IBD *and Biosimilars*

What Health Care Providers Need to Know

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Learning Objectives

Section 2: Summarizing the Evidence

- Summarize the evidence from pre-clinical to clinical assessment of biosimilarity
- Review the data from non-IBD indications that led to FDA approval for biosimilars and indication extrapolation
- Discuss the biosimilar studies, to date, in IBD

Summarizing the Evidence

Section 2

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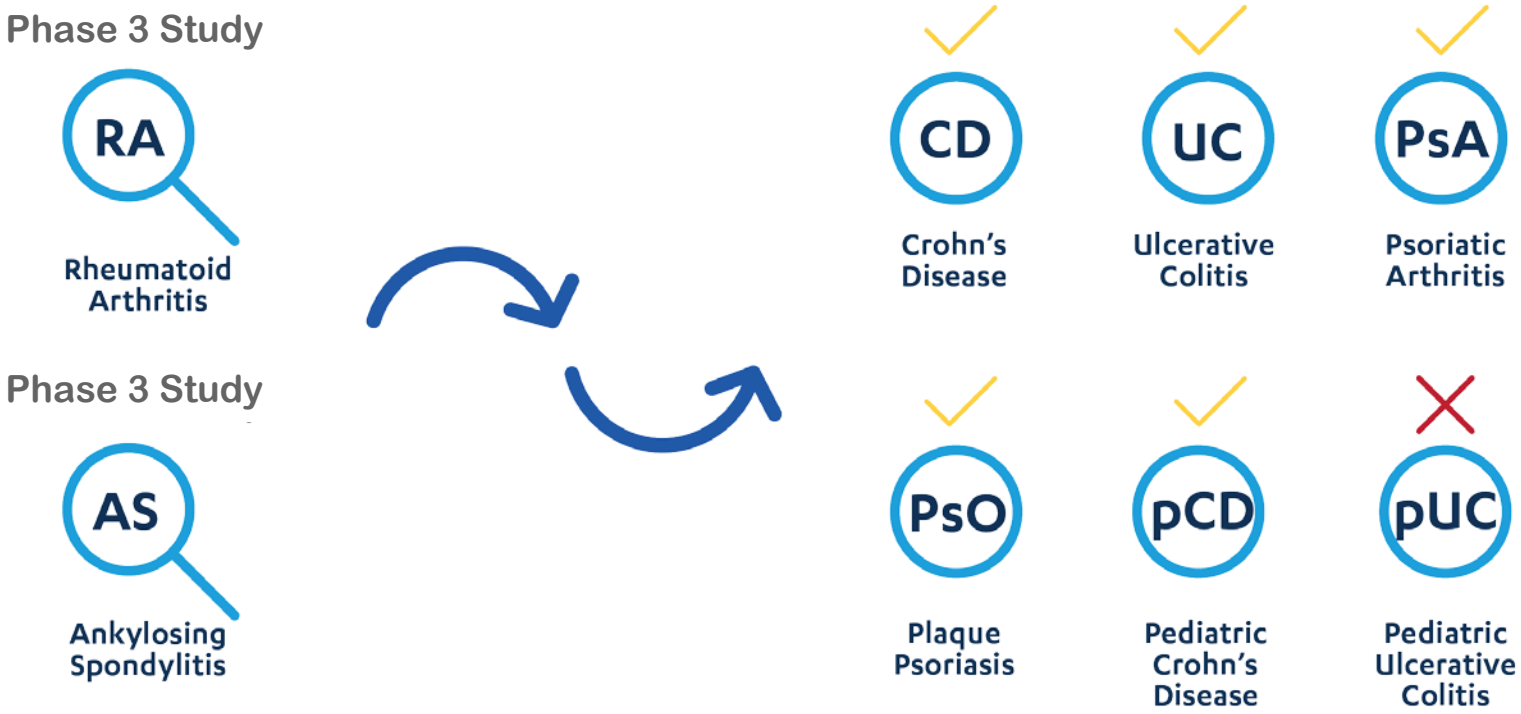
Most indications for infliximab-dyyb were extrapolated based on the biosimilarity exercise by comparing it with reference product



1. Yoo D et al. Ann Rheum Dis, 2013. **2.** Park W et al. Ann Rheum Dis, 2013. **3.** FDA approves Inflectra, a biosimilar to Remicade [news release]. Silver Spring, MD: US Food and Drug Administration; April 5, 2016. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/UCM494227.htm. Accessed February 26, 2018

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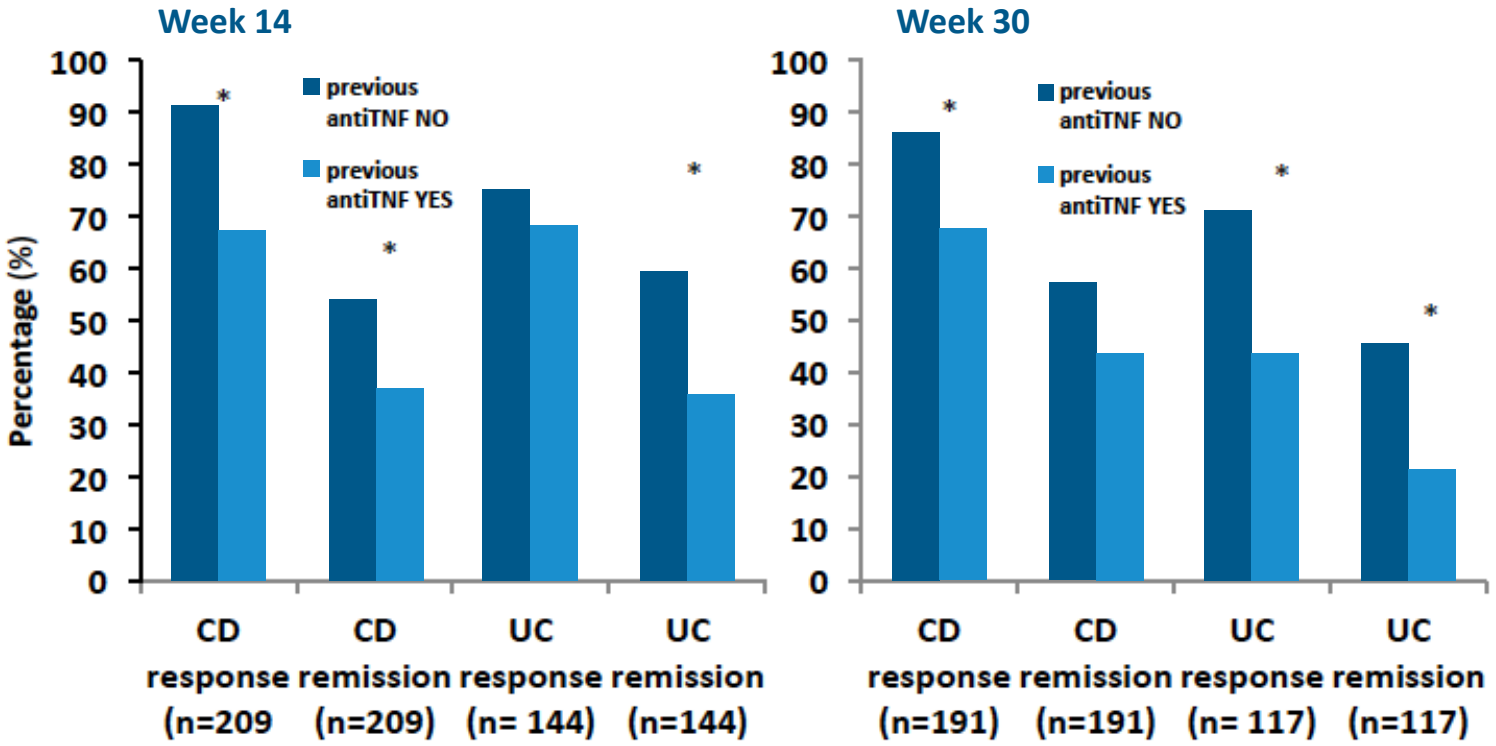
Efficacy and safety of biosimilar Infliximab-dyyb (CT-P13) in CD and UC after one-year: Results from a prospective nationwide cohort



