Supplemental Methods and Results

Research Priority Addressed

The James Lind Alliance supports partnerships between healthcare providers, patients, and patient support organizations to determine priorities for research.8 This Alliance has identified research priorities in the treatment of patients with inflammatory bowel disease.9 The consortium used to conduct the current study was built to directly address the top research priority identified (“What is the optimal treatment strategy considering efficacy, safety, and cost-effectiveness in inflammatory bowel disease management?”) through the generation of real-world evidence that supports the use and positioning of biologic agents in patients treated in routine practice who are often excluded from traditional clinical trials.7,9 The specific question being addressed in this proposal was identified to be the highest priority research question for ulcerative colitis (UC) in the current landscape of medical therapeutic options.9

We had the a priori hypothesis that vedolizumab is associated with a lower risk of serious infections than TNF-antagonist therapy in UC, and that vedolizumab is superior to TNF-antagonist therapy for achieving clinical remission in UC.8,9 This hypothesis was derived prior to the completion of the phase 3 head-to-head trial,6 and it was informed by prior network meta-analyses of phase 3 clinical trials and comparison of point estimates for developing an infectious adverse event or achieving clinical remission with vedolizumab relative to TNF-antagonist therapy.10-12

Variables

Data on variables of interest were collected from the sites, including patient characteristics (age at diagnosis, age at biologic initiation, sex, smoking status, body mass index), disease characteristics (prior hospitalizations, extraintestinal manifestations, and phenotype classified according to Montreal subclassifications of E1 through E3), and treatment history (steroids, immunomodulators, and tumor necrosis factor [TNF] antagonists; duration of use; indication for discontinuation; and complications). Variables of interest specific to the use of biologic agents included baseline disease severity or activity (endoscopic, biochemical, or clinical assessments), concomitant treatments (steroids and/or immunomodulators: azathioprine, 6-mercaptopurine, methotrexate), and follow-up assessments (endoscopic or clinical assessments). Steroid dependency or refractoriness was defined as current users of concomitant steroids who had more than 3 courses of steroids in the previous year and had been unable to remain off steroids for >3 months. Age was transformed into a binary variable (>60 years) to classify patients as elderly or non-elderly given the known association between age and risk of adverse events.19

Outcome Definitions

Serious infection was defined as any infection occurring after biologic initiation that required antibiotics, antifungals, or antivirals or that resulted in discontinuation of biologic therapy, hospitalization, or death. Serious adverse events were defined as the occurrence of any infectious or noninfectious adverse event after biologic initiation that required antibiotics, antifungals, or antivirals for a documented infection, or resulted in discontinuation of biologic therapy, hospitalization, or death.19 Exposure to antibiotics, antifungals, and antivirals was used in the definition given the need to use antibiotics, antifungals, and antivirals indicates a need for the provider to intervene to prevent damage which is in accordance with clinical trial definitions for adverse events, and that exposure to antibiotics increases the risk of developing Clostridium difficile, and the development of an infection with Clostridium difficile in UC patients is more severe and associated with a significant increase in risk for hospitalization, colectomy, and mortality.21-23
Clinical remission was defined by complete resolution of diarrhea, rectal bleeding, and urgency as per the European Crohn’s and Colitis Organization Consensus definition. Steroid-free remission was assessed only in those patients taking either prednisone or budesonide-MMX at the initiation of biologic therapy, and was defined as achieving clinical remission, tapering off steroids, and the absence of a steroid prescription within the subsequent 1 month of achieving remission. Deep remission was defined as achieving clinical remission (resolution of diarrhea, rectal bleeding, and/or urgency) and endoscopic remission (Mayo endoscopic subscore 0 or 1). The coordinating site used de-identified endoscopy reports to confirm endoscopic Mayo scores, and any discrepancies were resolved through consensus between the study sites and the coordinating site. If patients underwent dose escalation for non-response or partial response they were censored and considered a non-responder to standard of care labeled dosing for vedolizumab or TNF-antagonist therapy.

Handling Missing Data for Outcome Assessments

All patients received follow-up assessments for safety outcomes. A single patient had missing data for the assessment of clinical remission and was not included in the comparative effectiveness estimates. A follow-up assessment for endoscopic remission was performed in 59% of vedolizumab-treated patients and 69% of TNF-antagonist–treated patients ($P = .007$). Patients who did not undergo a follow-up assessment for endoscopic remission had less baseline inflammation as measured by baseline C-reactive protein (CRP) and baseline endoscopy (Supplemental Table S1). Comparative effectiveness outcomes including endoscopic remission in the definition were therefore limited to patients with documented baseline moderate-severe endoscopic inflammation (Mayo endoscopic subscore 2 or 3) within 4 weeks of starting vedolizumab or TNF-antagonist therapy to account for this differential attrition rate and the impact of missing data on comparative estimates.

