Upadacitinib and ustekinumab combination treatment for a refractory case of spondyloarthritis and Crohn’s disease

Sirs,

The safety of biological drug-modifying anti-rheumatic drugs (bDMARDs) and of targeted synthetic(s) DMARDs has been extensively described in the literature in many branches, including rheumatology, gastroenterology, and dermatology. However, data about safety of any combinations of these drugs are currently lacking.

In this regard, we report the clinical history of a patient with seronegative spondyloarthritis and Crohn’s disease, who was treated with a combination of ustekinumab and upadacitinib.

A 30-year-old female patient with type 2 diabetes mellitus and Crohn’s disease, in treatment with adalimumab 40 mg every 2 weeks, was admitted to our rheumatology department in February 2019 for severe inflammatory lower back pain. During the hospitalisation, a diagnosis of spondyloarthritis was established for the presence of active bilateral sacroiliitis on magnetic resonance imaging. The patient was negative for HLA-B27 and she had significantly and persistently elevated inflammation markers [erythrocyte sedimentation rate (ESR): 73 mm/h and C-reactive protein (CRP): 5.00 mg/dl], as well as very high disease activity (ASDAS 5.6 and BASDAI 8). Consequently, adalimumab was discontinued, and therapy with golimumab 50 mg every 4 weeks was initiated. Over the following six months, no clinical (ASDAS 5.3 and BASDAI 7.6) or laboratory improvements were observed (ESR: 106 mm/h, CRP: 3.76 mg/dl), despite the addition of sulfasalazine 2 g/day. Consequently, golimumab was discontinued, and the treatment was switched to infliximab 5 mg/kg every 8 weeks, which was later adjusted to 5 mg/kg every 6 weeks due to loss of efficacy at the end of the dosing interval. After 20 months of infliximab, our patient was switched to tofacitinib 5 mg bis in die, but this led to a new exacerbation of intestinal disease, requiring hospitalisation for active Crohn’s disease. As a consequence, tofacitinib was discontinued, and therapy with ustekinumab 90 mg every 12 weeks, was initiated. This led to remission of Crohn’s disease but had no effect on the lower back pain (ASDAS 4.4 and BASDAI 6.6) or on inflammation markers (ESR: 37 mm/h, CRP: 2.2 mm/h). Considering the patient’s pharmacological history and the lack therapeutic options, in agreement with the patient’s pharmacological history and the lack of any combination of anti-TNF-α agents (adalimumab, golimumab, certolizumab and anti-IL-12/23 ustekinumab) are practiced by gastroenterologists (1, 2), while dual biological therapy of anakinra and secukinumab, tocilizumab or certolizumab in familiar Mediterranean fever (3) has been attempted, as well as the combination of tofacitinib and adalimumab in resistant RA (4). Moreover, there is an ongoing clinical trial evaluating the efficacy of golimumab plus guselkumab in refractory PsA (NCT05071664). Nevertheless, the combination of p40 inhibitors does not raise particular concerns of adverse reactions, given the remarkable safety profile of these bDMARDs. To date, the available literature does not report an increase of adverse events when combining b/tdDMARDs with p40 inhibitors, but further studies, including randomised controlled trials are needed to better evaluate the safety and efficacy of such treatments.

Fig. 1. MRI: sacroiliac joints; T2 sequence: bilateral bone oedema on the sacral side.


References

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