

# Wopereis H, van Ampting MTJ, Cetinyurek-Yavuz A, et al. A specific synbiotic-containing amino acid-based formula restores gut microbiota in non-IgE-mediated cow milk allergic infants: a randomized controlled trial. Clin Transl Allergy. 2019;9:27.

## The ASSIGN Trial

### Background:

Altered gut microbiota is implicated in cow milk allergy (CMA) and differs markedly from healthy, breastfed infants. Infants who suffer from severe CMA often rely on cow milk protein avoidance and, when breastfeeding is not possible, on specialized infant formulas such as amino acid-based formulas (AAF). Herein, we report the effects of an AAF including specific synbiotics on oral and gastrointestinal microbiota of infants with non-IgE-mediated CMA with reference to healthy, breastfed infants.

### Methods:

In this prospective, randomized, double-blind controlled trial, infants with suspected non-IgE-mediated CMA received test or control formula. Test formula was AAF with synbiotics (prebiotic fructooligosaccharides and probiotic *Bifidobacterium breve* M-16V). Control formula was AAF without synbiotics. Healthy, breastfed infants were used as a separate reference group (HBR). Bacterial compositions of fecal and salivary samples were analyzed by 16S rRNA-gene sequencing. Fecal analysis was complemented with the analysis of pH, short chain fatty acids (SCFAs) and lactic acids.

### Results:

The trial included 35 test subjects, 36 controls, and 51 HBR. The 16S rRNA-gene sequencing revealed moderate effects of test formula on oral microbiota. In contrast, the gut microbiota was substantially affected across time comparing test with control. In both groups bacterial diversity increased over time but was characterized by a more gradual increment in test compared to control. Compositionally this reflected an enhancement of *Bifidobacterium* spp. and *Veillonella* spp. in the test group. In contrast, the control-fed infants showed increased abundance of adult-like species, mainly within the *Lachnospiraceae* family, as well as within the *Ruminococcus* and *Alistipes* genus. The effects on *Bifidobacterium* spp. and *Lachnospiraceae* spp. were previously confirmed through enumeration by fluorescent in situ hybridization and were shown for test to approximate the proportions observed in the HBR. Additionally, microbial activity was affected as evidenced by an increase of L-lactate, a decrease of valerate, and reduced concentrations of branched-chain SCFAs in test versus control.

### Conclusions:

The AAF including specific synbiotics effectively modulates the gut microbiota and its metabolic activity in non-IgE-mediated CMA infants bringing it closer to a healthy, breastfed profile.

**Neocate® Syneo® Infant positively changed the gut microbiota composition and its metabolic activity in infants with cow milk allergy bringing it closer to a healthy, breastfed profile.**

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ASSIGN = Amino acid-based formula with Synbiotics – Study in Infants with Gastrointestinal Non-IgE-mediated cow's milk allergy

Nutricia North America supports the use of breast milk wherever possible. Neocate® Syneo® is a hypoallergenic, amino acid-based medical food for use under medical supervision. Neocate® Syneo® Infant is indicated for the dietary management of cow milk allergy, multiple food allergies and related GI and allergic conditions, including food protein-induced enterocolitis syndrome, eosinophilic esophagitis and gastroesophageal reflux.