Power Calculation for Safety Outcomes

In this observational nonrandomised cohort study, we used the observed event rates in the control group (TNF-antagonist–treated UC patients) to determine power calculations for unweighted comparisons of safety outcomes using the methodology described by Cohen et al. For serious infections and serious adverse events we would need an observed event rate of 5% and 11%, respectively, in the vedolizumab-treatment group to be powered for the comparison.

Propensity Score Model and Statistical Analyses

The final set of variables used for the clinical remission propensity score model included age at initiation (>60 years), disease extent (left-sided colitis E1 or E2, or pancolitis E3), clinical disease severity (severe vs non-severe based on the physician global assessment), UC-related hospitalization within the preceding 1 year, prior TNF-antagonist exposure, baseline steroid dependency or refractoriness, concomitant steroid use, or concomitant immunomodulator use. Baseline CRP, albumin, and body mass index were not included because >25% of the cohort had missing baseline data for these variables. Post hoc assessment of these variables revealed that they had no prognostic significance for the primary treatment outcomes (clinical remission or serious infection), and therefore were unlikely to create an unmeasured confounder bias on the comparative estimates.

Comparative effectiveness between vedolizumab and TNF-antagonist therapy for the primary analysis and all subgroup or sensitivity analyses for effectiveness was done using the Cox-proportional hazard competing risk model. Colectomy is a preference sensitive decision and therefore variation is likely to have occurred as to when a patient may consider surgery and when a provider may offer surgery, creating a one-way competing risk for allowing treatment to take effect and observing clinical remission or treatment-related safety events. Furthermore, a larger proportion of the vedolizumab-treated UC patients had multiple prior TNF-antagonist exposures, and vedolizumab represented last-line biologic therapy in these patients prior to surgery. It was
further hypothesized that lack of availability for additional biologic therapy could therefore lead to surgery more often and earlier in the treatment course in the vedolizumab group. Therefore, this differential risk for surgery between the vedolizumab- and TNF-antagonist–treatment groups was accounted for by using a competing risk model with surgery functioning as a non-fatal competing risk.

Baseline Demographics

The median number of follow-up visits was comparable between the vedolizumab- (median number of visits 2; interquartile range [IQR] 1-3) and TNF-antagonist (median number of visits 2, IQR 1-3)–treated patients. The median duration of follow-up was comparable between the vedolizumab- (276 days, IQR 143-418) and TNF-antagonist (349 days, IQR 137-581)–treated patients. Vedolizumab-treated patients with UC were more often steroid refractory or dependent (48% vs 31%) and more often had prior TNF-antagonist exposure (69% vs 40%) or prior TNF-antagonist failure (57% vs 23%) than TNF-antagonist–treated patients. Among patients on concomitant steroids at baseline, the median dose was comparable between vedolizumab-treated (28 mg) and TNF-antagonist–treated (32 mg) patients.

Looking specifically at the TNF-antagonist–naïve patients, UC patients treated with vedolizumab were more often female (60% vs 49%), had less often been hospitalized within the previous year (25% vs 38%), and less often had severe endoscopic disease activity at baseline (21% vs 42%) compared to the TNF-antagonist–treated UC patients (Supplemental Tables S2 and S3).

Looking specifically at the TNF-antagonist–exposed patients, UC patients treated with vedolizumab were more comparable to the TNF-antagonist–treated patients in baseline demographics, with the exception of the vedolizumab-treated patients being more often steroid dependent at baseline (49% vs 21%) (Supplemental Tables S2 and S3).
**Supplemental Table 1**: Differences in Baseline Characteristics Between Patients Who Did and Those Who Did Not Have a Follow-up Assessment for Endoscopic Remission

