Vedolizumab has longer persistence than infliximab as a first-line biological agent but not as a second-line biological agent in moderate-to-severe ulcerative colitis: real-world registry data from the Persistence Australian National IBD Cohort (PANIC) study

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Abstract

Background: The choice between infliximab (IFX) and vedolizumab (VED) as a first-line biological agent in moderate-to-severe ulcerative colitis (UC) can be difficult. Second-line vedolizumab (VED) efficacy may decline following prior infliximab (IFX) treatment failure in UC patients. However, it is not known whether second-line IFX efficacy declines after failure of first-line VED.

Aims: We aimed to compare first-line and second-line persistence of IFX and VED, in particular whether second-line IFX persistence declines after failure of first-line VED.

Methods: Persistence of IFX and VED was analysed from the Australian Pharmaceutical Benefits Scheme registry data as either first- or second-line treatment in UC. Propensity score matching (1:1) was conducted in the comparison of first-line treatments. Cox proportional hazard regression analysis was used to identify significant predictors and expressed as a hazard ratio (HR and 95% CI).

Results: There were 420 subjects with moderate-to-severe UC who received either first-line IFX (n = 251) or VED (n = 169), with 774 patient-years of follow-up. First-line VED had significantly longer persistence than first-line IFX (>50.2 versus 22.2 months, p = 0.001). Fifty-three subjects failed first-line IFX and swapped to second-line VED (IFX → VED group). Twenty-two subjects failed first-line VED group and swapped to second-line IFX (VED → IFX group). First-line VED persistence was significantly longer than second-line VED (>50.2 versus 32.0 months, p = 0.03), but first-line IFX persistence was not statistically significantly different to second-line IFX (>27.6 months versus >38.6 months, p = 0.30). Immunomodulator co-therapy was significantly associated with a lower risk of nonpersistence of first-line VED (HR: 0.55, 95% CI: 0.33–0.89, p = 0.02) and IFX (HR: 0.63, 95%CI: 0.33–0.92, p = 0.02).

Conclusion: VED had a significantly longer persistence than IFX as first-line biological agent but does not disadvantage second-line IFX use in moderate-to-severe UC. VED after IFX is associated with significantly poorer persistence. VED, therefore, should be considered as the first-line biological agent of choice in UC.

Keywords: infliximab, sequencing, ulcerative colitis, vedolizumab
**Introduction**

Ulcerative colitis (UC) is an increasingly prevalent chronic inflammatory bowel disease (IBD) with 15% of patients having an aggressive disease course. The cumulative risk of relapse is 70–80% at 10 years and as such, many patients require maintenance treatment with an advanced therapy. Recent guidelines recommend the use of infliximab (IFX) or vedolizumab (VED) as a first-line biological agent for patients with moderate-to-severe UC who are naïve to biological therapy. However, 10–40% of patients have a primary nonresponse to IFX, while 23–46% of patients have a secondary loss of response to IFX at 12 months after induction. Furthermore, 35% of patients lose response to VED at 12 months. Therefore, many patients will switch to a second-line biological agent. VED may be less effective in those who have failed prior anti-tumour necrosis factor-alpha (anti-TNFα) therapy including IFX. The effectiveness of second-line IFX after failure of VED, however, is less well-known. The optimal sequencing of these agents as first- and second-line agents is a key knowledge gap that requires addressing to reduce disease burden.

Persistence data, in some respects, may be even more informative than head-to-head trials. Persistence reflects willingness by patient and their physician to continue a medication in the absence of significant adverse effects. Persistence reflects real-world practice that allows for treatment optimisation including dose-adjustment, addition of temporary induction treatments and other strategies. The rate of failure and duration of persistence for various drugs are different and provide important comparative efficacy data given the paucity of head-to-head trials of advanced therapies in UC.

