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

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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 Bio-NTech and 11 after placebo developed non-allergic manifestations (median onset: 3 minutes) such as numbness, tingling, dizziness, throat tightness, dysphagia, and transient hypertension consistent with Immunization Stress-Related Response (ISRR). 45% of these were categorized as moderate-severe owing to significant distress. Only 3 developed recurrent allergic reaction (median onset: 4 minutes) after vaccine including one Consortium of Food Allergy for Research (CoFAR) Grade 1 and two Grade 2 reactions, and none after placebo. Following unblinded booster, 10 of 13 developed ISRR symptoms (median onset: 7 mins; 20% moderate) and 1 had a recurrent allergic reaction (CoFAR Grade 3, onset: 2 mins). Two tested positive with Pfizer-BioNTech intradermal testing while all had negative excipient 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

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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 wheal size was reduced from 120 to 57 mm^2. 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.

680 Systemic Reactions in Infants and Toddlers: A Prospective Study of Oral Food Challenge Outcomes

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RATIONALE: Recognition of anaphylaxis in young children has unique challenges and may delay epinephrine administration, which is a known risk factor for adverse outcomes.

Specific challenges apply to anaphylaxis recognition in infants and toddlers. This is a non-verbal population that cannot communicate subjective symptoms; normal behavior in this age group can overlap with symptoms and signs of anaphylaxis, and current anaphylaxis diagnostic criteria has not been validated for those under 2 years of age.

METHODS: This is a prospective study of 523 oral food challenges (OFCs) in children under 36 months of age with a focus on those that experienced a systemic allergic reaction requiring epinephrine. OFCs were conducted at the Massachusetts General Hospital *for* Children Food Allergy Center between November 15, 2019 and July 22, 2022. Signs and symptoms were serially documented until resolution.

RESULTS: Of 523 OFCs, 14 (2.7%) resulted in systemic reactions, consisting of 3 infants and 11 toddlers. Thirteen (92.9%) had dermatologic symptoms, and of those, 8 (61.5%) had urticaria and 2 (15.4%) angioedema. Nine (64.3%) had respiratory symptoms, and of those, 2 had (22.2%) wheezing, 4 (44.4%) nasal congestion, 4 (44.4%) cough, and 1 (7.1%) stridor. Two (14.3%) had gastrointestinal symptoms and 13 had (92.9%) behavioral changes. Seven (50%) had mild cardiovascular symptoms all of which included tachycardia prior to epinephrine administration.

CONCLUSIONS: Signs and symptoms of anaphylaxis in infants differ from older age groups and may have greater than previously recognized cardiovascular system involvement.