Effectiveness of a once weekly double dose of etanercept in patients with juvenile idiopathic arthritis: a clinical study

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Etanercept is effective in juvenile idiopathic arthritis (JIA).^{1–3} Currently it is administered subcutaneously at a dose of 0.4 mg/kg (maximum of 25 mg) twice a week. Clinical trials in adults show that administration of a double dose once a week is effective enough to induce and retain remission.^{4,5} A pharmacokinetic model developed by Yim *et al*⁶ indicates that the same dosing regimen could be used in children. Wallace⁷ mentions the once weekly double dose in patients with JIA, but this is not supported by clinical trials. Therefore we evaluated the efficacy of etanercept administered subcutaneously once a week at a dose of 0.8 mg/kg (maximum of 50 mg) to retain and induce remission in patients with JIA.

Eleven patients with JIA, in remission, who had already been treated with etanercept twice a week at the usual dose were switched to the double dose of 0.8 mg/kg subcutaneously once a week. Two patients with JIA in whom etanercept at a dose of 0.8 mg/kg subcutaneously once a week was initiated were observed from the start of the treatment, to see if remission could be induced.

Table 1 shows the patient and disease characteristics. The outcome measures used to assess disease activity consisted of the following set of seven response variables: global assessment of disease activity by the physician and of pain and well-being by the patient all by visual analogue scale, Children Health Assessment Questionnaire, number of active joints, number of limited joints, and erythrocyte sedimentation rate. Patients were evaluated at the start of the study and after three months.

Table 1A summarises the data for patients for whom the administration of etanercept was switched to a double dose once a week. The equality between the response variables at the start of the study and after 3 months indicates remission according to the criteria of Wallace *et al*.⁸ None of the patients had a flare during the 3-month course of the study according to the definition of Brunner *et al*.⁹

Table 1B summarises the data for patients for whom etanercept was initiated at a double dose once a week. It is notable that there was a major improvement in all the response variables, except for the number of limited joints, which stayed the same. Lovell *et al*¹ modified this variable in their study because it is not a quick response variable and therefore not a good marker for short-term studies. The improvement in both patients met the definition of Giannini *et al*.¹⁰

There were no serious adverse events.

A limitation of this study is the open-label design, but a double-blind comparison of the two regimens would require a

number of patients with JIA that is almost impossible to recruit.

In conclusion, our clinical study supports what has been reported in theory in the literature, namely that the once weekly double dose of etanercept is just as effective at retaining remission in patients with JIA. Considering the good outcome in the two patients in whom etanercept was initiated at the once weekly double dose, it can also induce remission of JIA.

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Table 1 Patients characteristics, disease characteristics and disease activity variables; at start of study/after 3 months

A Patients switched from twice weekly usual dose to once weekly double dose etanercept														
Patient no	Sex	Age (years)	Disease duration (years)	Subtype	Etanercept use (years)	Co-medication at study start	Co-medication after 3 months	VAS physician	CHAQ (0-3)	VAS pain	VAS well-being	No of active joints	No of limited joints	ESR (mm/h)
1	Male	15.0	9.5	sJIA	4.4			0/0	0/0	0/0	0/0	0/0	2/1	2/5
2	Male	12.4	8.3	sJIA	4.3			0/0	0.1/0	21/2	0/2	0/0	2/0	4/6
3	Female	15.1	9.6	sJIA	4.7	15 mg MTX/week, NSAID	15 mg MTX/week, dose NSAID lowered	0/0	0.1/0.125	3/2	2/5	0/0	5/5	2/8
4	Male	18.2	9.9	pJIA RF+	0.4	5 mg MTX/week	MTX stopped	0/0	0/0	0/2	0/1	0/0	3/2	3/10
5	Female	13.5	3.4	pJIA RF-	0.8			0/0	0.3/0.3	0/0	0/0	0/0	2/1	5/3
6	Female	14.5	8.4	pJIA RF-	1.4	7.5 mg MTX/week, NSAID	7.5 mg MTX/week, NSAID	3/9	0.25/0.3	1/6	0/4	0/0	12/12	3/12
7	Female	12.9	2.9	pJIA RF-	1.3			0/0	0/0	0/0	2/1	0/0	4/0	17/12
8	Female	11.9	3.5	pJIA RF-	0.6			0/0	0/0	0/12	0/0	0/0	2/1	9/20
9	Male	17.0	8.0	oJIA ext	2.1			0/0	0/0.25	3/0	2/3	0/0	6/7	1/2
10	Male	10.6	4.9	oJIA ext	1.3			0/0	0.8/0.125	671/48	38/41	0/0	1/0	3/5
11	Female	8.5	2.0	PsJIA	0.9	5 mg MTX/week	5 mg MTX/week	0/0	0.1/0.4	0/0.7	0/0	0/0	0/0	2/5
Mean		13.6	6.4		2.0			0.27/0.82	0.15/0.136	8.64/6.61	4/5.18	0/0	3.55/2.64	4.64/8
B Patients in whom etanercept therapy was initiated in once weekly double dose														
Patient no	Sex	Age (years)	Disease duration (years)	Subtype	Co-medication at study start	Co-medication after 3 months	VAS physician	CHAQ (0-3)	VAS pain	VAS well-being	No of active joints	No of limited joints	ESR (mm/h)	
12	Female	17.3	5.0	pJIA RF+	25 mg MTX/week, NSAID	MTX stop, NSAID	58/16	2.5/1.5	100/13	61/1	35/11	14/14	38/34	
13	Female	14.3	1.4	pJIA RF+	25 mg MTX/week, prednisone, NSAID	15 mg MTX/week, prednisone, dose NSAID lowered	72.4% 83/0	40.0% 2.4/0	87.0% 81/0	98.4% 98/0	68.6% 23/0	0% 5/5	10.5% 4/2	
						Improvement	100%	100%	100%	100%	100%	0%	50%	

CHAQ, Children's Health Assessment Questionnaire; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; oJIA ext, oligoarticular extended JIA; pJIA RF+, polyarticular rheumatoid factor positive JIA; pJIA RF-, polyarticular rheumatoid factor negative JIA; PsJIA, juvenile arthritis psoriatic; RF, rheumatoid factor; sJIA, systemic JIA; VAS, visual analogue scale (1-100 mm).

CHAQ, Children's Health Assessment Questionnaire; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; oJIA ext, oligoarticular extended JIA; pJIA RF+, polyarticular rheumatoid factor positive JIA; pJIA RF-, polyarticular rheumatoid factor negative JIA; PsJIA, juvenile arthritis psoriatica; RF, rheumatoid factor; sJIA, systemic JIA; VAS, visual analogue scale (1-100 mm).