020 Genetic polymorphisms associated with the development of immunotoxicity following immune checkpoint blockade

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RATIONALE: Risk factors associated with immunotherapy-related adverse events (IRAE) resulting from immune checkpoint blockade (ICB) are not well understood with no screening tests to characterize vulnerability to toxicity. This study monitored patients treated for various cancers with ICB for the development of IRAE and investigated correlations with single nucleotide polymorphisms (SNPs).

METHODS: 159 patients treated with ICB were investigated for development of IRAE within one year of ICB initiation and toxicity severity grade through electronic medical record review. Patient DNA was subjected to genetic microarray for whole genome sequencing and analyzed utilizing PLINK and R scripts. Correlations of SNPs were compared between patients who developed IRAE and those who did not.

RESULTS: The mean age of patients was 64.1 years old with 96 women and 61 men included. 90 lung, 32 breast, 22 gastrointestinal, 5 miscellaneous, 4 gynecological, 4 melanoma, and 2 renal primary cancer types were represented. 51 of the 159 (32.1%) patients experienced an IRAE with a mean severity grade of 2.2. Genetic analysis demonstrated correlations of elevated risk of toxicity associated with SNPs within the THEMIS gene (rs10769115), REG1A gene (multiple), KCTD14 gene (multiple), and GRAMD4 gene (rs5767272). Reduced risk of toxicity was associated with SNPs within the TRIM5 gene (rs10769115) and JAKMIP3 gene (rs7087791).

CONCLUSIONS: Several SNPs correlated with development of IRAE in this study and may be useful screening biomarkers or pharmacologic targets with implicated genes including THEMIS, involved in T-cell receptor development/repertoire, TRIM5 involved in pattern recognition of the innate immune system, and JAKMIP3, involved in janus kinus signaling.

021 Diagnosis of Hypersensitivity to Components of Anti-COVID Vaccines

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RATIONALE: Serious allergic reactions to vaccines are rare but mechanisms of safety issues need to be explored.

METHODS: 25 subjects with allergic reactions to COVID vaccine were examined. 9 had a vector vaccine containing TWEEN 80; 8 had an inactivated vaccine with aluminum hydroxide. 19 healthy volunteers were controls. All underwent SPT and patch tests with polysorbate 80 (Tween 80), aluminum hydroxide, and polyethylene glycol (PEG 2000).

RESULTS: 16 (64%) patients had local burning and swelling where the vaccines were administered, shortness of breath, dizziness, and flu-like symptoms. 5 (20%) had urticaria within 12 hours of vaccination; 2 (8%) felt dyspnea; 2 (8%) had subcutaneous nodules. Patch tests in 24 (96%) were negative for all vaccine components. SPT with vaccine components were positive in 7 (28%) including TWEEN 80 in 2 (8%) patients with dyspnea and asthma. One had a positive SPT with PEG2000. In 2 (8%) with urticaria after vector vaccine Gam-Covid-Vac, SPT with Tween 80 was positive. In 3 (12%) with urticaria, SPTs were negative for all components. SPT testing with aluminum hydroxide was negative in 23 (92%) patients. 18 (72%) believing they were allergic to the vaccine tested negative.

CONCLUSIONS: Patients with a history of anaphylaxis following vaccination should undergo allergy testing for vaccine components.

022 Impact of reported penicillin allergy on patient outcomes and antibiotic costs in a large cohort in the outpatient setting

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RATIONALE: Penicillin allergy (PA) is the most commonly documented drug sensitivity and yet its diagnosis is largely inaccurate. Data on medical aspects and expenditure outcomes of PA in the outpatient setting is important for optimizing healthcare policy.

METHODS: We conducted a retrospective, matched cohort study on a population of 2.6 million members of a single Health Maintenance Organization (HMO) in Israel. We investigated medical records of subjects with reported PA in 2022.

RESULTS: A total of 96,773 subjects with PA were included in the study. Most were women (63.3%) with a median age of 49 years and medium to high socioeconomic status (85.6%). Matching for age group, gender, ethnicity, socioeconomic status, and co-morbidities included 96,675 individuals. Patients with PA demonstrated more encounters with family physicians (OR 1.42 [1.38, 1.46], p<0.001), pediatrician (OR 1.1 [1.07, 1.14], p<0.001), and secondary care physicians, (OR 1.21 [1.19,1.24], p<0.001). They were hospitalized more than the non-allergy group (OR 1.12 [1.07, 1.17], p<0.001), with no significant difference in the length of stay. No significant difference was found in death events. PA subjects purchased more antibiotics than matched non-allegy subjects (average 0.93 ± 1.79 versus 0.8 ± 1.58, p<0.001), at higher costs (10.05 ± 46.50 versus 13.00 ± 270.19 USD, p<0.01). They also demonstrated increased use of clindamycin (OR 5.66 [5.38,5.95], p<0.001), macrolides (OR 4.20 [4.08,4.32], p<0.001) and quinolones (OR 1.50 [1.44,1.55], p<0.001).

CONCLUSIONS: In the outpatient setting, penicillin allergy label is associated with increased burden on healthcare resources and costs but not with increased mortality. Active, large-scale penicillin allergy delabeling strategies are warranted.