Do You Know Pixantrone?

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Pixantrone is a novel anthracenedione, and as such it is popularly referred to as an “anthracycline-like” drug. Pixantrone has been obtained by extensive chemical modifications of the prototypic anthracenedione, mitoxantrone, and it has been approved by the European Medicines Agency (EMA), but not by the US Food and Drug Administration (FDA), for the treatment of refractory or relapsed non-Hodgkin lymphoma (r/r NHL).

For patients with newly diagnosed NHL, frontline therapy rests with an immuno-chemotherapy regimen that is called R-CHOP, where R reads rituximab (an anti-CD20 antibody) and CHOP reads a cocktail of cyclophosphamide, doxorubicin, vincristine, and prednisone. The reasons pixantrone was rejected by the FDA were quite multifaceted. The phase 3 study of pixantrone versus investigator-choice chemotherapeutics for the treatment of patients with r/r NHL recruited much fewer than planned patients, and in addition, only half of the patients were recruited in countries where rituximab was available for combination with CHOP at the time when NHL was diagnosed and CHOP was commenced. Thus, the FDA felt that the registration trial was both underpowered and structurally inadequate to provide a real representation of patients with r/r NHL. Further concerns were due to the incidence of grade 3–4 cardiotoxicity, which seemed to be higher in the pixantrone arm compared to investigator-choice drugs, as if pixantrone retained an anthracycline-like cardiotoxicity and precipitated subclinical cardiac damage induced by the doxorubicin-containing CHOP [1].

Following approval by the EMA, which maintained a role for pixantrone in a difficult-to-treat condition like r/r NHL, the drug became available in many countries, but its popularity with hematologists remained disappointing to say the least. It goes without too many words that the FDA decision counts, particularly in days when new drugs are running in the pipeline and hold promise for important twists in the field. Many doctors actually do not know pixantrone, and if they do, they believe it is one more anthracycline. In this issue of the journal, Appio et al. [2] report on a clinical case that clearly shows the might of pixantrone. They describe the case of a 56-year-old NHL patient who relapsed after R-CHOP, underwent second-line salvage therapy with rituximab, dexamethasone, high-dose cytarabine, and cisplatin (or oxaliplatin), but progressed before autologous stem cell transplantation could be performed. Third-line therapy with pixantrone and a single dose of rituximab offered a complete response and allowed the doctors to submit the patient to successful high-dose chemotherapy, followed by autologous stem cell transplantation and involved-field consolidation radiotherapy as appropriate. The patient enjoys a remission longer than a year, and his cardiac function is fully preserved. Thus, pixantrone was an excellent tool to bridge the patient to transplant – not bad for a little-known drug.

This is a case report and to be honest with our readers, we must recognize that one swallow does not make a summer. This having been acknowledged, the report by Appio et al. [2] raises a number of positive issues. The
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References


