INFLIXIMAB FOR PREVENTION OF POST-OPERATIVE CROHN'S DISEASE RECURRENCE: THE PREVENT TRIAL

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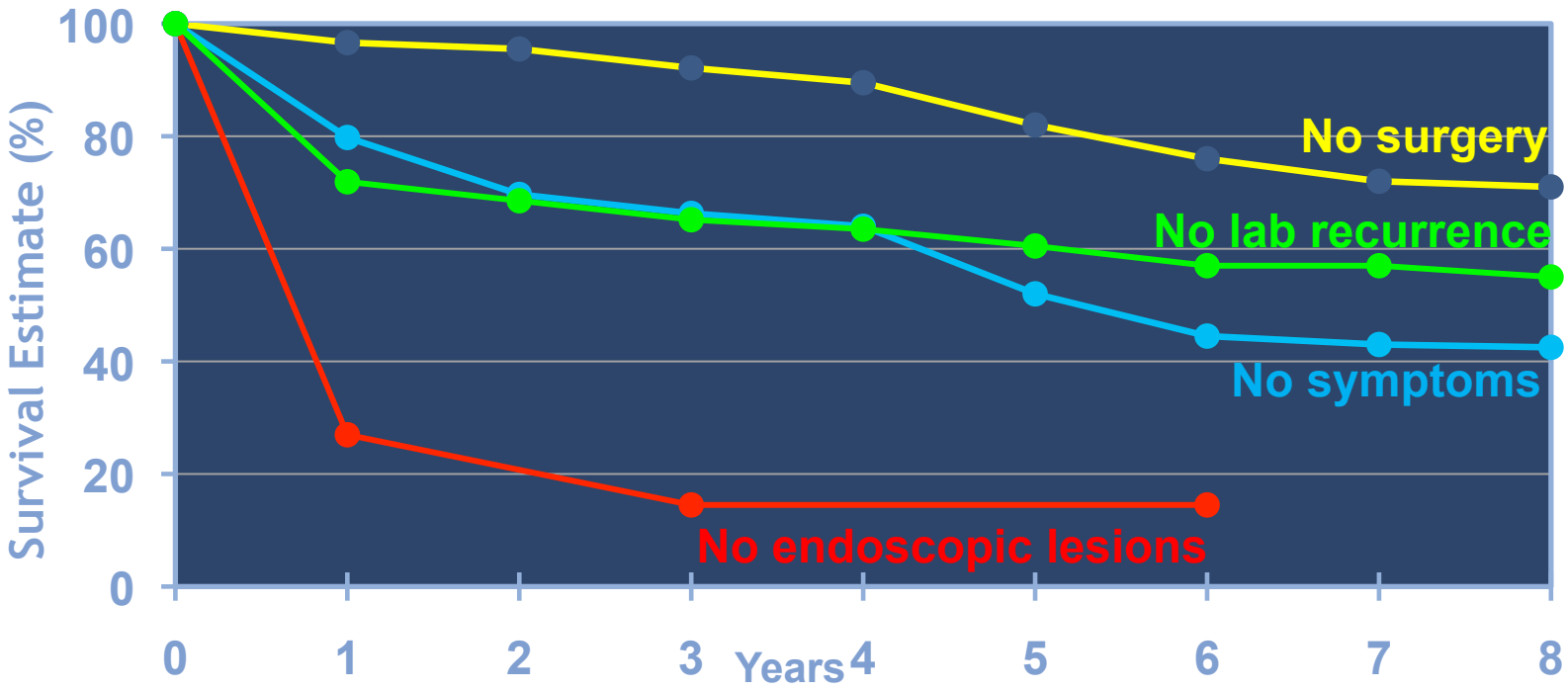
Objectives

- Discuss the current medical management of Crohn's disease following surgery
- Review the results of the PREVENT trial
- Discuss the place of infliximab in the post-operative management of Crohn's disease

