2006. TACRO UC

RCT/Tacrolimus/UC/Induction

A randomised dose finding study of oral tacrolimus (FK506) therapy in refractory ulcerative colitis

2-week study. Placebo-controlled, double-blind randomized trial.
Refractory active UC patients randomised to:
- Tacrolimus 0.05mg/kg, high trough (HT) (levels 10-15ng/ml) vs low-trough (LT) (5-10ng/ml) or placebo. Followed by an open-label 10 week extension in which all patients received tacrolimus.

Primary endpoint: improvement of DAI score w2, w10

Results:
- Improvement of DAI at w2, 68.4% in HT vs 10% placebo, p<0.001
- OLE at w10, 55.2% improved DAI
- Higher incidence of side effects in the HT than placebo.

Conclusions:
A dose dependent efficacy and safety of oral tacrolimus for remission-induction therapy of refractory UC was observed. The optimal target range appears to be 10–15 ng/ml in terms of efficacy with two week therapy.

Table 4 Clinical responses to therapy in the two week double blind study

Clinical response*	High trough group	Low trough group	Placebo group
No of patients (%)			
(n=60)†	19	21	20
Complete	0 (0)	0 (0)	0 (0)
Partial	13 (68.4) (p<0.001§)	8 (38.1) (p=0.067¶)	2 (10.0)
None	6 (31.6)	13 (61.9)	18 (90.0)
Severe patients (DAI score 10–12)			
(n=27)	6	10	11
Complete	0 (0)	0 (0)	0 (0)
Partial	4 (66.7) (p=0.086§)	5 (50.0) (p=0.219¶)	2 (18.2)
None	2 (33.3)	5 (50.0)	9 (81.8)
Moderate patients (DAI score 6–9)			
(n=33)	13	11	9
Complete	0 (0)	0 (0)	0 (0)
Partial	9 (69.2) (p=0.002§)	3 (27.3) (p=0.155¶)	0 (0)
None	4 (30.8)	8 (72.7)	9 (100.0)
Steroid resistant‡			
(n=15)	5	5	5
Complete	0 (0)	0 (0)	0 (0)
Partial	4 (80.0) (p=0.106§)	2 (40.0) (p=0.718¶)	1 (20.0)
None	1 (20.0)	3 (60.0)	4 (80.0)
Steroid dependent			
(n=45)	14	16	15
Complete	0 (0)	0 (0)	0 (0)
Partial	9 (64.3) (p=0.002§)	6 (37.5) (p=0.074¶)	1 (6.7)
None	5 (35.7)	10 (62.5)	14 (93.3)

Ogata H et al. Gut 2006;55:1255–1262