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Biologics Sequencing in Clinical Units (BISCUITS): UK IBD Registry Agile Research

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IBD Registry

Background

A growing number of pharmacological agents are available for Crohn's Disease (CD), but there is little evidence to guide decision-making when a patient does not respond to first line therapy with TNF-α inhibitors (TNF-i)[1]. Options include staying in class using an alternative TNF-i or switching to a drug with a different mode of action such as ustekinumab (anti-IL12/23), vedolizumab (anti-integrin) or more recently upadacitnib (JaK inhibitor).

The UK IBD Registry (IBDR) holds records for 40,000 CD patients. In BISCUITS, real world data from a cohort of the records held on the registry was analysed to compare outcomes in patients on different biologics after failing first line TNF-i therapy, stratified by type of failure.

Methods

The primary outcome was time to treatment failure after within-class (WCS) or out-of-class switch (OCS), defined as the time in days between initiation of second-line biologic and its cessation. Secondary outcomes include corticosteroid-free drug survival (no recorded drug stop date and no steroid treatment within 365 days) and IBD-related surgery.

A feasibility study was carried out on the existing IBDR data, identifying a cohort of 2,678 CD patients who switched from a TNF-i to a second biologic. Sites contacted patients to obtain consent (electronically or on paper) for use of their data for research, as well as for quality improvement. The registry has research ethics approval for use of consented patients' data for research with pharmaceutical companies with restrictions such as not sharing patient identifiable data and only sharing aggregated results (REC number 22/NE/0009). Cases were validated and reviewed to ensure data accuracy and completeness.

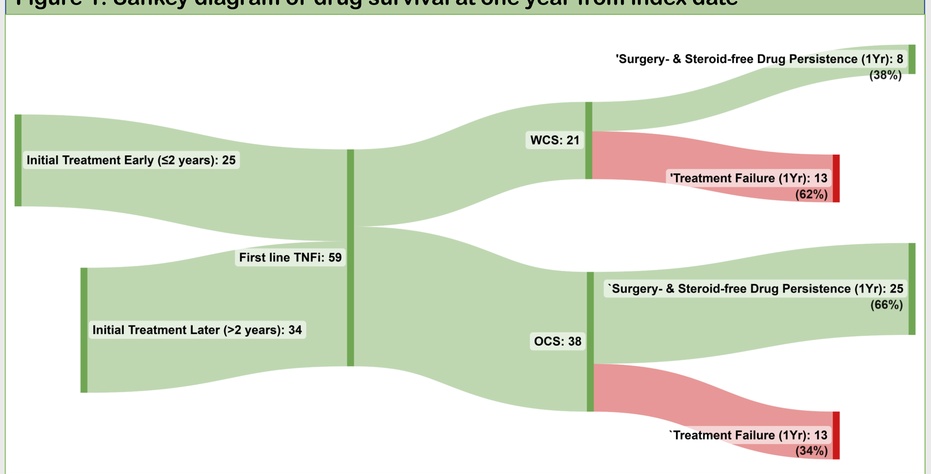
Results

A preliminary exploratory analysis was conducted on validated data received from one pilot site comprising 59 patients.

Table 1. Demographic and baseline variables

Characteristic	WCS N = 21	OCS N = 38
Age (at index), *median (IQR)*	33 (24, 45)	42 (26, 51)
Sex (assigned at birth), *n (%)*		
- Male	12 (57%)	15 (39%)
- Female	9 (43%)	23 (61%)
Past surgery for Crohn's disease, *n (%)*		
- Yes	4 (19%)	7 (18%)
- No	17 (81%)	31 (82%)
Timing of first-line TNFi, *n (%)*		
- **Early** (≤2 years)	12 (57%)	13 (34%)
- **Later** (>2 years)	9 (43%)	25 (66%)
Duration of first-line TNFi, *n (%)*		
- ≤6 months (**PNR**)	5 (24%)	12 (32%)
- >6 months (**SLOR**)	16 (76%)	26 (68%)
Choice of second-line treatment, *n (%)*		
- Infliximab	10 (48%)	n/a
- Adalimumab	11 (52%)	n/a
- Vedolizumab	n/a	6 (16%)
- Ustekinumab	n/a	32 (84%)
Concomitant treatment (at time of switch), *n (%)*		
- Steroids	1 (4.8%)	2 (5.3%)
- Immunosuppressants	13 (62%)	13 (34%)
- Steroids & Immunosuppressants	1 (4.8%)	2 (5.3%)
- None	6 (29%)	21 (55%)
Drug persistence at one year from index date, *n (%)*		
- Yes	10 (48%)	34 (89%)
- No	11 (52%)	4 (11%)
Steroid-free persistence at one year from index date, *n (%)*		
- Yes	8 (38%)	27 (71%)
- No	13 (62%)	11 (29%)
Surgery-free persistence at one year from index date, *n (%)*		
- Yes	10 (48%)	32 (84%)
- No	11 (52%)	6 (16%)
Surgery- & steroid-free drug persistence at one year from index date, *n (%)*		
- Yes	8 (38%)	25 (66%)
- No	13 (62%)	13 (34%)
Time to Treatment Failure of second-line biologic treatment in days, *median (IQR)*	348 (189, 831)	847 (498, 1248)

Figure 1. Sankey diagram of drug survival at one year from index date



Preliminary analysis of the first 59 patients (unadjusted for confounding) shows differences in rates of drug persistence at one year of 48% and 89% between WCS and OCS cohorts. Similarly, steroid- and surgery-free drug persistence at one year also differed between the cohorts: 38% vs 71% patients were steroid free and 48% vs 84% were surgery free in the WCS and OCS groups respectively (see Table 1), while 38% vs 66% were both surgery- & steroid-free (see Figure 1).

Conclusions

Using the UK IBDR dataset and infrastructure, we have developed an agile research framework to deliver high quality, validated data for real world evidence generation at pace and scale with academic and industry partners.

Upon completion of data collection, planned analysis will include time to treatment failure of second-line biologic, employing Kaplan-Meier survival curves and Cox-Proportional Hazards Models with propensity score weighting to adjust for potentially confounding covariates. Binary outcomes at one-year following initiation of second-line biologic will also be analysed using propensity score weighted logistic regression.

Key to the success of this research model is the pre-existing data sharing agreements between sites and the Registry, a robust data submission framework, research ethics approval and e-consent as well as analytics capability to not only assess feasibility of the study but deliver the results at speed. This study demonstrates the potential of the IBDR infrastructure as a study platform, facilitating delivery of efficient multicentre research.

References

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