Double Blind Placebo Controlled Food Challenge (DBPCFC)
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Background: In Phase II/III clinical development, the Double Blind Placebo Controlled Food Challenge (DBPCFC) is the generally accepted primary measure to evaluate the effectivity of immunotherapy with relevant food allergens. The DBPCFC is a challenge procedure with increasing doses of food allergen to determine the reactivity and threshold dose to food a specific food allergen and serves as the gold standard to confirm diagnosis of food allergy. HAL Allergy is developing a chemically modified peanut allergen preparation for immunotherapy and requires a standardised, pharmaceutical-grade oral challenge test to determine efficacy during clinical development.

Methods: A systematic literature search was performed to grade (scale 0-11) the relevance and quality of food challenge tests being published to define a standardised food challenge protocol, an adequate methodology for standardised DBFPCFC. Grading was performed independently by two viewers.

Results: Peanut material should be roasted and ground into a powder. The allergens will be administered to the patient in a matrix. Matrices (such as vanilla, cinnamon and cocoa) need to be capable of blinding the sensory properties of the food in a small volume compatible with use in the target patient group. Hypoallergenic pudding, applesauce or oatmeal are very suitable vehicles. The amount of incremental steps in a DBPCFC, with a dosing interval of preferably 20 minutes, should not exceed 10 dosages. For our peanut immunotherapy clinical studies, a dosing schedule ranging from 0.1-300 mg is proposed for the DBPCFC before treatment and from 1-3000 mg (or possibly 6000 mg) of peanut protein post-treatment. Placebo and active should be administered on separate days in random order, with at least 48 hours between challenges. DBPCFCs need standardisation regarding the interpretation of objective and subjective symptoms. Standard criteria to define a positive challenge outcome do not exist and the variability in symptom assessment is relatively high.

Conclusions: The literature search has resulted in recommendations for the design of the food challenge protocol to be used in our peanut immunotherapy in upcoming Phase II/III clinical studies, especially with regards to dosing schedules, matrix, physical and psychological health, contraindications and other logistic considerations. Further research is needed to standardize signs and symptoms to define a positive food challenge.