Persistence data, in some respects, may be even more informative than head-to-head trials. Population-based persistence data are cost-efficient and might include sufficient statistical power to identify clear clinical differences through long-term follow-up. Persistence data may be similar to clinical drug trials in that both have strict inclusion and exclusion eligibility criteria, collect data prospectively, include data on prior or ongoing use of conventional and biological agents, and are multicentre and generalizable. The Persistence in Australian National IBD Cohort (PANIC) study used prospective script data, including co-therapy with immunomodulators, collected from the Australian Pharmaceutical Benefits Scheme (PBS) database from December 2014 to September 2019. The PBS subsidises treatment with biological agents under the National Health Act 1953. Patients with UC and a partial Mayo score of ≥6 are provided biological agents at no cost if they fail to achieve adequate treatment response following a 3-month course of mesalazine and either 3 months of thiopurine (or shorter due to toxicity) or at least a 6-week course of a corticosteroid. Following induction therapy, demonstration of response to PBS subsidised treatment must be conducted 6-monthly in order to continuing maintenance treatment. The PBS does not enforce hierarchical prescribing order so there is no need to prescribe anti-TNFα agents or biosimilars prior to VED. Script data were linked to the patients’ unique Medicare number. Data were analysed using a 10% random sample, which is a standardised accepted strategy. PBS data were acquired and collated by an independent provider (Model Solutions, Australia) and
validated through a second provider to ensure robustness of data. All analyses, however, were performed by the researchers.

**Study definitions**

Persistence was defined as the duration of time from initiation to discontinuation of biological therapy for moderate-to-severe UC.11 Nonpersistence was defined as discontinuation of that agent and represented objectively as a switch in or out of biological class or complete cessation. Persistence rate was the proportion of patients who continued on a biological agent at a particular time point. Immunomodulator co-therapy was defined as the concurrent use of a thiopurine or methotrexate during the period of biological agent use.

**Sample size calculation**

Sample size calculation was based on results from a retrospective real-world study that found a persistence rate of 78% for VED patients and 64% for IFX patients with IBD at 24 months.16 Assuming a two-sided alpha of 0.05 and a power of 80%, a total of 249 IFX and 166 VED patients would be required at a ratio of three IFX patients to every two VED patients. The 3:2 ratio of IFX:VED was based on PBS biological agent prescription use for UC in Australia.17

**Study outcomes, propensity score matching and statistical analysis**

Baseline characteristics of continuous variables were described as medians with interquartile ranges (IQR). Categorical variables were described as percentages. Outcomes comparing the persistence of first-line and second-line IFX and VED were analysed using unadjusted Kaplan–Meier survival curves and statistically significant differences in persistence were identified using the log-rank test. Cox proportional hazard regression was used to identify factors affecting persistence, adjusting for covariates and described as hazard ratios (HR) and 95% confidence intervals (CI). Secondary outcomes included comparing the persistence rates between each biological agent at 12, 24, 36 and 48 months using chi-square testing. We also analysed the persistence of first-line IFX and VED stratified by immunomodulator co-therapy using unadjusted Kaplan–Meier survival curves and log-rank testing. Propensity score matching was also performed in first-line therapy comparisons to control for age and gender as possible confounders of medication persistence. Using the propensity scores, first-line VED patients were matched with first-line IFX patients using a 1:1 matching algorithm, with a proximity calliper of 0.1. A p value of <0.05 was considered statistically significant. Bonferroni correction was applied in the setting of multiple comparisons during analysis of persistence rates. Statistical analysis was performed using IBM SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA).

**Results**

**Study population and baseline characteristics**

In total, 420 patients were prescribed either IFX (251 patients) or VED (169 patients) as a first-line biological agent for moderate-to-severe UC, equating to 774 person-years of follow-up. Males comprised 54.2% (136/251) of the IFX group and 49.7% (84/169) of the VED group (p = 0.38). The median age of the VED group (44.0 years, IQR: 33.0–56.0) was older than the IFX group (37.0 years, IQR: 28.0–54.0, p = 0.003). The baseline characteristics of the study population are shown in Table 1.

Figure 1 illustrates the PBS prescription of IFX and VED as first-line and second-line biological agents. From the 251 patients who used IFX as a first-line biological agent, 53 used VED as a second-line biological agent (IFX → VED group). From the 169 patients who used VED as a first-line biological agent, 22 used IFX as a second-line biological agent (VED → IFX group). The baseline characteristics of the IFX → VED and VED → IFX groups are shown in Table 2. The median ages of the IFX → VED and VED → IFX groups were 38.0 years (IQR: 28.5–55.0) and 41.5 years (IQR: 29.5–58.8), respectively (p = 0.30). About 67.9% (36/53) of the IFX → VED group were treated with immunomodulator co-therapy during first-line biological agent use,
compared with 36.4% (8/22) of the VED→IFX group ($p=0.01$). About 52.8% (28/53) of the IFX→VED group were treated with immunomodulator co-therapy during second-line biological agent use, compared with 50.0% (11/22) of the VED→IFX group ($p=0.82$).