Infusion reactions 6.6%
Infections 7.9%

Conclusion:

Infliximab-dyyb (CT-P13) biosimilar of infliximab is effective and safe in maintaining remission in UC and CD (**no comparison group in this study**)

Gecse et al. J Crohn's Colitis, 2016.

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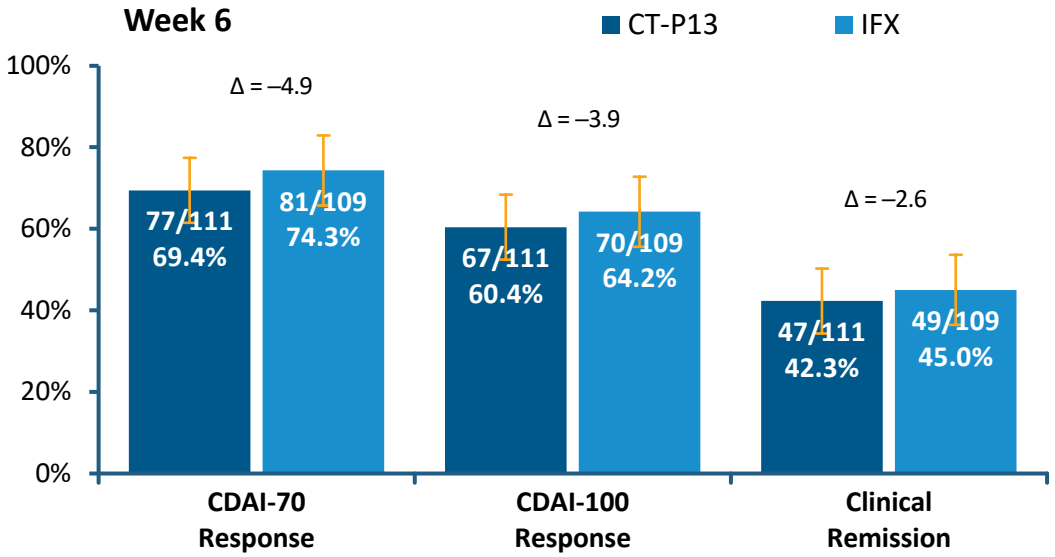
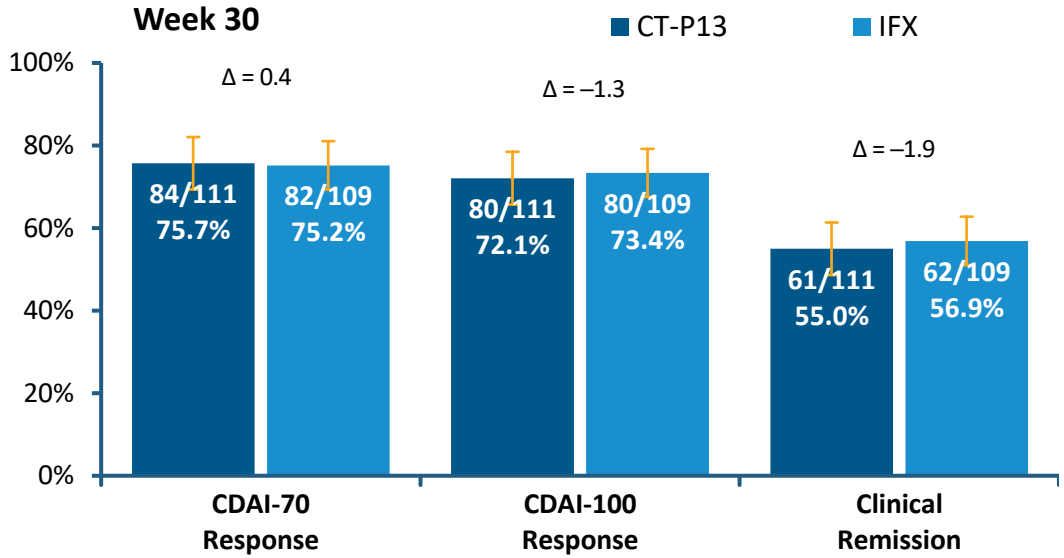
The efficacy and safety of Infliximab-dyyb (CT-P13) is similar to Infliximab RP (IFX): randomized controlled trial

Study design: Randomized, double-blind, trial of 220 moderate to severe CD with infliximab-dyyb or infliximab RP

Primary Endpoint: **CLINICAL** response and remission at week 6 (defined by CDAI) and week 30





No differences in FCP/CRP, adverse events, drug levels or ATIs

Ye BD et al. Lancet, 2019.

