Best of DDW 2017-IBD

Northern California Society of Clinical Gastroenterology
June 3, 2017

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2. Will oral tofacitinib be the next approved therapy for UC?

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4. Better to get resection than medical therapy for ileal CD?

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Benefit of Combination Therapy Depends on Disease Phenotype and Duration: Prospective Cohort Study

- Prospective Cohort; 7 referral centers
- 391 monotherapy vs. 316 combination therapy
- Groups balanced
  - First anti-TNF (63% vs 61%)
  - Disease duration, phenotype
  - Exception slightly more combo in perianal
- Type combo therapy-75% AZA/6MP/25% MTX
- Outcome-composite “bad outcome”
  - Surgery
  - Hospitalization
  - Penetrating disease
  - Steroids, new biologic

Ananthakrishnan et al DDW 2007 #200

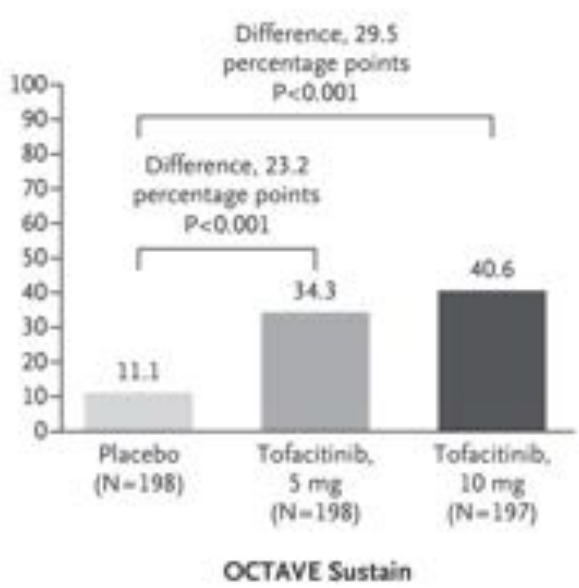
Benefit of Combination Therapy Depends on Disease Phenotype and Duration: Prospective Cohort Study

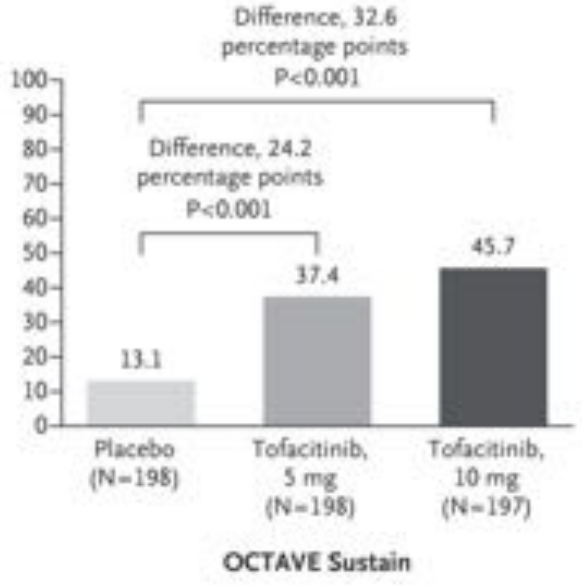
- Combo therapy did not reduce composite “bad outcome” in overall Crohn’s population (OR 0.9; 95%CI: 0.6-1.2)
- BUT-there was benefit in certain phenotypes
  - B1 (inflammatory): no difference
  - B2/B3 (structuring/penetrating): 42% reduction in composite “bad outcome”-(OR 0.58; 95%CI: 0.4-0.9)
    - Outcome driven by reduction in hospitalizations and surgery
    - Phenotype driven by those with disease < 5 years
    - <5 years: 65% reduction (OR 0.35: 95%CI: 0.2-0.9)
    - >5 years: no difference (OR 0.75; 95%CI: 0.5-1.3)

Ananthakrishnan et al DDW 2007 #200

Efficacy and safety of oral tofacitinib: results from phase III RCT

- WHAT: Tofacitinib
  - Oral, small molecule
  - JAK 1-3 inhibitor
- Pathway:
  - Signal→ JAK kinases→activate signal→mRNA-→proinflammatory cytokines
- WHO:
  - Patients with UC who responded to tofacitinib induction trial
  - Rerandomized to PBO/ 5 mg bid/ 10 mg bid





- SAFETY:
- Same % AE
  - Increased infections
  - Increased zoster
  - Increased lipids
  - Increased CK
- No intestinal perforations

