Absence of efficacy of thalidomide monotherapy in patients with extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT lymphoma)

Mucosa-associated lymphoid tissue (MALT) lymphoma accounts for 7% of newly diagnosed lymphomas and is thought to arise from marginal zone B cells, which probably constitute the precursors of plasma cells [1]. Accordingly, MALT lymphoma shares some common features with multiple myeloma, i.e. the potential to produce monoclonal immunoglobulins as well as plasmacytic differentiation [2, 3]. In a recent case report, pronounced activity of thalidomide plus dexamethasone has been described in pulmonary MALT lymphoma, resulting in a near-complete remission [4]. These data have prompted us to initiate a phase II study (registered with www.clinicaltrials.gov) of thalidomide in patients with MALT lymphoma either failing *Helicobacter pylori* eradication or presenting with a priori disseminated disease. Primary end point was the rate of objective responses, with time to progression and toxic effects being the secondary end points.

Thalidomide was started at a daily dose of 100 mg given orally and was increased to 200 mg after 4 weeks in the absence of severe toxic effects. After the initial restaging scheduled after 3 months, an increase to 400 mg was allowed in patients who did neither show signs of regression nor progression of the lymphoma and who did not have severe toxic effects, while maintenance at 200 mg was carried out in responders.

A total of 16 patients were planned for enrolment, and an interim analysis was carried out after eight patients were enrolled. Six patients were male and two female, with the median age being 60 years (range 36–73 years). Five patients had gastric MALT lymphoma, two of the conjunctiva and one of the duodenum. One patient did not receive therapy before the initiation of therapy due to diagnosis of colon carcinoma (stage I) during staging colonoscopy, but was included as a treatment failure according to the intent-to-treat analysis. Only one patient was able to increase the daily dose to 400 mg, while three patients required dose reductions from 200 mg. Toxic effects included neuropathy grade I and II in three patients, dizziness in two, visual disturbance and taste changes in one and fatigue in four cases. One patient developed acute renal failure due to an infectious enteritis and discontinued treatment prematurely. No objective responses were seen, and at a median follow-up of 19 months (range 2–32 months), all patients are alive except one, who died from myocardial infarction unrelated to treatment. Four patients had stable disease for 3, 5, 7 and 8 months, respectively, and four patients were rated as progressive disease, including the one patient who was not treated was also rated as treatment failure.

In view of the absence of activity along with a higher than expected toxicity, the study was stopped after eight patients were enrolled. As opposed to a case report in the current literature [4], these data indicate that monotherapy with thalidomide is not effective in patients MALT lymphoma. In this case report, however, one might speculate that the activity of thalidomide was partly due to the combination with steroid treatment that had been applied in this patient, as combination treatment with thalidomide plus dexamethasone has also demonstrated enhanced activity on multiple myeloma.

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references


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