

# CT-P13 Biosimilar Infliximab, a European and UK perspective: Lessons learnt over the last two years

Dr Nick Kennedy  
Consultant Gastroenterologist, Exeter



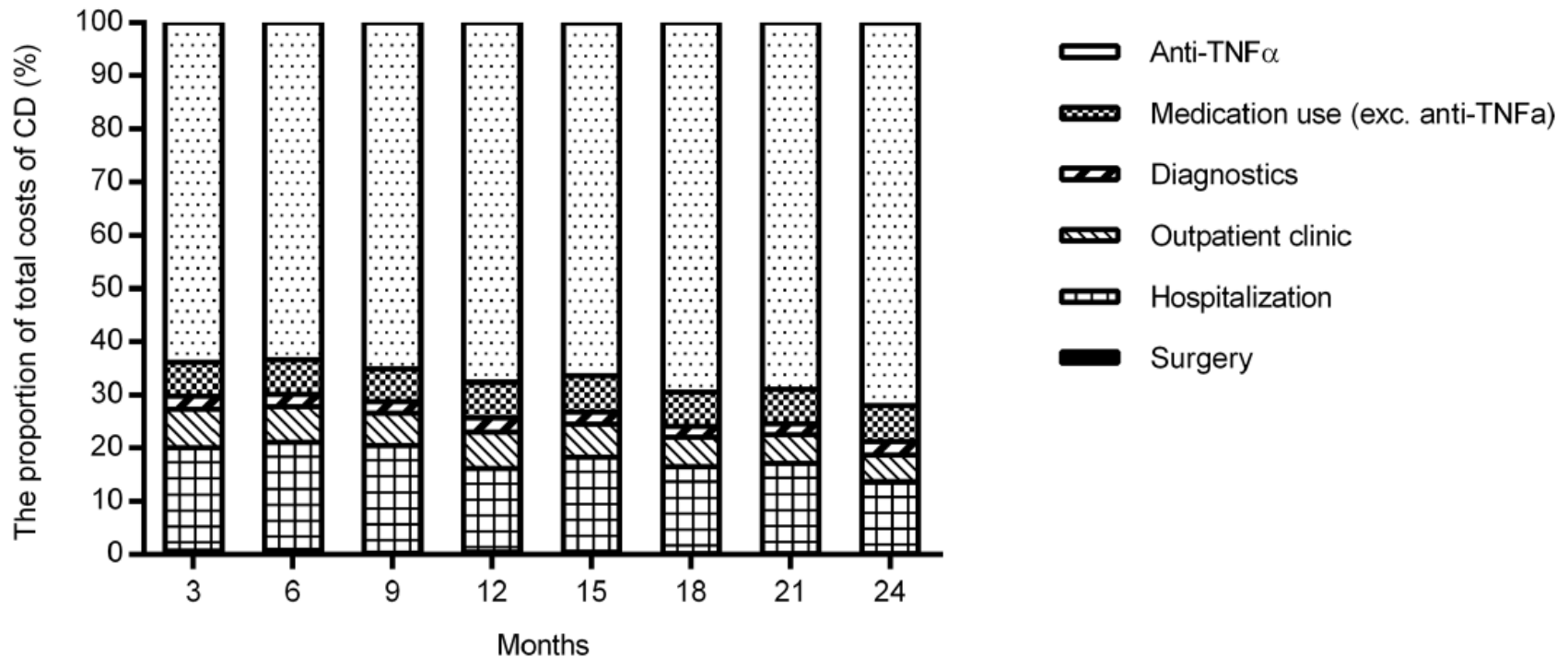
# Anti-TNFs in NHS England 2016/17

| Medicine    | Total cost (£000s) |
|-------------|--------------------|
| Adalimumab  | 461,973.9          |
| Aflibercept | 292,140.4          |
| Etanercept  | 202,859.3          |
| Infliximab  | 185,847.1          |
| Ranibizumab | 185,170.2          |

# Anti-TNFs in NHS England 2016/17

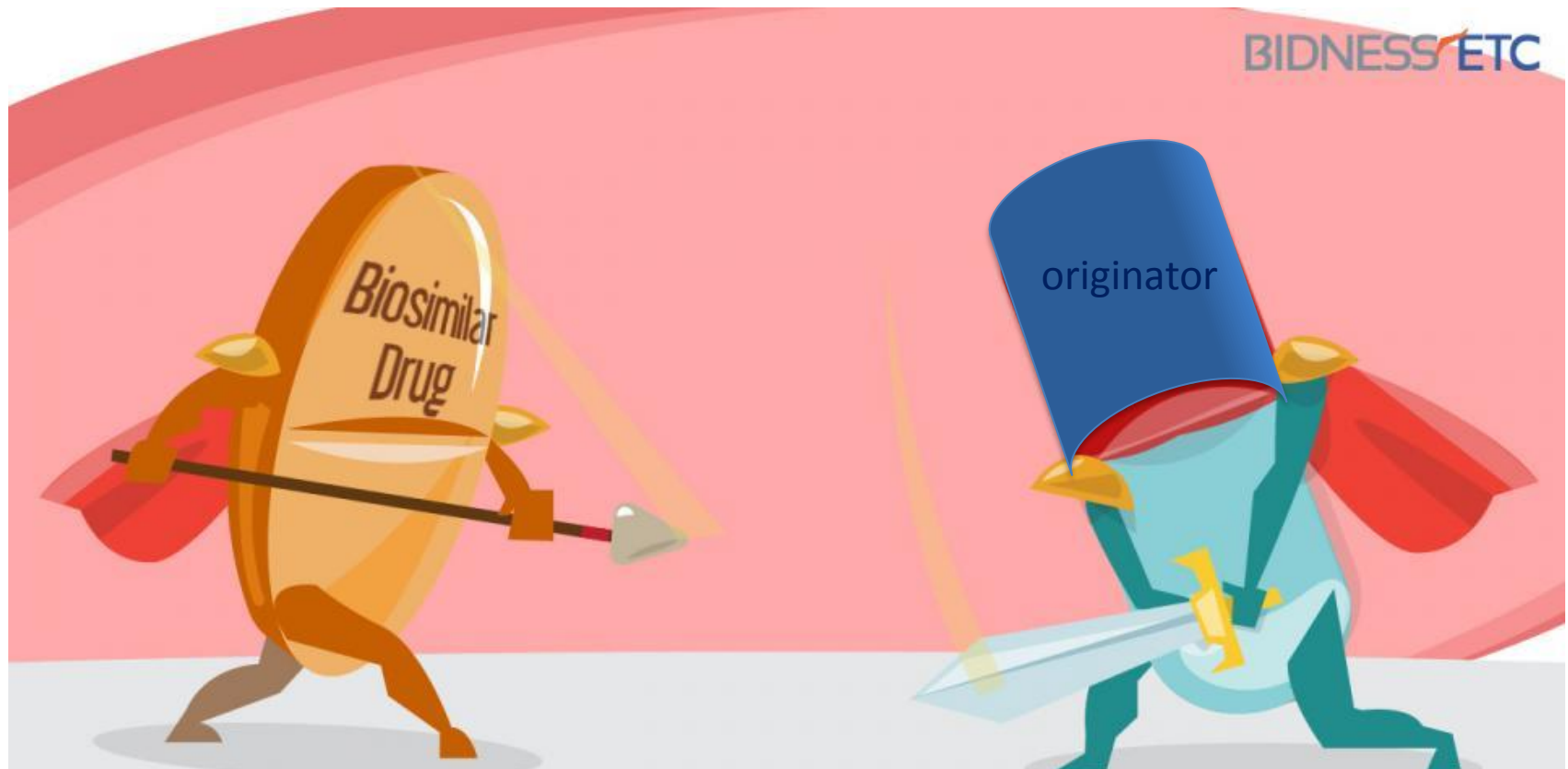
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# Biologics represent a significant proportion of IBD costs