Surgery is Not a Cure: CD Recurrence Following Resection



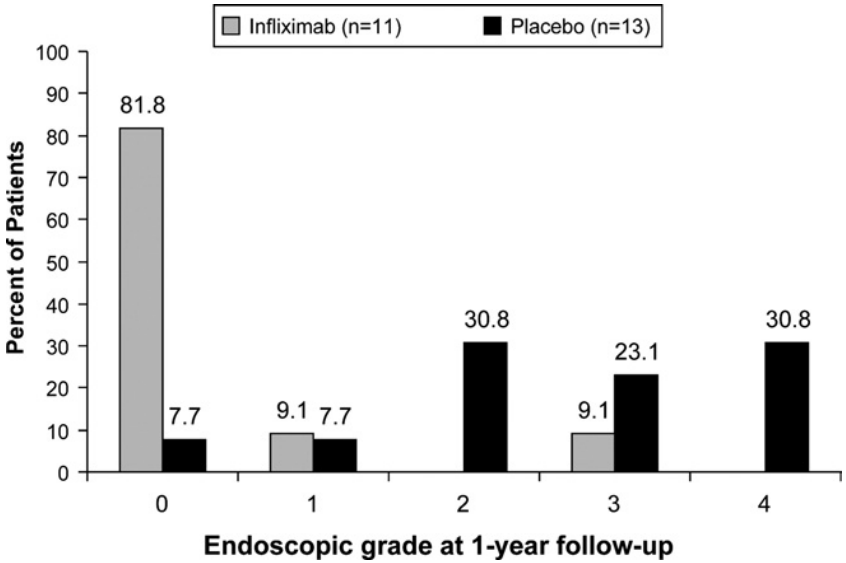
- At least 50% of patients require surgical treatment in the first 10 years of disease and approximately 70–80% will require surgery within their lifetime.[2]
- The post-operative clinical course is predicted by the severity of endoscopic lesions during the first year after resection

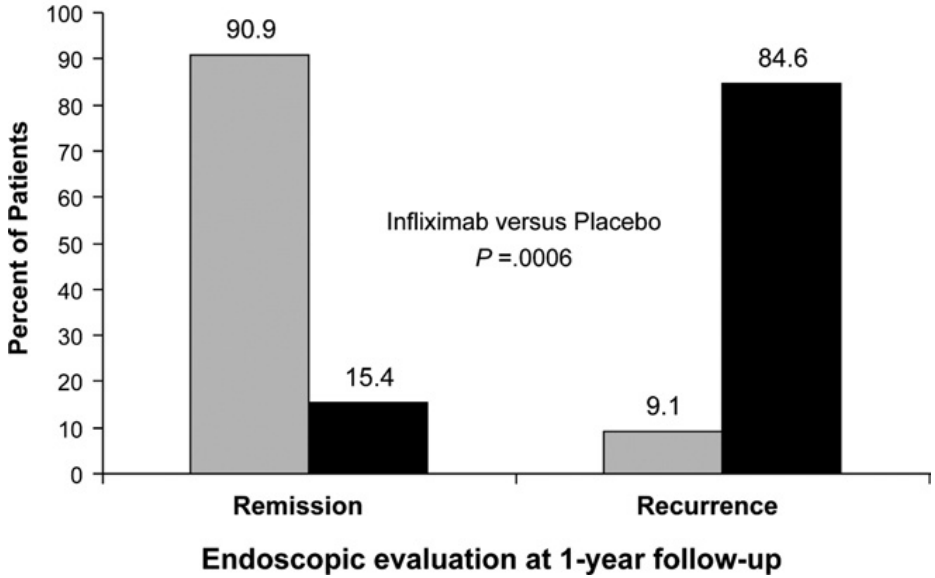
1. Rutgeerts et al. (1990) Gastroenterol;99:956-963; [2]Carter et al. Gut 2004;53:V1–16

Management of Post-operative CD Options

- No therapy
  - clinical assessment only
  - endoscopic / radiologic / biomarker follow-up
- 5-ASA
- Antiobiotics (metronidazole / ornidazole)
- Thiopurine analogs
- Anti-TNF agents

Anti-TNF Therapy for Prevention of Post-operative CD Recurrence: Infliximab vs Placebo





