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Effect of an antenatal maternal supplementation with GOS/inulin prebiotics on atopic dermatitis in high-risk children (PREGRALL): study protocol for a randomized controlled trial.

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Background: Allergies are increasing worldwide affecting 30-40% of the population. Among these, Atopic Dermatitis (AD) is the earliest and the most common manifestation of allergic diseases (prevalence 20%). Recent studies have shown that allergies were associated with a disruption of the gut microbial 'balance' suggesting that the use of nutritional intervention very early in life may restore an optimal pattern of microflora aiming at improving the host's health. So far, most human intervention studies have mainly focused on improving postnatal infant colonization.

Aim: Our study will test the hypothesis that a maternal antenatal prebiotics (GOS/inulin) supplementation may be superior to placebo for AD prevention in high-risk children (PREGRALL study).

Methods: The PREGRALL study is a parallel multicentre double-blind randomized controlled trial funded by the French Ministry of Health. It will recruit 376 pregnant women, at risk of having an allergic infant. Participants will be randomized to be given prebiotics supplementation or placebo, from 20 weeks of pregnancy to delivery (fig.1 and 2) . Primary outcome is AD prevalence at one year old. Secondary outcomes are AD severity, quality of life, prebiotics tolerance (fig.1). PREGRALL will lead a translational study based on biological samples from at least 60 infant-mother dyads (30 per group). Samples will be collected at different times(table).

Fig.1: Study progress

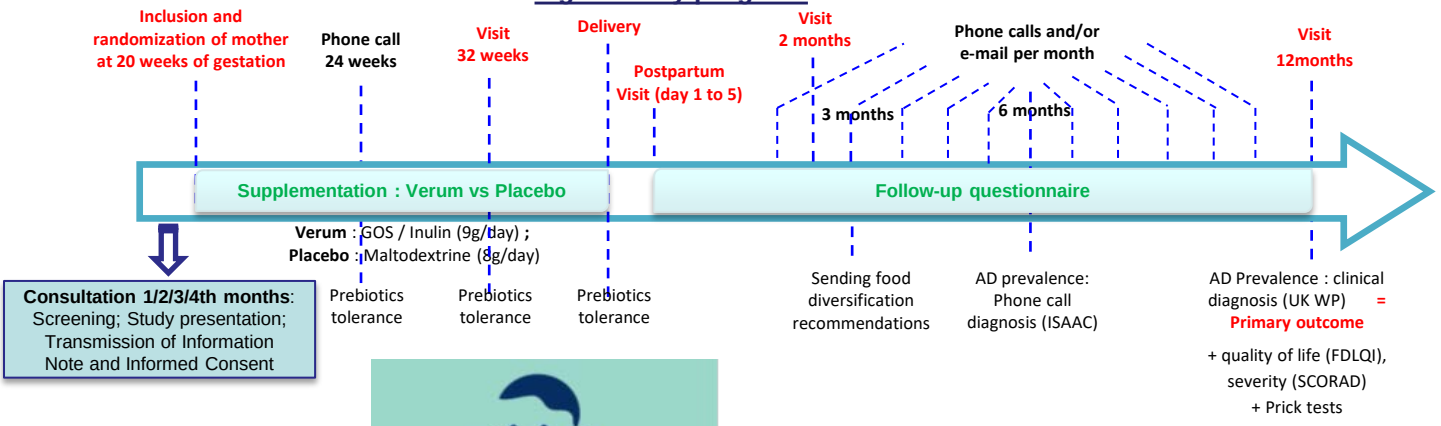

Fig.2: Study design

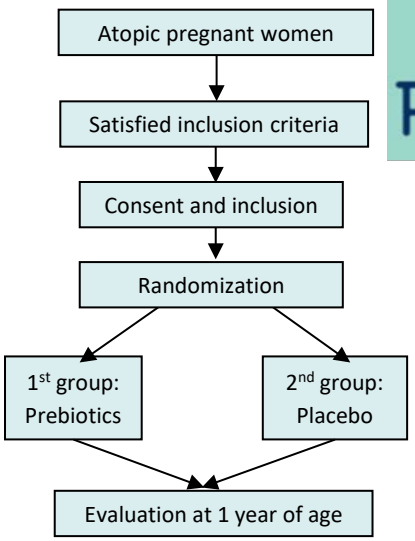

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Table: Biocollection

		Inclusion 20 weeks	Follow up 32 weeks	Delivery Day 0	Postpartum Day 1 to day 5	1 month	Gynecological visit 2 months	Dermato-pediatric visit 1 year
Samples	Mother blood	X	X	X			X	
	Mother stools	X	X	X			X	
	Mother buccal swab	X	X	X			X	X
	Cord blood			X				
	Placenta			X				
	Colostrum/breastmilk				X	X		
	Newborn stools				X		X	X
	Newborn buccal swab				X		X	X
	Newborn blood							X

Results: We hypothesize that the intervention will (i) reduce AD prevalence in high-risk children; (ii) favourably influence maternal gut colonization and increase SCFA metabolites thereby facilitating microbiota species richness during early infant colonization; (iii) have immunomodulatory effects associated with markers of immune homeostasis (at birth and during the postnatal period) in blood of mother and offspring as well as in breastmilk. The 60 dyads will be used for an ancillary study to analyze the mechanistic effects of prebiotics on immune system, gut microbiota's and milk's composition and function.

Conclusions: To our knowledge, PREGRALL will be the first clinical trial assessing the effects of prebiotics for allergy prevention during pregnancy exclusively. It will contribute to our understanding of mechanisms involved in allergy prevention and may help to define new strategies involving prebiotics use during the antenatal period for reducing the incidence of AD in high-risk families.