**678 COVID-19 mRNA Vaccine-induced Immunization Stress-Related Response (ISRR) and Anaphylaxis: An Early Look at COVAAR Clinical Outcomes**

Muhammad Khalid, MD1, Joanna Utoh, MSN, CRNP1, Ellen Zeketser, RN, BSN, MPH1, Pamela Guerrero, MD PhD1, 1National Institute of Health.

**RATIONALE:** COVID-19 mRNA vaccine anaphylaxis has been estimated to occur at a higher rate compared to conventional vaccines. We aimed to assess safety of subsequent dose administration in individuals who experienced a systemic allergic reaction after 1st dose of an mRNA vaccine.

**METHODS:** Sixteen individuals with history of a systemic allergic reaction after 1st dose of COVID-19 mRNA vaccine received a 2nd dose of Pfizer-BioNTech and placebo in a randomized, double-blinded, cross-over fashion in the ICU. 13 subjects additionally received an unblinded Pfizer-BioNTech booster dose and underwent skin testing.

**RESULTS:** Of 16 participants (15 females; mean age: 45 years), 9 after 2nd dose of Pfizer BioNTech and 11 after placebo developed non-allergic reaction after 1st dose of COVID-19 mRNA vaccine. Of 16 participants (15 females; mean age: 45 years), 9 after Pfizer-BioNTech booster dose and underwent skin testing.

**CONCLUSIONS:** ISRR is an underrecognized vaccine-induced anaphylaxis mimic that likely contributes to the elevated rate of “allergic” reactions reported following COVID-19 mRNA vaccination. Recognizing ISRRs is essential to reduce vaccine hesitancy and allow subsequent vaccination.

---

**679 The BTK inhibitor acalabrutinib reduces or eliminates clinical reactivity during oral challenge to peanut in allergic adults**

Ragha Suresh, MD1, Collin Dunnam, MS1, Dhananjay Vaidya, MBBS, PhD, MPH2, Donald MacGlashan, MD PhD2, Robert Wood, MD, MD FAAAAI3, Bruce Bochner, MD FAAAAI4, Melanie Dispenza, MD PhD1, 1Johns Hopkins University School of Medicine, Department of Medicine, Division of Allergy and Immunology, 2Johns Hopkins University School of Medicine, Department of Medicine, Division of General Internal Medicine, 3Johns Hopkins University School Medicine, Department of Pediatrics, Division of Allergy and Immunology, 4Northwestern University Feinberg School of Medicine, Department of Medicine, Division of Allergy and Immunology.

**RATIONALE:** There are no known therapies that can reliably prevent IgE-mediated anaphylaxis. Bruton’s tyrosine kinase (BTK) is an essential enzyme for the FcεRI signaling pathway and is an ideal target to prevent IgE-mediated allergic reactions. We hypothesized that acalabrutinib, an FDA-approved BTK inhibitor, can prevent clinical reactivity to peanut in peanut-allergic adults.

**METHODS:** Adults with peanut allergy confirmed by specific IgE and/or skin prick testing (SPT) were enrolled in an open-label clinical trial. Subjects underwent a baseline placebo-controlled single-blinded graded oral food challenge (OFC) to peanut to establish their baseline level of clinical reactivity, as well as SPT and basophil activation testing (BAT) to peanut extract. After a minimum 6-week rest period, subjects received four standard oral doses of 100 mg acalabrutinib twice daily and underwent repeat OFC, SPT, and BAT.

**RESULTS:** At baseline, subjects tolerated a median 44 mg (range 1 to 444) of peanut protein before objective clinical reaction. During subsequent OFC while taking acalabrutinib, 7/9 subjects tolerated the maximum amount (4,044 mg) of peanut protein with no objective clinical reaction, and the last 2 subjects’ tolerant peanut dose increased from 14 to 1,044 and 3,044 mg, respectively. Average peanut SPT wheat size was reduced from 120 to 57 mm². Peanut- and anti-IgE antibody-induced BAT were negative on acalabrutinib in all subjects. No serious adverse events occurred.

**CONCLUSIONS:** Pharmacologic inhibition of BTK can reduce or prevent clinical reactivity to peanut during OFC in peanut-allergic adults. BTK inhibitors could be used as short-term therapies for high-risk procedures including allergen immunotherapy and drug desensitizations.