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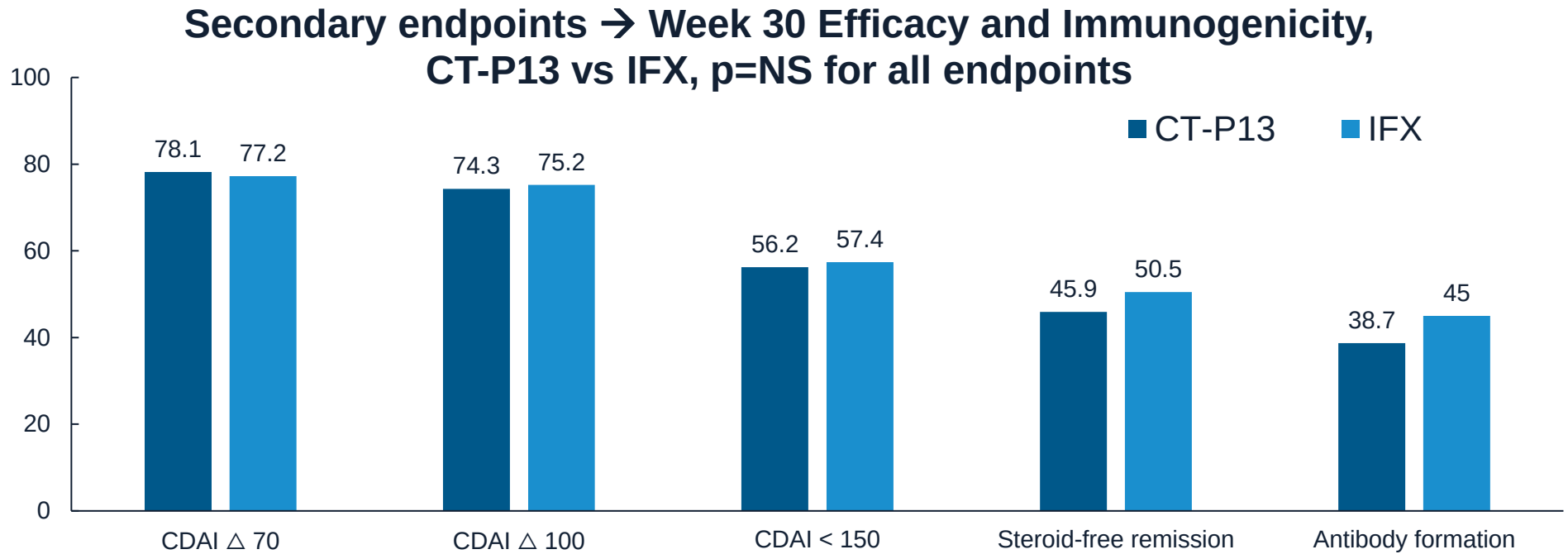
Phase III randomized, double-blind, controlled trial to compare biosimilar infliximab-dyyb (CT-P13) with infliximab RP (IFX) in patients with active Crohn's Disease: early efficacy and safety results



No differences in adverse events, week 14 drug levels (max or trough)

Ye BD et al. Lancet, 2019.

Switching of patients with inflammatory bowel disease from reference product Infliximab to biosimilar Infliximab-dyyb is effective and safe

Study design: Retrospective observational cohort

Aim: Evaluate efficacy and safety of switching from reference product to biosimilar in CD and UC

Population: 74 IBD patients (56 CD, 18 UC) on infliximab RP therapy that were switched to biosimilar

- **Mean time of 3 $\pm$ 2.2 yrs of orignator IFX**
- 46% on concomitant azathioprine
- 72% clinical remission, 22% mild-mod active dz; 5% severe dz

Outcomes of interest: Disease activity and adverse events

Results: Comparing week 0 to week 24 after starting the biosimilar **No Differences in:**

- Calprotectin
- Infliximab levels (3.4 vs 3.8 pg/mL)
- Antibodies (9.5% vs 10%)
- Remission at week 0 - 72%, week 24 - 78%
- Infusion reactions

Conclusion: Switching to biosimilar IFX appears to be effective and safe

Limitations: No control IFX brand group for comparison; no long-term data on efficacy.

Kolar M et al. Dig Dis, 2017.

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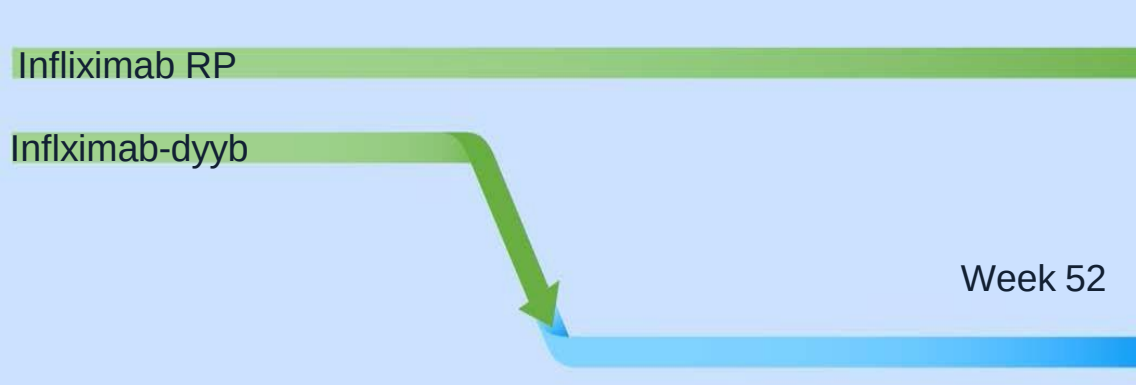
A Phase IV Multi-Indication Prospective NOR-SWITCH Study

52-week randomized, double-blind non-inferiority study



Disease Worsening at 12 months

	Infliximab RP	Infliximab-dyyb
CD (n=155)	14 (21%)	23 (36.5%)
UC (n=93)	3 (9.1%)	5 (11.9%)
Primary outcome	53/202 (26.2%)	61/206 (29.6%)

Jorgensen K et al. Lancet, 2017.

