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Rheumatoid Arthritis Patients With Inadequate Response to Oral Methotrexate Maintain Satisfactory Disease Control and Durable Long-term Response When Switched to Subcutaneous Methotrexate Monotherapy

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BACKGROUND

Methotrexate (MTX) is the cornerstone of rheumatoid arthritis (RA) therapy, although many patients do not achieve an adequate response to oral MTX for reasons of tolerability or efficacy.[1,2]

Subcutaneous (SC) MTX has been shown to provide greater bioavailability than oral MTX at high doses,[3] and may offer benefits with respect to both tolerability and efficacy. SC MTX should be considered for patients with RA who have an unsatisfactory response to oral MTX.[4]

OBJECTIVES

- In this analysis, patients with RA were switched from oral MTX to SC MTX monotherapy, and their durability of response and level of disease control were evaluated

METHODS

- A retrospective analysis was performed from patient data collected between 2003 and 2011 at a single site in the United Kingdom[5]
- Per institutional practice, an incremental increase in the oral MTX dose was followed by a switch to SC MTX
- As a matter of routine practice, folic acid (5-15 mg) was given 1 day after SC MTX treatment
- Patients who switched from oral MTX to SC MTX monotherapy because of intolerance or inefficacy were included in the analysis, and data were obtained via patient record review
- Pre-switch and 6-month post-switch Disease Activity Scores including 28 joints (DAS28) were examined
  - Pre-switch and post-switch DAS28 were compared by Wilcoxon signed-rank analysis
  - Low disease activity (LDA) was defined as DAS28 ≤3.2; remission was defined as DAS28 ≤2.6
- Mean duration of SC MTX monotherapy following the switch from oral MTX was examined

RESULTS

Demographics and Disease Characteristics

- 112 Patients with RA were eligible for analysis (**Table 1**)
  - Mean age was 60.1 years (range, 26-83 y), mean disease duration was 9.6 years (range, 0.5-48 y), and mean MTX dose was 19.35 mg/week (range, 7.5-30 mg/wk)

Table 1. Baseline Demographics and Disease Characteristics

	All	Switched From Oral MTX to SC MTX Monotherapy		
		Total	Switched Because of Intolerability	Switched Because of Inefficacy
n	112	49	20	29
Age, y				
Mean	60.1	60.0	59.4	60.5
Range	26-83	30-83	31-74	30-83
Disease duration, y				
Mean	9.6	9.6	10.9	8.7
Range	0.5-48	0.5-48	0.5-48	0.5-23
MTX dose, mg/wk				
Mean	19.35	19.23	17.13	20.69
Range	7.5-30	7.5-30	7.5-25	10-30

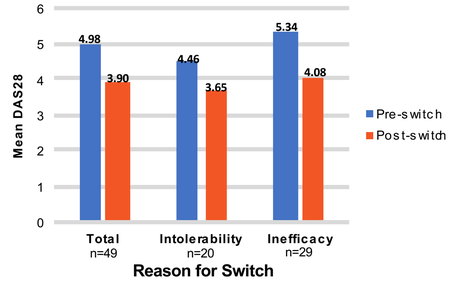
MTX, methotrexate; SC, subcutaneous.

- 49 Patients (44%) switched from oral MTX to SC MTX monotherapy for reasons of intolerance or inefficacy and were included in this analysis
- Among these 49 patients, 20 (41%) switched from oral MTX to SC MTX because of intolerability, and 29 (59%) switched because of inefficacy

DAS28

- Six months after the switch to SC MTX monotherapy, mean DAS28 decreased from 4.98 to 3.90 (**Figure 1**)
  - Mean changes in DAS28 were -1.05 among patients who switched because of intolerance and -1.26 among patients who switched because of inefficacy
  - Median DAS28 significantly improved overall (P<0.01) and among patients who switched because of inefficacy (P<0.01) (**Table 2**)

Figure 1. Mean DAS28 Among Patients Who Switched From Oral MTX to SC MTX Monotherapy



DAS28, Disease Activity Score including 28 joints; MTX, methotrexate; SC, subcutaneous.