8 patients (3 IFX; 5 placebo) had received
1 – 4 doses of IFX prior to surgery

Rugeiro M, et al. Gastroenterology 2009;136:441-450

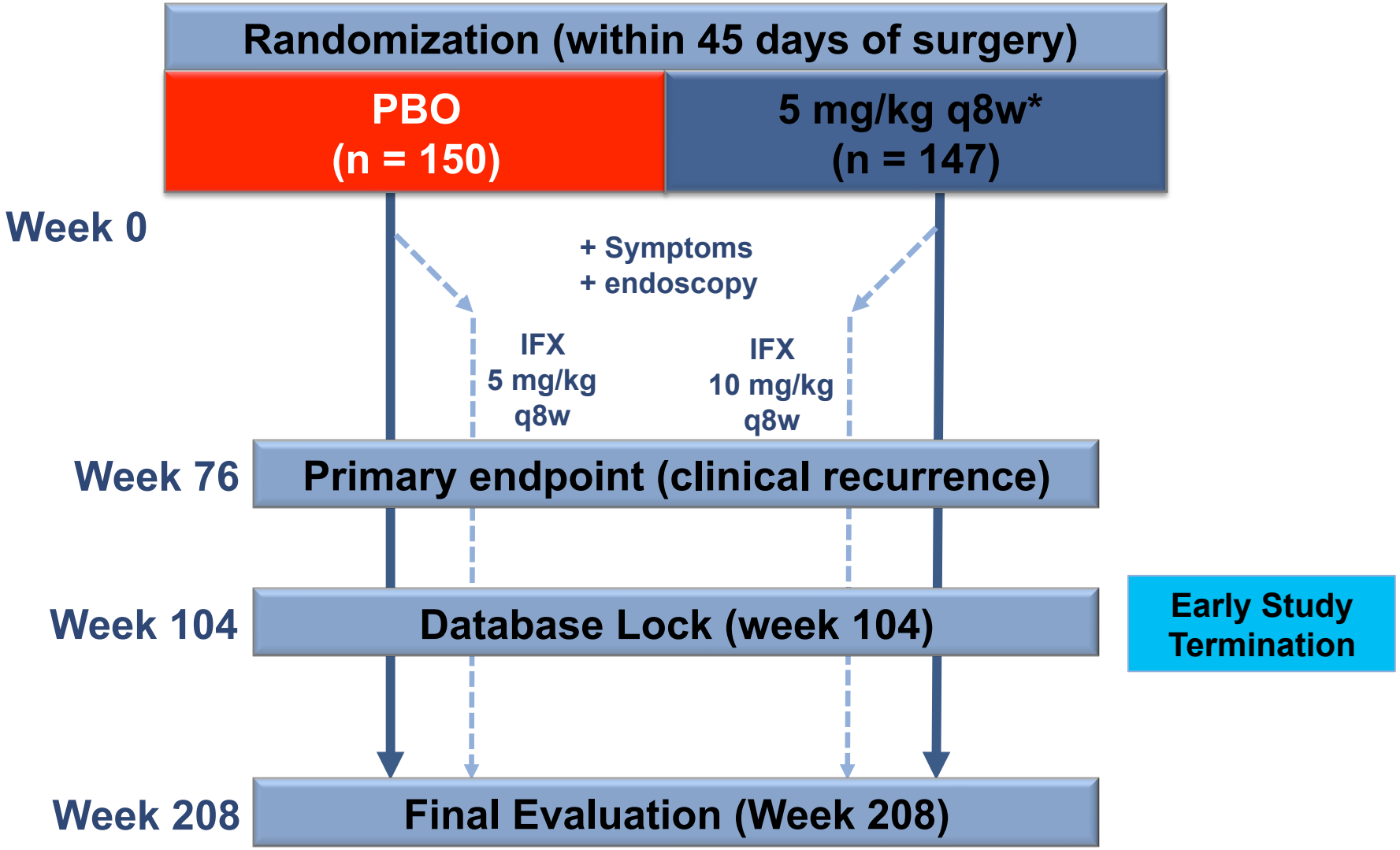
PREVENT TRIAL

- Prospective, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial Comparing REMICADE® (infliximab) and Placebo in the Prevention of Recurrence in Crohn's Disease Subjects Undergoing Surgical Resection Who Are at an Increased Risk of Recurrence
- study aim - to assess combined endoscopic and clinical outcome over 76 weeks of treatment in patients at increased risk of recurrence

Increased Risk of CD Recurrence: Criteria

- Qualifying surgery was 2nd operation in past 10 years
- Qualifying surgery was 3rd (or more) operation in past 10 years
- Qualifying surgery was for penetrating complication of CD
- Any history of fistulizing CD provided it was not active in 3 months prior to study
- Cigarette smoker and unable or unwilling to stop

PREVENT: STUDY DESIGN



** No IFX induction dosing was used

Regueiro M, et al. DDW 2015, Abstract 749

PREVENT Study: Baseline Demographics

Patient characteristics	Placebo (n = 150)	Infliximab (n = 147)
Male gender, n (%)	81 (54%)	77 (52%)
Caucasian, n (%)	138 (92%)	138 (94%)
Disease duration (yrs), median	3.3	6.5
CDAI, median	109.5	102.5
Prior intra-abdominal surgeries, N	150	146
0	91 (60%)	79 (54%)
1-2	51 (34%)	63 (43%)
>2	8 (5%)	4 (2%)
CD medication at baseline*		
Corticosteroids (excluding budesonide)	4 (3%)	10 (7%)
Immunosuppressant, n (%)	88 (59%)	85 (58%)
Aminosalicylate, n (%)	101 (67%)	100 (69%)
History of Anti-TNF use, n (%)	30 (20%)	37 (25%)

