XPERT PERSPECTIVES

...from DDW

Reporting on IBD

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This activity is supported by Abbott, Centocor Ortho Biotech, and UCB, Inc.

GastroIntestinal Health Foundation

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Reporting on IBD

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Xpert Perspectives ...from DDW

Reporting on IBD

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Reporting on IBD

In Vivo Constitutive Expression of an IBD Associated Gene TNFSF15 Causes Severe Inflammation and Induces Fibrostenotic Disease in 2 Murine Models of Chronic Colitis

Barret R et al. Abstract Sa1803

Design

- Background
  - Elevated expression of TNFSF15 (TL1A) is seen in the inflamed colonic and intestinal mucosa of IBD patients
  - TL1A haplotype B is associated with enhanced production and is also characterized by fibrostenotic disease and need for surgery in IBD patients
  - Transgenic mice with constitutive expression of TL1A in T cells or antigen presenting cells leads to spontaneous ileitis
- Objective
  - Assess whether *in vivo* constitutive TL1A expression exacerbates inflammation/causes fibrostenotic disease in murine models of chronic colitis

Key Results

- Compared to WT, Tl1a overexpression:
  - Led to significantly enhanced weight loss and worsened DAI
  - Significantly enhanced gross inflammatory score in the intestine
- Mucosal Tl1a transgenic T cells and APCs had a more activated phenotype and higher IFN-γ expression
- Gross strictures were only present in the Tl1a transgenic mice
- Enhanced histologic fibrosis was observed in Tl1a transgenic mice
- Consistent with increased fibrosis, increased expression of fibrogenic factors TGF-β1 and IGF-1 were found in the intestine and colon of transgenic mice

Conclusions

- Tl1a modulates the development of both severe gut mucosal inflammation and marked fibrosis by enhancing Th1 effector functions and expression of pro-fibrogenic factors

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Reporting on IBD

NOD2 Genotype is Associated With Shifts in Human Ileal Mucosa-Associated Microbial Composition

Li E et al. Abstract 110

Design

- Objective
  - Examine whether CD risk alleles underlie changes in ileal-associated microbiota prior to the development of macroscopic disease
- Methods
  - Sequencing of bacterial 16S rRNA gene and hypervariable regions in macroscopically disease-unaffected ileal tissues from 52 ileal CD, 58 colitis, and 60 control patients

Key Results

- Both disease phenotype and NOD2 genotype as having a significant effect on overall ileal microbial composition
- Ileal CD phenotype was associated with decreased relative frequency of *Clostridium* group IV clade
  - *Faecalibacterium* spp. represented a major subset
- NOD2 genotype was associated with increased relative frequency of this taxon in ileal CD patients

Conclusions

- These results suggest that the effect of NOD2 genotype on ileal microbiota is not mediated by its association with ileal CD phenotype

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Natural History of IBD and Complications

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Reporting on IBD

Are We Exposing Inflammatory Bowel Disease Patients to *Clostridium difficile* During Clinic Visits?

Curry S et al. Abstract Sa1803

Design

- Objective
  - Determine whether a hospital based Gastroenterology (GI) Clinic may also be contaminated with CD spores and pose a risk for acquisition of infection
- Methods
  - Epidemiologic analysis of hospital based GI and dermatology (DERM) clinics for environmental contamination with CD

Key Results

- 3 of the 6 GI clinic ER (50%) were positive for toxigenic *C difficile*
- The remaining GI and dermatology clinic sites were negative
- The 3 positive GI ER had been decontaminated with bleach wipes prior to sampling
- Upon sampling of the 10 high-contact sites within the positive rooms, only 1 of the 10 sites, the computer keyboard, was positive

Conclusions

- Contamination of GI outpatient clinics with CD may be an under-recognized source of exposure complicating the care of patients with IBD
- Improved health care provider hand-washing, use of gloves during patient examination and improved disinfection techniques (effective bleaching and use of washable computer keyboards/covers) may be important for reducing exposure and potential infection in patients with IBD

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Reporting on IBD

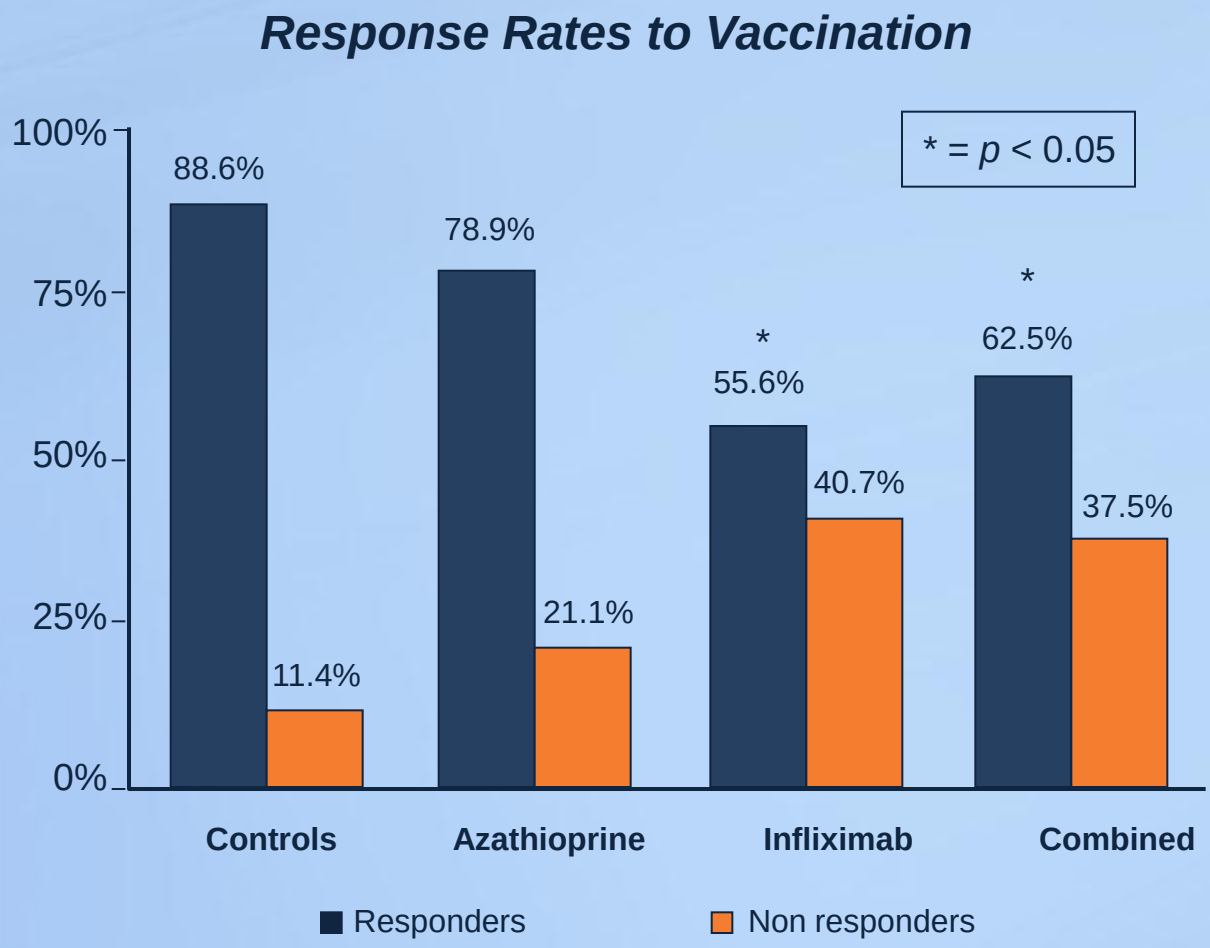
Immunosuppression Does Not Influence the Decay of Pneumococcal Antibodies 3 Years After Vaccination in Patients With Inflammatory Bowel Disease