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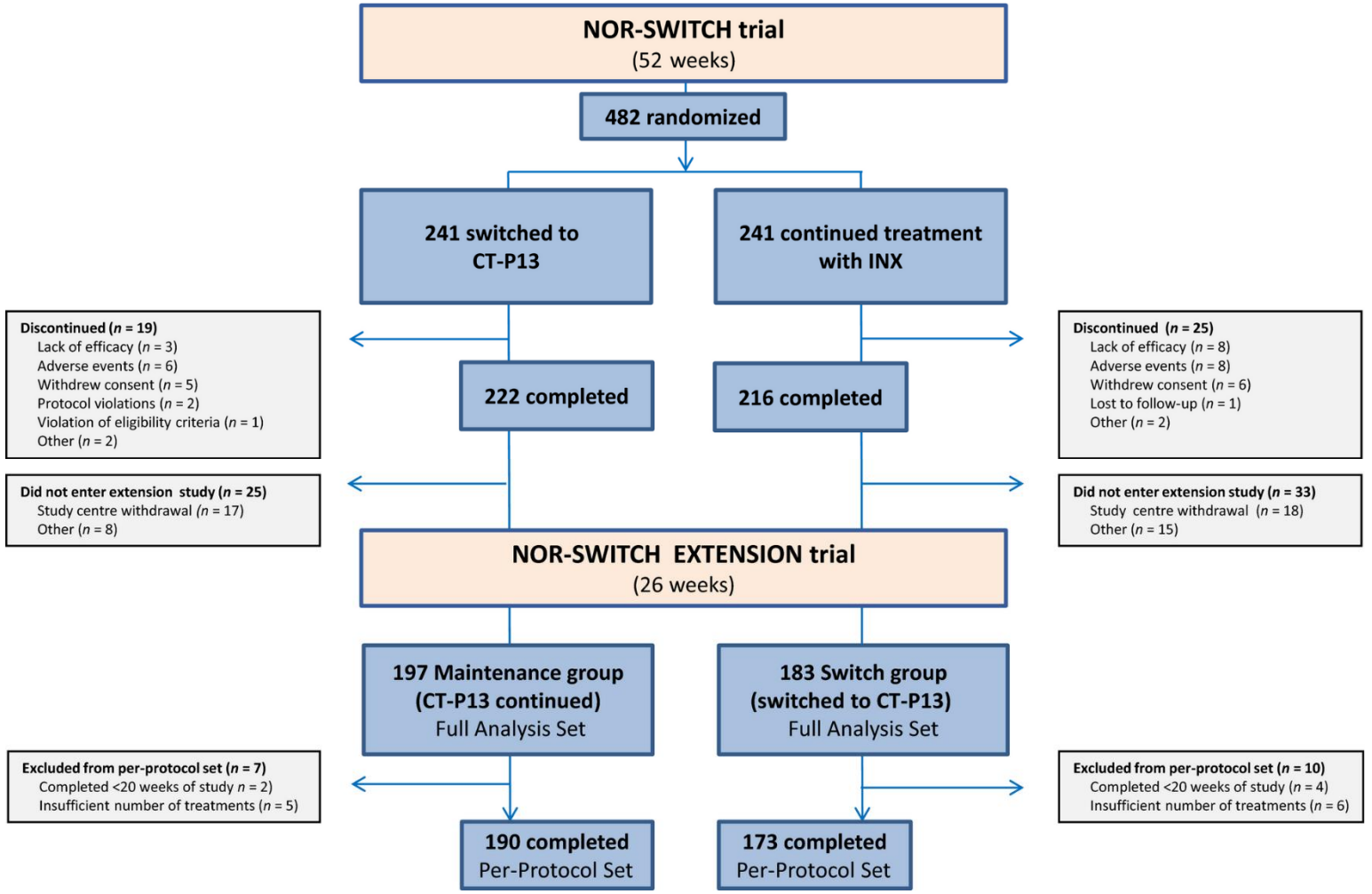
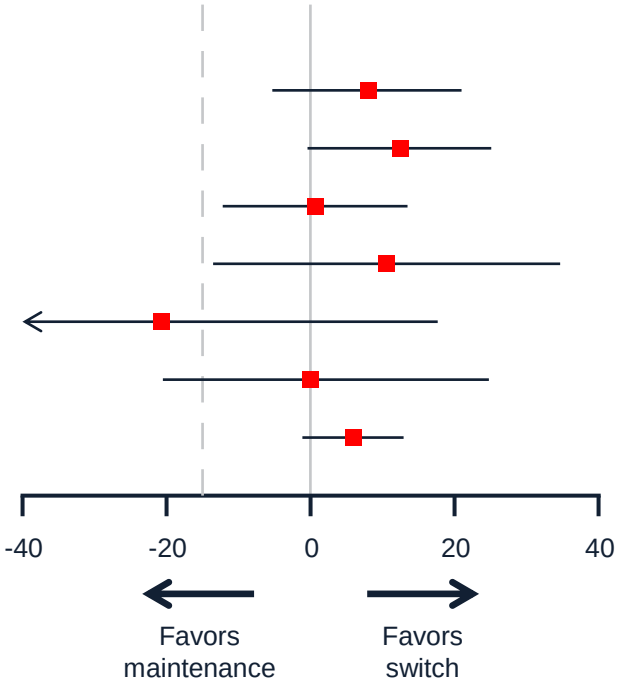
Switch: NOR-SWITCH / Open Label Extension (OLE)



Goll GL et al. J Intern Med, 2019.

Switch: NOR-SWITCH / OLE Outcomes

Diagnosis	Maintenance (*n*=190)	Switch (*n*=173)	Risk difference (95% CI)
Crohn's disease	13/63 (20.6%)	8/61 (13.1%)	7.9% (-5.2 to 21)
Ulcerative colitis	6/39 (15.4%)	1/35 (2.9%)	12.4% (-0.1 to 25)
Spondyloarthritis	3/38 (7.9%)	2/28 (7.1%)	0.6% (-12.2 to 13.5)
Rheumatoid arthritis	9/26 (34.6%)	6/27 (22.2%)	10.5% (-13.6 to 34.6)
Psoriatic arthritis	1/8 (12.5%)	3/9 (33.3%)	-20.8% (-59.1 to 17.6)
Psoriasis	0/16 (0%)	0/13 (0%)	0% (-20.6,24.7)
Overall	**32/190 (16.8%)**	**20/173 (11.6%)**	**5.9% (-1.1 to 12.9)**



Goll GL et al. J Intern Med, 2019.