van der Valk ME et al. Cominelli F, editor. PLoS One. 2016 Apr 21;11(4):e0142481  
doi:10.1371/journal.pone.0142481.

# 2013 first monoclonal biosimilar



no clinically meaningful differences to the licensed originator in structure, pharmacokinetics, quality, safety or efficacy

# Extrapolation to IBD – 2013 Concerns

The pathological roles of TNF $\alpha$  may vary by disease.

The mechanism of action of Infliximab might vary by indication

“Questions remain as to whether PK, efficacy and safety data for CT-P13 can be extrapolated and provide justification for use in IBD...a more conservative approach is warranted”<sup>1</sup>

ECCO position statement “Biosimilars will require testing in patients with IBD with comparison to the innovator product”<sup>2</sup>

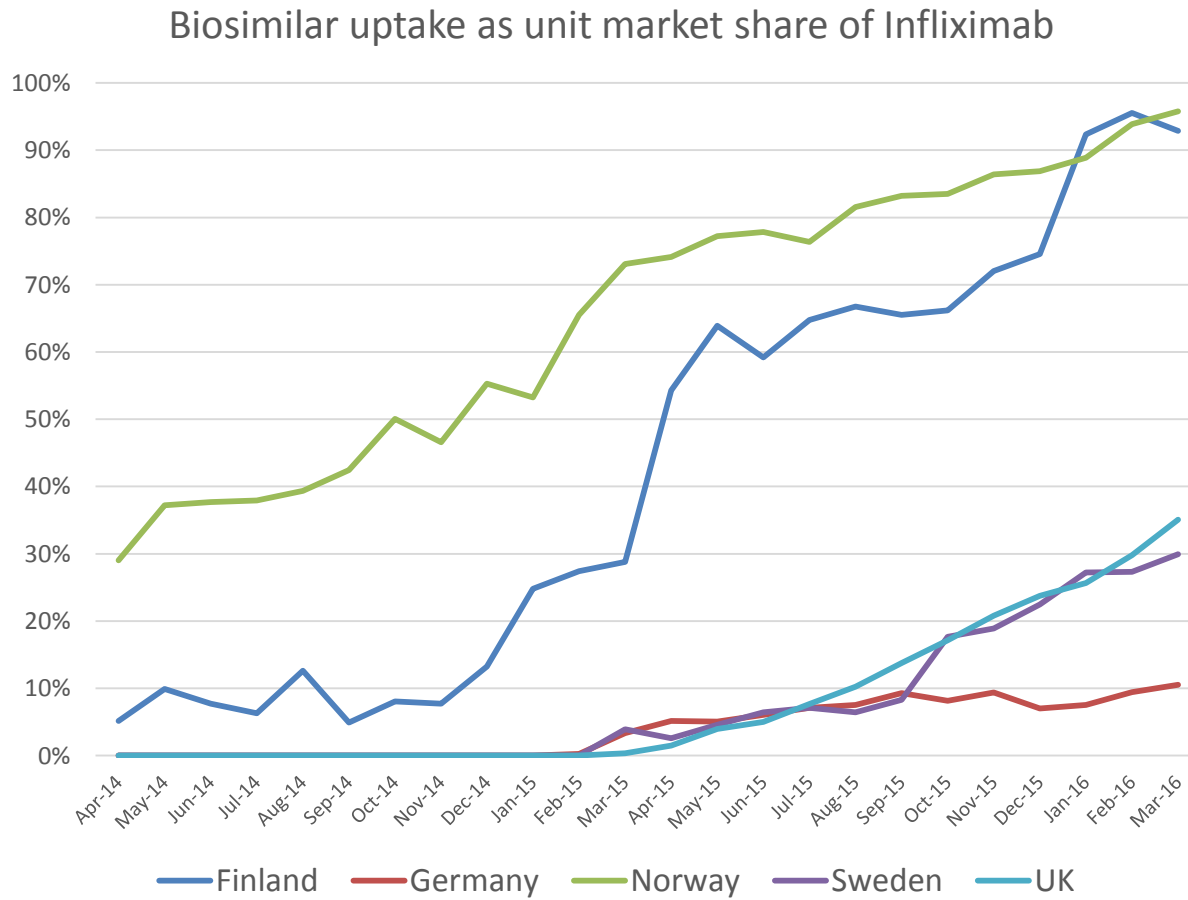
ECCO survey of 118 members – 19.5% felt little or no confidence in use of Biosimilars”<sup>3</sup>