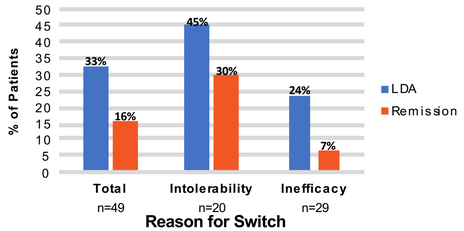
Table 2. Median DAS28 Among Patients Who Switched From Oral MTX to SC MTX Monotherapy

Reason for Switch	Pre-switch	Post-switch	*P* Value
Total	5.05	3.68	<0.01
Intolerability	4.97	3.65	Not significant
Inefficacy	5.65	4.21	<0.01

LDA and Remission

- 16 Patients (33%) achieved LDA, and 8 patients (16%) achieved remission (**Figure 2**)
  - Among patients who switched to SC MTX monotherapy because of intolerability, 9 (45%) achieved LDA and 6 (30%) achieved remission
  - Among patients who switched to SC MTX monotherapy because of inefficacy, 7 (24%) achieved LDA and 2 (7%) achieved remission

Figure 2. LDA and Remission Among Patients Who Switched From Oral MTX to SC MTX Monotherapy

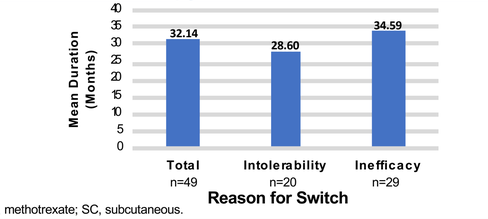


LDA, low disease activity; MTX, methotrexate; SC, subcutaneous.

Duration of SC MTX Monotherapy

- Patients remained on SC MTX monotherapy for a mean of 32.14 months (**Figure 3**)
  - Patients who switched from oral MTX because of intolerability remained on SC MTX monotherapy for a mean of 28.60 months
  - Patients who switched from oral MTX because of inefficacy remained on SC MTX monotherapy for a mean of 34.59 months

Figure 3. Duration of SC MTX Monotherapy Among Patients Who Switched From Oral MTX to SC MTX Monotherapy



MTX, methotrexate; SC, subcutaneous.

CONCLUSIONS

- In this single-center analysis, patients with RA who experienced an inadequate response to oral MTX for reasons of efficacy or tolerability maintained satisfactory disease control and a durable long-term response when switched to SC MTX monotherapy
- Among patients who switched from oral MTX to SC MTX monotherapy because of intolerability, DAS28 responses improved with SC MTX use
  - This improvement was numerically greater among patients who switched because of inefficacy
- DAS remission rates were higher among patients who switched because of intolerability (30%) than among patients who switched because of inefficacy (7%)
- Among patients with RA who tolerated oral MTX monotherapy poorly, a switch to SC MTX allowed them to continue on MTX monotherapy for approximately 29 months after oral MTX failure

DISCUSSION

Among patients with RA, those who experience intolerance to oral MTX may have the greatest potential to benefit from SC MTX monotherapy. This is broadly in line with clinician expectations and experience from switching in other studies.[6,7] In our practice, patients failing oral MTX because of nausea seem particularly suitable for the use of SC MTX.

Patients who discontinue oral MTX because of inefficacy may receive similar benefits from SC MTX, although fewer of these patients may be able to achieve LDA or remission. The patients identified in this study who switched to SC MTX because of inefficacy experienced a clinically important mean change in DAS28 of -1.26.

Many of the patients responding to SC MTX would have been eligible in the United Kingdom for progression to TNFα-blocking therapy. SC MTX is therefore likely to be cost-effective in comparison to alternative treatment strategies.

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DISCLOSURES

The authors have no conflicts of interest to disclose.

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