Immunogenicity

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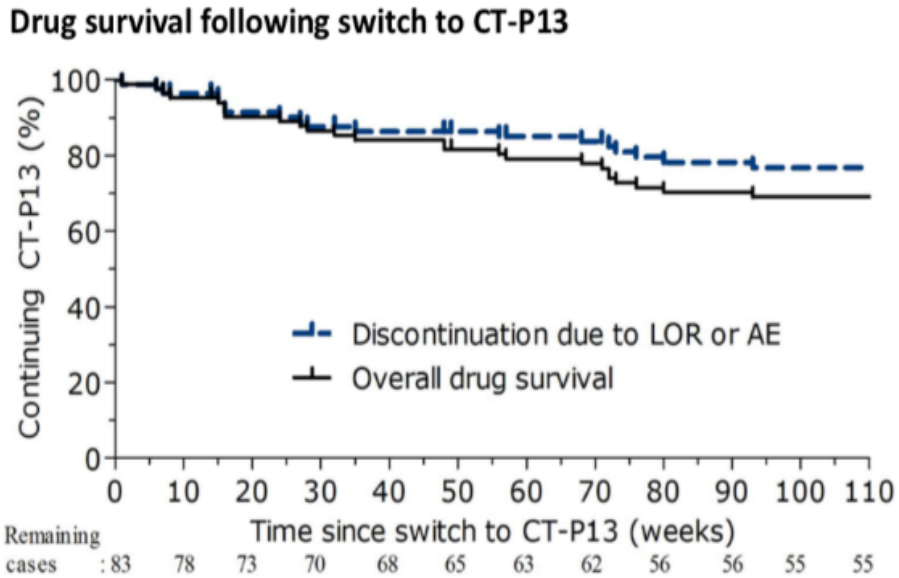
Switching to biosimilar IFX does not alter outcomes, levels or immunogenicity → for patients in stable remission

Prospective study of adult CD patients in stable remission (> 30 weeks, HBI ≤ 4) with stable dosing of infliximab RP switched to biosimilar IFX[1]

- **IFX level at week 0 (pre-switch):**
  - **mean 2.97 (2.78-3.18)**
- **IFX level at week 16 w/CT-P13 biosimilar:**
  - **mean 3.25 (3.04-3.48)**
- **At week 16:**
  - **86% of CD patients still in remission**
  - No significant differences in CRP or FC
  - 3.2% (n=2) serious adverse events
  - 1 patient developed antibodies to IFX

83 (57 CD, 24 UC, 2 IBDU) infliximab RP treated patients switched to IFX biosimilar [2]

- Stable dosing & interval, 104-week follow-up



Only 2 patients with antibody formation by week 104

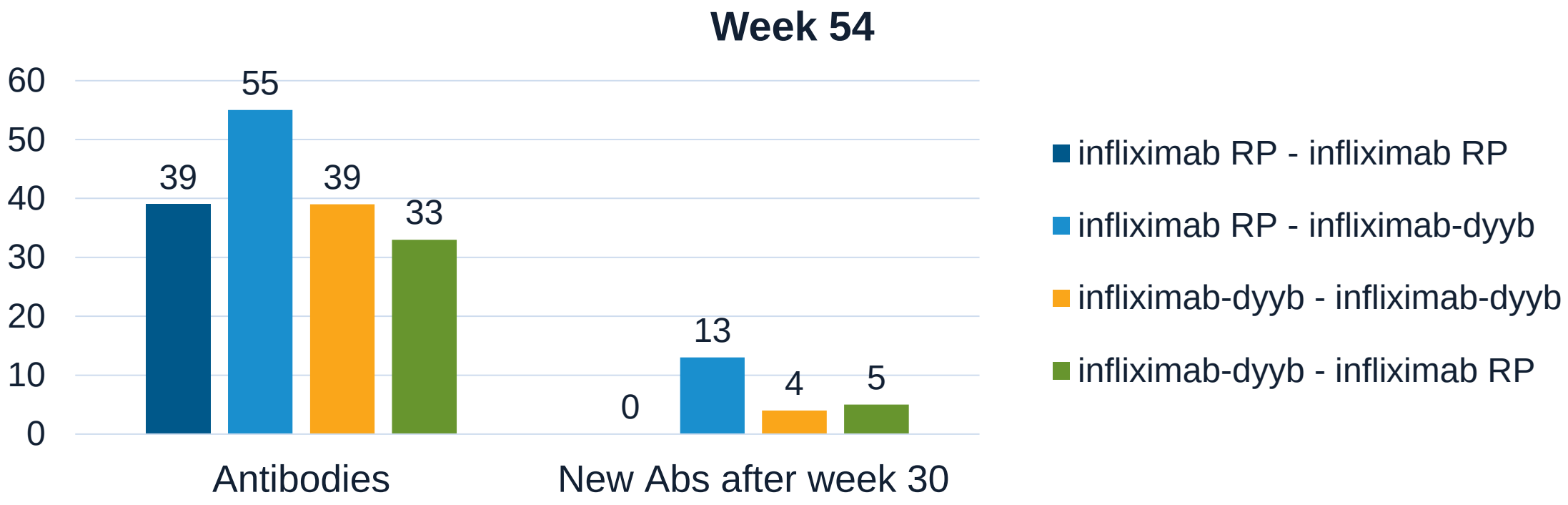
1. Strik et al. Lancet Gastroenterol Hepatol, 2018. **2.** Smits is Smits LT et al. Inflamm Bowel Dis, 2019.

Therapeutic drug monitoring (TDM) targets for IFX and ADA (Same as originators)

	Parameter	Target Value
IFX / ADA Level	Clin + Endo Remission	≥ 5 µg/mL
	Clin not Endo Remission	≥ 10 µg/mL
	Clin + Endo Active	≥ 15-20 µg/mL
Antibodies	IFX	≤ 9 µg/mL
	ADA	≤ 4 µg/mL

Gastroenterology. 2017 Sep;153(3):858-859. Mulcahy, Andrew W., Zachary Predmore and Soeren Mattke. The Cost Savings Potential of Biosimilar Drugs in the United States. Santa Monica, CA: RAND Corporation, 2014. https://www.rand.org/pubs/perspectives/PE127.html.

Immunogenicity In Crossover Study with Infliximab RP and Biosimilar



Ye BD et al. Lancet, 2019.