**Table 1.** Baseline characteristics of moderate-to-severe UC patients using first-line and second-line infliximab or vedolizumab.

| Biological agent | Infliximab $n=251$ | Vedolizumab $n=169$ | $p$-value |
|------------------|---------------------|---------------------|-----------|
| Male, n (%)      | 136 (54.2%)         | 84 (49.7%)          | 0.38      |
| Median age, years (IQR) | 37.0 (28.0–54.0) | 44.0 (33.0–56.0) | 0.003     |
| Immunomodulator co-therapy, n (%) | 160 (63.7%) | 80 (47.3%) | 0.001     |
| Thiopurine, n (%) | 145 (57.8%)         | 75 (44.4%)          | 0.01      |
| Methotrexate, n (%) | 21 (8.4%)         | 7 (4.1%)            | 0.09      |
| Time on combination therapy between biological agent and immunomodulator, months (IQR) | 17.3 (5.1–27.6) | 13.3 (5.6–17.5) | 0.03      |

IQR, interquartile range; UC, ulcerative colitis.

**Figure 1.** Flow diagram of infliximab and vedolizumab choice in moderate-to-severe UC from PBS.

Persistence of infliximab and vedolizumab as first-line biological agents in moderate-to-severe UC

VED had a significantly longer persistence than IFX when used as a first-line biological agent in moderate-to-severe UC (>50.2 months) versus...
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27.6 months (95% CI: 18.7–36.6), \( p = 0.004 \) (Figure 2). VED use was associated with a 43% lower risk of nonpersistence than IFX (HR: 0.57, 95% CI: 0.41–0.80, \( p = 0.001 \)) (Table 3). Persistence rates and their 95% CIs at 12, 24, 36 and 48 months are reported in Figure 2. Immunomodulator co-therapy use was higher in the IFX group (63.7%, 160/251) than the VED group (47.3%, 80/169; \( p = 0.001 \)) and was associated with a 44% lower risk of nonpersistence of first-line biological therapy (HR: 0.56, 95% CI: 0.42–0.77, \( p < 0.001 \)).

Using propensity score matching, 169 IFX patients were matched with 169 VED patients using age and gender as covariates. VED had a significant longer persistence than IFX as a first-line biological agent (>50.2 months versus 32.0 months, \( p = 0.03 \), Figure 5). First-line VED use was associated with a 44% lower risk of nonpersistence compared with second-line VED use (HR: 0.56, 95% CI: 0.34–0.92, \( p = 0.02 \)). Persistence rates at 12, 24 and 36 months between first-line VED and second-line VED are shown in Figure 5. Immunomodulator co-therapy occurred in 47.3% (80/169) of the first-line VED group versus 52.8% (28/53, \( p = 0.49 \)) of the second-line VED group, and was associated with a 45% lower risk of nonpersistence of VED therapy (HR: 0.55, 95% CI: 0.33–0.89, \( p = 0.02 \)).

Persistence comparison between first-line infliximab and second-line infliximab

There was no significant difference between first-line IFX and second-line IFX persistence [27.6 months (95% CI: 18.7–36.6) versus >38.6 months, \( p = 0.30 \), Figure 6]. The use of IFX as a first- versus second-line agent did not significantly predict for nonpersistence (HR: 1.49, 95% CI: 0.61–3.67, \( p = 0.39 \)). Immunomodulator co-therapy occurred in 64.7% (160/251) of the first-line IFX group versus 50.0% (11/22, \( p = 0.20 \)) of the second-line IFX group and was associated with a 37% lower risk of nonpersistence of IFX therapy (HR: 0.63, 95% CI: 0.44–0.92, \( p = 0.02 \)).

Persistence comparison between first-line vedolizumab and second-line vedolizumab

First-line VED use had a significantly longer persistence than when used as a second-line biological agent (>50.2 months versus 32.0 months, \( p = 0.03 \), Figure 5). First-line VED use was associated with a 44% lower risk of nonpersistence compared with second-line VED use (HR: 0.56, 95% CI: 0.34–0.92, \( p = 0.02 \)). Persistence rates at 12, 24 and 36 months between first-line VED and second-line VED are shown in Figure 5. Immunomodulator co-therapy occurred in 47.3% (80/169) of the first-line VED group versus 52.8% (28/53, \( p = 0.49 \)) of the second-line VED group, and was associated with a 45% lower risk of nonpersistence of VED therapy (HR: 0.55, 95% CI: 0.33–0.89, \( p = 0.02 \)).

