2003.IV steroids & Immunogenicity

RCT/IV steroid/CD/Immunogenicity

Intravenous Hydrocortisone Premedication Reduces Antibodies to Infliximab in Crohn's Disease: A Randomized Controlled Trial

Study 1: Response and ATI formation in CD treated with IFX.
IFX for luminal disease 1 infusion and for fistulous 3 (0,2,6) and thereafter on-demand basis *
Study 2: Subsequent 16 week, double blind placebo controlled trial.
IV hydrocortisone 200mg or placebo inmediately before IV IFX

Primary endpoints: Reduction in median antibodies to infliximab (ATI) levels at week 16. ITT analysis.

Results:
- Study 1: continuous responders had lower median ATI levels than partial responders and nonresponders, p <0.0001
- Study 1: patients on concurrent immunosupressants had lower incidence of ATI 24% vs 63%, p =0.007 and IFX infusion within 8 weeks of the first OR 0.13, p=0.0007
- Study 2 (RCT): ATI levels were lower in the hydrocortisone group at w8 and w16, p=0.002 and p=0.02 respectively.

Conclusion:
Loss of initial response and infusion reactions post-IFX is strongly related to ATI formation and level. Administering a second infusion within 8 weeks of the first and concurrent immunosuppressant therapy significantly reduce ATI formation. Intravenous hydrocortisone premedication significantly reduces ATI levels but does not eliminate ATI formation or infusion reactions.

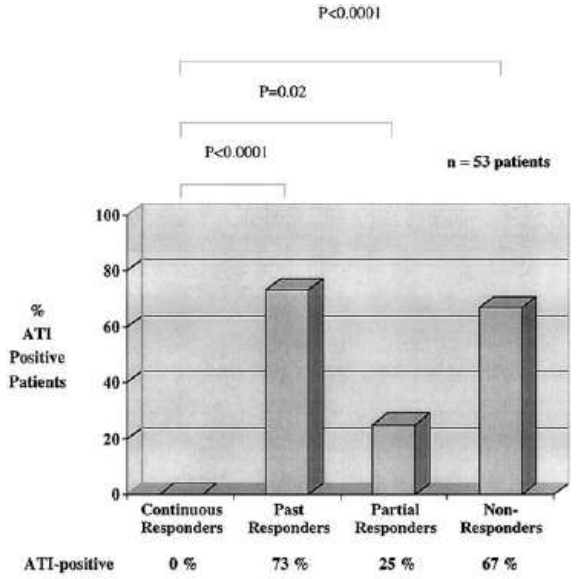

Figure 1. Relationship between response patterns and ATI formation in initial observational cohort of 53 patients. At follow-up, none of 21 continuous responders (0%) were ATI positive compared with 11 of 15 past responders (73%) ($P < 0.0001$), 2 of 8 partial responders (25%) ($P = 0.02$), and 6 of 9 nonresponders (67%), ($P < 0.0001$).

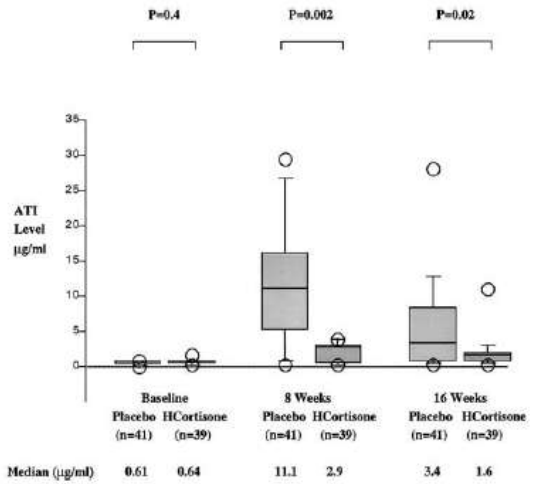

Figure 4. Median ATI concentration levels at baseline and at 8 and 16 weeks post-first infusion according to treatment (placebo/hydrocortisone) group. The *boxes* indicate the 25th percentiles, median values, and 75th percentiles; the *bars* indicate the 10th and 90th percentiles; and the *circles* indicate outliers. Median ATI levels were significantly lower in the hydrocortisone group compared with the placebo group at 8 weeks, (2.9 vs. 11.1 µg/mL, respectively; $P = 0.002$) and at 16 weeks (1.6 vs. 3.4 µg/mL, $P = 0.02$).

Farrel RJ et al. Gastroenterology. 2003; 124: 917-924