Prolonged clinical remission in patients with extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type treated with cladribine: 6 year follow-up of a phase II trial

A median 80 months follow-up with updated time to progression (TTP) and survival data is presented from a multicenter phase II trial using 2-Chlorodeoxyadenosine (2-CdA) in the treatment of extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type (MALT lymphoma) [1].

With the exception of Helicobacter pylori (HP) eradication therapy in localized gastric disease no established guidelines for the management of MALT lymphoma patients exist.
New insights in the pathophysiology and genetics [2] of the disease together with the emergence of precise diagnostic tools [3] have led to the development of risk adapted therapeutic concepts, favouring organ preservation.

Between March 1997 and August 2000 26 patients with histologically verified chemonaive MALT lymphoma were enrolled. For lymphomas in stage EI1 according to the Ann Arbor staging system modified by Musshoff and Radaszkiewicz et al. [4], the treatment was restricted to persistent MALT-lymphoma for at least 1 year following successful HP-eradication, progressive- and HP-negative disease.

2-CdA was administered at a dose of 0.12 mg/kg body weight intravenous (i.v.) infusion over 2 h given on days 1–5, four to six cycles every 28 days.

Twenty-five evaluable patients responded to therapy with twenty one patients (84%; 95% CI 63% to 96%) achieving complete remission (CR). Whereas patients with primary gastric lymphoma displayed a CR rate of 100% (95%; CI 81% to 100%), only three out of seven patients (= 43%) with initial extragastric manifestation achieved CR (95% CI 18% to 91%).

After a median follow-up time of 80 months (range; 64–107 months), 21 (84%) patients are alive. Seven patients (4 of 7 with extragastric primary and 3 of 19 with gastric primary) have relapsed or progressed. However, in three relapsing patients (two of them with gastric primary) a reduced dose had to be administered because of pronounced haematotoxicity. Six of the relapsing patients are still in remission after successful salvage therapy. Five patients have died, all of unrelated causes.

The median overall survival (including the 95% CI), as well as the median TTP, have not yet been reached (TTP 95% CI 5.5 years to not reached). Disease-free survival at 6.7 years was 68.5% (95% CI 41.8–84.9) for the entire group, 78.5% (12/15, 95% CI 37.1–87.7%) for patients with gastric primary and 33.3% (3/6, 95% CI 1.4–75.5%) for patients with extragastric tumor manifestation.

To our knowledge, this is the largest prospective study on chemotherapy in MALT lymphoma with the longest follow-up. In conclusion 2-CdA exerts excellent tumor control and long lasting remission in the majority of patients with gastric MALT lymphomas, which might potentially translate into cure. The latter assumption is based on the fact that our median follow-up of 80 months is much longer than the median time to relapse (47 months) reported for MALT-lymphoma in recent series [5]. The favourable toxicity profile and the convenient application mode suggest 2-CdA as a promising alternative to radiation. Recent data showing subcutaneous administration of 2-CdA as equally effective in comparison to i.v. application might further facilitate clinical use in MALT lymphoma. For extragastric manifestations however, combined modality therapies, i.e. including rituximab or combination with mitoxantrone should be investigated in prospective trials.

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