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Reduction of 5-azacitidine induced skin reactions in MDS patients with evening primrose oil

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Dear Editor,

5-Azacitidine has become the standard of care for patients with high-risk myelodysplastic syndromes (MDS), because it has shown an impressive survival benefit compared to three conventional care regimens [1]. In the pivotal trial by Fenaux et al. [1], 5-azacitidine was administered subcutaneously (s.c.) for 7 days. Other trials [2] have tested administration over a cumulative period of up to 10 days. In general, in case of response, the treatment needs to be continued until disease progression. Although an oral formulation is under development [3] and i.v. administration is also possible, the majority of patients receive the drug s.c., according to the phase III trial that was the basis for approval in the European Union. The drug appears to be very well tolerated, however, and in agreements with a recent report in this journal [4], local injection site skin reactions are observed within the most common non-hematological adverse events. This side effect, although usually completely and spontaneously reversible, often is of

inflammatory nature and can be painful, displaying therefore a challenge in the daily clinical care of these patients. Although several recommendations exist in order to prevent this complication (like preventing drug residues in the injection channel), still, this side effect occurs in the majority of the patients [5]. In fact, in our own experience with more than 50 patients, around 60% experienced skin reactions.

As a result and based on the recommendation of an MDS patient (who made this observation by chance), we used evening primrose oil (*Oenothera biennis*) administered topically and immediately after each 5-azacitidine injection in ten patients, who had already experienced skin reactions during their previous 5-azacitidine cycles. Evening primrose oil consists mainly of unsaturated fatty acids (predominately gamma-linoleic acid), which has anti-inflammatory properties. In Germany, it is an over-the-counter drug sold in pharmacies and has been successfully used in patients with atopic dermatitis [6, 7]. As shown in Fig. 1, evening primrose oil can successfully alleviate inflammatory skin reactions in these patients. In fact, six out of ten consecutive patients showed an impressive reduction in injection site reactions compared to previous cycles. Although the patient numbers are still limited and the data preliminary and not a result of a true randomized trial, we wanted to share our observations with other colleagues involved in the care of MDS patients. We strongly believe that evening primrose oil might be a safe and inexpensive local therapy which could improve patient compliance and adherence to the scheduled s.c. drug protocol.

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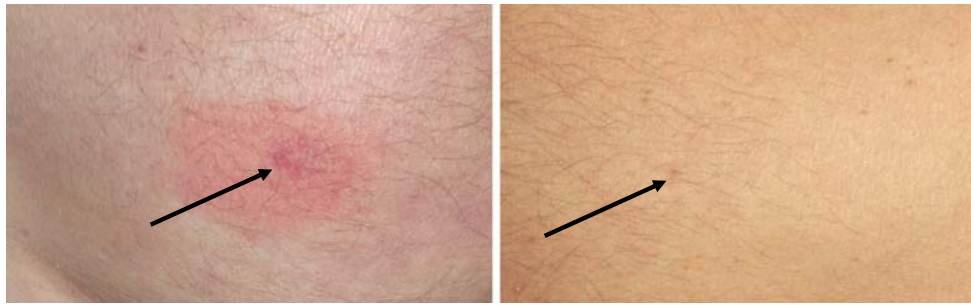


Fig. 1 Example of an MDS patient receiving 5-azacitidine *without* (left shows the injection site of the belly in a patient 24 h after s.c. injection) or *with* (right shows a different injection site of the belly in

the same patient 24 h after s.c. injection) local evening primrose oil treatment administration immediately after s.c. injection; the *arrow* marks the injection site

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