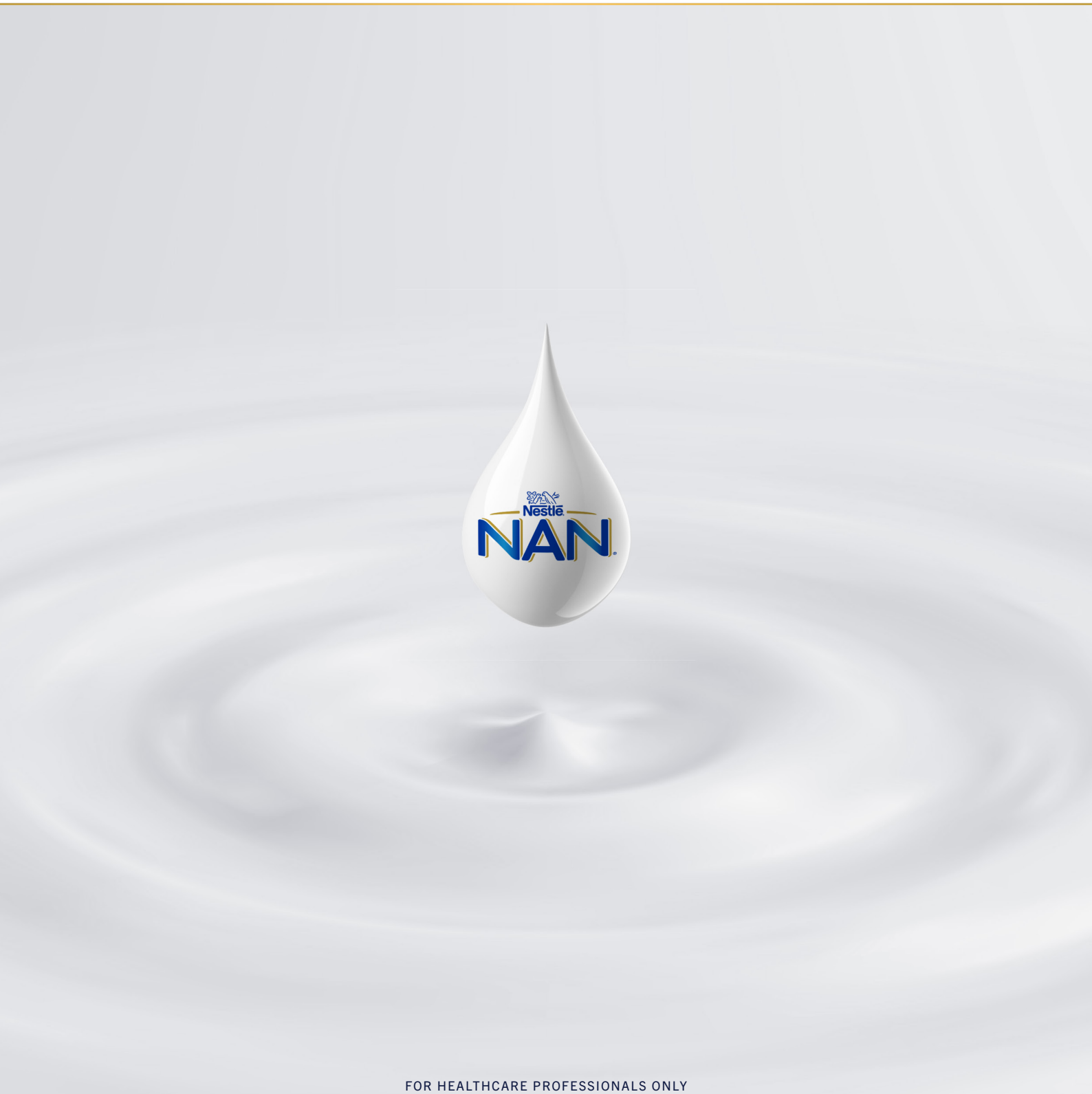
BREAST MILK IS BEST FOR BABIES

Nestlé research on HMOs and age-adapted protein

NEW abstracts from clinical trials of NAN® infant and follow-up formulae



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BREAST MILK IS BEST FOR BABIES

HMOs and age-adapted protein – Scientific evidence

Nestlé is one of the early pioneers of infant nutrition research and development. Nestlé continues to relentlessly pursue innovations to make sure that infants and children around the world can benefit from the most advanced science-based products.

