Pegylated, liposomal doxorubicin in the treatment of primary cutaneous T-cell lymphoma: an update

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Pegylated liposomal doxorubicin (Peg-Doxo) is a new delivery system, able to improve the anthracycline concentration inside the tumor as well as its tolerability. The efficacy and safety of Peg-Doxo have been tested with remarkable results in a large spectrum of solid tumors and hematologic malignancies, both as single agent and in combination with other cytotoxic agents.[1-3] In the last 10 years, Peg-Doxo has been increasingly used in the heterogeneous group of primary cutaneous T-cell lymphomas (CTCL): advanced mycosis fungoides (MF, stage IIB-IV), Sézary syndrome (SS), primary cutaneous $CD30^+$ anaplastic large cell lymphoma with disseminated lesions, subcutaneous panniculitis-like T-cell lymphoma with progressive lesions, peripheral T-cell lymphoma, unspecified (PTL-U), and any refractory CTCL.[4-13] From the analysis of the results of the published case series and studies, some key points should be stressed. First of all, the overall response rate (ORR), which range from 56% to 88% (with 17% to 44% complete responses, CR) in stage I to IVA CTCL patients. This is the highest rate in monotherapy, with that obtained by gemcitabine in front line (75%)[14] as the only comparable, both superior with those obtained by the most commonly used polychemotherapy schemes. In addition, the response rate – and in particular, the CR rate – were overall not influenced by the stage of disease (I vs. IVA), while the prognostic category (MF vs. SS and PTL-U) influenced the response rate in some studies,[11] different from others.[12] The second point concerns the remarkable overall survival, ranging from 17-34 months, although the progression-free survival was much more variable (3-19 months). Third and last, the tolerability, which was overall very good, with max. 26% side effects and only 11% grade III-IV toxicities. In this regard, the dose escalation of Peg-Doxo (40 mg/m^2, instead of the classic 20 mg/m^2 dose) clearly increased toxicity, while did not produce any advantage in terms of clinical response.[12] In conclusion, Peg-Doxo can play a considerable role in the panorama of the available treatments of CTCL, with a high response rate and an excellent toxicity profile. This is of great importance in relation to the possible combination treatment (association and/or sequential) with different biologic response modifiers.[15-17] According to the preliminary results of a pilot study in 4 patients [Pimpinelli N *et al.*, manuscript in preparation], the association of Peg-Doxo with low dose oral bexarotene (150 mg/m^2/die) was able to produce long-term remissions in 3 of 4 patients, with an excellent benefit/risk profile.

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