“At present, we urge caution until we have more data” – BSG

Health Canada does not accept extrapolation to IBD

1. Feagan Biologicals 2014;42(4):177-83
2. Danese S et al. J Crohns Colitis. 2013;7(7):586-9.
3. Danese S et al. J Crohns Colitis. 2014;8(11):1548-50

# Despite initial concerns CT-P13 uptake has increased



# Real world evidence: IBD (adults)

| Author               | Country     | Total patient numbers (n=665) | No. of switch patients | No. of anti-TNF naïve patients | Efficacy assessed at |
|----------------------|-------------|-------------------------------|------------------------|--------------------------------|----------------------|
| Park <sup>1</sup>    | South Korea | 173<br>(CD=95, UC=78)         | 60                     | 113                            | 30 weeks             |
| Jung <sup>2</sup>    | South Korea | 110<br>(CD=59, UC=51)         | 36                     | 74                             | 2, 8, 30, 54 weeks   |
| Jahnsen <sup>3</sup> | Norway      | 78<br>(CD=46, UC=32)          | 0                      | 78                             | 14 weeks             |
| Kang <sup>4</sup>    | South Korea | 17<br>(CD=8, UC=9)            | 9                      | 8                              | 8 weeks              |
| Farkas <sup>5</sup>  | Hungary     | 39<br>(CD=18, UC=21)          | 0                      | 39                             | 8 weeks              |
| Gesce <sup>6</sup>   | Hungary     | 210<br>(CD=126, UC=84)        | 0                      | 210                            | 14 +30 weeks         |
| Smits <sup>7</sup>   | Netherlands | 83<br>(57 CD, 24 UC, 2 IBD-U) | 83                     | 0                              | 16 weeks             |

1. Park SH, *et al.* Expert Rev Gastroenterol Hepatol 2015; 9 (S1): S34-S44. 2. Jung YS, *et al.* J Gastroenterol Hepatol 2015 Dec; 30(12): 1705-12 3. Jahnsen J, *et al.* Expert Rev Gastroenterol Hepatol 2015; 9 (S1): S45-S52. 4. Kang Y-S, *et al.* Dig Dis Sci. 2015 Apr; 60(4): 951-6. doi: 10.1007/s10620-014-3392-z. Epub 2014 Oct 18 . 5. Farkas K, *et al.* Expert Opin Biol Ther 2015 15(9):1257-62. doi: 10.1517/14712598.2015.1064893. [Epub 2015 Jul 2]. 6. Gecse KB, *et al.* J Crohns Colitis 2016 Feb; 10(2): 133-140 doi:10.1093/ecco-jcc/jjv220. Epub 2015 Dec 10 7. Smits *et al.*, J Crohns Colitis. 2016 Apr 19. pii: jjw087. [Epub ahead of print]



# ECCO 2016 - Real-world experience

- 10 studies report experience using biosimilar infliximab in 325 IBD patients<sup>1-10</sup>
- The majority small retrospective studies
- Majority of cohorts include patients with past exposure, new starts and switchers
- All studies are uncontrolled
- Limited drug and antibody level data
- **No clear adverse efficacy, safety, immunogenicity signal.**

1. Bettey M, et al [Abstract DOP029]. Presented at the 11<sup>th</sup> Congress of ECCO, Mar 2016, Amsterdam, Netherlands.

2. Kolar M, et al. [Abstract DOP032]. Presented at the 11<sup>th</sup> Congress of ECCO, Mar 2016, Amsterdam, Netherlands.

3. Hamanaka S, et al. [Abstract P329]. Presented at the 11<sup>th</sup> Congress of ECCO, Mar 2016, Amsterdam, Netherlands.

4. Smits L, et al. [Abstract DOP030]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 March 2016, Amsterdam, Netherlands.

5. Diaz Hernández L, et al. [Abstract P449]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar 2016, Amsterdam, Netherlands.

6. Guerra Veloz M.F, et al. [Abstract P452]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar 2016, Amsterdam, Netherlands.

7. Fiorino G, et al. [Abstract P544]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar 2016 Amsterdam, Netherlands.

8. Guerra Veloz M.F, et al. [Abstract P600]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar 2016, Amsterdam, Netherlands.

9. Siczekowska J, et al. [Abstract P617]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar2016, Amsterdam, Netherlands.