This booklet consolidates Nestlé abstracts on HMOs and age-adapted protein, accepted for 56th ESPGHAN annual meeting.

OVER 150 YEARS SCIENCE LEADER

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HMOs and age-adapted protein – Scientific evidence

Infant formulas with age-adapted protein concentrations fed from birth to 12 months of age support adequate growth and body composition at 36-48 months of age

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Objectives:

Breast-milk protein content varies over the course of lactation but remains static in infant formula (IF). We developed a series of age-adapted IFs replicating breast-milk's protein content. Long-term growth and safety outcomes were examined in infants fed IFs containing modified sweet whey with either standard or age-adapted protein content for 0-360 days, comparing them to breastfed infants.

Methods:

Healthy term infants were randomized to two groups:

1. Standard Regimen: Standard-IF (1.85g protein/100kcal; 0-90 days) + Follow-up formula (1.50g protein/100kcal; 90-360 days).
2. Age-adapted Regimen: New-IF (2.50g protein/100kcal; 0-30 days) + Standard-IF (30-90 days) + Follow-up formula (90-360 days).

Breastfed infants served as a reference.

Growth outcomes (Z-scores at 36 and 48 months of age) and body composition (36 months) were determined.

Results:

Anthropometric outcomes in each regimen were non-inferior (non-inferiority margin of -0.5 SD) to WHO standards and breastfed infants. The three study groups were not statistically different for any outcome (**Table-1**).

Conclusions:

Both regimens of modified sweet whey containing IFs support adequate long-term growth, comparable to breastfed infants.

Table-1. Data from two IF regimens and breastfed infants (FAS data). No significant differences between study groups. Data from n=125-145 participants/group for Z-scores (48 months) and n=75-95 participants/group for body composition (36 months).

Outcomes	Adjusted Means [95% CI]		
	Standard Regimen	Age-Adapted Regimen	Breastfed
Weight-for-age Z-score	0.00 [-0.11; 0.12]	0.03 [-0.08; 0.15]	-0.03 [-0.15; 0.09]
Length-for-age Z-score	0.09 [-0.02; 0.20]	0.06 [-0.05; 0.17]	-0.06 [-0.18; 0.07]
Head circumference-for-age Z-score	0.58 [0.46; 0.69]	0.58 [0.46; 0.69]	0.67 [0.55; 0.80]
BMI-for-age Z-score	-0.06 [-0.19; 0.06]	0.00 [-0.12; 0.13]	-0.01 [-0.14; 0.13]
Weight-for-length Z-score	-0.05 [-0.18; 0.08]	0.02 [-0.11; 0.15]	-0.01 [-0.15; 0.13]
Fat Free Mass (grams)	10755.72 [10502.04; 11009.41]	10564.93 [10331.27; 10798.59]	10582.45 [10317.93; 10846.97]
Fat Mass (grams)	3954.10 [3757.90; 4150.31]	4055.72 [3875.00; 4236.43]	4129.95 [3925.37; 4334.54]
%Fat	26.76 [25.79; 27.73]	27.56 [26.66; 28.45]	28.08 [27.06; 29.09]

Disclosure:

Jibran A. Wali, J. Manuel Ramos-Nieves and Nicholas P. Hays are employees of Société des Produits Nestlé S.A., the sponsor of the study.

An age-adapted synbiotic blend of human milk oligosaccharides and *B. infantis* LMG11588 plus *B. lactis* may contribute to immune cell homeostasis in formula-fed infants

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[1]Clara study group: Javier Miranda, Olivier Claris, Mercedes Gil-Campos, Ignacio Salamanca, Luc Cornette, Philippe Alliet, André Léké, Mireille Castanet, Hugues Piloquet, Virginie de Halleux, Delphine Mitanchez, Yvan Vandenplas, Pierre Maton, Frank Jochum, Dirk Olbertz, Sergio Negre. [2]Société des Produits Nestlé S.A., Nestlé Research, Nestlé Institute of Health Sciences, Department of Gastrointestinal Health - Immunology, Lausanne, Switzerland. [3]Clinical Microbiomics, Copenhagen, Denmark. [4]Clinical Research Unit, Nestlé Research, Lausanne, Switzerland. [5]Research & Development, Nestlé Product Technology Center Nutrition, Vevey, Switzerland.