Fiorino G et al. Abstract 989

Design

- Objective
  - Evaluate the response rates to pneumococcal vaccination and the impact of IBD-related medications (azathioprine and/or infliximab)
- Patients (N=96)
  - IBD (54 CD, 42 UC)
- Methods
  - 23-PSV administered
  - Blood samples collected before and >3 weeks after vaccination (mean interval, 8 weeks)
  - Antibody titers compared to baseline

Key Results


Response Rates to Vaccination
* = p < 0.05
100%
75%
50%
25%
0%
88.6%
11.4%
78.9%
21.1%
*
55.6%
40.7%
*
62.5%
37.5%
Controls
Azathioprine
Infliximab
Combined
Responders
Non responders

Conclusions

- Anti-TNF therapy alone or in combination with azathioprine impairs response to pneumococcal vaccination in IBD patients
- All IBD patients should be vaccinated >3 weeks before starting with anti-TNF therapy

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Reporting on IBD

Risk of Solid Organ and Hematological Malignancy in Patients With Inflammatory Bowel Diseases

Kappelman M et al. Abstract 180

Risk of Squamous and Basal Cell Carcinomas in Patients With Inflammatory Bowel Disorders Exposed to Thiopurines: The CESAME National Cohort Study

Biroulet LP et al. Abstract 181

Design

- Risk of Solid Organ and Hematological Malignancy in Patients With Inflammatory Bowel Diseases (Kappelman et al)
  - Data derived from Danish Cancer registry (N=35,461)
  - Patients followed from date that CD or UC was first recorded until occurrence of cancer, death from other causes, emigration, or end of study period
- Risk of Squamous and Basal Cell Carcinomas in Patients With Inflammatory Bowel Disorders Exposed to Thiopurines: The CESAME National Cohort Study
  - Data derived from nationwide French cohort (60.3% CD, 39.7% UC), N=19,486
  - Details of immunosuppressive therapy and cases of cancer reported

Key Results: Risk for Squamous and Basal Cell Carcinomas in Patients With IBD Exposed to Thiopurines: The CESAME National Cohort Study

- Before age 50, the incidence of skin carcinomas among patients receiving thiopurine therapy and those previously exposed was 0.59 (95% CI: 0.25-1.16) and 0.50 (95% CI: 0.14-1.29) per 10,000 patient-years, respectively
- The incidence of skin cancer in patients who had never received thiopurines was 0
- Risk factors for squamous and basal cell cancer:
  - Ongoing thiopurine treatment (OR: 7.3; 95% CI: 2.7-19.8; *p*=0.0001)
  - Past exposure to thiopurines (OR: 5.1; 95% CI: 1.7-15.3; *p*=0.004)
  - Age (OR: 1.1; 95% CI: 1.04-1.09; p<0.0001)

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5-ASA is Not Chemoprotective for Colorectal Cancer in IBD: A Meta-Analysis of Population-Based Studies

Gulamhusein A et al. Abstract 289

Design

- Objective
  - Conduct an updated systematic review and meta-analysis that includes only population-based studies of the effects of 5-ASA on colorectal cancer
- Studies included (N=6)
  - Assessed for exposure to 5-ASA
  - Reported CRC or dysplasia outcomes
  - Population based

Key Results

- There were a combined 605 cases and 2174 controls in the 4 studies included in analysis
- Pooled crude (unadjusted) odds ratio was 0.93 (95%CI, 0.75-1.15)
- Pooled adjusted odds ratio was 0.92 (95% CI, 0.62-1.35)

Conclusions

- Meta-analysis of population-based studies suggests 5-ASA is not associated with reduced risk of CRC in IBD patients
- Contrasts with a previous meta-analysis
- 5-ASA should not be routinely offered solely as a chemopreventive measure against colorectal cancer

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Biologics and Ulcerative Colitis

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A Randomized, Multicenter, Open-Label Phase 3 Study to Evaluate the Safety and Efficacy of Infliximab in Pediatric Patients With Moderate to Severe Ulcerative Colitis

Hyams JS et al. Abstract 747

Design

- Objectives
  - Evaluate efficacy of a 3-dose IFX regimen in inducing clinical response in pediatric patients with moderately-to-severe UC
  - Evaluate safety of IFX regimen
- Patients (N=60)
  - Age 6-17 years
  - Active UC (Mayo score 6-12; endoscopic subscore ≥2)
  - Failed to respond to or tolerate treatment with 6-MP, AZA, corticosteroids, and/or 5-ASA
- Treatments
  - IFX 5mg/kg at weeks 0, 2, and 6
  - Patients who achieved clinical response at week 8 were randomized to IFX 5mg/kg q8 weeks through week 46 or q12 weeks through week 42
- Primary end point
  - Clinical response at week 8 (decrease from baseline in the Mayo score ≥30% and ≥3 points, with a decrease in rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0/1

Key Results

- Week 8 results
  - Clinical response in 73.3% patients [95% CI: 62.1%, 84.5%]
  - Clinical remission in 40.0% by Mayo score and 33.3% by PUCAI
  - Mucosal healing in 68.3%
- At week 54, among patients who continued treatment, a numerically greater proportion of patients were in remission in the 5mg/kg q8wk grp(38.1%) vs 5mg/kg q12wk group(18.2%)
  - Did not reach statistical significance (p=0.146)
- More patients on corticosteroids at baseline were in remission and off corticosteroids at wk54 in the q8wk maintenance group (38.5%) than in the q12 wk maintenance group (0.0%)
- No difference in AEs across maintenance groups

Conclusions

- IFX is effective and safe in the treatment of pediatric patients with moderately to severely active UC with results comparable to those of the ACT trials
- At week54, twice as many patients were in remission following q8wk vs q12w therapy

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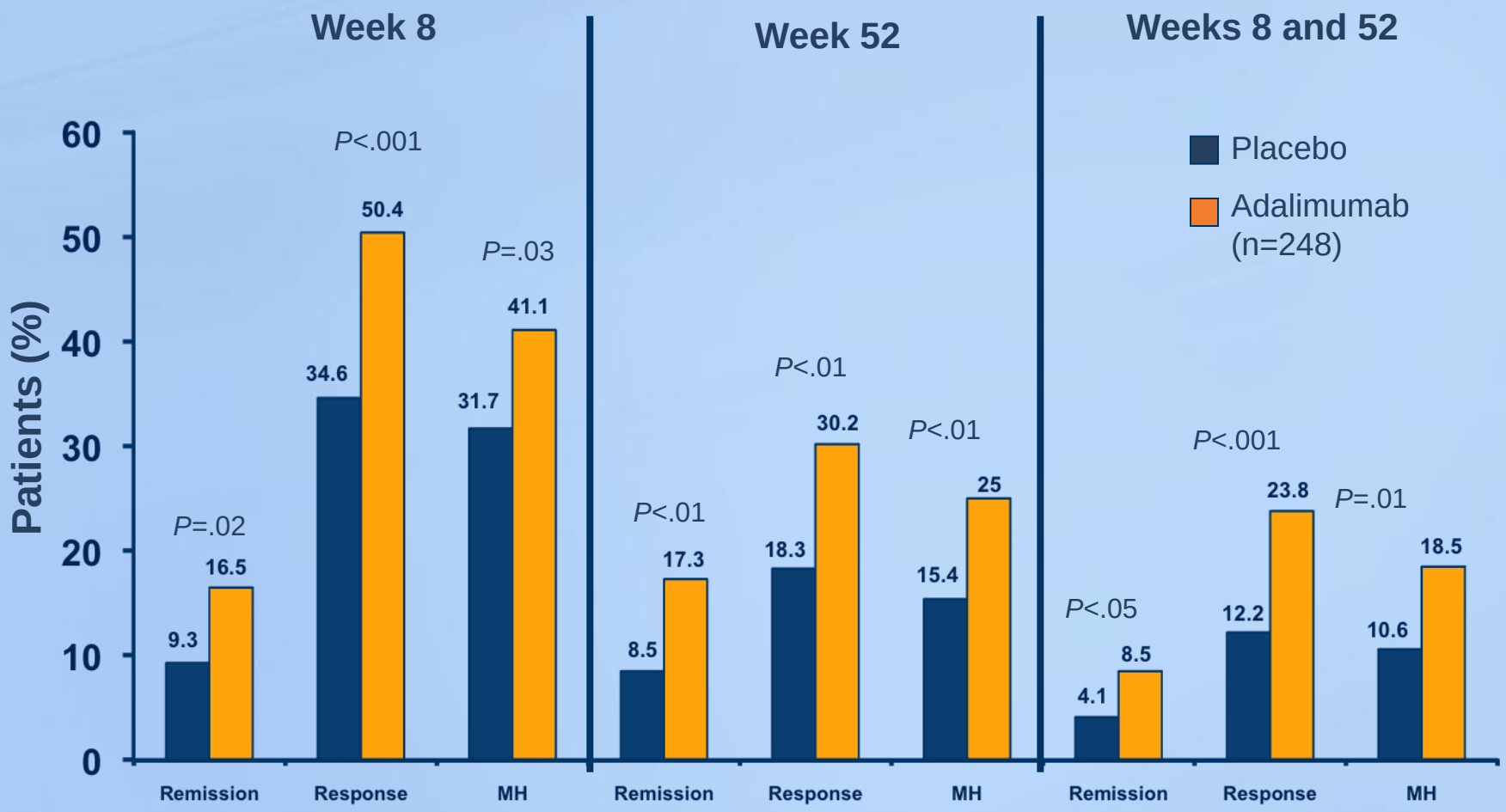
Induction and Maintenance of Clinical Remission by Adalimumab in Patients With Moderate-to-Severe Ulcerative Colitis