Sandborn et al DDW 2007 #1080

Fistula healing in pivotal studies of ustekinumab in Crohn's disease

- METHODS: Subgroup analysis of ustekinumab induction studies (UNITI 1/2) & 2b study (CERTIFI)
  - 13% patients with fistulas
- Outcomes
  - Fistula response (>50% reduction in drainage)
  - Fistula resolution

FISTULA RESPONSE
28%
(11% better PBO-NS)

FISTULA RESOLUTION
28%
(14% better PBO-p=0.052)

Sands et al DDW 2007 #981

Cost-effectiveness of laparoscopic ileal resection vs IFX

- METHODS: RCT 143 patients (2008-2015) laparascopic ileal resection vs IFX
  - CD of TI only
  - > 3 months thiopurine or steroid failure
  - <40 cm affected, no prior resection, no critical stenosis
- Outcomes:
  - IBDQ
  - SF-36
  - Cost/QALY
- Results:
  - IFX: 30% discontinues/19% surg at 1 year
  - Surgery: 4% IFX at 1 year

Same Disease Specific QOL (IBDQ)
4.9 pts better resection (NS)

Better Overall QOL
Better Physical Scale*
Better Mental Scale*

Less Expensive
$8431 Saved
$77,221/QALY

De Groof et al DDW 2007 #980

Phase III RCT to compare biosimilar IFX (CT-P13) with innovator IFX in CD

- METHODS:
  - RCT,
  - 200 pts moderate-severe CD
  - Multicenter, international
  - CPT-13 vs. IFX
- Outcomes-week 6 and 30
  - CDA-100 response
  - Remission
  - Safety

RESPONSE-SAME
Week 6-72 v. 75% IFX
Week 30-72 v. 73%

REMISSION-SAME
Week 6- 43 v. 45%
Week 30- 55 v. 57%

SAFETY-SAME
Same % infusion reactions

Kim et al DDW 2007 #248

Correlation of clinical and endoscopic outcomes in patients with CD treated with GED-0301

- WHAT: Mongerson
  - Oral, small molecule
  - Anti-SMAD7 oligonucleotide
- Pathway:
  - TGF-B1 suppresses gut inflammation
  - SMAD7 binds TGF-B1 receptor
  - Prevents TGF-B1 anti-inflammation response
- WHO:
  - Active CD, 63 pts
  - RCT 4,8.12 wks followed by observation period without
  - 160 mg daily, no PBO
  - Central reading
  - CDAI assessment

