SHORT COMMUNICATION

Dimethyl Fumarate Treatment in Patients with Moderate-to-Severe Psoriasis: A 52-week Real-life Study

Laura GNESOTTO[1#], Guido MIOSO[1#*], Federico BARDAZZI[2], Federica FILIPPI[2], Vito DI LERNIA[3], Alberto MOTOLESE[3], Sergio DI NUZZO[4], Andrea CONTI[5], Federica ARGINELLI[5], Monica CORAZZA[6], Giulia ODORICI[6], Alessandro BORGHI[6], Paolo GISONDI[7], Luigi NALDI[8], Paolo DAPAVO[9], Aurora PARODI[10], Martina BURLANDO[10] and Stefano PIASERICO[1]

[1]Dermatology Unit, Department of Medicine, University of Padova, Via Cesare Battisti 206, IT-35128 Padua, [2]Department of Experimental, Diagnostic and Specialty Medicine- Division of Dermatology, University of Bologna, Bologna, [3]Dermatology Unit, Arcispedale S. Maria Nuova, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, [4]Dermatology, Department of Medicine and Surgery, University of Parma, Parma, [5]Section of Dermatology, Department of Specialized Medicine, University of Modena and Reggio Emilia, Modena, [6]Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University of Ferrara, Ferrara, [7]Section of Dermatology, Department of Medicine, University of Verona, Verona, [8]Dermatology Unit, San Bortolo Hospital, Vicenza, [9]Section of Dermatology, Department of Medical Sciences, University of Turin, Turin and [10]University of Genova, DiSSal Section of Dermatology, San Martino Polyclinic Hospital IRCCS, Largo R. Benzi 10 16132 Genova, Italy. E-mail: guido.mioso@gmail.com

[#]These authors contributed equally to this work.

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Psoriasis is a chronic inflammatory immune-mediated disease, with an estimated prevalence of 2–4% in Europe. Recently, a new oral formulation of dimethyl fumarate (DMF) has been approved for treating adults with moderate-to-severe chronic plaque psoriasis (1). The aim of this multicentre retrospective study was to evaluate the effectiveness and safety of DMF in a real-life setting, through collecting and analysing data from DMF-treated patients with moderate-to-severe psoriasis.

MATERIALS AND METHODS

The study retrospectively collected data from DMF-treated adult patients with moderate-to-severe psoriasis presenting to 10 dermatological referral centres located in the central parts of Northern Italy (Bologna, Ferrara, Genova, Modena, Padova, Parma, Reggio-Emilia, Torino, Verona, Vicenza) from January 2019 to March 2021.

Psoriasis Area and Severity Index (PASI) was evaluated at weeks 0, 12, 24, and 52. The study protocol was approved by the local ethics committee (protocol 0053012/ 2022) and informed consent was obtained by the participating subjects. The following data were extracted from electronic medical records: demographics (sex and age), body mass index (BMI), comorbidities, psoriasis duration, psoriatic arthritis (PsA), clinical or laboratory side-effects.

Statistical analysis

PASI reduction $\geq$50% and $\geq$75% from baseline (PASI 50 and PASI 75, respectively) were assessed using both intention-to-treat (ITT) and per-protocol analysis (PP). In the ITT analysis, patients who withdrew from the study for any reason were defined as non-responders. Differences between psoriasis patients at baseline and at short-term or intermediate-term therapy were analysed using repeated measures of 1-way analysis of variance (ANOVA). Analyses were performed using IBM-SPSS software v.25 (Chicago, IL, USA). A p-value <0.05 was considered statistically significant.

RESULTS

Patient characteristics

The current study included 270 patients, 170 (63%) men, and 100 (37%) women, mean age ± standard deviation (SD) 55.8 ± 15.3 years (range 19–88 years), BMI 26.8 ± 4.4 kg/m^2 and psoriasis duration 17.4 ± 12.9 years.

A total of 160 patients (69.9%) underwent systemic therapy before DMF initiation, whereas 14 patients (6.1%) had previously been treated with biological drugs. Co-morbid conditions were reported in 198 (73.3%) patients (Table SI). In the study population, 90 were elderly patients (>65 years), 58 (64.4%) men, and 32 (35.6%) women, mean age ± SD 72.2 ± 5.9 years (range 65–88 years), BMI 27±3.9 kg/m^2 and psoriasis duration 20.8±14.4 years.

Efficacy of dimethyl fumarate

Mean baseline PASI was 9.9 ± 5.7, which decreased to 4.6, 2.9, and 2.3 after 12, 24 and 52 weeks of treatment, respectively ($p<0.001$). At 12 weeks, PASI 50 was achieved by 109 patients (40.4% of the ITT population and 61.9% of the PP population), while PASI 75 was obtained by 46 patients (17% ITT, 25.8% PP).

At 52 weeks, PASI 50 and PASI 75 were achieved by 53 patients (19.6% ITT, 88.3% PP) and 40 patients (14.8% ITT, 66.7% PP), respectively (**Fig. 1**). Among the 90 elderly patients, PASI 50 and PASI 75 were achieved by 42 (46.7% ITT, 71.2% PP) and 22 patients (24.4% ITT, 36.7% PP), respectively, at 12 weeks. At 52 weeks, PASI 50 and 75 were achieved by 22 (24.4% ITT, 95.7% PP) and 16 patients (17.8% ITT, 69.6%PP), respectively (**Fig. 2**).

Safety profile of dimethyl fumarate

At least 1 adverse event was experienced by 163 (60.4%) patients, while 71 patients (26.6%) experienced laboratory side-effects. Overall, 116 (42.9%) patients interrupted the treatment because of side-effects.