Sandborn WJ et al. Abstract 744

Design

- Objective
  - Assess efficacy and safety of adalimumab for induction and maintenance of clinical remission in patients with moderate-to-severe UC
- Patients (N=494 ITT patients)
  - Moderate to severe UC (Mayo score 6-12, endoscopy subscore 2-3 points despite concurrent treatment with oral corticosteroids/ immunosuppressants)
  - Previous anti-TNF use was allowed
- Treatments
  - Placebo
  - Adalimumab (160 mg, Week 0; 80 mg, Week 2; 40 mg eow starting Week 4)

Key Results


Week 8
Week 52
Weeks 8 and 52
Patients (%)
60
50
40
30
20
10
0
Placebo
Adalimumab (n=248)
P=.02
9.3
16.5
P<.001
34.6
50.4
P=.03
31.7
41.1
P<.01
8.5
17.3
P<.01
18.3
30.2
P<.01
15.4
25
P<.05
4.1
8.5
P<.001
12.2
23.8
P=.01
10.6
18.5
Remission
Response
MH
Remission
Response
MH
Remission
Response
MH

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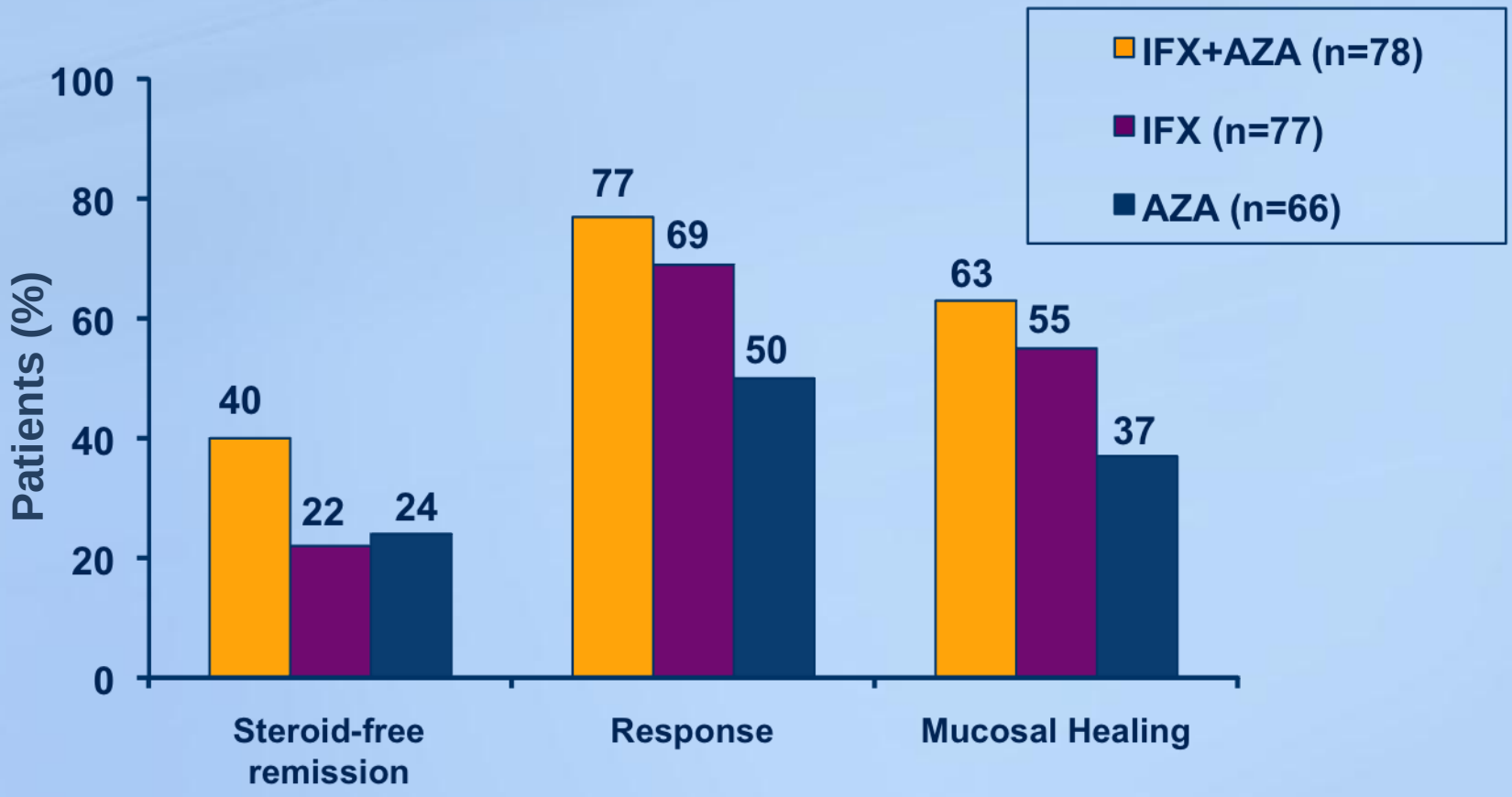
Infliximab, Azathioprine, or Infliximab + Azathioprine for Treatment of Moderate to Severe Ulcerative Colitis: The UC Success Trial

Panccione R et al. Abstract 835

Design

- Objective
  - To assess the best treatment strategy in patients with moderate-severe UC who are failing corticosteroids
- Patients (N=231)
  - Severe UC (Mayo score ≥6)
  - Failing corticosteroids
  - Naive to azathioprine or had stopped ≥3 months prior to entry
- Treatments
  - AZA 2.5 mg/kg + placebo
  - IFX 5 mg/kg + placebo
  - IFX 5 mg/kg + AZA 2.5 mg/kg
  - At week 8, nonresponders in the AZA arm were eligible for IFX 5 mg/kg at weeks 8, 10, and 14
- Primary end point
  - Steroid-free remission at week 16 (total Mayo score ≤2)

