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Summary

TOWARD PRECISION THERAPY IN ULCERATIVE COLITIS: GENOTYPE-BASED SINGLE-NUCLEOTIDE POLYMORPHISM (SNPS) SIGNATURES PREDICT DEEP RESPONSE TO USTEKINUMAB - A POST-HOC ANALYSIS OF THE UNIFI TRIAL

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Genome-wide association analysis of 654 ulcerative colitis patients from the UNIFI trial identified 99 SNPs associated with response to ustekinumab at maintenance week 44, with the RGS1 locus emerging as a predictor across all six clinical, endoscopic, and histological endpoints.

KEY POINTS

- RGS1 was associated with all six treatment response endpoints (clinical remission, endoscopic improvement, endoscopic remission, histological improvement, histological remission, and mucosal healing), implicating lymphocyte trafficking in ustekinumab response.
- Clinical remission at week 44 was associated with 41 SNPs (9 protective, 32 risk-increasing), while mucosal healing was associated with 14 SNPs (8 protective, 6 risk-increasing) in 102 patients (15.69%).
- Additional immune regulatory genes identified included IL7R and HLA-DQA1 (known IBD loci involved in T-cell activity and antigen presentation), MAPT, and FHIT, suggesting epithelial integrity and immune regulation are important in achieving remission.
- The analysis included 1,528,830 variants from 650 patients with moderate-to-severe UC, using logistic regression adjusted for sex and genetic variability with a suggestive threshold of 1 × 10^-5.
- These are suggestive associations from a discovery study requiring independent replication and biological validation before clinical translation; transcriptomic validation is ongoing.

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