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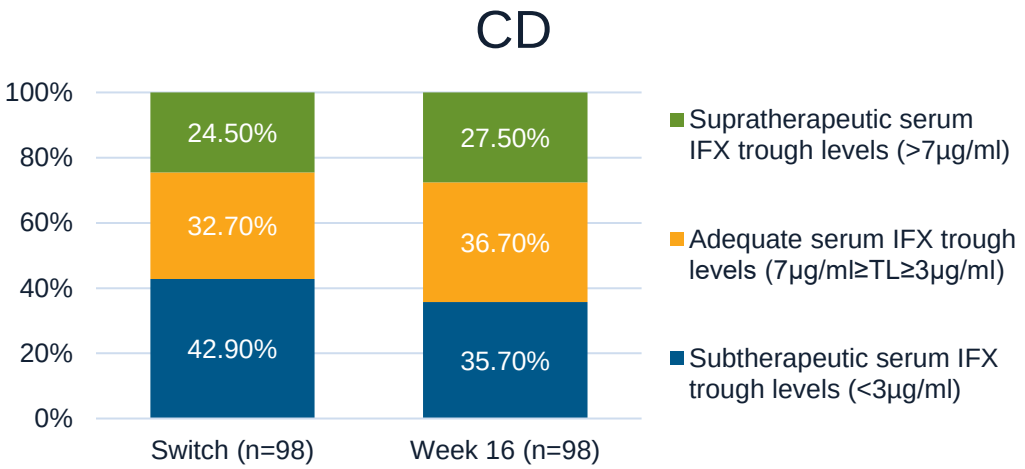
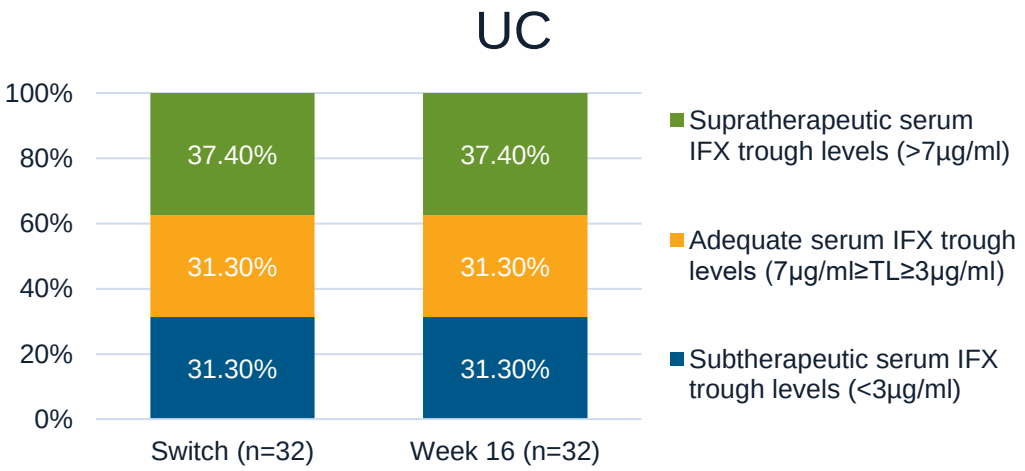
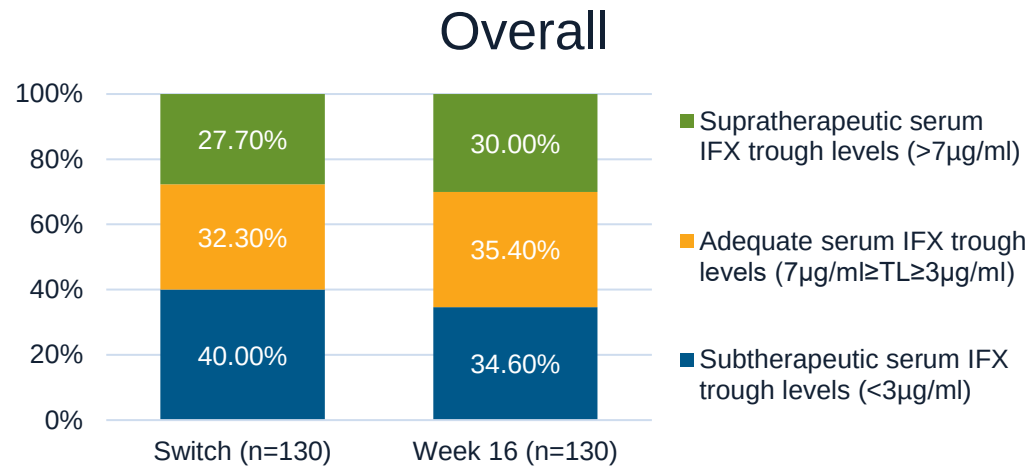
PK and Immunogenicity Switch from CT-P13 to Infliximab RP in CD and UC