Key Results



*P<.05 compared to IFX; #P<.05 compared to AZA

Conclusions

- IFX+AZA was superior to AZA and IFX monotherapy in inducing steroid-free remission in patients with moderate-severe UC
- Patients treated with IFX both as monotherapy and in combination with AZA are more likely to achieve response and mucosal healing than those treated with AZA monotherapy

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Predictors of Response to Infliximab in Patients With Ulcerative Colitis in Remission After at Least 6 Months of Combination Therapy (Infliximab Plus Azathioprine)

Roblin X et al. Abstract Mo1245

Design

- Objective
  - Identify predictive factors associated with favorable outcomes in patients with UC in remission after >6 months of combination therapy
- Design
  - Retrospective study including all patients with UC in clinical remission after >6 months of therapy with IFX + AZA (N=55)
  - Median follow-up of 14 months

Key Results

Factors associated with favorable response during follow-up (univariate analysis)

	Odds of favorable response (95% CI)	P
Duration of combined therapy ≥1 year	0.24 (0.007-0.77)	.024
Severity of disease	1.67 (0.42-6.66)	.7
Extent of disease	0.67 (0.23-1.96)	.46
CRP >20 mg/L	1.52 (0.48-4.81)	.47
Hemoglobin > g/dL on IFX initiation	0.96 (0.32-2.93)	.95

In multivariate analysis, only duration of combined therapy ≥1 year remained significant for predicting good response (OR 0.24 [.07-.78]; P=.018)

Conclusions

- In UC patients in clinical remission after 6 months of combined therapy with IFX and AZA, a combined therapy ≥1 year is associated with a 76% diminution of the risk of relapse

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Cyclosporin Versus Infliximab in Severe Acute Ulcerative Colitis Refractory to Intravenous Steroids: A Randomized Trial

Laharie D et al. Abstract 619

Design

- Objective
  - Compare cyclosporin to infliximab in iv steroid-resistant severe acute UC
- Patients (N=111)
  - Severe, acute UC
  - IV steroid resistant
- Treatments
  - IV cyclosporin (2 mg/kg/d for 1 week, then switched to oral for 98 days)
  - IFX (5mg/kg at weeks 0-2-6)
  - In patients with a clinical response at week 7, azathioprine initiated and steroids decreased
- Outcomes
  - Rate of treatment failure

Key Results

- Treatment failure
  - 60% with cyclosporin vs 54% with IFX (*P*=.49)
- Day 7 response rates
  - 84% with cyclosporine and 86% with IFX (*P*=.76)
- Day 98 results
  - 10 patients treated with cyclosporine and 13 with IFX were colectomized
- Severe adverse events
  - 10 in cyclosporine patients; 16 in IFX patients

Conclusions

- In patients with acute, severe UC refractory to IV steroids, cyclosporine is not more effective than IFX to achieve short-term remission and avoid urgent colectomy

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Short and Long Term Outcome of Infliximab Scheduled Therapy for Acute, Severe Ulcerative Colitis. A Prospective, Open Label, Single-Centre, Two-Year Study

Papamichael K et al. Abstract Sa1295

Design

- Objective
  - Assess the short and long term outcome of IFX rescue therapy in patients with acute, severe UC
- Patients (N=37)
  - Acute, severe UC (Truelove & Witts criteria plus an endoscopic Mayo score of 3)
- Treatments
  - Single dose of IFX (5 mg/kg)
  - Responders received additional induction doses (5 mg/kg at weeks 2 and 6) and then scheduled IFX maintenance therapy (5 mg/kg q8weeks)
  - Steroids tapered
  - Azathioprine continued in previous users
- Outcomes
  - Steroid-free remission
  - Complete mucosal healing

Key Results

- Steroid-free remission (SFR)
  - 67.5% at 6 months
  - 54% at 2 years
- Mucosal healing
  - Complete mucosal healing (CMH) observed in 12/37 patients
  - Near-complete mucosal healing observed in 8/37 patients
- 12 patients proceeded to colectomy
  - 5 did not respond to first infusion
  - 1 developed a severe allergic reaction during second infusion
  - 6 relapsed before the fourth infusion after partial response to IFX induction

Conclusions

- In this study which mirrors real life experience, approximately 2/3 of patients who received rescue IFX for AS-UC avoided emergency colectomy
- Over 50% were maintained in long-term SFR and achieved CMH or near CMH

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Biologics in Crohn's Disease

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Reporting on IBD

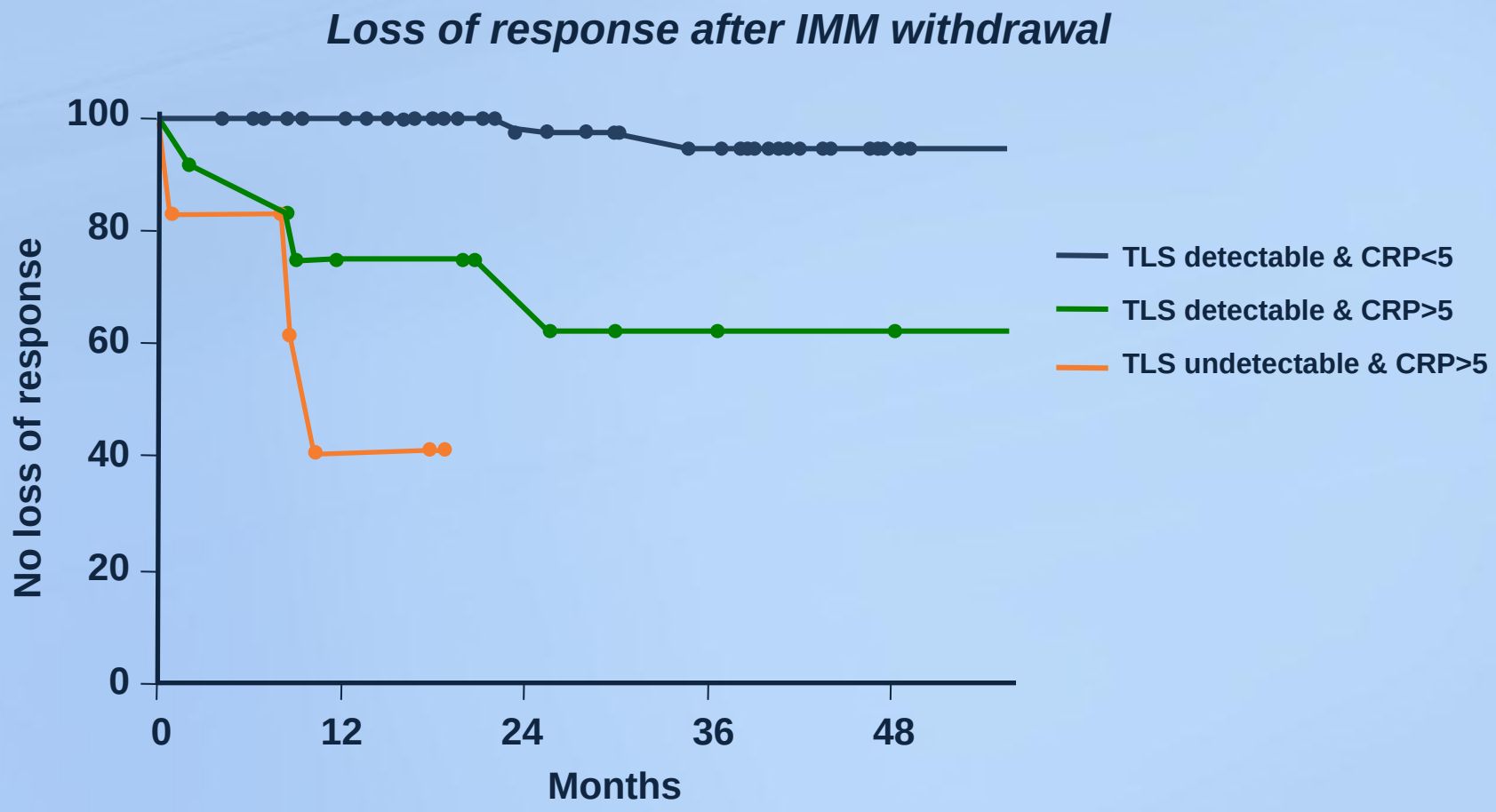
Crohn's Disease: Infliximab Trough Levels and CRP During Infliximab-Immunomodulator Combination Treatment Are Associated With Clinical Outcome After Immunomodulator Withdrawal

