Hypoallergenicity of A Whey-Based, Extensively Hydrolysed Infant Formula Containing Two Human Milk Oligosaccharides

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ABSTRACT

Background: We sought to determine whether an extensively hydrolysed formula (EHF) supplemented with two HMO (human milk oligosaccharides) was tolerated by infants with cow's milk protein allergy (CMPA).

Methods: A whey-based EHF (Test formula) containing 2'fucosyl-lactose (2'FL) and lacto-N-neotetraose (LNnT) was assessed for clinical hypoallergenicity and safety. The Control formula was a currently marketed EHF without HMO (Althéra®). Children aged 2 months to 4 years with CMPA were assessed by double-blind, placebo-controlled food challenges (DBPCFC) to both formulas, in randomized order. If both DBPCFC were negative, subjects participated in a one-week, open food challenge (OFC) with Test formula. Symptoms and adverse events were recorded. Hypoallergenicity was accepted if at least 90% (with 95% confidence intervals) of subjects tolerated the Test formula.

Results: Of 82 children with CMPA screened, 67 (intention-to-treat [ITT] cohort: mean age 24.5 ± 13.6 months, range 2-57; 45 [67.2%] male) were randomized to receive either Test or Control formula during the first DBPCFC. Of these, 64 children completed at least one DBPCFC (modified intention-to-treat [mITT] cohort). Three children were excluded due to protocol deviations (per protocol [PP] cohort; n=61). There was one allergic reaction to the Test, and one to Control formula. On mITT analysis, 63/64 (98.4%; 95% CI lower bound 92.8%), and on PP analysis 60/61 (98.4%; 95% CI lower bound 92.5%) of participants tolerated the Test formula, confirming hypoallergenicity.*

Conclusion: The whey-based EHF supplemented with 2'FL and LNnT meets the clinical hypoallergenicity criteria and is suitable for the management of CMPA in infants and young children.

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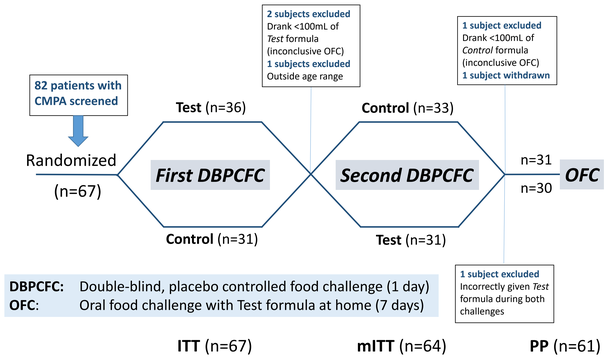
FIGURE 1: Study flow and analysis populations



ITT = Intention-to-treat, **mITT** = modified intention-to-treat and **PP** = per protocol analysis cohorts

FIGURE 2: Percentage of subjects tolerating the Test and Control formulas (mITT; arrows indicate percentage and 95% confidence interval lower bound)

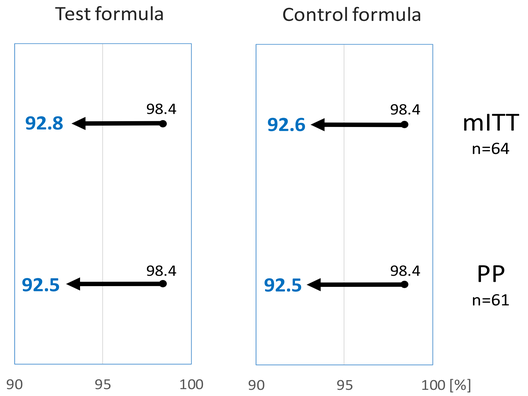


TABLE 1: Age distribution and diagnostic criteria

Age at enrolment [mean ± SD]	24.1 ± 13.2 months
Age distribution [n (%)]	
< 12 months	8 (12.5%)
12-36 months	39 (60.9%)
> 36 months	17 (26.6%)
Diagnostic criteria [n (%)]	
• Reported convincing allergic symptoms following ingestion of cow's milk or milk-containing food product and presence of milk-specific serum IgE (>0.7 kUA/L), or positive skin prick test (wheal >5mm)	58 (90.6%)
• Milk-specific serum IgE level >15 kUA/L(>95% PPV) or skin prick test wheal >10mm (>95% PPV)	6 (9.4%)

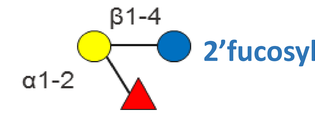
More than 90% of subjects (95% CI lower bound = 92.8%) tolerated the novel EHF with two HMO, confirming its safety and efficacy in infants and young children with CMPA.

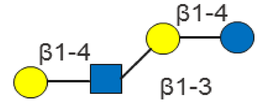
TABLE 2: Formula challenge outcome (mITT analysis)

	Challenge outcome	DBPCFC 1 n (%)	DBPCFC 2 n (%)	Total n (%)	95% CI lower bound
Test Formula	Positive	1 (3.0%)	0 (0.0%)	1 (1.6%)	**92.8%**
	Negative	32 (97.0%)	31 (100%)	63 (98.4%)	
Control Formula	Positive	0 (0.0%)	1 (3.2%)	1 (1.6%)	**92.6%**
	Negative	31 (100%)	30 (96.8%)	61 (98.4%)	

Human milk oligosaccharides (HMO)

- Made by microbial biofermentation
- Structure identical to naturally occurring HMO in breast milk
- Highly purified and free from milk allergens





Glucose Galactose Fucose N-acetylglucosamine

KEY MESSAGES

- Human milk oligosaccharides (HMO) are non-digestible carbohydrates in breast milk which provide the host-specific substrate for the developing gut microbiome of young infants.
- The present study is the first clinical trial which assessed the hypoallergenicity of an extensively hydrolysed formula (EHF) containing HMO.
- The study formula supplemented with 2'FL and LNnT was tolerated by >90% of infants and children with CMPA, confirming the hypoallergenicity of the EHF according to the AAP guidelines.