Introduction:

- Interleukin-1 inhibitors are immunosuppressive drugs that target the proinflammatory cytokines IL-1α and IL-1β.
- IL-1 inhibitors can be used to treat various rheumatologic disorders.
- The three available IL-1 inhibitors are anakinra, canakinumab and rilonacept.
- Although there are a few reports implicating IL-1 inhibitors as causes of inflammatory bowel disease (IBD), this is not a well-established adverse effect.
- The FDA Adverse Event Reporting System (FAERS) is a publicly available database for post-marketing surveillance of drug safety.

Objectives:

- Evaluate FAERS reports to examine the possible relationship between incidence of de novo IBD and treatment with IL-1 inhibitor therapies for various rheumatologic conditions.

Methods:

- All FAERS reports for patients receiving anakinra, canakinumab or rilonacept were investigated.
- Only "primary suspect" reports of IBD as an adverse event were selected.
- Subsequently, files were queried for inflammatory bowel disease, Crohn’s disease and ulcerative colitis as reaction terms.
- Detailed reports of these cases were requested from the FDA.
- The Adverse Drug Reaction Probability Score (Naranjo Scale), was applied to each case to assess the likelihood of a causal relationship between the IL-1 inhibitor and the adverse effect of de novo IBD (see Table 1).
- The probability of the drug reaction is assigned via a score for a definite (≥9), probable (5-8), possible (1-4), or doubtful (≤0) reaction.

Results:

- Of the 34 cases of IBD reported in patients from IL-1 inhibitor therapy, 6 were excluded because patients had a prior history of IBD.
- There were 12 reports of IBD from anakinra. Based on the Naranjo scale, 11 were possible anakinra-induced IBD and 1 was a doubtful case.
- There were 18 reports of canakinumab-induced IBD. Based on the Naranjo scale 17 were possible canakinumab-induced IBD and one was a probable case.
- There were no reports linking rilonacept therapy to IBD in the FAERS database (Table 2, Figure 1).

Conclusions:

- Review of the collected FAERS reports suggests a possible causal relationship between treatment with IL-1 inhibitors and de novo IBD.
- These results are significant, as the underlying pharmacodynamics of these medications may either unmask or initiate IBD in these patient populations being treated for various rheumatologic disorders.
- Further investigation of the mechanisms driving the development of IBD in patients on IL-1 inhibitor therapy is needed.