Drobne D et al. Abstract 279

Design

- Objective
  - To study the influence of immunomodulator (IMM) withdrawal on IFX trough levels and to identify predictors of disease flare and loss of response to IFX after withdrawal of IMM
- Patients (N=223)
  - On IFX maintenance therapy for CD, of whom 155 were cotreated with IMMs
- Treatments
  - IMMs discontinued in 117 patients when durable clinical remission was achieved after >6 months of cotreatment

Key Results



TL=trough levels

Conclusions

- Undetectable IFX trough levels and CRP>5 mg/l during IFX-IMM combination therapy are associated with an increased loss of response to IFX after IMM withdrawal

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Induction and Maintenance Adalimumab Therapy for the Treatment of Moderate to Severe Crohn's Disease in Children

Drobne D et al. Abstract 279

Design

- Objective
  - Compare 2 adalimumab dosage regimens for induction and maintenance of clinical remission in children with moderate to severe CD
- Patients (N=192)
  - Age 6-17
  - CD (PCDAI >30 at baseline for ≥12 weeks despite treatment with or failure/intolerance of oral corticosteroids or immunosuppressants)
- Treatments
  - Open-label ADA induction per BL body weight
  - At week 4, patients randomized to double-blind adalimumab maintenance therapy (high dose or low dose)
- Primary end point
  - Clinical remission for high- vs low-dose groups

Key Results

Clinical Remission at Week 26 in Randomized Patients

Prior IFX	W4 response	ADA low dose (%)	ADA high dose (%)	P[a,b,c]
Yes		20	17	.736
	Yes	22	19	.756
	No	11	10	
No		35	57	.026*
	Yes	38	63	.016*
	No	17	25	

[a]Cochran-Mantel-Haenszel test adjusted for prior IFX use and Wk4 response status for overall. [b]Chi-square test (or Fisher's exact test for small cell counts) within each category of prior IFX use or Wk4 response. [c]If blank, test not performed due to small sample size. *Statistically significant at an α=5% level.

Conclusions

- In this pediatric trial, ADA was efficacious for inducing and maintaining remission of CD, with a safety profile comparable to that observed in adult CD patients
- The greatest efficacy was observed for IFX-naive patients in the high-dose group, especially responders to induction

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Economic Impact of Deep Remission in Adalimumab-Treated Patients With Crohn's Disease: Key Results From Extend

Sandborn WJ et al. Abstract Sa1019

Design

- Objective
  - To evaluate the economic impact of deep remission in adalimumab (ADA)-treated patients with CD
- Design
  - Data derived from EXTEND trial
  - Early “deep remission” defined as mucosal healing and clinical remission (CDAI <150) at Week 12
- Treatments
  - Open-label ADA 160-/80-mg induction therapy at Weeks 0/2 followed by randomization at Week 4 to maintenance therapy with ADA 40 mg eow or placebo through Week 52
- Outcomes
  - Hospitalization costs (at a rate of $36,195/hospitalization)
  - Direct non-hospitalization costs
  - Indirect costs

Key Results

Health Care Costs Over 40 Weeks for Patients who did and did not Achieve "Deep Remission" at Week 12

Week-52 Costs (US $ 2009)	Deep Remission Achievers (N=11)	Deep Remission Non-Achievers (N=53)	Difference
Total direct costs	5,735	11,404	-5,669
Direct non-hospitalization costs	5,735	7,992	-2,257
Hospitalization costs	0	3,411	-3,411
Total indirect costs	8,958	13,201	-4,243
Total costs (direct+indirect)	14,693	24,604	-9,912

Conclusions

- Adalimumab-treated patients who achieved deep remission at Week 12 had health care costs savings of about $9,900 at 1 year vs. those who did not achieve deep remission

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Reporting on IBD

Preoperative Use of Anti-TNF Therapy in Crohn's Disease Patients is Associated With Increased Infectious and Surgical Complications

Syed A et al. Abstract 154

Shorter Time Interval From Exposure to Biological Treatment to Surgery in Patients With IBD is Not Associated With Increased Short-Term Surgical Complications

Waterman M et al. Abstract 152

Methods

- Preoperative Use of Anti-TNF Therapy in Crohn's Disease Patients is Associated With Increased Infectious and Surgical Complications
  - Data collected from prospective IBD clinical database
  - Postoperative complications compared in patients exposed and unexposed to TNF less than 8 weeks before surgery
- Shorter Time Interval From Exposure to Biological Treatment to Surgery in Patients With IBD is Not Associated With Increased Short-Term Surgical Complications
  - Data collected from IBD surgical database
  - Retrospective chart review
  - Procedures grouped into categories based on time interval from last biologic dose to surgery (<14 days, 15-30 days, 31-180 days)
  - LOS, UTI, pneumonia, other serious infections, need for post-op antibiotics, wound infection, anastomotic leak, reoperation, readmission, intra-abdominal abcesses, and mortality recorded

Preoperative Use of Anti-TNF *is not* Associated With Increased Infectious and Surgical Complications (Waterman et al)

- Complication rates were similar regardless of time elapsed since last dose of anti-TNF

Complication	Overall Rate (%)
UTI	5
Pneumonia	2.8
Septic shock	1.7
Bacteremia	4
Wound infection	20.3
Other serious infections	2.9
Need for antibiotics	17.9

Preoperative Use of Anti-TNF *is* *Associated* With Increased Infectious and Surgical Complications (Syed et al)

- Preoperative use of anti-TNF was an independent predictor of:
  - Overall infectious (OR 1.97; 95% CI 1.09-3.55)
  - Surgical site complications (OR 1.94; 95% CI 1.06-3.54)
- In patients who underwent intestinal resection revealed that preoperative use of anti-TNF was an independent predictor of:
  - Overall infectious (OR 2.10; 95% CI 1.02-4.34)
  - Surgical site complications (OR 2.17; 95% CI 1.03-4.56)
  - Overall major complications (OR 2.14; 95% CI 1.03-4.47)
- A trend towards a significant association with intra-abdominal penetrating complications was also seen (OR 2.18; 95% CI 0.95-4.99)

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Insights into Thiopurine Therapy

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Early Use of Azathioprine Has a Steroid Sparing Effect on Recently Diagnosed Crohn's Disease Patients

Sans M et al. Abstract 590

Design

- Objective
  - To evaluate the usefulness of azathioprine in recently diagnosed adult CD patients
- Design
  - Multicenter, randomized, double-blind, placebo-controlled
- Patients (N=131)
  - CD diagnosed within 8 weeks prior to inclusion
- Treatments (18 months)
  - Azathioprine 2.5 mg/kg/d
  - Placebo
- Primary end point
  - Proportion of patients with steroid-free sustained remission until month 18

Key Results

- Primary outcome met in 67.7% of azathioprine patients and 57.1% of placebo patients (*P*=.2) (LOCF)
  - There were no differences in the proportion of patients in remission at other time points
- The mean cumulative dose of prednisone was higher in the placebo group (1995 mg) than in the azathioprine group (717 mg, *P*=.002)
- No differences between groups in penetrating behaviour, perianal disease, hospitalization or bowel resection
- No deaths occurred and the number or adverse events and serious adverse events was similar in the two groups
  - Macrocitic anemia, leucopenia, and acute pancreatitis were significantly more frequent in the azathioprine group