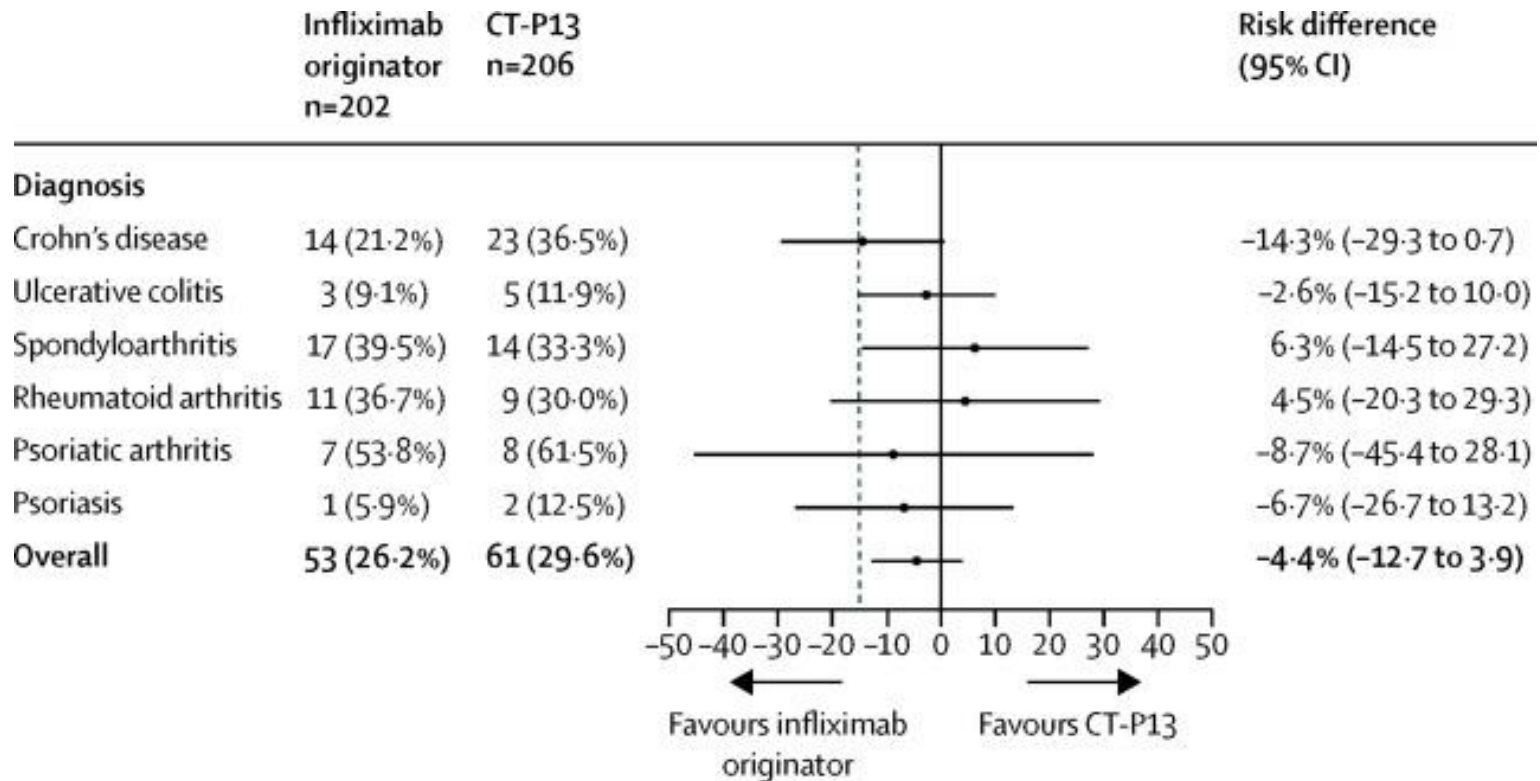
10. Hlavaty T, et al. [Abstract P655]. Presented at the 11<sup>th</sup> Congress of ECCO, 16-19 Mar2016, Amsterdam, Netherlands.

# NOR-SWITCH

- 52-week randomised, double-blind parallel-group, multicentre, non-inferiority
- Randomisation to continue Remicade vs. switch to CT-P13
- Primary endpoint disease worsening

Jørgensen KK et al. Lancet. 2017;389(10086):2304–16  
doi:10.1016/S0140-6736(17)30068-5.

# NOR-SWITCH



# Growing confidence in the use of Biosimilar IFX among 118 ECCO members

|   | 2013  | 2015  |
|---|-------|-------|
| Main advantage of Biosimilars = cost reduction                          | 89.5% | 92.4% |
| Concerns about immunogenicity of Biosimilar IFX                         | 67.1% | 27.1% |
| Originator and Biosimilar are interchangeable for patients in remission | 5.9%  | 44.4% |
| Against extrapolation across indications                                | -     | 32.2% |
| Little or no confidence in Biosimilars                                  | 63%   | 19.5% |

60% of respondents had prescribed Biosimilar IFX

22% had access but not yet prescribed

18% had no access to Biosimilar IFX

# 2016 BSG Guidance – CT-P13 in IBD<sup>1</sup>

“There are sufficient data from observational studies to show that safety and efficacy of CT-P13 are comparable to Remicade, with similar immunogenicity, and that switching is also safe and effective.”

Small differences in afucosylation, resulting in lower binding affinity to Fc receptors and lower ADCC activity – not clinically meaningful

1. [http://www.bsg.org.uk/images/stories/docs/clinical/guidance/bsg\\_infliximab\\_guidance\\_16.pdf](http://www.bsg.org.uk/images/stories/docs/clinical/guidance/bsg_infliximab_guidance_16.pdf)

