Michaelis LJ, Wopereis H, van Ampting MTJ, et al. An amino acid-based formula with synbiotics affects faecal microbiota in non-IgE mediated cow's milk allergic infants. EAACI Annual Meeting. Jun 11-15; Vienna, Austria. Allergy. 2016;71(S102):58(114).

The ASSIGN Trial

Background:

Hypoallergenic infant formulas – based on extensively hydrolyzed protein or amino acids - are used in the dietary management of cow milk allergy (CMA) in infants. Research has shown that infants and children with CMA have an imbalanced gut microbiota associated with their allergic condition. This study sought to determine whether an amino acid-based formula (AAF) supplemented with a specific synbiotic blend, designed for CMA patients, will improve the gut microbiota as it develops in CMA subjects.

Methods:

The study was prospective, randomized, double-blind and controlled, lasting 8 weeks (registered as NTR3979). Infants (6.00+/- 2.98 months) with non-IgE-mediated CMA were randomized to either a control AAF (n=36) or a test AAF supplemented with a specific synbiotic blend of short-chain fructooligosaccharides (scFOS), long-chain fructooligosaccharides (lcFOS) and *Bifidobacterium breve* M-16V (n=35). As the study was blinded, participants were unaware of the AAF they were assigned. The primary outcome measures were bifidobacteria, as a marker of a gut microbiota of a healthy infant, and the *Eubacterium rectale/Clostridium coccoides* (ER/CC) group, representing an adult-like gut microbial group, as percentages of total fecal bacteria. Secondary outcomes included stool characteristics, fecal short-chain fatty acid (SCFA) levels, fecal secretory IgA levels, and concomitant medication use.

Results:

CMA symptoms were primarily gastrointestinal (90% of subjects) as well as dermatological (10% of subjects), and subjects were stratified based on these factors. Sixty subjects completed the 8-week intervention (test n = 28; control n = 32). The study demonstrated that, following an 8-week intervention, test group subjects' fecal microbiota shifted in levels of both *Bifidobacterium* species and the ER/CC group to be closer to levels seen in a reference group of age-matched, healthy breastfed infants vs. control group subjects. Test group subjects demonstrated significantly higher levels of bifidobacteria (35.6%) after 8 weeks compared to control group subjects (14.7%) ($p<0.001$). The test group also demonstrated significantly lower ER/CC levels (12.1%) compared to the control group (26.6%) ($p<0.001$). Secondary and clinical outcome measures of the study are pending. Similar numbers of subjects in both groups experienced (serious) adverse events.

Conclusions:

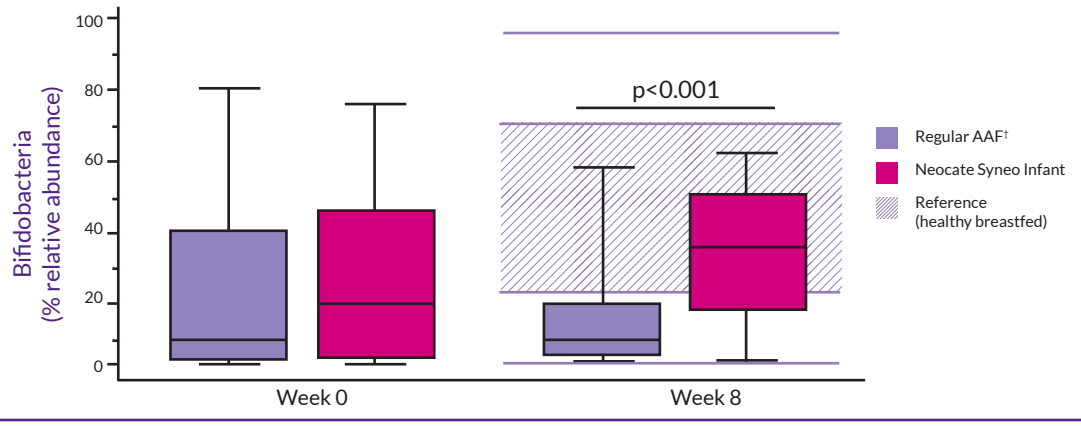
This study demonstrated that an AAF with an added specific synbiotic mixture is suitable for CMA infants and will help to rebalance the gut microbiota by significantly increasing fecal bifidobacteria levels and lowering the ER/CC group vs. a standard AAF, bringing the gut microbiota composition closer to that seen in age-matched, healthy breastfed infants*.

Neocate® Syneo® Infant is an amino acid-based formula with synbiotics that has been clinically shown to help address the hidden gut dysbiosis seen with CMA.

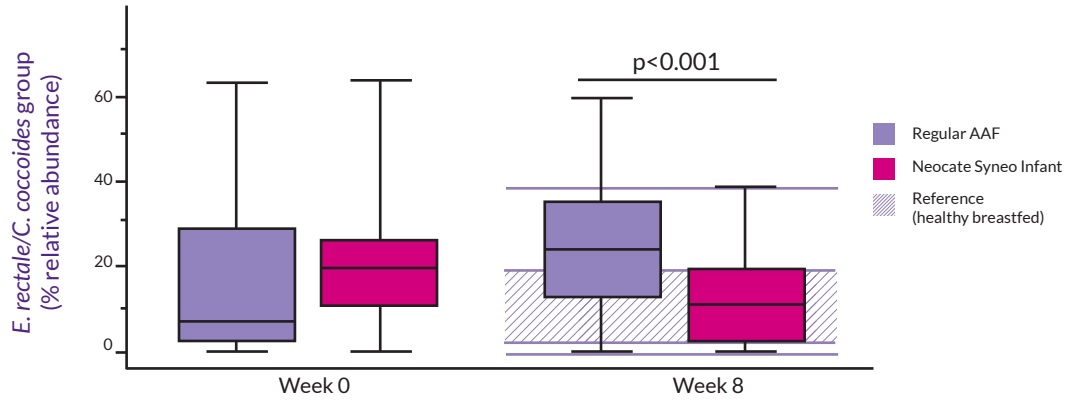
NUTRICIA Neocate® Syneo® INFANT

* Candy DCA, Van Ampting MTJ, Oude Nijhuis MM, et al. A synbiotic-containing amino-acid-based formula improves gut microbiota in non-IgE-mediated allergic infants. Pediatr Res. 2017 Dec 6.

Increased levels of infant-like bifidobacteria*



Decrease of adult-like *E. rectale/C. coccoides* group*



Neocate Syneo Infant has been clinically shown to help bring the gut microbiota of infants with CMA closer to that of healthy, breastfed infants.

Figures adapted from: Candy DCA, Van Ampting MTJ, Oude Nijhuis MM, et al. A synbiotic-containing amino-acid-based formula improves gut microbiota in non-IgE-mediated allergic infants. Pediatr Res. 2017 Dec 6.

*Statistics are based on ANCOVA comparing test vs. control with Week 8 values as outcome, stratification factor (skin or gastrointestinal symptoms) and imputed baseline values as covariate and treatment as fixed effect. The grey shaded area represents the sample 25th to 75th percentile of the reference group (healthy subjects) and the grey horizontal lines represent the minimum and maximum values of this reference group.

†AAF = amino acid-based formula

Adapted from publicly available abstract - http://onlinelibrary.wiley.com/doi/10.1111/all.12970/epdf (abstract 114)
Full text available at https://www.nature.com/articles/pr2017270

9497350-20511 ZMSA 03/18

NUTRICIA Neocate® Syneo® INFANT