Conclusions

- Early treatment with azathioprine results in a steroid-sparing effect but does not significantly decrease the proportion of patients achieving steroid-free sustained remission over 18 months

Novel, Evolving Therapies

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Reporting on IBD

Budesonide Mxx® 9 mg for the Induction of Remission of Mild-to-Moderate Ulcerative Colitis (UC): Data From a Multicenter, Randomized, Double-Blind Placebo-Controlled Study in North America and India

Sandborn WJ et al. Abstract 746

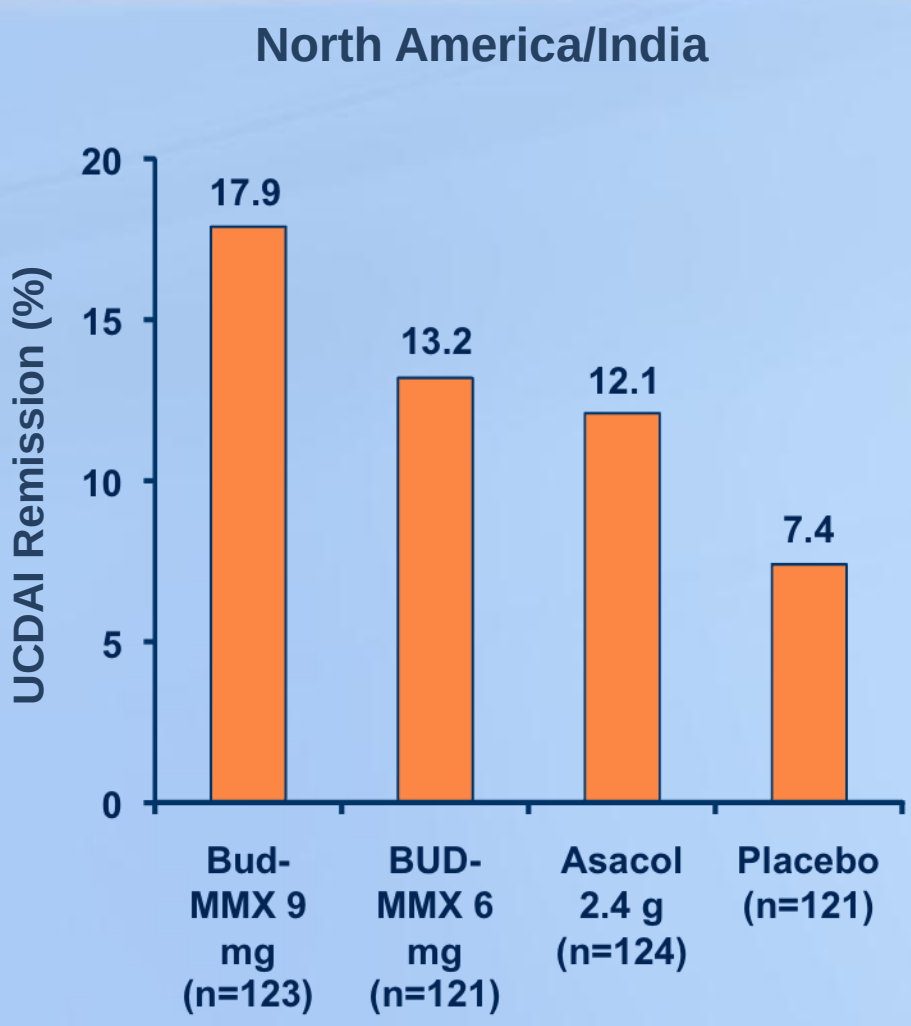
Budesonide-MMx® 9 mg for Induction of Remission of Mild-to-Moderate Ulcerative Colitis (UC): Data From a Multicenter, Randomized, Double-Blind Placebo-Controlled Study in the Europe, Russia, Israel and Australia

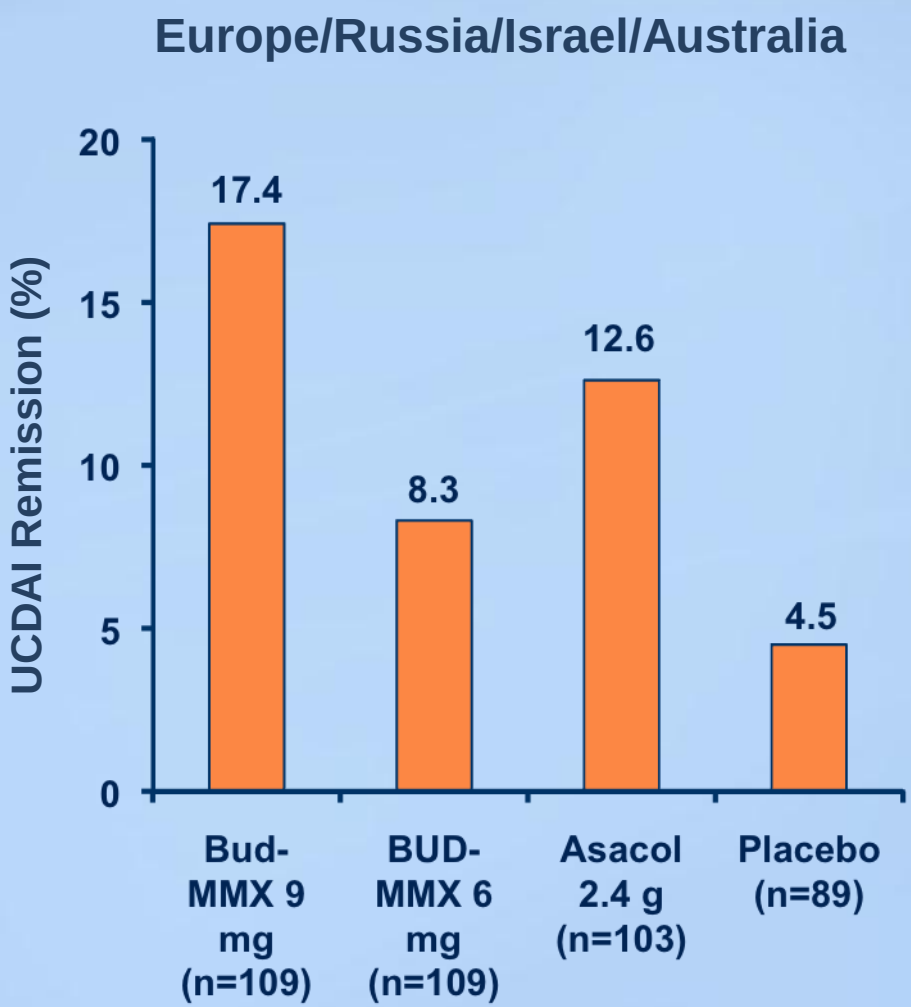
Sandborn WJ et al. Abstract 292

Design

- Design
  - 2 randomized, controlled, double-blind, placebo controlled studies (North America/India, Europe/Russia/Israel/Australia)
- Objective
  - Evaluate the efficacy of a budesonide formulation (Budesonide MMX) in mild-to-moderate UC
- Patients
  - Mild-to-moderate UC
  - North America/India: N=509
  - Europe/Russia/Israel/Australia: N=511
- Treatments
  - North America/India: Bud-MMX 9 mg, Bud-MMX 6 mg, Asacol 2.4 g, placebo
  - Europe/Russia/Israel/Australia: Bud-MMX 9 mg, Bud-MMX 6 mg, Entocort 9 mg, placebo

