

Title: A Multi-Database, Retrospective, Long-term, Observational Safety Study of Pediatric Patients with Inflammatory Bowel Disease

Authors: Kevin Haynes (khaynes2@its.jnj.com), Tim Hoops (thoops2@its.jnj.com), Pankti Bhatt (pbhatt19@its.jnj.com), Robert Suruki (rsuruki@its.jnj.com), Patrick Ryan (pryan4@its.jnj.com), Jared Houghtaling (jhoughta@its.jnj.com)

Abstract:

Background: Infliximab is widely used for the treatment of pediatric inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). However, long-term safety data in real-world pediatric populations remain limited. Concerns persist regarding the potential risks of serious infections, malignancies, and autoimmune diseases associated with TNF inhibitor therapy in children. Additional real-world evidence is needed to complement existing clinical trial and post-marketing data. The primary objective was to compare the incidence of safety outcomes of interest, including any hospitalization, serious infections, tuberculosis (TB), new malignancy, and new autoimmune disease, among pediatric IBD patients who were new users of infliximab versus new users of comparator non-TNF inhibitor (non-TNFi) therapies. A second primary analysis compared infliximab to adalimumab.

Methods: This was a retrospective, observational, new-user, non-interventional safety study utilizing five large U.S. electronic healthcare databases (Health Verity, CCAE, MDCCD, Optum EHR, and Optum Clinformatics). The analysis was run as a distributed data network study using the OMOP CDM v5.4 and the Strategus workflow, specifically the CohortMethod package and the EvidenceSynthesis package. The study population included patients aged <17 years with incident IBD and at least one IBD complication. The target cohort was defined as those newly treated with infliximab. The comparator cohorts were defined as non-TNF therapies and separately adalimumab. Treatment pathways were explored to ensure comparability across the exposure groups. Propensity score stratification, statistical adjustment for baseline confounders, pre-specified analytic diagnostics to prevent biased analyses, and Bayesian meta-analysis across databases were employed. Both as-treated and intent-to-treat time-at-risk windows were assessed.

Results: Over 9,000 new infliximab pediatric patients were followed for a mean of 3.1 years (SD: 2.5). The mean age ranged from 12.4 to 12.8 years, and the population was predominantly male (52%–59%). Treatment pathways across the databases and cohorts are presented in Figure 1. Patients largely adhered to their treatments with notable real world therapeutic switching. The non-TNF group mostly switched to infliximab and other antiTNF inhibitors (eg, adalimumab). Bayesian meta-analysis hazard ratios (Figure 2)

comparing infliximab to non-TNF comparators were: any hospitalization 0.91 (95% CI: 0.69–1.22), serious infection 0.66 (95% CI: 0.38–1.14), new malignancy 1.03 (95% CI: 0.46–2.28), and new autoimmune disease 2.25 (95% CI: 1.18–4.30). Figure 3 shows the database heterogeneity of the autoimmune disease outcome. The majority of autoimmune events were driven by new-onset psoriasis. No significant differences were identified between infliximab and adalimumab.

Conclusions: Infliximab exposure was associated with an approximately two-fold increased risk of newly diagnosed autoimmune disease compared with non-TNF therapies, consistent with its established safety profile and known paradoxical effects of TNF inhibitors. No increased risk was observed for hospitalization, serious infection, or malignancy. These findings support the established benefit-risk profile of infliximab in pediatric IBD and provide robust real-world evidence complementing existing clinical and post-marketing data.