# 2016 BSG Guidance – CT-P13 in IBD<sup>1</sup>

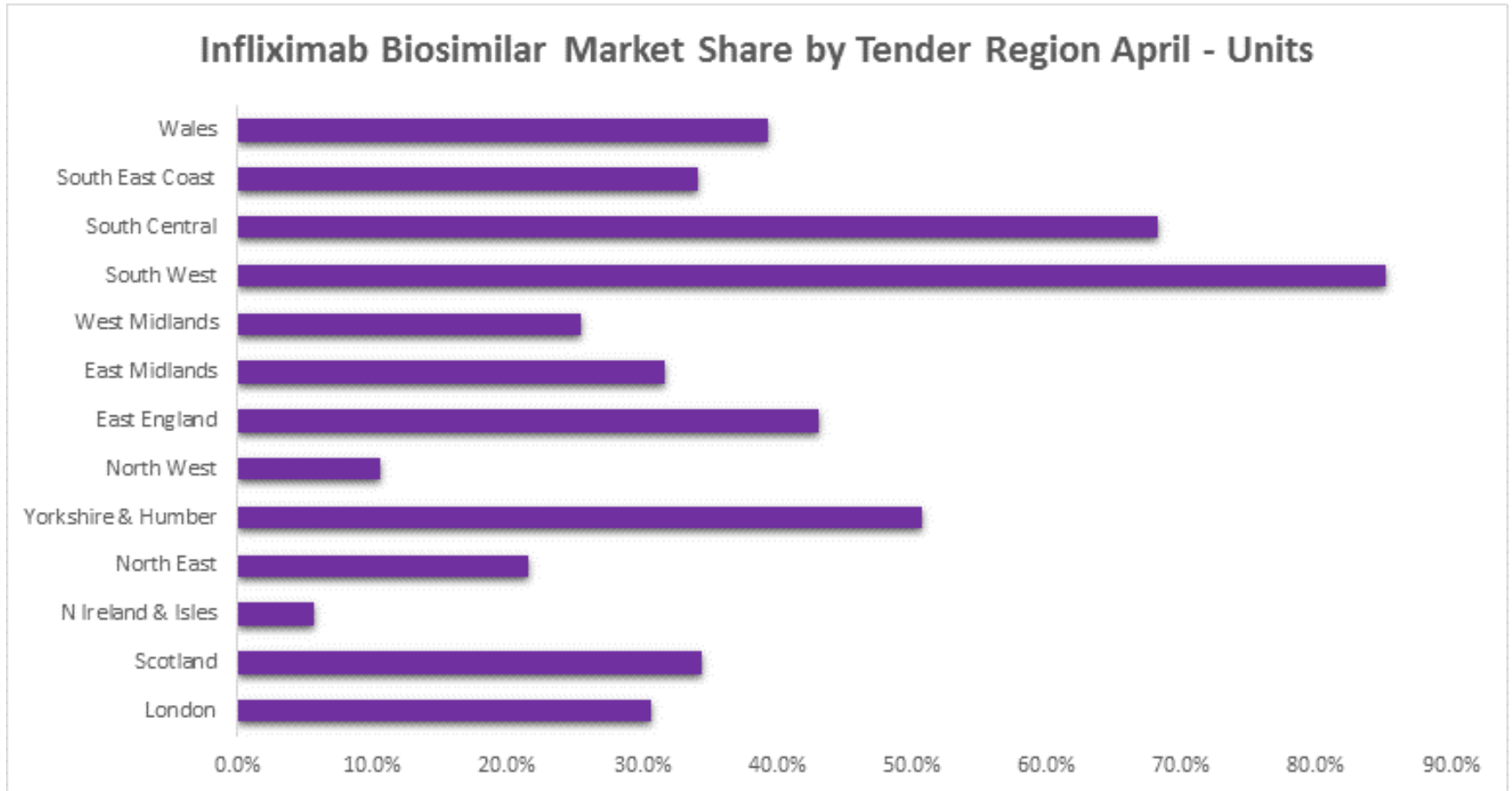
## Recommendations:

1. Infliximab must be prescribed by brand name.
2. For patients starting IFX, Remicade, Remsima® ▼ or Inflectra® ▼ may be prescribed...the choice should take into account the cost and its administration.
3. There is sufficient evidence to recommend that patients who are in a stable clinical response or remission on Remicade therapy may be switched to Remsima or Inflectra at the same dose and interval. This should be done after discussion with individual patients, with explanation for the reason for switching.
4. Automatic substitution (at the pharmacy level) is not appropriate.
5. Pharmacovigilance is essential and patients should be followed for safety in a registry such as the UK National IBD registry.

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©INFLECTRA is a registered trade mark of Hospira UK Limited

# UK Regional variation of CT-P13 uptake



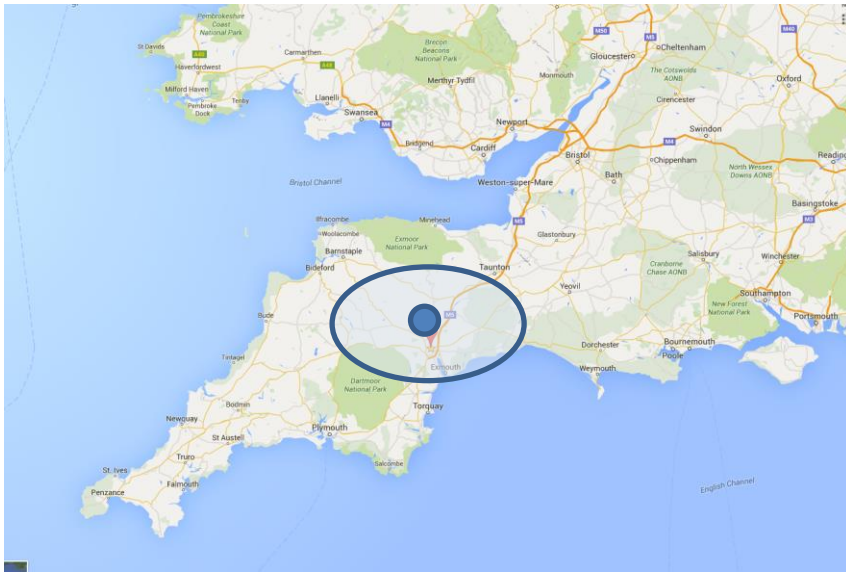
# Steps to introducing Biosimilar IFX

## RD&E Experience

- Identify, consult and educate stakeholders (inc patients)
  - EMA, NHS publications
- Build a switch team
  - Clinicians, Senior pharmacist, senior manager, commissioning lead, IBD nurse, patient
- Identify potential cost-saving
- Secure gain-share with CCG and your hospital
- Seek approval at local D&T
- Letter / information to patients
- Collect pre and post treatment clinical and lab data and enter into registry

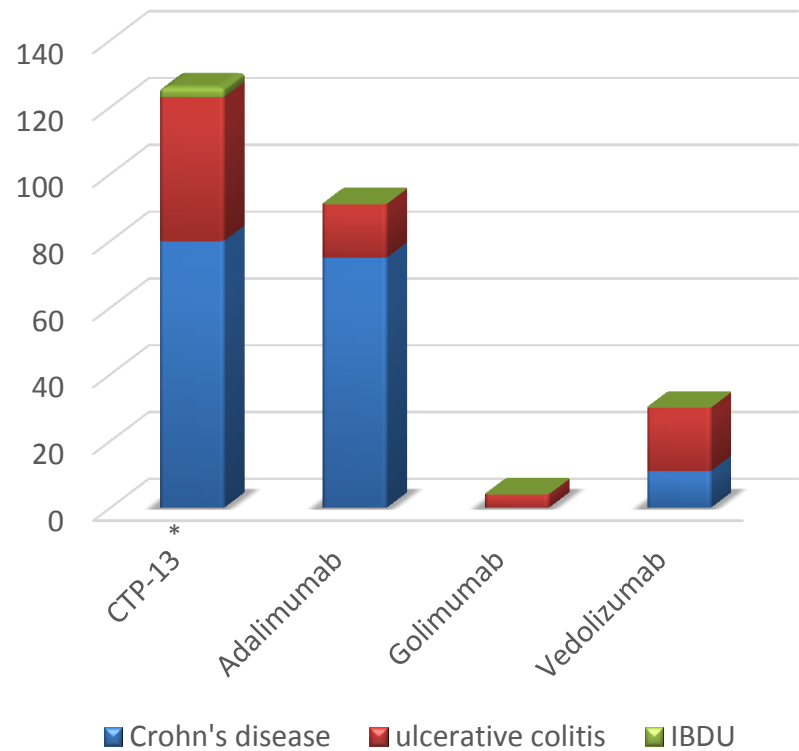


# Exeter IBD Service



- **Catchment area = 450,000 patients**
- **4 WTE IBD nurses**
- **8 luminal gastroenterologists**