Response (CDAI-100) begins week 2: 21%/26%/29%

Response highest in 12 wk group: 53%/44%/67%

37% endoscopic response at week 12 among all groups

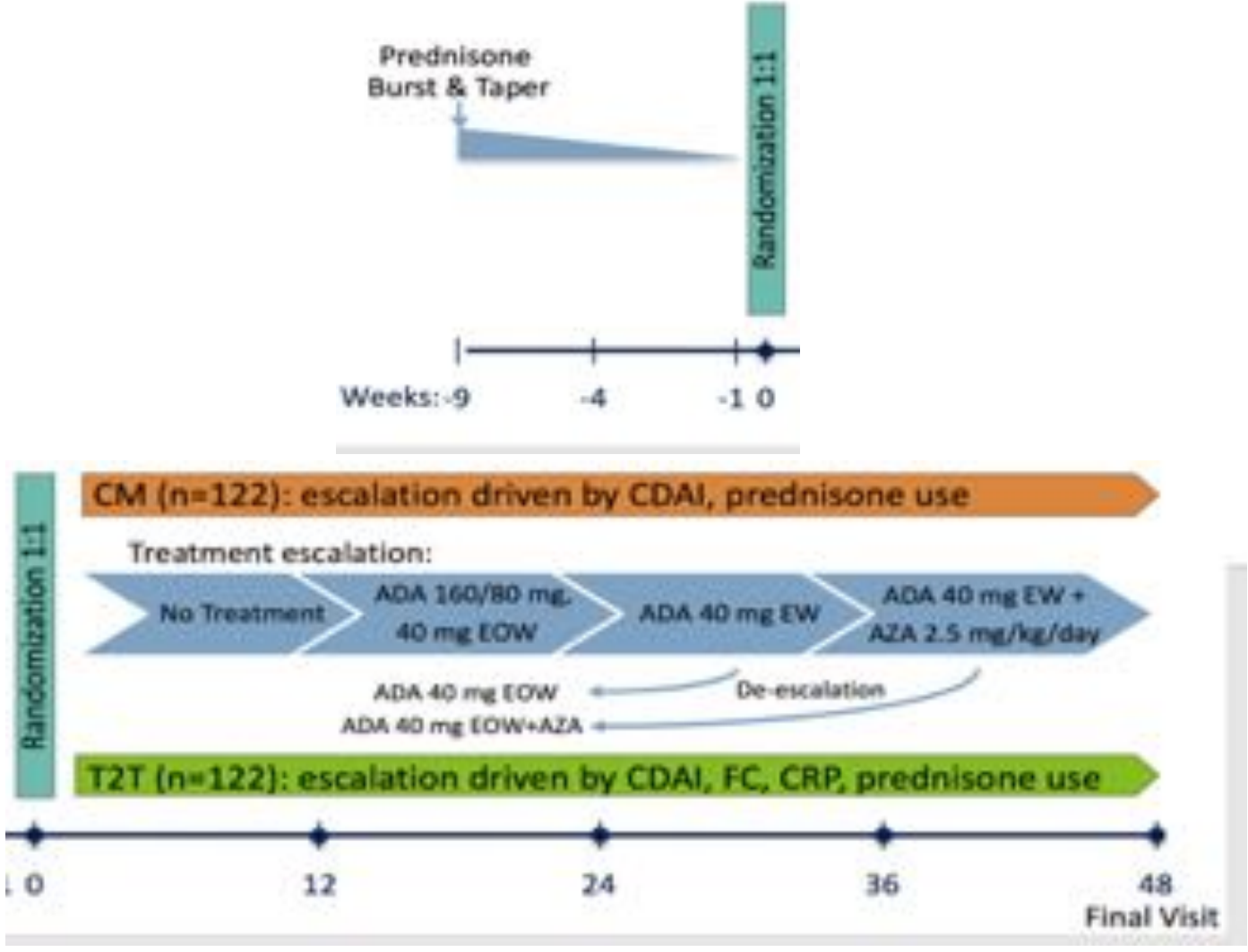
No safety signals

Feagan et al DDW 2007 #1076

A Treat-to-target approach leads to superior endoscopic and deep remission outcomes compared with symptom-driven care

CALM: A prospective, multicenter, open-label randomized study of treatment strategies

- Prospective, multicenter, open-label
- 244 biologic and immunomodulator naïve patients with CD
  - All had clinical, endoscopic (CDEIS > 6) and biochemical (CRP > 5 and or FC>250) disease activity
- Primary endpoint: CDEIS < 4 and no deep ulceration at week 48



A Treat-to-target approach leads to superior endoscopic and deep remission outcomes compared with symptom-driven care

CALM: A prospective, multicenter, open-label randomized study of treatment strategies

Lab visits	Clinical Management	Treat to Target
Week -1 (prior to randomization)	CDAI decrease < 70 points compared to BL or CDAI > 200	CDAI ≥ 150 CRP ≥ 5mg/L FC ≥ 250 µg/g Prednisone use at week 0
Weeks 11, 23, and 35	CDAI decrease < 100 points compared to BL or CDAI ≥ 200 Prednisone use a week prior to visit	CDAI ≥ 150 CRP ≥ 5mg/L FC ≥ 250 µg/g Prednisone use a week prior to visit

