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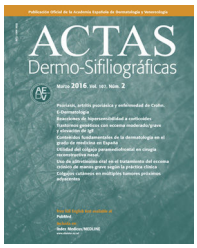

RESIDENT'S FORUM

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 Clínic, Universitat de Barcelona, Barcelona, Spain

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PALABRAS CLAVE
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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%.[1] 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 $\geq$ 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

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

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.

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