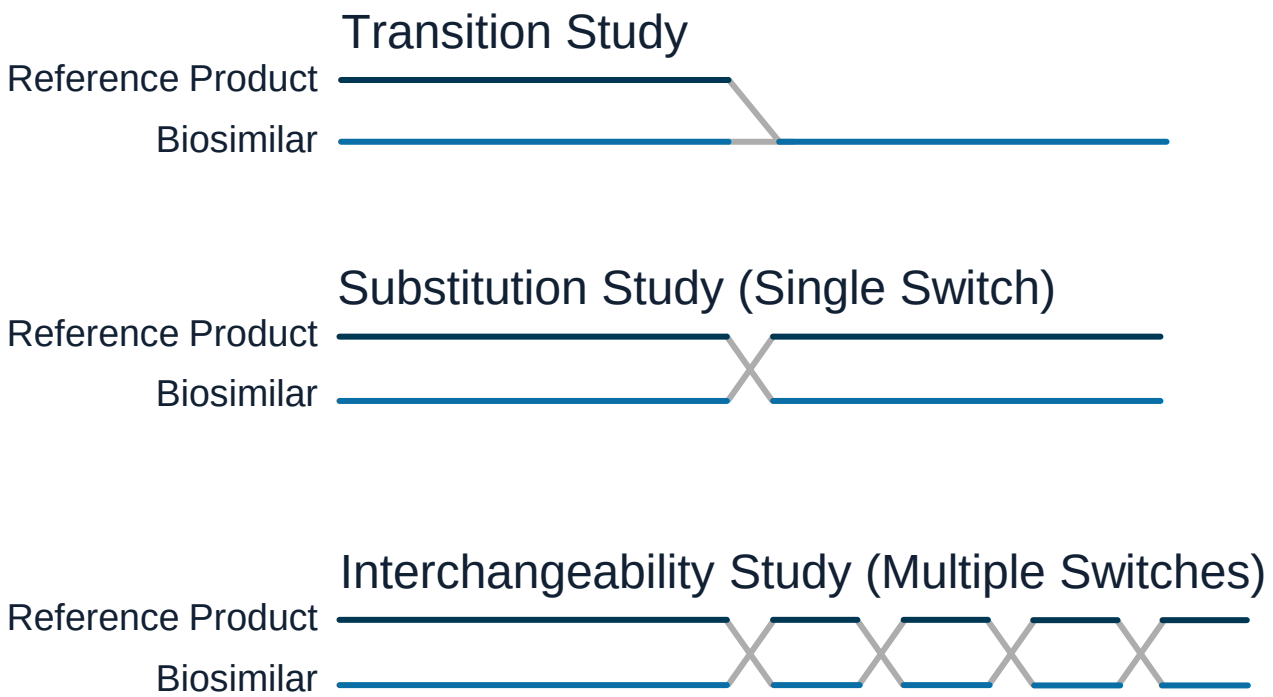




Mean µg/mL	5.33 ± 4.70	5.69 ± 4.94

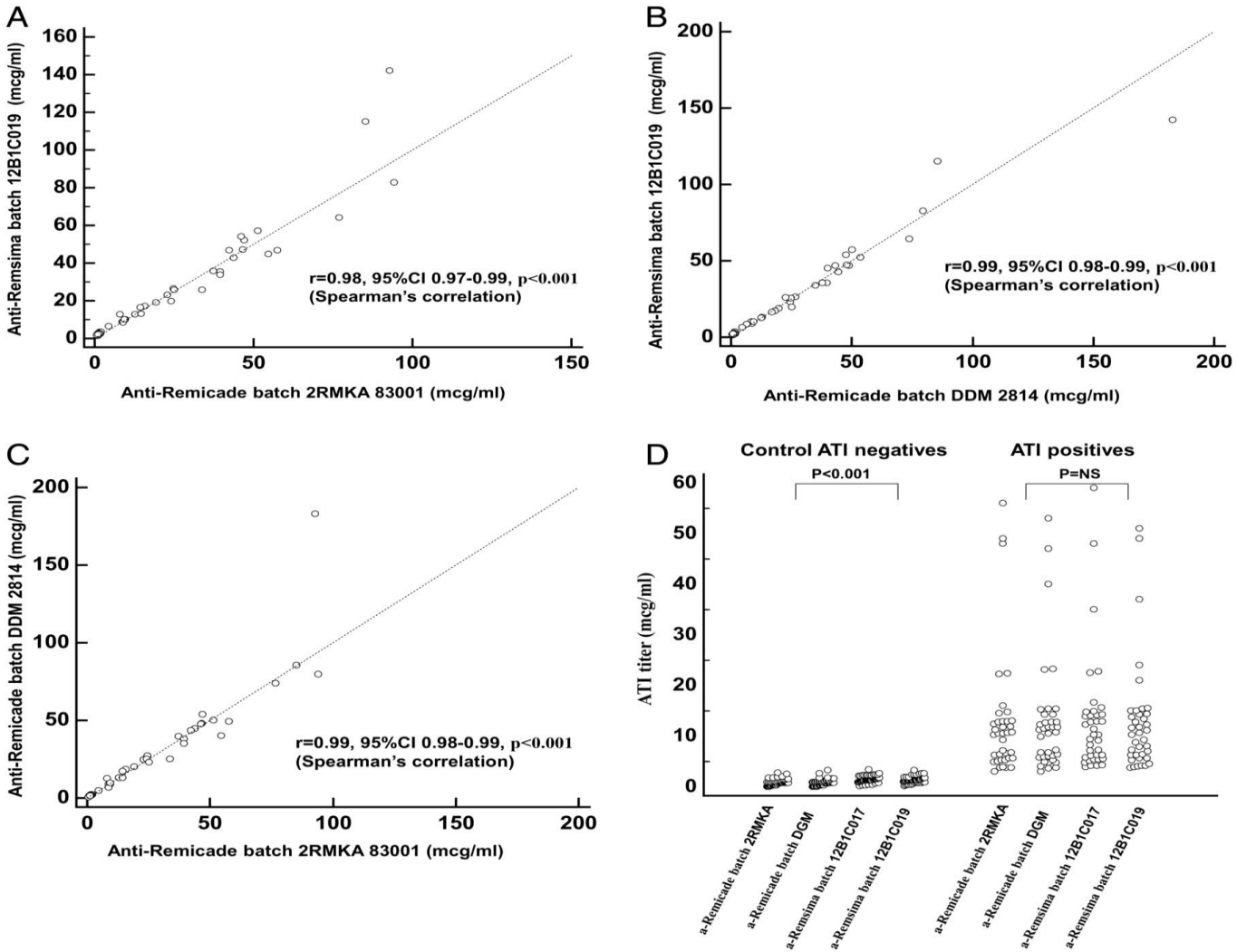
Ilias A et al. Clin Gastroenterol Hepatol, 2019.

Transition-switching-interchangeability studies



Faccin F et al. Expert Opin Biol Ther, 2016.

