Treatment of mycosis fungoides and Sézary syndrome with romidepsin: a series of 32 cases from the French Study Group for Cutaneous Lymphoma

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Research letter

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Dear Editor, Treatment of cutaneous T-cell lymphoma is based on skin-directed therapies for early-stage disease and systemic therapies for advanced-stage disease. Romidepsin is a histone deacetylase inhibitor approved by the U.S. Food and Drug Administration. This is based on two phase II pivotal studies for the treatment of mycosis fungoides (MF) and Sézary syndrome (SS) after at least one prior line of systemic therapy.[1,2] In France, romidepsin is available only on Temporary Use Authorization. Until now, few data have been available as to its use in a real-life setting.

We evaluated the efficacy and the safety profiles of romidepsin in a series of patients from the French Study Group for Cutaneous Lymphoma. Thirty-two patients treated between 2014 and 2017 were included in a retrospective multicentre study, including 20 with MF (seven stage I, three stage II, nine stage III and one stage IV) and 12 with SS. Romidepsin was delivered by intravenous infusion at a dose of 14 mg m^{-2} on days 1, 8 and 15 then every 28 days. Evaluation of efficacy and tolerance was performed at each cycle with pictures, evaluation of skin involvement by a physician, and blood tests, including red and white cell count, platelets, Sézary cell count, serum electrolytes, liver tests, lactate dehydrogenase and immunophenotyping of peripheral lymphocyte populations.

Complete response (CR) was defined as > 95% improvement of skin disease, partial response (PR) as > 50% improvement and progressive disease as > 25% progression. In the other cases, the disease was deemed stable.[3] We considered the best overall response during all of the treatment, and the time to response (TTR). Data were reported and analysed retrospectively using medical records. Progression-free survival (PFS) was defined as the time without skin progression from the best overall response, and TTR as the time to response after the beginning of treatment.

The patients had received a median of five prior lines of systemic treatment, and a median of five cycles of romidepsin (range 1–14). The median follow-up was 10·5 months (range 1–29). A response was observed in 15 patients (47%), including 12 PR (38%) and three CR (9%). The disease was stable in nine patients (28%) and progressed in eight patients (25%) (Fig. 1a). The rate of best overall response was 60% in MF and 25% in SS, P = 0·05 (Fig. 1b). The median TTR was 3 months (range 1–10). Among patients with MF, six of eight with early MF were responders vs. six of 12 with advanced MF, with no statistical difference (P = 0·37) (Fig. 1c).

Six of the 32 patients received romidepsin after fewer than three prior lines of systemic therapies, of whom three experienced an objective response (50%). This compared with 12 responders out of 26 who were more heavily pretreated, with no significant difference. The median PFS was 5 months (range 1–27) (Fig. 1d), and was similar between patients with MF (4·2 months) and SS (5·8 months, P = 0·70; Fig. 1e). A long-term response (> 12 months) was observed in seven patients (five MF and two SS). Almost all patients (31 of 32) experienced at least one adverse event (AE) during the treatment, with a median of 4·5 AEs (range 0–10) and a total of 137 AEs. Among these, 125 were grade 1 or 2 and 12 were grade 3 or 4 (nausea or vomiting, asthenia and cytopenia). Twelve patients permanently discontinued treatment because of AEs of grade 3–4 (four of 12) or because of cumulative AEs resulting in quality-of-life impairment (eight of 12).

This first French evaluation of the use of romidepsin in a real-life setting confirms its efficacy, as 47% of patients presented a response. These results were better than in the two pivotal studies[1,2] (response rate of 34%). The real-life setting compared with a trial situation could in part explain the observed difference. In our study the modified Severity-Weighted Assessment Tool was not used, because the study was retrospective and this score was not systematically indicated in the medical records. Our study confirms the existence of long-term responders (especially in patients with MF).[4,5] Although romidepsin seems to be more effective for MF, we did not find any predictive factor for efficacy. Similar efficacy was observed in patients treated before or after the fourth-line therapy (as proved in a recent study showing similar response rates in patients pretreated by chemotherapy or not),[6] and similar efficacy was also seen in patients with early- and advanced-stage disease. The safety profile was similar to that in other studies.

Larger studies should be useful to find predictive response factors, but although this treatment is easily accessible in France, the special request is a limiting factor for realization of such studies. However, our series confirms that romidepsin represents an interesting additional treatment line for patients with a cutaneous T-cell lymphoma.

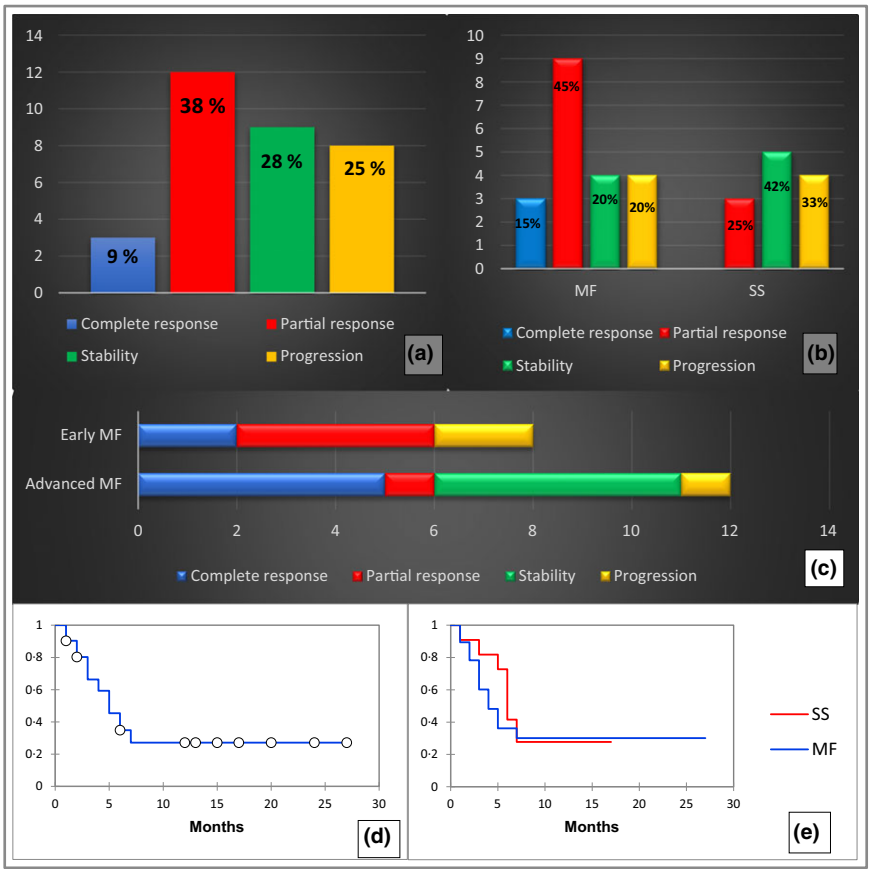

Fig 1. (a) Overall best response rates. (b) Overall best response rates in the mycosis fungoides (MF) and Sézary syndrome (SS) subgroups. (c) Overall best response rates: early vs. advanced MF. (d) Overall progression-free survival. (e) Progression-free survival in the MF and SS subgroups.

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