Figure 1: Treatment pathways

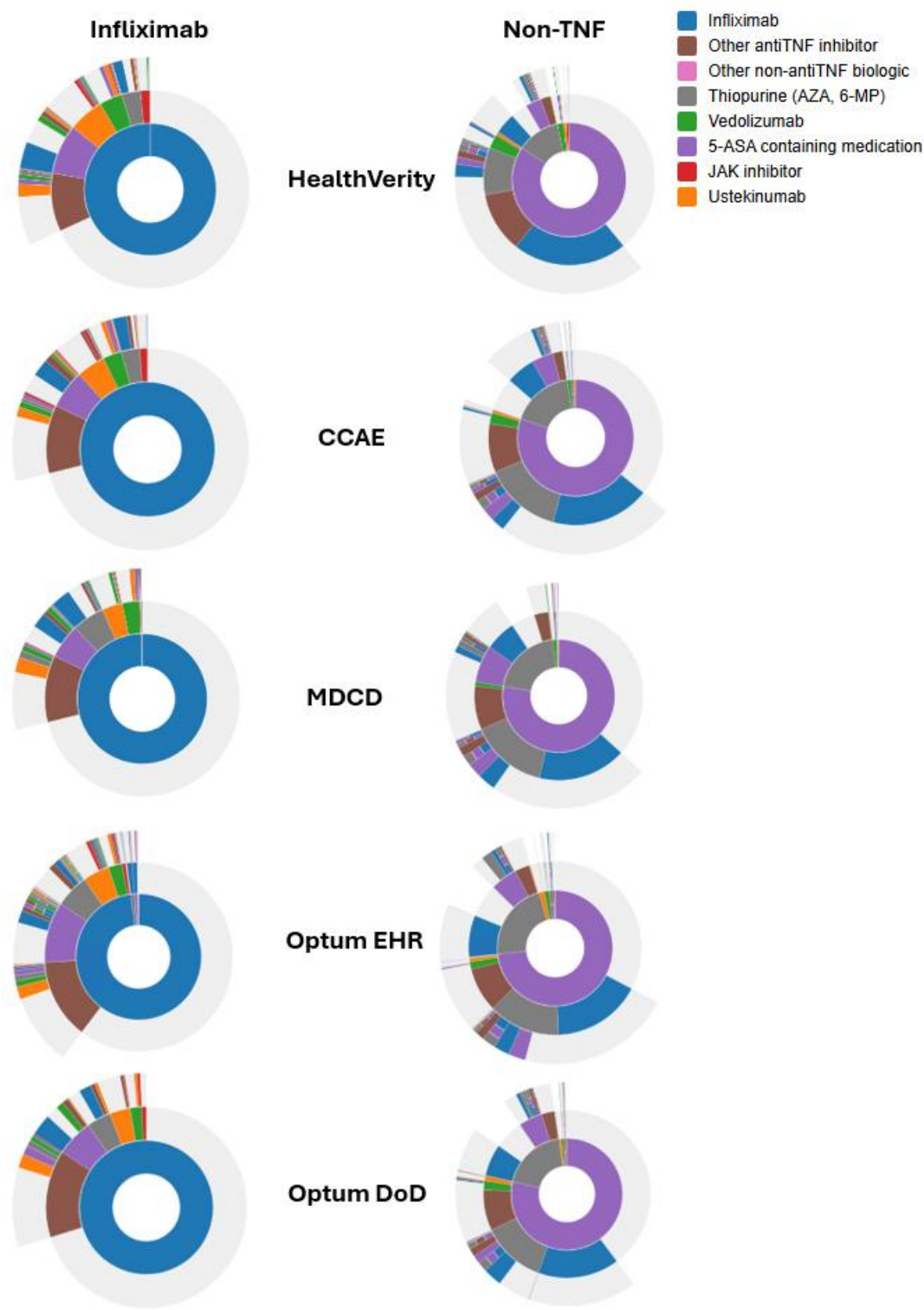


Figure 2: Bayesian meta-analysis results for on-treatment and intent-to-treat analyses

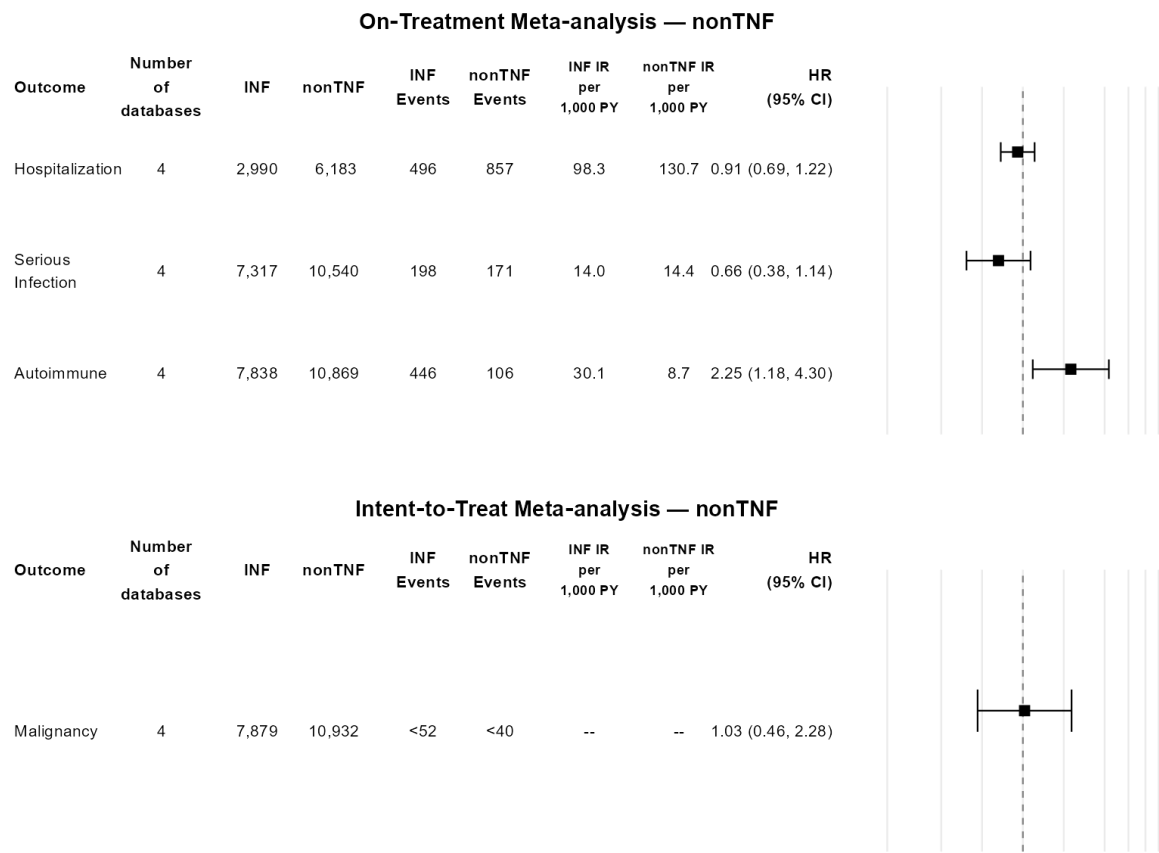


Figure 3: Infliximab Compared to Non-TNF Initiators in Pediatric IBD for New Events of Autoimmune Disease (SLE, MS, ON, PsO, PsA, JIA, or AH) On-treatment

Earliest event of a new autoimmune diagnosis of SLE, MS, ON, PsO, PsA, JIA, or AH — On-Treatment