**252 / ~3300 (7.6%) patients receiving biologics June 2016**

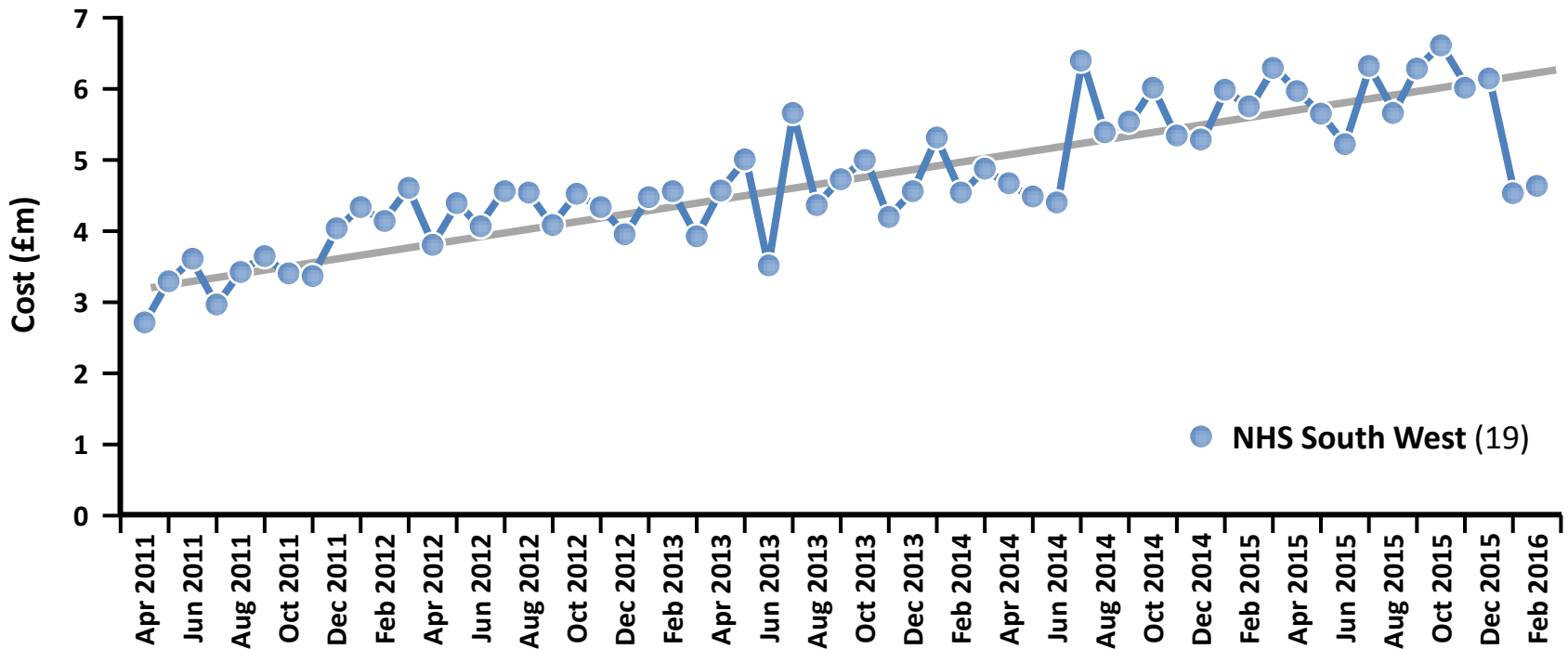


\*CT-P13 = biosimilar infliximab, marketed in the UK as Inflectra™ (Hospira) and Remsima™ (Napp)

# Increased costs were the driver for early adoption of biosimilar infliximab\* in April 2015

- Increasing incidence
- Increasing longevity, particularly in South West results in compounding prevalence – 1 in 130
- Increased uptake of biologics

Monthly spend on anti-TNF therapy in SW England



\*CT-P13, marketed in the UK as Inflectra™ (Hospira) and Remsima™ (Napp)

