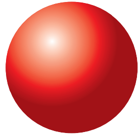

Management of Patients with Past or Present **History of Ileocolonic Disease**

Evidence Based Medicine | Official recommendations | Expert opinion

As with other biotherapies, the risk of infection is increased during tocilizumab therapy. Diverticulitis was one of the infectious events seen during tocilizumab therapy, albeit at a far lower rate than upper respiratory tract infections. Thus, diverticulitis is classified among the “uncommon” adverse events, i.e., those having rates of occurrence lower than 1/1000 but greater than 1/100.

Based on the clinical development program for tocilizumab, the FDA estimated the incidence of lower intestinal tract perforation at 0.15/100 patient-years. In the two North-American databases of RA patients who had not received tocilizumab therapy *(United Health Care Database and Marketscan Database)*, the incidences were 0.16 and 0.14 events/100 patient-years, respectively [(70)]. Lower intestinal tract perforation occurred only in the tocilizumab groups. However, all patients with lower gastrointestinal tract perforation had a history of bowel disease or current treatment with NSAIDs and/or glucocorticoids [(40)].

An even smaller number of patients experienced complications of diverticulitis, some of which were fatal. These complications consisted of generalized suppurative peritonitis, bowel perforation (usually of the colon), fistulas, and abscesses.

It should be borne in mind that NSAID therapy increases the risk of such complications in the general population [(71)]. More specifically, in RA patients the widespread use of NSAIDs and glucocorticoid therapy in combination is associated with an increased risk of these complications [(72-76)].

What steps should be taken before tocilizumab therapy in patients with a history of ileocolonic disease?

- Routinely ask the patient about a known history of diverticular disease, particularly with episodes of diverticulitis, or of perforation or ulcers.
- Routinely inform the patient about the risk of ileocolonic complications and ask the patient to seek medical help promptly in the event of abdominal pain, bleeding, or a change in bowel habits, particularly if there is also a fever; the patient should immediately inform the physician that he/she is on tocilizumab therapy.
- Inform the patient’s primary-care physician via the guide for physicians and pharmacists, which can be communicated via the patient or another means. This guide draws attention to the risk of diverticulitis and other complications, to the possibility that tocilizumab may mask classic signs of infection (fever and CRP elevation), and to the potentially devastating impact on patient outcomes of any delay in initiating appropriate treatment.

- In patients with a history of diverticulitis:
  - reappraise the risk/benefit ratio; in this situation, a discussion with the gastroenterologist and primary-care physician may be helpful;
  - to the extent possible, correct any other risk factors for superinfection or perforation such as poorly controlled diabetes, glucocorticoid therapy, or NSAID therapy;
  - in patients who have had a prior episode of diverticular sigmoiditis, consider sigmoid colon resection surgery. Although surgery is generally indicated only in the event of a second episode, prophylactic surgery after the first episode should be considered in patients who are scheduled to receive treatment with tocilizumab (or another immunosuppressive agent).
  - careful attention should be directed to informing and educating the patient and primary-care physician, as described above.

What are the warning signs of ileocolonic disease?

Before each tocilizumab infusion, the absence of abdominal symptoms or signs should be checked. It should be borne in mind that the classic signs of infection (fever, CRP elevation) may be missing in patients on tocilizumab therapy, and the slightest suspicion should lead to the infusion being postponed until the patient is evaluated by a specialist.

Course of action when ileocolonic disease is diagnosed

- If abdominal symptoms develop, discontinue tocilizumab therapy and refer the patient to a gastroenterologist; evaluation by a gastroenterologist should be obtained very promptly in patients with a fever, bleeding, or abnormal abdominal physical findings;
- The initial diagnostic and therapeutic strategy should be developed by the gastroenterologist based on national recommendations [77] then by the primary-care physician if there are no complications.

When can tocilizumab therapy be re-started?

In patients who experience diverticulitis while on tocilizumab therapy, the available data are inadequate to recommend re-starting the drug.

Prophylactic surgical resection should be considered.