- Antibiotics not permitted
- Cholestyramine was permitted

Regueiro M et al. DDW 2015, Abstract 749

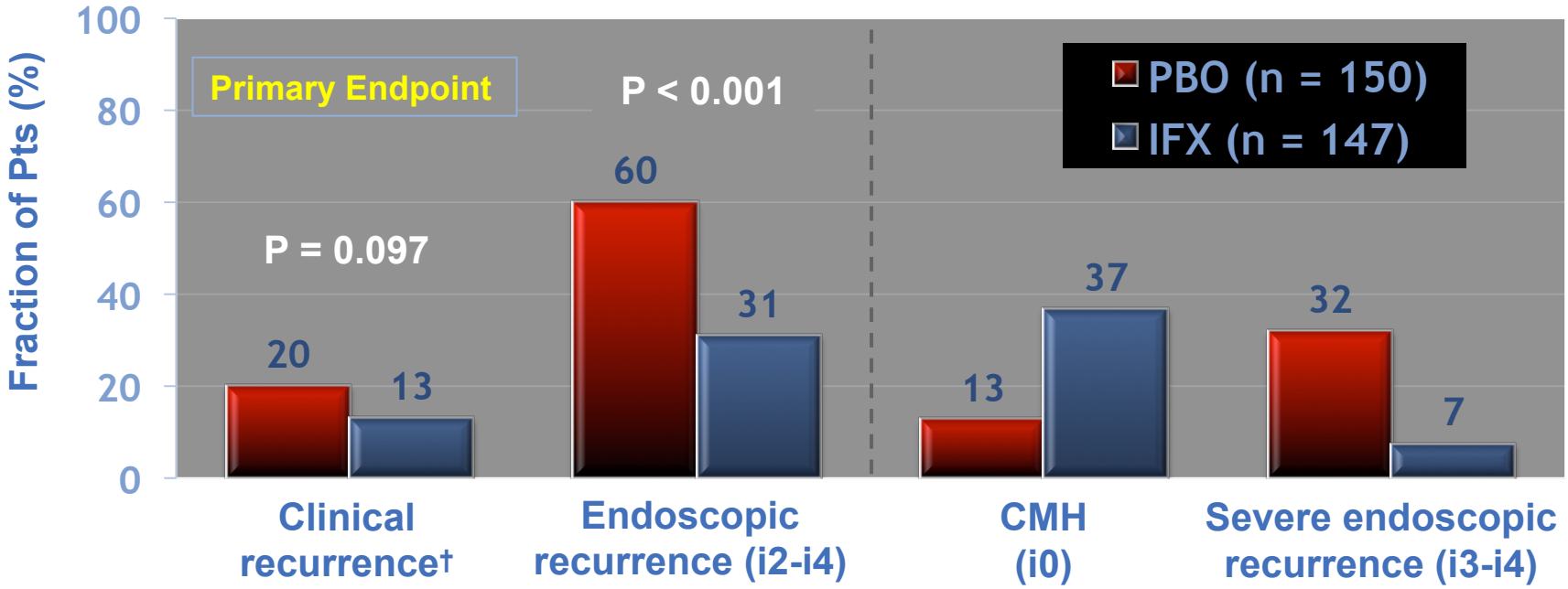
Summary of Risk Factors for Recurrence of Active CD in Randomized Subjects

Patient characteristics	Placebo (n = 150)	Infliximab (n = 147)
Randomized	150	147
Subjects with risk factor	150	146
Qualifying surgery was 2nd operation in past 10 yrs	30 (20%)	31 (21%)
Qualifying surgery was 3rd (or more) operation in past 10 yrs	12 (8%)	14 (10%)
Qualifying surgery was for penetrating complication of CD	106 (71%)	98 (67%)
Any history of fistulizing CD provided not active in 3 months prior to study	12 (8%)	16 (11%)
Cigarette smoker and unable or unwilling to stop	37 (25%)	38 (26%)

Regueiro M et al. DDW 2015, Abstract 749

IFX for Prevention Recurrence in CD Following Ileocolonic Resection

Presence of Clinical and Endoscopic Recurrence at Week 76



* CDAI ≥ 200 or 70-pt increase, endoscopic recurrence or complication
† Smoker, B2 or B3 disease or > 1 operation: ~30% > 1 risk factor
** No induction dosing was used

Regueiro M et al. DDW 2015, Abstract 749

PREVENT Study: Conclusions

- Primary endpoint (clinical & endoscopic recurrence not met) but trend toward reduced rate on IFX
- Endoscopic recurrence reduced by approximately half in IFX group and similar to prior study results
- No new safety signals

PREVENT Study: Discussion

- clinical recurrence overestimated leading to underpowered study
- follow-up may not be long enough to see clinical impact
- no loading dose
- no therapeutic drug monitoring
- need to differentiate IFX naïve versus experienced patients
- impact of combination therapy
- definition of ‘increased risk’ of recurrence may not be adequately identifying very high risk patients and may result in overtreatment
- role of early endoscopic evaluation not assessed
- required duration of treatment not assessed

PREVENT Study: Incorporating it into practice

- not all patients require infliximab (anti-TNF therapy) after surgery
- use risk stratification to identify high risk patients
  - high risk of recurrence
  - high risk of bad outcome of recurrent disease
- consider infliximab (anti-TNF therapy) in high risk patients