The most common were gastrointestinal disorders (Table SII). Among the elderly group, 35 patients (38.9%) interrupted the treatment because of side-effects. However, the percentage was lower, albeit not significantly, compared with that of the younger patients (45.8%).

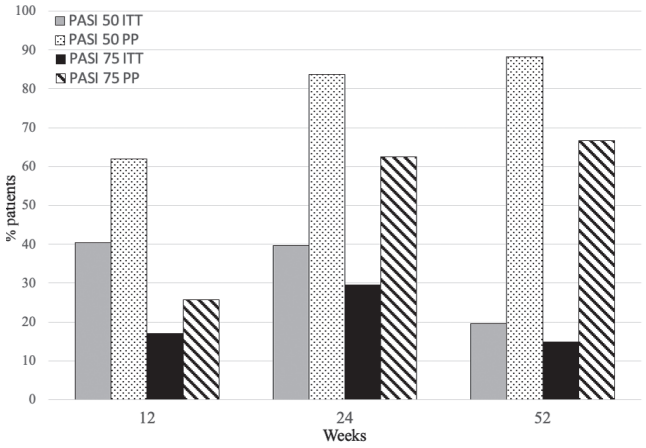

Fig. 1. Psoriasis Area and Severity Index (PASI) 50 and 75 rates after 12, 24 and 52 weeks (intention-to-treat (ITT) and per-protocol (PP) analysis).

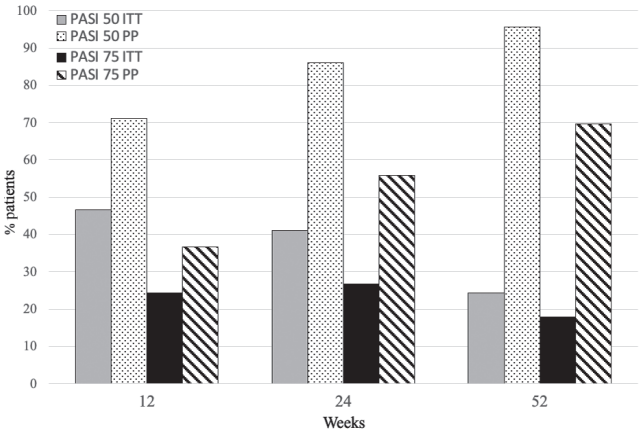

Fig. 2. Psoriasis Area and Severity Index (PASI) 50 and 75 rates in elderly patients (>65 years) after 12, 24 and 52 weeks (intention-to-treat (ITT) and per-protocol (PP) analysis).

DISCUSSION

This is the largest study of real-life use of DMF in adult patients with moderate-to-severe psoriasis, and the first to compare different evaluation methods (ITT and PP analyses) to handle a loss to follow-up. ITT and PP analyses revealed that PASI 75 was achieved by 14.8% and 66.7% of patients at 52 weeks, respectively.

Sparse data have been published regarding the real-world use of DMF (2–6). Moreover, most studies have focused on fumaric acid esters (FAE) (7–11). The findings of the current study are in agreement with those of a few studies on DMF. A real-life study by Malara et al. (2) on 36 patients reported a PASI 75 reached by 16% of patients at 16 weeks and by 61% of patients at 52 weeks (PP analysis). Other studies (3–6) confirmed DMF efficacy in a real-life scenario, revealing PASI 75 responses ranging from 17.5% to 33.3% of patients at the end of the observation period. Overall, PASI 75 achieved with DMF may not seem remarkable compared with other therapies for psoriasis. However, in a long-term analysis, a recent study showed that DMF has an efficacy comparable to other systemic treatments (6). In a subgroup population of 90 elderly patients it was found that PASI 50 and PASI 75 at 12, 24 and 52 weeks were higher than the entire population. DMF efficacy in elderly patients was also evaluated in a recent smaller retrospective multicentre study by Ricceri et al. (12). The mean PASI score at baseline was 9.8±4.1, which decreased to 4.3±3.2 at 16 weeks and 2.7±3.2 at 24 weeks. Previous randomized clinical trials reported that the main adverse events related to DMF therapy were gastrointestinal disorders (62.7%), especially diarrhoea (38.8%), upper abdominal pain (20.1%), and abdominal pain (19.7%) (13). Lijnen et al. (3) confirmed the high incidence of gastrointestinal disorders (58%) and reported a particularly great frequency of skin flushing (65%) and neutrophilia (65%).

The current study observed that 86.7% of patients experienced at least 1 side-effect; nausea (23.7%), diarrhoea (27.8%) and flushing (16.7%) being the most common. Overall, 43% of the patients studied had to discontinue the treatment due to side-effects. Similarly to the current study results, Walker et al. (8) reported that 43.4% of patients stopped FAE therapy due to an adverse event, mostly gastrointestinal disorders. In the current study population, 38 patients treated with DMF had an oncological history, and none experienced a relapse of malignancy during the follow-up period, as also reported by Corazza et al. (4). This may be related to the mild immunosuppressant effect of DMF.

The strengths of the current study include the large cohort of patients and the long period of observation (up to 52 weeks). Study limitations include the retrospective design and its multicentric nature, which could not allow a homogeneous patient selection.

In conclusion, the results of this study demonstrate the good effectiveness and excellent safety of treatment with DMF in a real-life setting in adult patients with moderate-to-severe psoriasis. DMF might not be the best choice when a high efficacy is needed, but its advantage may be the possibility to use this treatment in patients with multiple comorbidities and malignancy, even in elderly patients. However, further real-life studies are required to investigate treatment response patterns according to the heterogeneous psoriasis phenotypes, the long-term effectiveness and safety of the drug, and the identification of the best responder patient profile.

The authors have no conflicts of interest to declare.

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