Infliximab therapy in hematologic malignancies: handle with care (*Comment*)

We read with great interest the manuscript by Baron and colleagues entitled "Value of infliximab (Remicade®) in patients with low-risk myelodysplastic syndrome: final results of a randomized phase II trial (EORTC trial 06023) of the EORTC Leukemia Group".[1] The reported findings showed that infliximab displayed modest efficacy in patients with low-risk myelodysplastic syndrome (MDS). However, since a combination of infliximab and chemotherapy might represent a promising therapeutic strategy for MDS and acute myeloid leukemia (AML) patients, two safety issues should be considered.

The first issue concerns the possible risk of secondary malignancies associated with infliximab treatment. We recently diagnosed chronic myeloid leukemia (CML) in chronic phase (high Sokal risk; e14a2, high BCR-ABL^{IS} transcript 74.6%) in a 54-year old patient with rheumatoid arthritis who had been taken infliximab (5 mg/kg) for five years (from 2002 to 2007). Because of his newly diagnosed CML, he is now receiving tyrosine kinase inhibitor therapy (imatinib mesylate 400 mg daily) and has achieved a major molecular remission after 12 months. Thi is by no means an isolated case, since other accounts of lymphoproliferative or myeloproliferative disorders in patients receiving tumor necrosis alpha inhibitors have been published in the literature.[2-6] Therefore, although a direct causative link between infliximab and increased risk of second hematologic disorders has not been established, a warning should be raised.

A second issue relates to the potential risk of infections in patients treated with infliximab. Baron *et al.* reported a high cumulative incidence of grade 3-5 infections in both arms of their study (41% of patients in the 3 mg/kg arm and 19% of patients in the 5 mg/kg arm).[1] This finding might represent a second warning signal when using infliximab in patients with hematologic malignancies because of the suppressive effect that the drug might exert on normal hematopoietic progenitors.[7]

In conclusion, while infliximab might represent a promising agent with therapeutic activity in both MDS and AML, potential toxicities associated with this drug might warrant further assessment of its safety profile in specific subpopulations.

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References

1. Baron F, Suciu S, Amadori S, Muus P, Zwierzina H, Denzlinger C, et al. Value of infliximab (Remicade®) in patients with low-risk myelodysplastic syndrome: final results of a randomized phase II trial (EORTC trial 06023) of the EORTC Leukemia Group. Haematologica. 2012;97(4):529-33.
2. Brown SL, Greene MH, Gershon SK, Edwards ET, Braun MM. Tumor necrosis factor antagonist therapy and lymphoma development: twenty-six cases reprted to the Food and Drug Administration. Arthritis Rheum. 2002;46(12):3151-8.
3. Bakland G, Nassent H. Acute myelogenous leukemia following etanercept therapy. Rheumatology. 2003;42(7):900-1
4. Broussais F, Kawashima M, Marotte H, Miossec P. Chronic myeloid leukemia and tuberculosis in a patient with rheumatoid arthritis treated with infliximab. Ann Rheum Dis. 2005;64(3):509-10.
5. Fidder H, Schnitzler F, Ferrante M, Noman M, Katsanos K, Segaert S, et al. Long-term safety of infliximab for the treatment of inflammatory bowel disease: a single-centre cohort study. Gut. 2009;58(4):501-8.
6. Fischer M, Helper D, Chiorean MV. Myeloproliferative disorders in patients with inflammatory bowel disease on anti-TNF-α therapy: report of two cases and review of the literature. Inflamm Bowel Dis. 2011;17(2):674-5.
7. Murase T, Hotta T, Saito H, Ohno R. Effect of recombinant human tumor necrosis factor on the colony growth of human leukemia progenitor cells and normal hematopoietic progenitor cells. Blood. 1987;69(2):467-72.