Infliximab RP and Infliximab-dyyb show similar immunogenicity



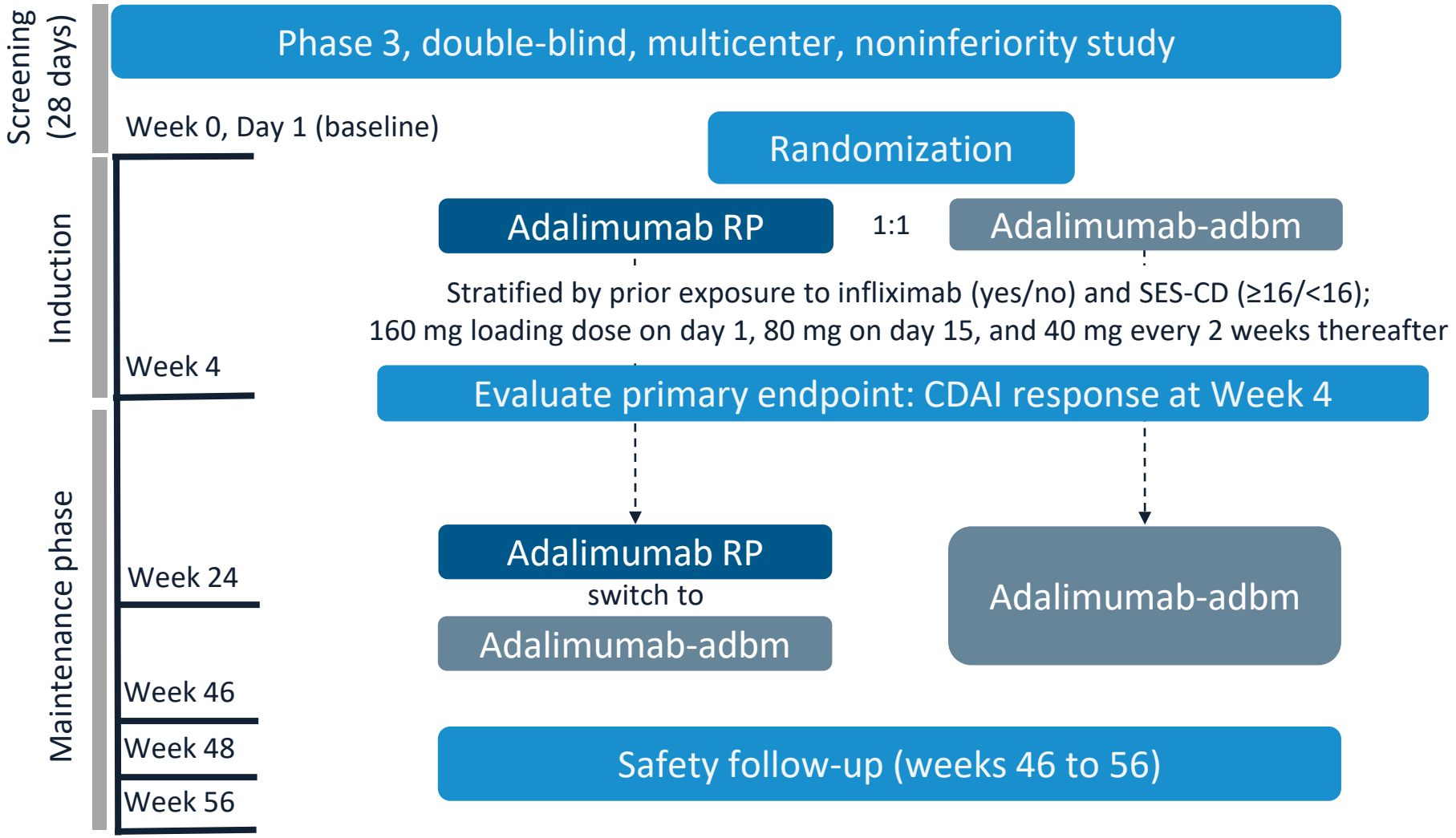
Ben-Horin S et al. Gut, 2016.

What does the real-world evidence say about using biosimilars in IBD?

Considerations

- The FDA allows for extrapolation of indication for biosimilars, and available data suggests that biosimilars to anti-TNFs will behave similarly to their reference products.
- No biosimilar in the U.S. yet has interchange-able designation, in patients with IBD.
- Safety remains uncertain with double and triple switches.
- Drug assays for reference products are expected to work similarly for biosimilars.
- Anti-drug antibodies to reference products WILL cross-react to biosimilars (and vice versa).
- Providers can feel as comfortable starting a new patient on a biosimilar as on its reference biologic.

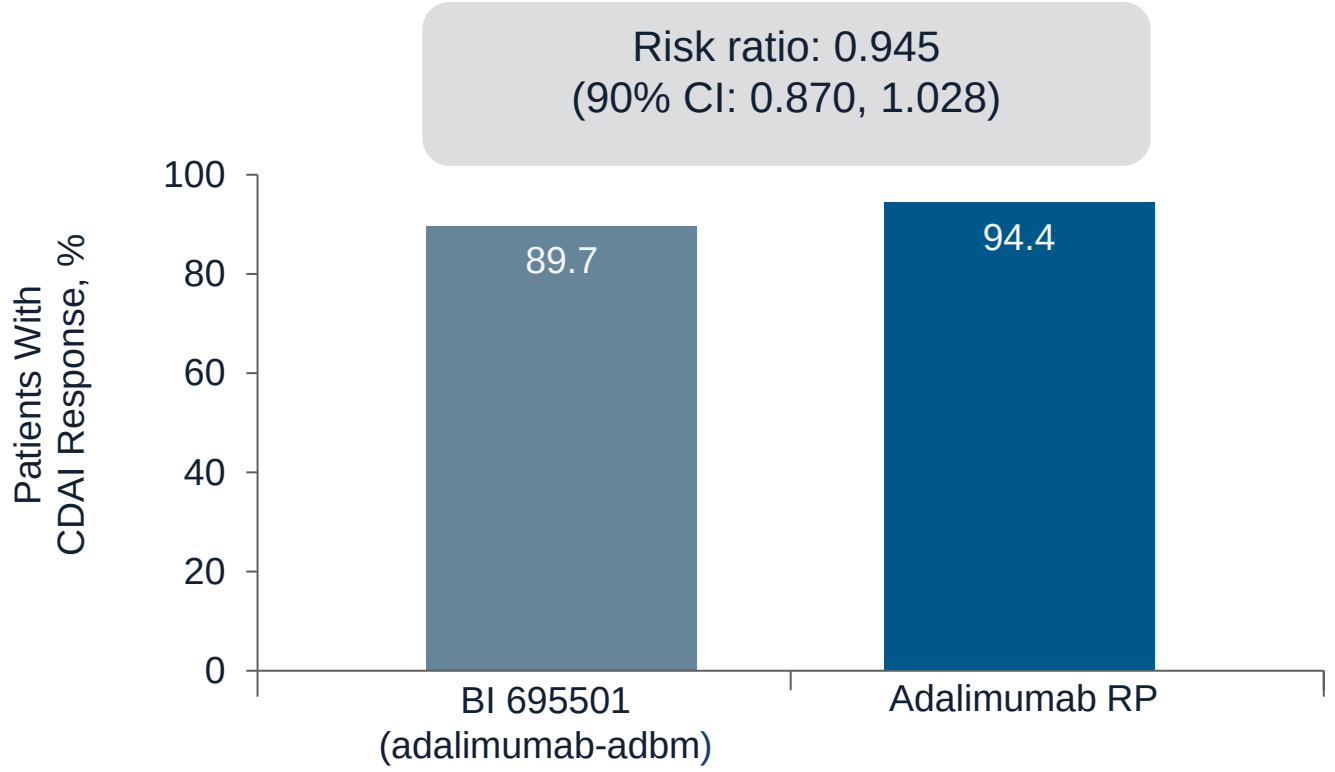
VOLTAIRE-CD study: Safety and efficacy of Adalimumab-adbm (BI 695501) compared with EU-approved Adalimumab RP



Hanauer SB, et al. DDW 2020. Abstract 1862.

Results: Primary endpoint analysis

Primary endpoint analysis: ≥70-point decrease in CDAI score between baseline and week 4 (full analysis set)



Safety profiles were similar between treatment arms, with no unexpected safety signals

Hanauer SB, et al. DDW 2020. Abstract 1862.