RESIDENT’S FORUM

RF-The METOP Study: Further Evidence for the Use of Subcutaneous Methotrexate in Psoriasis

FR-Estudio METOP: nuevas evidencias sobre el uso del metotrexato subcutáneo en psoriasis

D. Morgado-Carrasco, X. Fustà-Novell, J. Riera-Monroig, J.M. Mascaró Galy*

Dermatology Department, Hospital Clinic, Universitat de Barcelona, Barcelona, Spain

KEYWORDS
Methotrexate; Subcutaneous; Psoriasis; Metop

PALABRAS CLAVE
Metotrexato; Subcutáneo; Psoriasis; Metop

Methotrexate (MTX) has been a first-line treatment for psoriasis for half a century. However, little high-quality scientific evidence and few well-designed clinical trials have yet been performed to support its efficacy. A recent meta-analysis showed a 75% reduction in the baseline Psoriasis Area Severity Index (PASI75) at 12 to 16 weeks in 45% of patients, and side effects that required drug withdrawal in 6.9%. A clinical trial of briakinumab versus MTX found that only 23.9% of patients receiving MTX achieved a PASI75 at 52 weeks, and that 72% (118/163) discontinued the drug due to lack of efficacy (95/163), side effects (9/163), or other reasons.2 Regarding the route of administration, some studies in rheumatoid arthritis suggest greater efficacy of methotrexate when given by subcutaneous injection (MTXSC).3

Warren et al.4 recently published the results of the European METOP study, a multicenter randomized, double-blind clinical trial of MTXSC versus placebo in patients with moderate to severe plaque psoriasis (PASI ≥ 10). During the first 16 weeks, patients received placebo (n = 29) or MTXSC (n = 91) at a dose of 17.5 mg/week, increasing to 22.5 mg/week depending on the clinical response at week 8. Subsequently, all patients received MTXSC up to week 52. At week 16, 41% of the MTXSC group and 10% of the placebo group achieved PASI75 (relative risk: 3.93; 95% confidence interval, 1.31-11.81; P = .0026). At week 52, 45% (n = 41) of patients had achieved a PASI75, and 28% a PASI90. MTXSC was well tolerated, with no reports of death, serious infections, or major cardiovascular events. Of the patients who received the drug for 52 weeks, 3% (n = 3) presented gastrointestinal intolerance requiring treatment discontinuation. Biopsies were performed on 27 patients prior to treatment and during week 16, observing a marked reduction in interleukin 17 and interferon-γ mRNA levels in those individuals with MTXSC who achieved a PASI75.

These results after 12 to 16 weeks of treatment with MTXSC are similar to those observed previously with oral

* Corresponding author.
E-mail address: josemanuel.mascaro@gmail.com
(J.M. Mascaró Galy).

1578-2190/© 2017 Published by Elsevier España, S.L.U.
MTX,\(^1\) with a PASI75 of around 40%. However, at week 52, the subcutaneous route appears to be considerably superior, with a PASI75 of 45% compared to 23% with oral MTX in previous studies, and a lower rate of treatment interruption.\(^2\) Furthermore, a PASI75 of 27% was achieved at 8 weeks in the METOP study compared with only 20% in a clinical trial with oral MTX.\(^2\) This would suggest a more rapid clinical response with MTXSC. That study also supported the use of a higher starting dose of MTXSC, as has recently been proposed.\(^5\)

Although MTX does not show the efficacy of the latest-generation biologic agents, it does have an appreciable response rate, a good safety profile, and lower cost. The subcutaneous route would appear to have advantages over oral MTX and could be considered as first-line therapy in psoriasis, although high-quality clinical trials comparing the efficacy of oral vs subcutaneous MTX are still required in this disease.

References