or reduces the loss of nutrients caused by sustained allergic inflammation (19).

There was no difference in efficacy in terms of the incidence of CMA symptoms between the AAF administered with a yogurt-type texture for spoon-feeding compared to its usual administration as an oral liquid. The incidence of specific dermatological, gastrointestinal, and respiratory symptoms that are commonly associated with CMA was generally <50% at day 0, probably since an inclusion criterion required that all patients had been on an AAF diet for at least 1 month before enrolment. There was little change in

![Figure 3](https://www.jpgn.org/)

**FIGURE 3.** Mean ± standard deviation (SD) z scores for weight-for-height, weight-for-age, height-for-age, body mass index (BMI)-for-age at enrollment (day 0) and at day 28 (PP set).
the incidence of symptoms in either group during the study, and no discernible difference between groups except for gastroesophageal reflux, which showed greater improvement for the test formula.

Both formulae were well tolerated, although the incidence of TEAEs was higher in group 1 than group 2. This is likely to be a reflection of the open-label study design, with parents of infants receiving the test formula being more attentive to any reaction of the infant, and is not considered to be of clinical importance.

A limitation of the study is that the number of enrolled patients (17 per group) was lower than the planned sample size (24 per group). This was due to the stringent criteria for inclusion into the study only of infants with true severe CMA and the attendant difficulties in patient recruitment. Even if the planned sample size had, however, been reached it is unlikely that statistical significance would have been achieved for the analysis of the primary efficacy criterion between groups due to the high P values obtained. Although some statistical differences were observed for the anthropometric data, it is not possible to draw robust conclusions regarding the clinical significance since the study duration was limited to 28 days.

Overall there was no difference in efficacy, formula consumption, and tolerability between the new spoon-fed yogurt-type AAF formula and the reference formula, whereas significantly higher calcium intake was achieved with the new formula.

Acknowledgments: The authors acknowledge the study site personnel for the conduct of the study and also all enrolled infants and their caregivers for their participation. In particular, the authors acknowledge Florence Villard-Truc, MD, Marie-Hélène Thierry, MD, Céline Lagrange, MD, Anne-Sophie Brunet, MD, and Bénédicte Douvillez, MD for study conduct. This manuscript was prepared with the assistance of a professional medical writer, Dr Andrew Lane (Lane Medical Writing), in accordance with the European Medical Writers Association guidelines and Good Publication Practice.