# Challenges of 'gain share'

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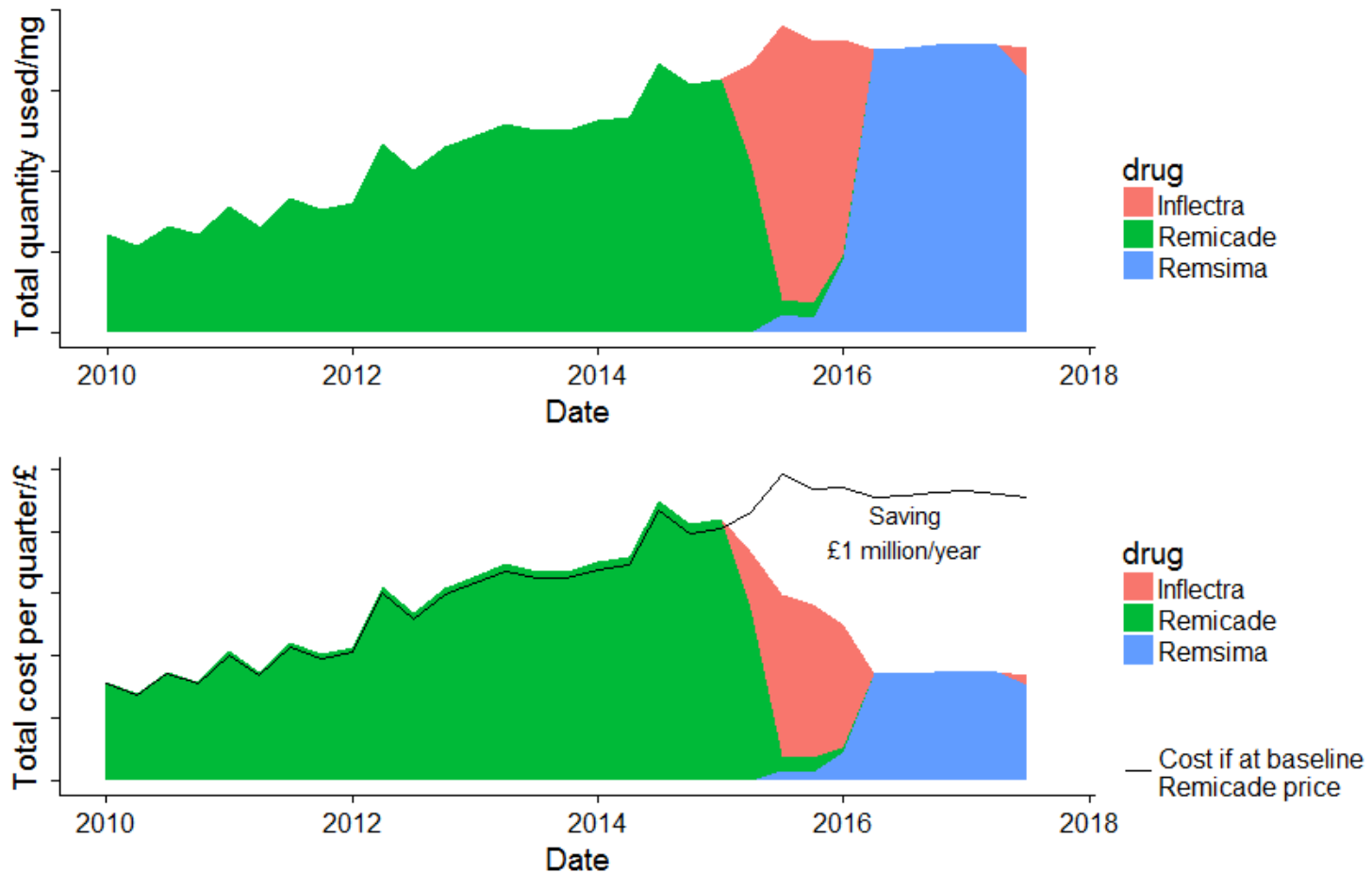
- How long is gain-share period?
  - Most are one year
- What happens when price falls again?
- What happens if the use of infliximab increases?
- Will the savings disappear in a hospital black hole?

# Exeter infliximab switch data (uncontrolled)

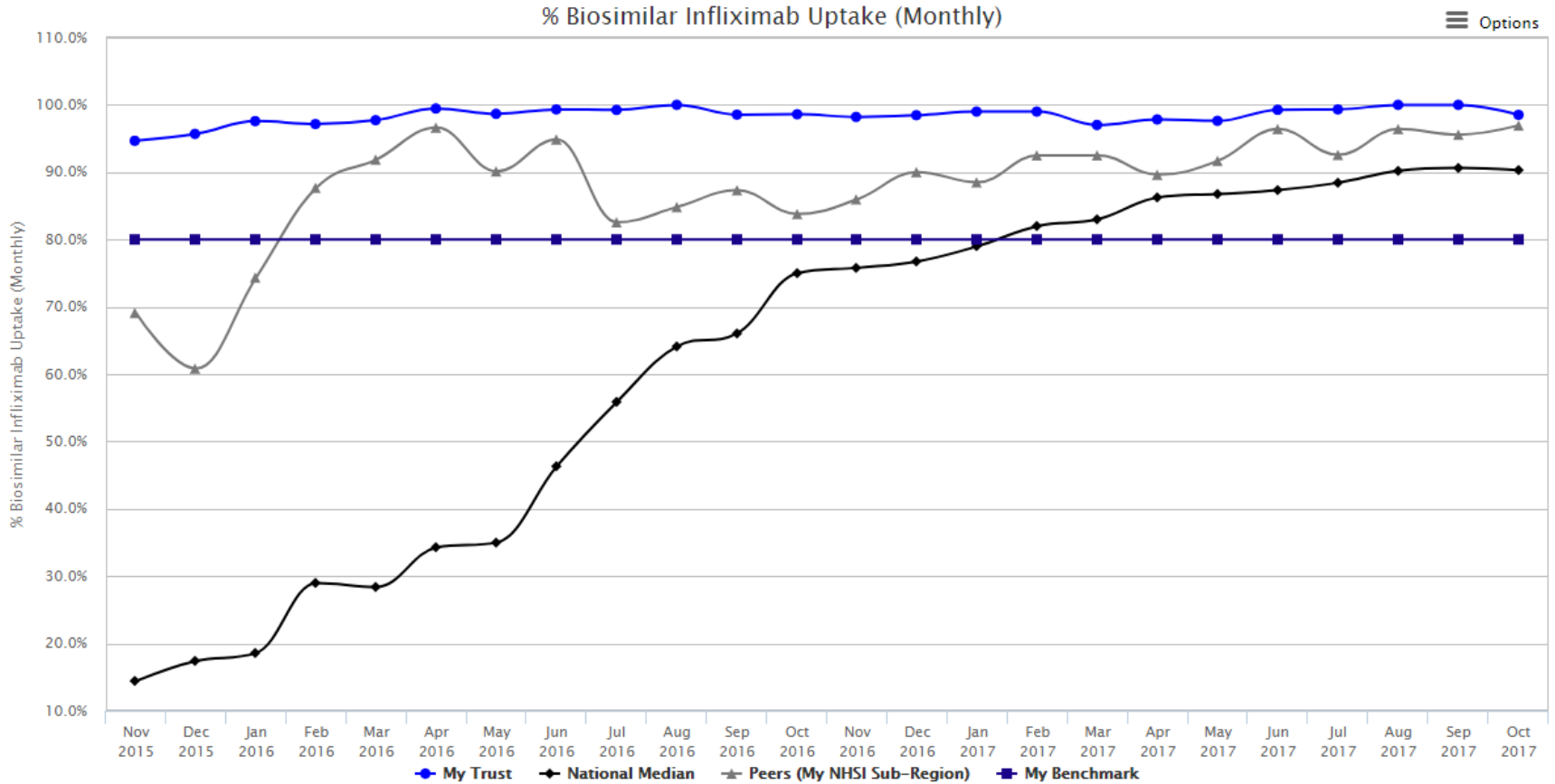
- 104 patients (73 CD, 29 UC and 2 IBDU) treated with Remicade™ for ≥ 6 months, switched April-November 2015
- Median Remicade™ duration prior to switch is 1136.5 days (range = 202 - 5728 days)
- Median CT-P13 duration since switch 353.5 days (range 198-394 days)
- Drug withdrawn in 22 patients (6 elective, 9 LOR, 7 other reasons)