Persistence comparison between first-line infliximab and second-line infliximab

There was no significant difference between first-line IFX and second-line IFX persistence [27.6 months (95% CI: 18.7–36.6) versus >38.6 months, \( p = 0.30 \), Figure 6]. The use of IFX as a first- versus second-line agent did not significantly predict for nonpersistence (HR: 1.49, 95% CI: 0.61–3.67, \( p = 0.39 \)). Immunomodulator co-therapy occurred in 64.7% (160/251) of the first-line IFX group versus 50.0% (11/22, \( p = 0.20 \)) of the second-line IFX group and was associated with a 37% lower risk of nonpersistence of IFX therapy (HR: 0.63, 95% CI: 0.44–0.92, \( p = 0.02 \)).

Persistence comparison between first-line vedolizumab and second-line vedolizumab

First-line VED use had a significantly longer persistence than when used as a second-line biological agent (>50.2 months versus 32.0 months, \( p = 0.03 \), Figure 5). First-line VED use was associated with a 44% lower risk of nonpersistence compared with second-line VED use (HR: 0.56, 95% CI: 0.34–0.92, \( p = 0.02 \)). Persistence rates at 12, 24 and 36 months between first-line VED and second-line VED are shown in Figure 5. Immunomodulator co-therapy occurred in 47.3% (80/169) of the first-line VED group versus 52.8% (28/53, \( p = 0.49 \)) of the second-line VED group, and was associated with a 45% lower risk of nonpersistence of VED therapy (HR: 0.55, 95% CI: 0.33–0.89, \( p = 0.02 \)).
for IFX group; > 50.2 months versus 40.8 months (95% CI: 10.3–71.3), \( p = 0.02 \) for VED group, Figures 7 and 8. There was no significant difference in persistence between second-line IFX (\( p = 0.95 \)) and VED (\( p = 0.30 \)) when stratified by immunomodulator co-therapy (Figures 9 and 10).

**Discussion**

In this large population-based prospective registry providing 774 patient-years of real-world follow-up, the persistence of VED was significantly longer than IFX as a first-line biological agent in moderate-to-severe UC. Persistence of second-line IFX after VED exposure was not significantly
impaired when compared against second-line VED after IFX exposure. First-line VED persistence had significantly longer persistence than second-line VED. There was no significant difference in persistence between first-line IFX and second-line IFX. These data support the use of VED as first-line biological treatment in moderate-to-severe UC given the longer persistence when used first-line and the decline in persistence when used second-line. Conversely, IFX persistence when used as a second-line agent after switch from VED was not impaired.

There is a lack of data on the long-term effectiveness of biological agents in UC, and persistence data provide an indirect approach for assessing the long-term therapeutic benefit and safety of therapies. The VARSITY (An Efficacy and Safety Study of Vedolizumab Intravenous [IV] Compared to Adalimumab Subcutaneous [SC] in Participants With Ulcerative Colitis) study recently demonstrated that VED was superior to adalimumab in achieving clinical remission and endoscopic improvement; however, there are no direct comparisons between IFX and VED. In the absence of head-to-head comparisons between IFX and VED, real-world persistence data act as a surrogate marker for treatment efficacy, safety and acceptability by patients and physicians. Our results demonstrate significantly greater persistence of

| Table 3. Predictors of medication nonpersistence. |
|-----------------------------------------------|
|                                           | HR (95% CI) | p-value |
| **First-line biological therapy of vedolizumab and infliximab** |             |         |
| Female versus male gender                   | 1.03 (0.76–1.39) | 0.84   |
| Age                                         | 1.00 (0.99–1.01) | 0.67   |
| VED versus IFX                              | 0.57 (0.41–0.80) | 0.001  |
| Immunomodulator co-therapy                  | 0.56 (0.42–0.77) | <0.001 |
| **Second-line biological therapy of infliximab (VED→IFX group) and vedolizumab (IFX→VED) group** |             |         |
| Female versus male gender                   | 0.61 (0.25–1.49) | 0.28   |
| Age                                         | 0.98 (0.96–1.01) | 0.34   |
| VED versus IFX                              | 1.66 (0.63–4.40) | 0.31   |
| Immunomodulator co-therapy                  | 0.66 (0.30–1.47) | 0.31   |
| **Vedolizumab use as a first-line or second-line biological therapy** |             |         |
| Female versus male gender                   | 0.85 (0.52–1.39) | 0.51   |
| Age                                         | 1.00 (0.98–1.01) | 0.59   |
| First-line VED versus second-line VED       | 0.56 (0.34–0.92) | 0.02   |
| Immunomodulator co-therapy                  | 0.55 (0.33–0.89) | 0.02   |
| **Infliximab use as a first-line or second-line biological therapy** |             |         |
| Female versus male gender                   | 0.86 (0.59–1.25) | 0.43   |
| Age                                         | 1.00 (0.99–1.01) | 0.90   |
| First-line IFX versus second-line IFX       | 1.49 (0.61–3.67) | 0.39   |
| Immunomodulator co-therapy                  | 0.63 (0.44–0.92) | 0.02   |