Key Results


North America/India
UCDAI Remission (%)
20
15
10
5
0
17.9
13.2
12.1
7.4
Bud-MMX 9 mg (n=123)
BUD-MMX 6 mg (n=121)
Asacol 2.4 g (n=124)
Placebo (n=121)


Europe/Russia/Israel/Australia
UCDAI Remission (%)
20
15
10
5
0
17.4
8.3
12.6
4.5
Bud-MMX 9 mg (n=109)
BUD-MMX 6 mg (n=109)
Asacol 2.4 g (n=103)
Placebo (n=89)

Conclusions

- Budesonide MMXR 9 mg administered once daily was safe and effective at inducing remission in patients with mild-to-moderate UC

XPERT PERSPECTIVES ...from DDW

Reporting on IBD

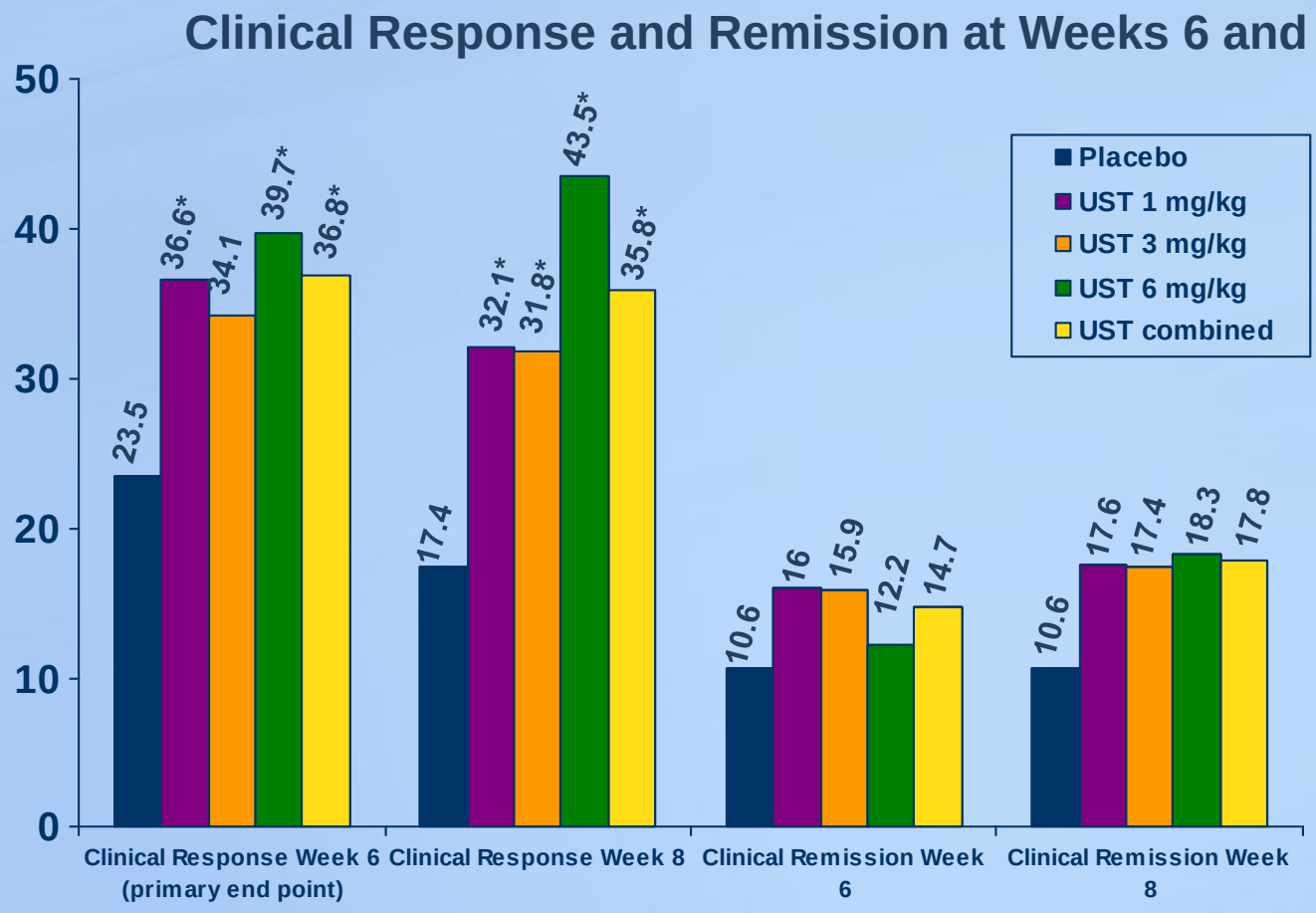
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase2b Study of Ustekinumab, a Human Monoclonal Antibody to IL-12/23p40, in Patients With Moderately to Severely Active Crohn's Disease: Key Results Through Week 22 From the Certifi Trial

Sandborn WJ et al. Abstract 592

Design

- Design
  - Phase 2b randomized, double-blind, placebo-controlled study
- Objective
  - Assess the efficacy of ustekinumab in patients with CD
- Patients (N=526)
- Treatment
  - IV placebo
  - IV UST 1, 3, 6 mg/kg
  - At week 8, patients who received IV UST induction and were either responders (≥100 CDAI decrease) or non-responders at week 6 were re-randomized separately to maintenance therapy with 90mg UST or PBO SC at weeks 8 and 16, and then followed through week 22
  - Responders to IV PBO received PBO SC at weeks 8 and 16 and non-responders received UST 270 mg SC at week 8 and UST 90 mg SC at week 16
- Primary end point
  - Response (≥100 CDAI decrease) at Week 6

Key Results



*$P<.05$

Conclusions

- In patients with moderate to severe CD who had previously failed TNF antagonist therapy, UST induced and maintained clinical response
- During the maintenance phase, a statistically significant greater proportion of week6 responders achieved clinical remission in the UST treated group compared to PBO treated patients
- Both IV and SC UST were well tolerated

XPERT PERSPECTIVES ...from DDW

Reporting on IBD

Phase 2 Study of CP-690,550, an Oral Janus Kinase Inhibitor, in Active Ulcerative Colitis