REFERENCES

1. Hill DJ, Firer MA, Shelton MJ, et al. Manifestations of milk allergy in infancy: clinical and immunologic findings. J Pediatr 1986;109:270–6.
2. Host A, Jacobsen HP, Halken S, et al. The natural history of cow’s milk protein allergy/intolerance. Eur J Clin Nutr 1995;49:S13–8.
3. Host A. Frequency of cow’s milk allergy in childhood. Ann Allergy Asthma Immunol 2002;89:53–7.
4. Dupont C, Chouraqui JP, De Boissieu D, et al. Dietary treatment of cow’s milk protein allergy in childhood: a commentary by the Committee on Nutrition of the French Society of Paediatrics. Br J Nutr 2012;107:325–38.
5. Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow’s milk protein allergy in infants and children: ESPGHAN Committee practical guidelines. J Pediatr Gastroenterol Nutr 2012;55:211–9.
6. Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy 2014;69:1008–25.
7. Commission of the European Communities Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC of 16 December 2006, http://eur-lex.europa.eu/eli/dir/ 2006/141/oj. Accessed October 13, 2017.
8. Aggett PJ, Haschke F, Heinze W, et al. Comment on antigen-reduced infant formulae. ESPGAN Committee on Nutrition. Acta Paediatr 1993;82:314–9.
9. Kleinman RE. Cow milk allergy in infancy and hypoallergenic formula. J Pediatr 1992;121:S116–21.
10. Sampson HA, Bernhisel-Broadbent J, Yang E, et al. Safety of casein hydrolysate formula in children with cow milk allergy. J Pediatr 1991;118:520–5.
11. de Boissieu D, Matarazzo P, Dupont C. Allergy to extensively hydrolyzed cow milk proteins in infants: identification and treatment with an amino acid-based formula. J Pediatr 1997;131:744–7.
12. Halken S, Host A. How hypoallergenic are hypoallergenic cow’s milk-based formulas? Allergy 1997;52:1175–83.
13. Vanderhoof JA, Murray ND, Kaufman SS, et al. Intolerance to protein hydrolysate infant formulas: an underrecognized cause of gastrointestinal symptoms in infants. J Pediatr 1997;131:741–4.
14. De Boissieu D, Dupont C. Allergy to extensively hydrolyzed cow’s milk proteins in infants: safety and duration of amino acid-based formula. J Pediatr 2002;141:271–3.
15. Hill DJ, Heine RG, Cameron DJ, et al. The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance. J Pediatr 1999;135:118–21.
16. Hill DJ, Murch SH, Rafferty K, et al. The efficacy of amino acid-based formulas in relieving the symptoms of cow’s milk allergy: a systematic review. Clin Exp Allergy 2007;37:808–22.
17. Isolauri E, Sutas Y, Makinen-Kiljunen S, et al. Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. J Pediatr 1995;127:550–7.
18. Fiocchi A, Brozek J, Schunemann H, et al. World Allergy Organization (WAO) diagnosis and rationale for action against cow’s milk allergy (DRACMA) guidelines. World Allergy Organ J 2010;3:57–161.
19. Isolauri E, Sutas Y, Salo MK, et al. Elimination diet in cow’s milk allergy: risk for impaired growth in young children. J Pediatr 1998;132:1004–9.
20. Niggemann B, Binder C, Dupont C, et al. Prospective, controlled, multicenter study on the effect of an amino-acid-based formula in infants with cow’s milk allergy/intolerance and atopic dermatitis. Pediatr Allergy Immunol 2001;12:78–82.
21. Sampson HA, James JM, Bernhisel-Broadbent J. Safety of an amino acid-derived infant formula in children allergic to cow milk. Pediatrics 1992;90:463–5.
22. Hill DJ, Cameron DJ, Francis DE, et al. Challenge confirmation of late-onset reactions to extensively hydrolyzed formulas in infants with multiple food protein intolerance. J Allergy Clin Immunol 1995;96:386–94.
23. Host A, Koletzko B, Dreeborg S, et al. Dietary products used in infants for treatment and prevention of food allergy. Joint Statement of the European Society for Paediatric Allergology and Clinical Immunology (ESCAPAC) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. Arch Dis Child 1999;81:80–4.
24. Le Reverend BJ, Edelson LR, Loret C. Anatomical, functional, physiological and behavioural aspects of the development of mastication in early childhood. Br J Nutr 2014;111:403–14.
25. Ambroziszewicz J, Rowicka G, Chelchowska M, et al. Biochemical markers of bone metabolism in children with cow’s milk allergy. Arch Med Sci 2014;10:1135–41.
26. WHO. Child growth standards: WHO Anthro (version 3.2.2, January 2011) and macros 2017. http://www.who.int/childgrowth/software/en/. Accessed October 13, 2017.
27. WHO Multicentre Growth Reference Study Group. WHO child growth standards: methods and development. Geneva: World Health Organization; 2006. http://www.who.int/childgrowth/standards/technical_report/en/. Accessed October 13, 2017.
28. Anmar F, de Boissieu D, Dupont C. Allergy to protein hydrolysates. Report of 30 cases [in French]. Arch Pediatr 1999;6:837–43.
29. Isolauri E, Tahvanainen A, Peltola T, et al. Breast-feeding of allergic infants. J Pediatr 1999;134:27–32.
30. Kanny G, Moneret-Vautrin DA, Flabbee J, et al. Use of an amino-acid-based formula in the treatment of cow’s milk protein allergy and multiple food allergy syndrome [in French]. Allergy Immunol (Paris) 2002;34:82–4.