CI, confidence interval; HR, hazard ratio; IFX, infliximab; VED, vedolizumab.
first-line VED over first-line IFX in both short term (12 months) and long term (24, 36 and 48 months) (Figure 2). The results from this PANIC study are supported by a retrospective study which also demonstrated that VED had higher persistence rates than IFX in biological-naïve IBD patients. The addition of propensity score matching was relevant due to the significant increased age of VED subjects compared with IFX in the PANIC registry. We previously demonstrated the increasing age of IBD subjects in developed countries and for age to be a significant determinant in the deciding a biological agent in IBD. Therefore, propensity score matching was performed to reduce the selection bias associated with older age and the risk of adverse effects. Consistent with other studies, we found VED had significantly longer persistence when used as a first-line agent versus second-line use following IFX failure. To our knowledge, however, there are no data comparing second-line biological agents in IFX→VED with VED→IFX sequences. There is a need to explore the correct positioning

Figure 3. Kaplan–Meier curve for persistence of first-line infliximab and vedolizumab in moderate-to-severe UC using propensity score matching.
of biological agents, as less than half of all UC patients continue their first-line biological agent after 1 year. The persistence of second-line IFX (after VED exposure) of 65.5% (95% CI: 59.6–71.4%) compared against second-line VED of 46.2% (95% CI: 38.7–53.7%) at 36 months (p = 0.15, Figure 3) suggests a trend of IFX being a better second-line agent than VED. There have been no studies that evaluated persistence up to 3 years previously with others limited to only 6 months of follow-up. The persistence of IFX was not dissimilar when used first-line or second-line following VED.

First-line VED use did not impair the effectiveness of second-line IFX use, as supported by the
E VOLVE study which also found that anti-TNF effectiveness may not be compromised by prior VED exposure.24 However, our study found that IFX therapy impaired subsequent VED persistence.7,8 A possible explanation is a pharmacokinetic impact of prior IFX exposure on VED trough levels, with one study noting lower VED trough levels at week 6 compared with biological-naive patients (22.5 versus 36.0 µg/ml, \( p = 0.03 \)).25 Previous research has also demonstrated that MAdCAM-1 is downregulated by TNFα blockade, so prior IFX-exposed patients may need higher doses of vedolizumab to bind a higher target burden.26 These detectable biological changes, therefore, support VED to be used as first-line biological agent in moderate-to-severe UC, followed by IFX as a second-line agent.

**Figure 5.** Kaplan–Meier curve for persistence of first-line vedolizumab compared with second-line vedolizumab in moderate-to-severe UC.
Immunomodulator use improved the persistence of first-line IFX and first-line VED. Immunomodulator co-therapy is known to reduce immunogenicity and improve the persistence and effectiveness of IFX. However, the benefit of combination immunotherapy with VED is less clear. This is the first study to demonstrate the increased persistence of first-line VED when combined with immunomodulators through the use of prospectively collected data for immunomodulators in our PANIC registry. We found larger differences in persistence rates between combination VED and immunomodulator co-therapy versus VED monotherapy after 12 months of VED use (Figure 8), suggesting a greater benefit with long-term follow-up. Other studies suggest a lack of advantage of combination therapy versus monotherapy but were limited to 6–12 months of data and may not have verified ongoing

| Persistence Percentage (95%CI) (%) | Median survival time in months (95% CI) |
|----------------------------------|---------------------------------------|
| 12 months | 24 months | 36 months | 48 months |
| First-line IFX | 66.1 (60.2-71.9) | 52.5 (46.3-58.7) | 45.1 (38.9-51.3) | 35.3 (29.4-41.2) | 27.6 (18.7-36.6) |
| Second-line IFX | 73.7 (55.3-92.1) | 65.5 (45.6-85.4) | 65.5 (45.6-85.4) | - |
| P-value | 0.53 | 0.32 | 0.09 | n/a |

CI, confidence interval; IFX, infliximab; n/a, not applicable

*The median survival or its confidence interval cannot be exactly calculated when event rate is higher than 50%.