Sandborn WJ et al. Abstract 594

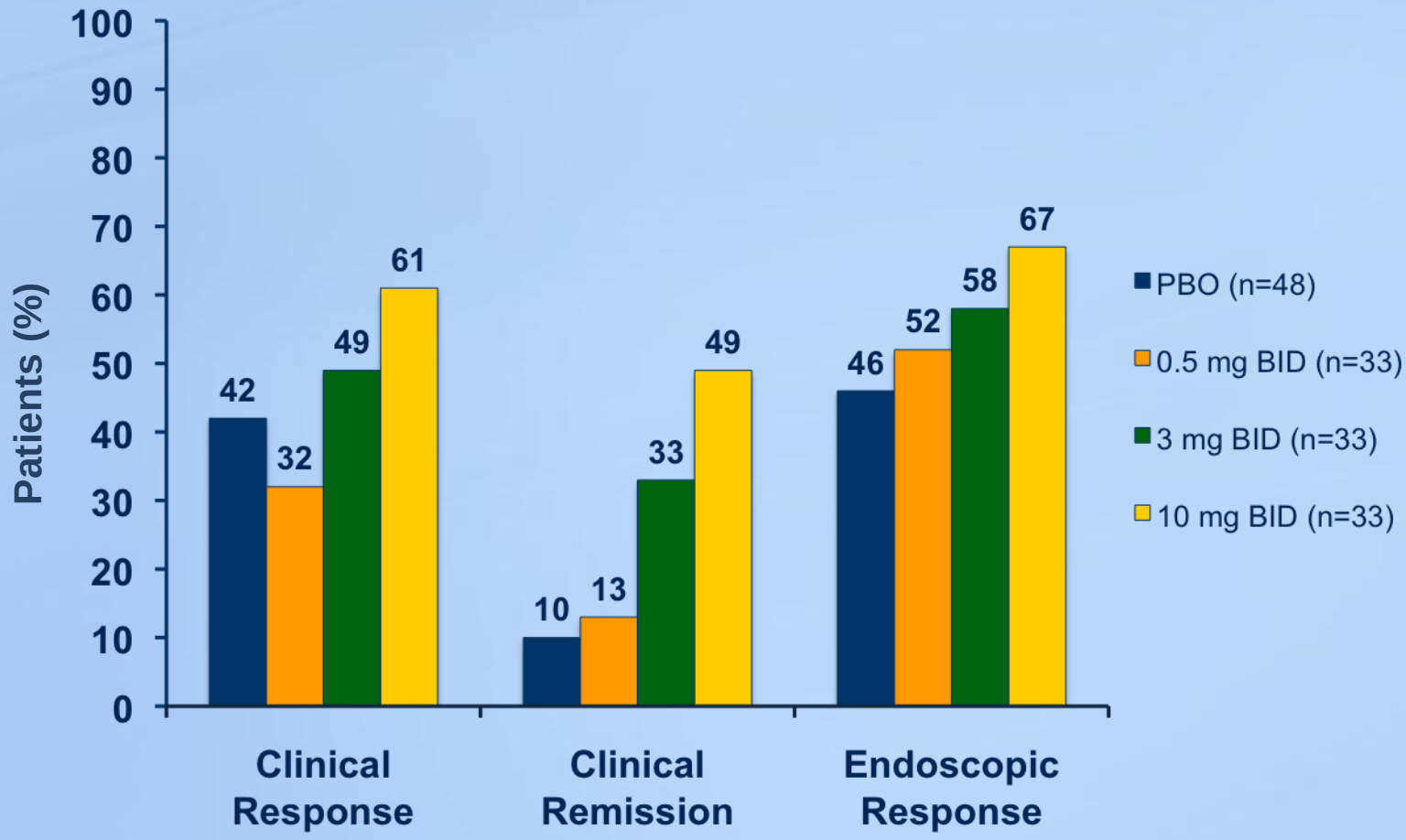
Phase 2 Randomized Study of CP-690,550, an Oral Janus Kinase Inhibitor, in Active Crohn's Disease

Sandborn WJ et al. Abstract 745

Design

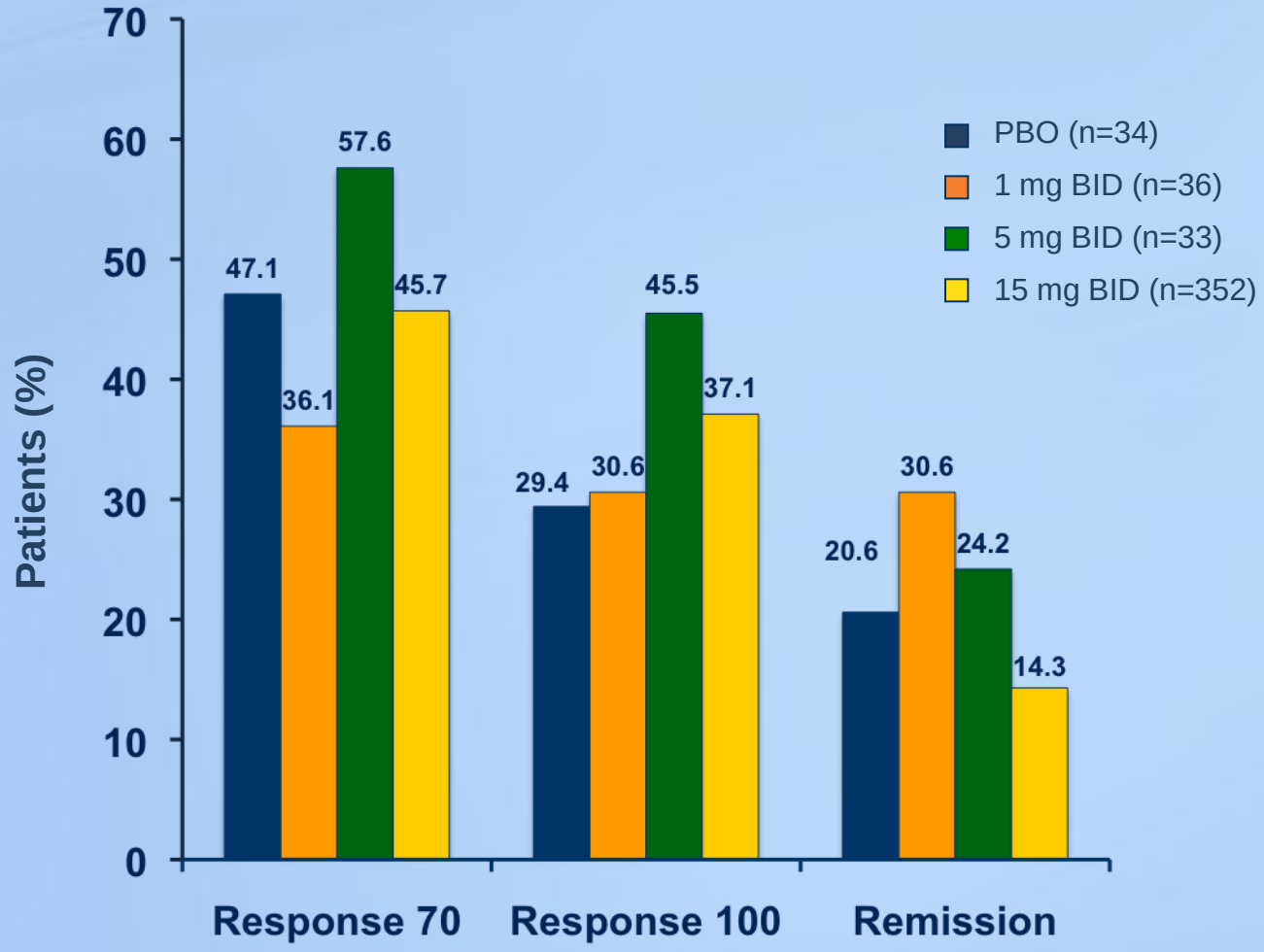
- Design
  - Two separate, phase 2 clinical studies
- Objectives
  - Evaluate the efficacy and safety of CP for induction of response and remission in patients with moderate-to-severe active UC
  - Evaluate the efficacy and safety of CP in patients with moderate-to-severe CD
- Patients
  - Moderate-to-severe active UC (N=189)
  - Moderate-to-severe CD (N=139)
- Treatments
  - UC: CP-690,550 0.5, 3, 10, 15, mg BID or placebo (8 weeks)
  - CD: CP 1, 5, 15 mg BID or placebo (4 weeks)
- Primary end point
  - UC: Clinical response rate (decrease in Mayo score ≥3 points and ≥30%; decrease in rectal bleeding subscore ≥1 point or absolute subscore ≤1) at week 8
  - CD: Percentage of patients with CDAI score reduction of ≥70 points at week 4

Key Results in Ulcerative Colitis (Week 8)



*P<.05; **P<.01

Key Results in Crohn's Disease (Week 4)



Conclusions

- UC
  - In patients with moderate-to-severe UC, treatment with CP-690,550 was associated with dose-dependent improvement in clinical response and remission rates
  - CP-690,550 as an induction therapy in UC was generally well tolerated
- CD
  - CP had no significant treatment effect within 4 weeks on clinical endpoints measured by CDAI in patients with active CD
  - There was a dose-dependent treatment effect on CRP levels, and a treatment effect on FeC levels with the 15 mg dose (data not shown)
  - CP was generally well tolerated

XPERT PERSPECTIVES
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Reporting on IBD

Closing Remarks

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