Colombel JF, et al. Presented at DDW. May 2017. Abstract 718

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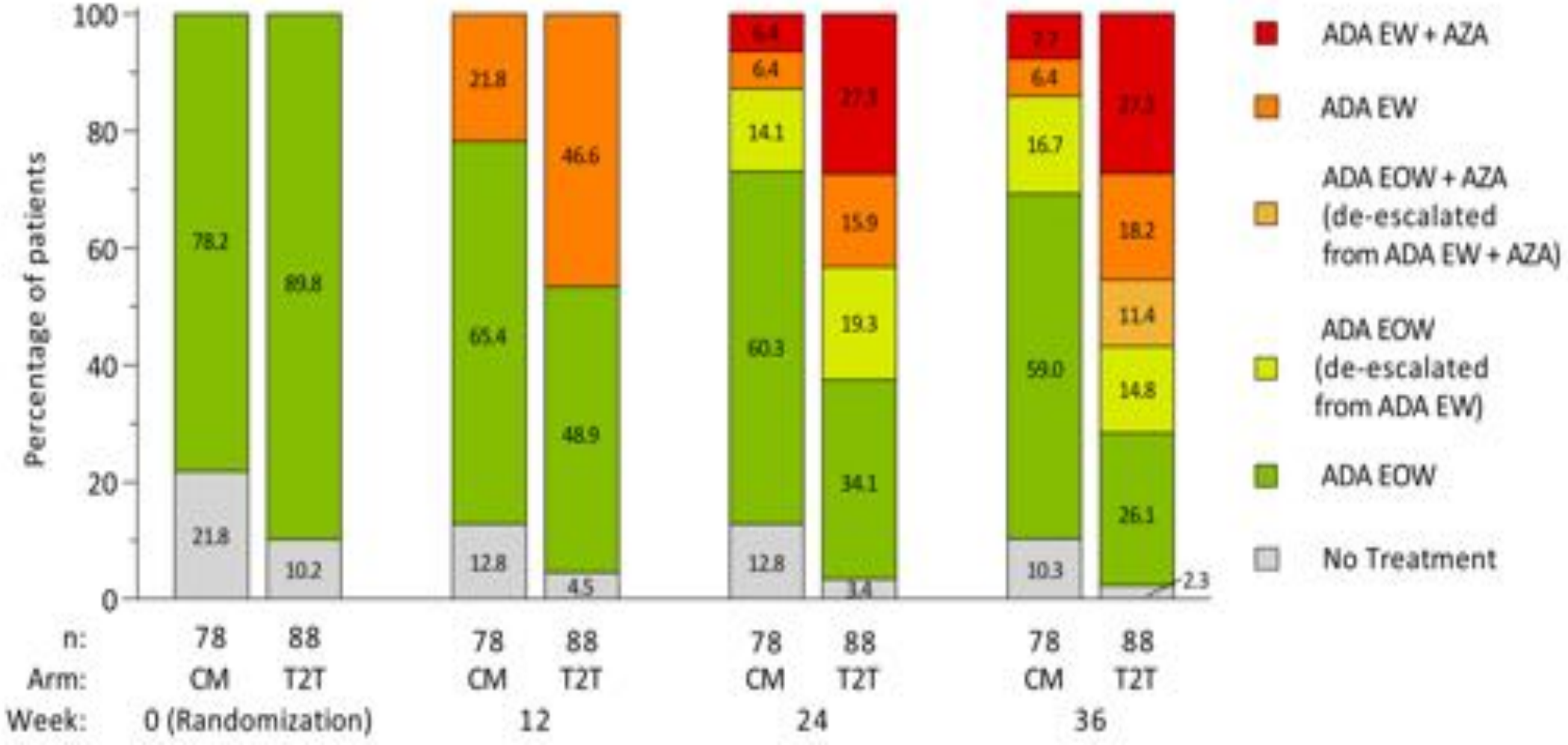

Colombel JF, et al. Presented at DDW. May 2017. Abstract 718

Hyperbaric O2 is safe and effective for hospitalized UC, a multicenter RCT, sham-controlled trial

- METHODS:
  - Hospitalized UC patients
  - Moderate-severe flare
- Intervention:
  - Steroids +daily HBO2 (10 sessions, 90 min) vs. steroids + sham
  - 18 patients
- Outcomes:
  - Day 5 clinical remission
  - Day 10 clinical response/remission/ endoscopic remission
  - In hospital progression (surgery/TNF/CSA)

Higher day 5 remission
50 vs 0% p=0.04

Higher day 10 outcomes
Remission (50 vs 0%)*
Response (80 vs 25%) p=0.05
Endo Remission (50 vs 13%) NS

Less in hospital progression
10 vs 63%*

Dulai et al DDW 2007 #1075

IBD Potpourri

SubQ α4β7 integrin (Abrilumab)
2b –no difference PBO UC/CD
Need explore higher doses

Vegetarian/ gluten free diet in IBD
↓ QOL, ↑ anxiety/depression, no improve dz activity/hosp/surg

Cx601 Mesenchymal Stem Cells
Injected into fistula after 2 EUA
56% vs 39% remission*

Supratherapeutic (>15) IFX levels not associated with higher risk of infections (12% vs 19% normal)

Telemedicine RCT using myIBDcoach resulted in fewer hospitalizations, outpatients visits, better medication adherence *

Dose escalation works for LOR with vedolizumab
81.4% recaptured response when increased to q4 or q6 weeks

Sandborn et al DDW 2007 #1077; Panes et al DDW 2007 #985
De Jong et al DDW 2007

Schrinet et al DDW 2007 #95, Greener et al DDW 2007 #452,
Shivashankar et al DDW 2007 #304

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