†Based on Bonferroni correction, statistical significance defined as P<0.017

Figure 6. Kaplan–Meier curve for persistence of first-line infliximab compared with second-line infliximab in moderate-to-severe UC.
immunomodulator use.²⁷ The smaller sample size of the EVOLVE study (22 patients in the combination group) identified numerically higher persistence in the combination group at 18 and 24 months but might be underpowered to demonstrate statistical significance.²⁸ It is possible that newer monoclonal antibodies, although less immunogenic than older anti-TNFα agents, are still complex glycoproteins that may result in the eventual development of antibodies. Additive anti-inflammatory effects of immunomodulators with VED are also possible. A prospective study primarily focusing on the benefits of combination therapy with VED is recommended.

This study has limitations. First, this study was not a randomised controlled trial controlling for patient characteristics and disease severity. However, there is no proposed randomised controlled trial of IFX versus VED currently planned, and it would not be possible to include a sufficient sample size and follow-up duration to be able to follow-up those that require switching to a second-line treatment. Real-world evidence with
sufficient patient-years of follow-up may address these data gaps. Second, the clinical, biochemical, and endoscopic outcomes are not known. Although patients with acute severe UC were excluded, it is possible that patients were prescribed IFX as they had a more severe phenotype, hence biasing the results. However, as only experienced gastroenterologists prescribe these agents in Australia, it is expected that relevant clinical information would be incorporated into any decision to continue or discontinue treatment. The population-based database also means data are not limited to specialised centres so that data can be generalised. Third, data on therapeutic drug monitoring and corticosteroid use are unknown. However, current conventional practice allows for treatment escalation of IFX and VED to be provided under compassionate access at no cost to the hospitals or subjects so it is likely that dose optimisation is performed prior to treatment switching. Whereas clinical trials might deem such dose escalations as treatment failure on intention-to-treat, persistence data allow these subjects to be included and provide a more realistic comparison of treatment efficacy. Ideally, correcting for clinical characteristics beyond age in

Figure 8. Kaplan–Meier curve for persistence of first-line vedolizumab stratified by immunomodulator co-therapy in moderate-to-severe UC.
Propensity score matching might further reduce bias in comparing subjects on VED versus IFX. However, age was the most important factor identified previously and subjected to propensity score matching. Also, there was a relatively small number of patients in the second-line groups which may impact on the results. However, there is limited available data on second-line use (particularly IFX) so our results will be beneficial. Finally, only a randomly selected 10% of the population database could be used for analysis due to national ethical criteria for data accessibility. However, this was a random sampling without selection bias and similar publications were deemed robust given the large patient-years of follow-up.

Strengths include the use of a large, national, population-based study where biological agents are prescribed without a hierarchical prescribing order and are fully reimbursed indefinitely. All subjects had verified Mayo scores of $\geq 6$ which
indicates consistency of disease severity. All data were collected prospectively with clinical remission being an absolute requirement for ongoing treatment. Whether treatment escalation was performed or concurrent immunomodulator was used was decided between the clinician and patients consistent with real-world practice. Furthermore, individual switches to other biological agents and immunomodulator co-therapy are prospectively recorded and long-term follow-up data beyond 4 years is an advantage over clinical trials that have relatively short durations of follow-up. The population-based data also mean the results are more generalizable. In the absence of large head-to-head studies with long-term follow-up, population-based persistence data can effectively compare the efficacy of IFX versus VED.

Conclusion
In summary, the PANIC cohort with real-world data set of nonhierarchical prescribing of biological agents supports the use of VED over IFX as a first-line biological agent in moderate-to-severe UC. Following failure of VED, there is no impact on IFX persistence when used second-line. Immunomodulator treatment significantly increases the persistence of VED, but further prospective data are required to confirm this observation. Our findings will assist in the positioning of biological therapies in moderate-to-severe UC.

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Author contributions
Aviv Pudipeddi: Data curation; Formal analysis; Methodology; Resources; Software; Writing – original draft; Writing – review & editing.
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Rupert Leong: Conceptualisation; Data curation; Formal analysis; Resources; Supervision; Visualisation; Writing – review & editing.

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Supplemental material
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