

Multicenter, randomized, double-blind placebo controlled trial. Patients with active perianal CD with draining perianal or enterocutaneous fistulas were randomized to treatment with oral tacrolimus 0.2mg/kg/d or placebo for 10 weeks.

Primary endpoint: Fistula improvement as defined by closure of over 50% of fistulas and maintenance of that closure for at least 4 w

#### Results: N=48

- Fistula improvement 43% tacrolimus vs 8% placebo, p=0.004
- Fistula remission 10% vs 8% placebo, p=0.86
- Adverse events were associated to tacrolimus including headache, leg cramps, tremor, increased creatinine that were managed decreasing the dose.

#### Conclusion:

Oral tacrolimus 0.2 mg/kg/day is effective for fistula improvement, but not fistula remission, in patients with perianal Crohn's disease. Adverse events associated with tacrolimus can be managed by dose reduction. Lower doses of tacrolimus should be evaluated.

**Table 3.** Adverse Events in the 2 Treatment Groups

Variable	Placebo group (n = 25)	Tacrolimus group (n = 21)	P
Mean (SD) no. of adverse events per patient	2.3 (2.3)	5.2 (4.2)	0.009
No. (%; 95% CI) of patients with adverse events	19 (76, 57–89)	20 (95, 79–100)	0.11
No. (%; 95% CI) of patients with serious adverse events	0 (0, 0–12)	1 (5, 0–21)	0.46
No. (%; 95% CI) of patients with severe adverse events	2 (8, 1–24)	6 (29, 13–51)	0.12
No. (%; 95% CI) of adverse events occurring in ≥10% of patients in at least one of the treatment groups			
Abdominal pain	2 (8, 1–24)	3 (14, 4–34)	0.65
Asthenia	1 (4, 0–19)	2 (10, 2–28)	0.58
Creatinine level increased	0 (0, 0–12)	8 (38, 20–60)	0.008
Diarrhea	3 (12, 3–30)	4 (19, 7–40)	0.69
Dizziness	0 (0, 0–12)	2 (10, 2–28)	0.20
Esophagitis	1 (4, 0–19)	2 (10, 2–28)	0.58
Headache	3 (12, 3–30)	10 (48, 28–72)	0.01
Hyperkalemia	0 (0, 0–12)	2 (10, 2–28)	0.20
Insomnia	0 (0, 0–12)	6 (29, 13–51)	0.006
Leg cramps	0 (0, 0–12)	5 (24, 10–46)	0.01
Leukocytosis	0 (0, 0–12)	2 (10, 2–28)	0.20
Nausea and/or vomiting	4 (16, 6–34)	6 (29, 13–51)	0.47
Paresthesias	1 (4, 0–19)	12 (57, 34–79)	<0.001
Peripheral edema	0 (0, 0–12)	2 (10, 2–28)	0.20
Pruritus	1 (4, 0–19)	4 (19, 7–40)	0.16
Rectal disorder	5 (20, 8–38)	3 (14, 4–34)	0.71
Rhinitis	3 (12, 3–30)	2 (10, 2–28)	1.00
Thinking abnormal	0 (0, 0–12)	2 (10, 2–28)	0.20
Tremor	0 (0, 0–12)	6 (29, 13–51)	0.006
Other	11 (44, 24–66)	11 (52, 28–72)	0.77

