Tofacitinib, celiac disease and the elderly: mind the gut!

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To the Editor,

We read with great attention the interesting case report by Lenfant et al. narrating the successful use of tofacitinib in a patient with microscopic colitis and celiac disease (1), and we would point some insights about this peculiar situation.

In fact, tofacitinib depicts potential side effects, including a higher risk of malignancies, and the FDA has even issued a warning about this drug's hazard (2).

Actually, a randomized open-label trial published in the *New England Journal of Medicine* in 2021 found that patients with rheumatoid arthritis who took tofacitinib had a higher risk of developing cancer than those who took a tumor necrosis factor (TNF) inhibitor (3).

Recently, two recent randmoized controlled trials from the ORAL Surveillance Trial and published in the *Annals of the Rheumatic Diseases* in 2023 also contributed to shed the light on this potential risk: that patients with rheumatoid arthritis aged > 50 with cardiovascular risk who took tofacitinib had a higher risk of developing any type of cancer than those who took a TNF inhibitor (4), and secondary stratification found that they were more likely to develop cancer if they were over the age of 65 years (5).

Adding insult to injury, the maligancies are also driven by the two peculiar forms of celiac disease: seronegative and refractory celiac disease (RCD), and this risk is also increased in CD diagnosed at adulthood: particularly, elder patients are prone to present a RCD, and giving immune checkpoint therapy might increase this risk (6).

In conclusion, RCD ought to be definetly ruled out before starting JAK inhibitor therapy, especially in aged population with seronegative celiac disease and microscopic colitis, two well-known conditions associated with RCD.

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