Objectives:

Decreased levels of human milk oligosaccharides (HMO)-utilizing bifidobacteria have been associated with inflammation and immune dysregulation in early life and may increase the risk of chronic inflammatory disorders including allergies. In an ongoing study, we examined systemic immune cell profiles in formula-fed infants supplemented with an age-adapted synbiotic.

Methods:

In a multicenter European trial (NCT04962594), healthy infants aged ≤14 days were randomly assigned to either a control formula group (CF; n=117, partially hydrolyzed 100% whey-based formula) or an experimental formula group (EF; n=119, CF supplemented with 1.77g/L of 6 HMOs [2'FL, DFL, 3-FL, LNT, 3'SL, 6'SL], *B. lactis* CNCM I-3446, and *B. infantis* LMG11588. In a sub-cohort, blood samples were collected from CF (n=39), EF (n=35) and a reference group of breast-fed infants (BF, n=16) at 4 months of age. Peripheral blood mononuclear cells (PBMCs) were isolated and immune cell frequencies analyzed by ChipCytometry. Spearman correlation matrices were calculated for immune cell-network analyses.

Results:

At 4 months of age, T-helper (Th) 2 cells were significantly decreased in EF compared to CF (p=0.033), following a comparable pattern in BF. Although the relative abundance of Th1 and Th17 cells was comparable among all feeding groups, cell-network analyses identified different modules of co-regulated immune cell populations in EF compared to CF infants. In EF, but not CF, Th1 cells positively correlated with Th2, Th17, regulatory T cells and antibody producing CD38$^+$ plasmablasts suggesting a balanced cross regulation among these populations.

Conclusions:

An age-adapted synbiotic blend composed of 6 HMOs, *B. infantis* plus *B. lactis* led to a decrease in systemic Th2 cells associated with a balanced cross-regulation of T-helper cell subsets, potentially contributing to immune homeostasis in formula fed infants. Future analyses up to 15 months of age may provide additional evidence on the impact of this blend on infant health.

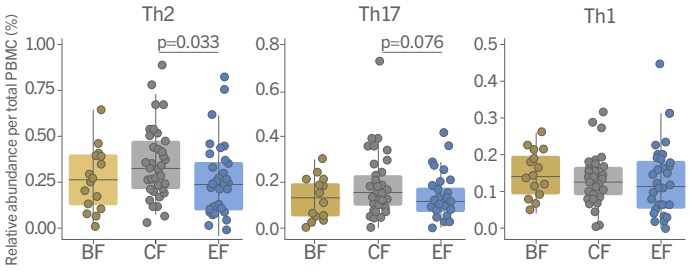

Figure 1. Relative abundance of T-helper type (Th) 2, Th17 and Th1 cells in peripheral blood mononuclear cells (PBMCs) of control formula (CF, n=39) and experimental formula (EF, n=35) fed infants at 4 months of age. Breastfed infants (n=16) served as reference control. Individual data are plotted with mean as bar and standard deviation. Non-parametric t-test was used to compare EF versus CF.

HMOs and age-adapted protein – Scientific evidence

Biomarkers of gut maturity, inflammation, and metabolic environment in infants fed formula containing six human milk oligosaccharides, *B. infantis* LMG11588, and *B. lactis* CNCM I-3446

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Objectives:

Formulas supplemented with human milk oligosaccharides (HMOs) and probiotics may promote favorable changes in biomarkers of gut maturity, inflammation, and metabolic environment in infants. Here, we report secondary, staged analysis results (baseline and age 3 months [mo]) from an ongoing trial of infants fed formulas supplemented with 6 HMOs and two probiotics from birth to 15mo.

