## METHODS

### **Study Design and Participants**

In this observational, prospective, multi-center study, eligible infants were provided with an amino acid based infant formula (Investigational formula: marketed Nutramigen AA, Mead Johnson Nutrition, Evansville, IN) for 12 weeks. Infants (1-12 months of age) with suspected cow’s milk protein allergy and a history of weight loss (≥ 0.5 WHO reference z-score) while on an EHP formula were recruited from 5 centers in France. Eligible infants had a birth weight of ≥1500 g, were experiencing at least one persistent CMPA symptom (atopic dermatitis, bloody stool, diarrhea, rash, vomiting/spitting up), and fed with an EHP formula for at least two weeks prior to the first study visit. Prior to Study Visit 1, eligible participants had not responded to four different extensively hydrolyzed formulas including whey hydrolysate (n = 4), rice hydrolysate (n = 10), and casein hydrolysate (n = 17). Exclusion criteria included history of metabolic disease, underlying disease, or congenital malformation likely to interfere with normal growth and development or participant evaluation.

Parents or guardians provided written informed consent prior to enrollment. The research protocol and informed consent forms adhered to the Declaration of Helsinki and were approved by the appropriate ethics committees. The study complied with good clinical practices (ClinicalTrials.gov Identifier: NCT01584245).

### **Growth and Allergy Symptoms**

Anthropometric measures (weight, length) and allergy symptoms were recorded at baseline (study visit 1), 4 weeks (study visit 2), and 12 weeks (study visit 3). AD severity was assessed by Scoring Atopic Dermatitis (SCORAD) Index, and the incidence of vomiting/spitting up was given a Gastrointestinal (GI) symptom score using the I-GERQ-R parental questionnaire ([15](#_ENREF_15)). The primary outcome was infant weight z-score change over the 12 weeks of feeding. Secondary outcomes included monitoring allergic manifestations (atopic dermatitis, bloody stools, and vomiting/spitting up), tolerance, and serious adverse events.

***Statistical Analysis***

Mean weight change z-score over the study period (week 0 to week 12) was compared to the inclusion criteria of 0.5 z-score history of weight loss. The trends for weight by z-score over the study period was analyzed by comparing the z-score means obtained at visits 1, 2, and 3, using analysis of variance (ANOVA) for repeated data. Bonferroni adjustment for multiple comparison was used to evaluate means. The SCORAD score and GI Symptom scores were recorded through the study period and analyzed using ANOVA. GI Symptom score changes from Visit 1 to Visit 3 were analyzed by McNemar’s Test. All tests were conducted at α = 0.05.