Comparison of two methotrexate initiation strategies in rheumatoid arthritis in current practice

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OBJETIVE

To compare the efficacy and tolerance at 3 and 6 months of two methotrexate (MTX) initiation strategies in rheumatoid arthritis (RA).

METHODS

Retrospective, monocentric, cross-sectional study including patients with RA who initiated MTX as first-line therapy during the last 2 years according to one of the following 2 strategies: a "classic" strategy defined by an initiation of oral MTX a dose of 10-15 mg/week or an "aggressive" strategy, defined by an initiation of subcutaneous (SC) MTX at a dose of 15 mg/week SC or >15 mg/week either orally or SC. Each strategy allowed the possibility to increase the doses and/or switch to the SC route at 3 months. Efficacy was assessed at 3 and 6 months using the DAS28-CRP. The tolerance of each strategy was also assessed at month 3 and 6.

RESULTS

We included 101 patients (85 women) with a mean age of 55±12 years and disease duration of 5±6 months. The frequency of rheumatoid factors, anti-CCP antibodies and erosions was 83%, 81% and 38% respectively. 61 patients initiated MTX according to the "classic" strategy, with an increase of dose and/or a switch to the SC route at 3 months for 31 patients, and 40 patients started treatment according to the "aggressive" strategy, with an increase of dose and/or switch to the SC route at 3 months for 14 patients. There was no difference between these 2 groups in terms of age, gender, disease duration, antibody status, frequency of bone erosions, body mass index, comorbidities and disease activity at baseline.

Efficacy at 3 months was significantly higher with the “aggressive” strategy (reduction of the DAS28-CRP from 4.34±0.91 to 2.39±0.75, mean difference of 1.95±1.21, p<0.001) compared to the “classic” strategy (reduction of the DAS28-CRP from 4.09±0.62 to 2.88±0.73, mean difference of 1.21±0.90, p=0.12) (Figure 1). The improvement of tender/swollen joint counts, patient global assessment and CRP levels was also significantly more important at 3 months with the “aggressive” strategy (Table 1).

	“Classic” strategy (n=61)	“Aggressive” strategy (n=40)	p-value
Variation of tender joint count	-2.6±3.4	-4.4±4.9	0.032
Variation of swollen joint count	-2.0±5	-4.7±4.0	0.005
Variation of PGA-VAS	-24±25	-40±35	0.009
Variation of CRP (mg/L)	-1.8±13	-15±20	<0.001

Table 1.Evaluation of efficacy parameter at 3 months according to the MTX initiation strategy

At 6 months, although the DAS28-CRP was similar in the 2 groups (Figure 1), less patients from the “aggressive” strategy subgroup required an escalation to a targeted biologic/synthetic therapy compared to the “classic” strategy (12/40, 30% vs. 29/61, 48%, p=0.073).

The frequency of digestive side effects at 3 months was significantly lower in the “aggressive” strategy (3/40, 7,5% vs. 16/61, 26%, p=0.021). The frequency of hepatic cytolysis at 3 month was higher in the aggressive strategy (4/40, 10% vs. 1/61, 1,6%, p=0.057). The frequency of asthenia at 3 months was similar in both groups (7/4, 18% vs. 6/61, 10%, p=0.25). Only one infection was observed in the “classic” strategy and no hematological side effect was recorded. At 6 months, the cumulative incidence of side effects was 23% with the “aggressive” strategy compared to 46% with the “classic” strategy (p=0.015). Only one treatment discontinuation was noted in the “aggressive” subgroup vs. 9 in the “classic” subgroup (p=0.042).

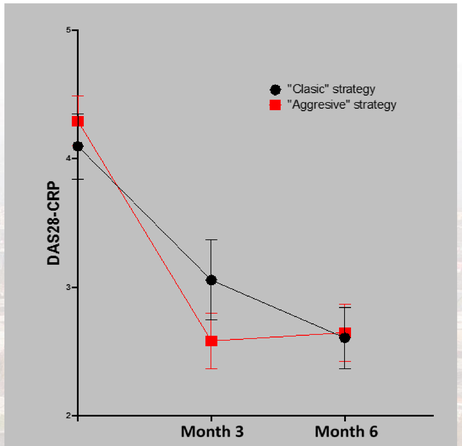

Figure 1: Evolution at 3 and 6 months of DAS28-CRP index according to the MTX initiation strategy

CONCLUSIONS

This study suggests that it is possible to use a more aggressive initiation strategy of MTX in RA in routine clinical practice. This strategy allows to obtain an earlier clinical response and it is associated with a better tolerance than the classic strategy. These results need to be confirmed in prospective studies.