Methods:

In a multicenter European trial (Clinical trials.gov: NCT04962594), formula-fed infants aged ≤14 days were randomized to control (CF, partially hydrolyzed 100% whey-based; n=117) or experimental formula (EF, same formula plus 1.77g/L HMOs [2'FL, DFL, 3-FL, LNT, 3'SL, 6'SL], *B. lactis* [CNCM I-3446; 1x106 CFU/g], and *B. infantis* [LMG11588; 5x105 CFU/g]; n=119). Non-randomized breastfed infants (BF; n=82) were a reference group. Stool samples were analyzed for biomarkers of intestinal immune response (total secretory immunoglobulin A [sIgA]), inflammation (calprotectin), and maturity (alpha-1 antitrypsin [AAT]), plus markers of gut metabolic environment (pH and short chain fatty acids [SFCA]). ANCOVA models were corrected for baseline value, age, and site; a propensity score was included to allow comparison with the non-randomized BF group.

Results:

No significant differences in sIgA or calprotectin (mg/kg dry stool) were observed (**Figure**); higher sIgA values in BF are likely due to breast milk intake. AAT (mg/g dry stool) in EF was significantly lower than CF (p=0.015; Figure), while not different than BF. Mean±SD fecal pH in EF (6.7±1.1) was lower than CF (7.0±0.8; p=0.032), while both groups were higher than BF (4.9±1.3; p<0.0001). EF and CF had lower acetate (% total SFCA) than BF (both p<0.033); propionate was higher in EF vs. BF (p=0.005).

Conclusions:

Partially hydrolyzed infant formula with a synbiotic blend of 6 HMOs and two probiotics positively supports gut maturity and lowers pH at age 3mo. Analyses at later timepoints will provide evidence of the impact of this formula on additional health-related outcomes.

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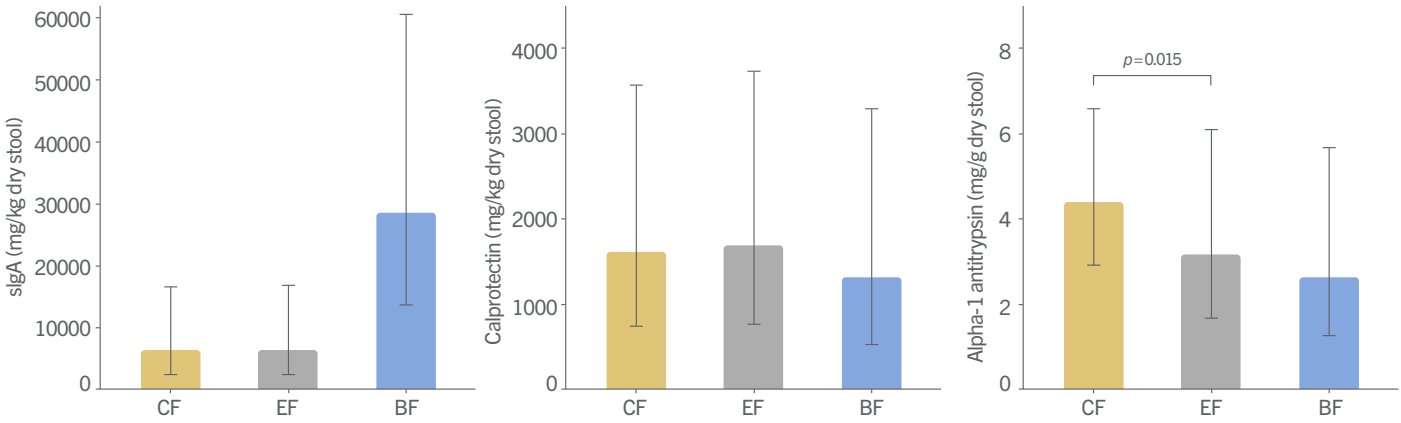

Figure. Geometric mean and geometric standard deviation values of fecal biomarkers of intestinal immune response (total secretory immunoglobulin A [sIgA]), gut inflammation (calprotectin), and gut maturity (alpha-1 antitrypsin) at 3 months of age.

CF, control formula group; EF, experimental formula group; BF, breastfed reference group. P-values from ANCOVA models with baseline value, age, site, and propensity score as covariates. P-values were adjusted for multiplicity using Benjamini-Hochberg correction.

Disclosure:

Anirban Lahiry, Irma Silva Zolezzi, Nicholas P. Hays and Norbert Sprenger are employees of Société des Produits Nestlé S.A., the sponsor of the trial.

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