|                                | Pre-switch   | Post-switch  | P Value |
|--------------------------------|--------------|--------------|---------|
| HBI                            | 1 (0-12)     | 0 (0-8)      | 0.30    |
| CRP                            | 1.5 (0-27)   | 2 (0-19)     | 0.86    |
| IFX drug level, median, range  | 5.2 (0-41.2) | 3.0 (0-35.3) | <0.01   |
| ADA level Au/mL, median, range | 0 (0-380)    | 0 (0-400)    | 0.77    |
| % ADA positive (>10Au/mL)      | 33%          | 29%          | 0.43    |
| % ADA positive (>50Au/mL)      | 9%           | 12%          | 0.54    |

# Effect of biosimilars in Exeter on prescribing and cost



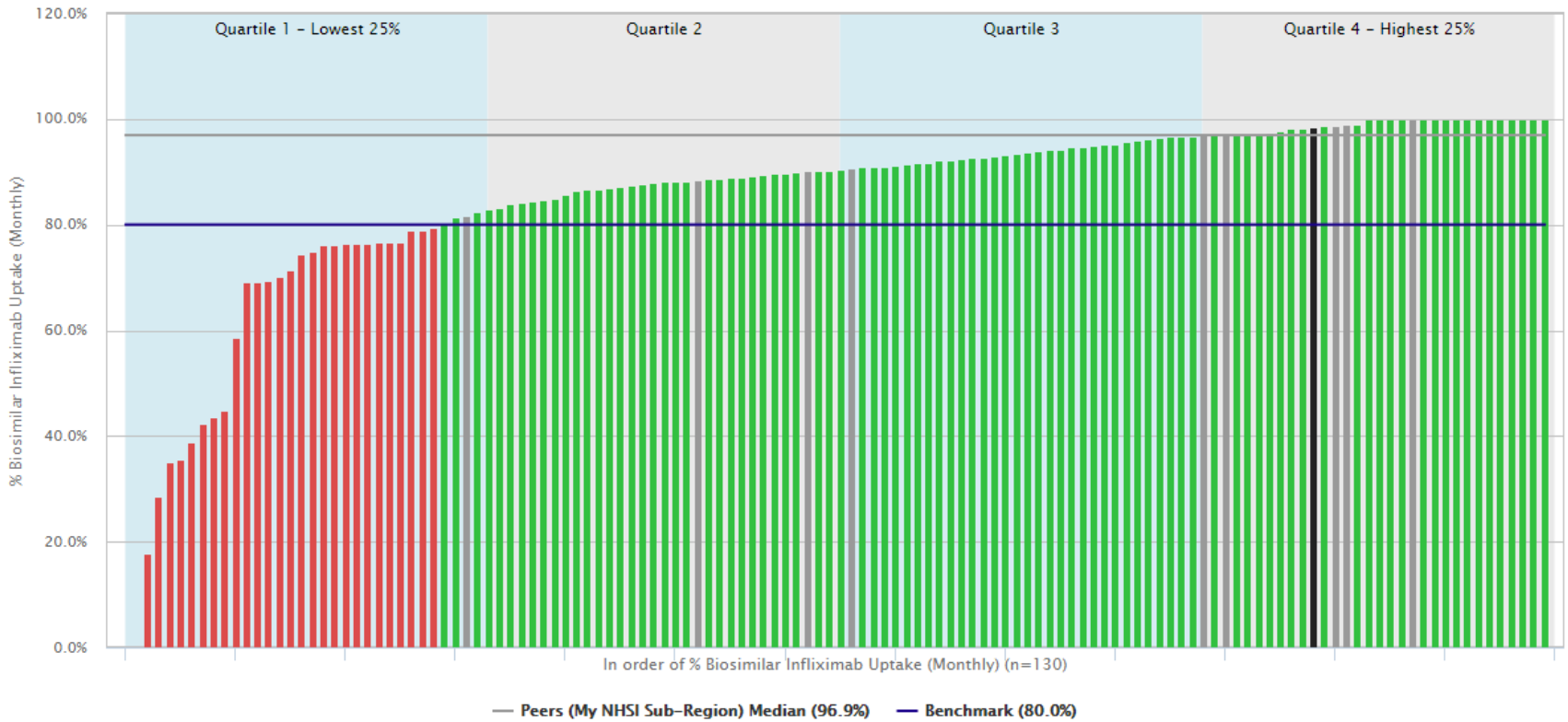
# Exeter in the national context



# Exeter in the national context

% Biosimilar Infiximab Uptake (Monthly), National Distribution

☰ Options



# Benefits of switching

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## Team expansion (£92K PA)

- 1.0 WTE additional band 6 IBD nurse post
- 0.5 WTE Band 7 pharmacist
- 0.5 WTE Band 3 clerical support

## Service development

- Virtual biologics meeting/clinic
- Early detection of anti-TNF failure
- Tighter monitoring of adalimumab usage
- Support for Blueteq process



# What's next?

- Further infliximab biosimilars
- Adalimumab – late 2018



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