|                                | Had follow-up assessment for endoscopic remission | No follow-up assessment for endoscopic remission | P-value |
|--------------------------------|--------------------------------------------------|-------------------------------------------------|---------|
| Age at biologic                | n = 455                                          | n = 267                                         | .586    |
|                                | 41.23 (16.62)                                    | 40.53 (16.75)                                  |         |
| Age at diagnosis               | n = 455                                          | n = 267                                         | .921    |
|                                | 32.49 (15.29)                                    | 32.37 (16.08)                                  |         |
| Sex (female)                   | n = 455                                          | n = 267                                         | .644    |
| Female                         | 224 (49.2%)                                      | 137 (51.3%)                                    |         |
| Male                           | 231 (50.8%)                                      | 130 (48.7%)                                    |         |
| BMI                            | n = 424                                          | n = 253                                         | .763    |
|                                | 25.65 (6.46)                                     | 25.51 (5.64)                                   |         |
| Smoking status                 | n = 455                                          | n = 267                                         | .948    |
| Current                        | 14 (3.1%)                                        | 9 (3.4%)                                        |         |
| Former                         | 120 (26.4%)                                      | 68 (25.5%)                                      |         |
| Never                          | 321 (70.5%)                                      | 190 (71.2%)                                    |         |
| Disease duration               | n = 455                                          | n = 267                                         | .396    |
|                                | 8.75 (9.12)                                      | 8.16 (8.71)                                    |         |
| Ever hospitalized?             | n = 455                                          | n = 267                                         | .844    |
| Never                          | 217 (47.7%)                                      | 125 (46.8%)                                    |         |
| Yes (in the last year)         | 124 (27.3%)                                      | 78 (29.2%)                                      |         |
| Yes (not in the last year)     | 114 (25.1%)                                      | 64 (24.0%)                                      |         |
| CRP                            | n = 356                                          | n = 193                                         | .013    |
|                                | 11.66 (30.85)                                    | 6.74 (15.19)                                   |         |
| Albumin                        | n = 391                                          | n = 236                                         | .749    |
|                                | 3.89 (0.56)                                      | 3.90 (0.61)                                    |         |
| Rheumatic EIM (Yes/No)         | n = 455                                          | n = 267                                         | .163    |
| No                             | 386 (84.8%)                                      | 215 (80.5%)                                    |         |
| Yes                            | 69 (15.2%)                                       | 52 (19.5%)                                     |         |
| Ophthalmologic EIM (Yes/No)    | n = 455                                          | n = 267                                         | .283    |
| No                             | 448 (98.5%)                                      | 266 (99.6%)                                    |         |
| Yes                            | 7 (1.5%)                                         | 1 (0.4%)                                       |         |
| Dermatologic EIM (Yes/No)      | n = 455                                          | n = 267                                         | 1.000   |
| No                             | 437 (96.0%)                                      | 257 (96.3%)                                    |         |
| Yes                            | 18 (4.0%)                                        | 10 (3.7%)                                      |         |
| Hepatic EIM (Yes/No)           | n = 455                                          | n = 267                                         | .733    |
| No                             | 436 (95.8%)                                      | 258 (96.6%)                                    |         |
| Yes                            | 19 (4.2%)                                        | 9 (3.4%)                                       |         |
| Disease extent                 | n = 454                                          | n = 265                                         | .707    |
| E1                             | 19 (4.2%)                                        | 14 (5.3%)                                      |         |
| E2                             | 164 (36.1%)                                      | 90 (34.0%)                                     |         |
| E3                             | 271 (59.7%)                                      | 161 (60.8%)                                    |         |
| Disease severity               | n = 455                                          | n = 267                                         | .057    |
| Mild                           | 42 (9.2%)                                        | 23 (8.6%)                                      |         |
| Moderate                       | 232 (51.0%)                                      | 160 (59.9%)                                    |         |
| Severe                         | 181 (39.8%)                                      | 84 (31.5%)                                     |         |
| Endoscopic severity            | n = 345                                          | n = 207                                         |         |
| Category                      | Mild   | Moderate | Severe   | p-Value |
|-------------------------------|--------|----------|----------|---------|
|                               | 51 (14.8%) | 137 (39.7%) | 157 (45.5%) | .031    |

**Combo. IM (Yes/No)**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| No               | 266 (58.5%) | 193 (72.3%) | <.001    |
| Yes              | 189 (41.5%) | 74 (27.7%)  |

**Combo. steroids (Yes/No)**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| No               | 212 (46.6%) | 122 (45.7%) | .875    |
| Yes              | 243 (53.4%) | 145 (54.3%) |

**Steroid dependency (Yes/No)**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| No               | 270 (59.3%) | 153 (57.3%) | .647    |
| Yes              | 185 (40.7%) | 114 (42.7%) |

**TNF antagonist exposed (Yes/No)**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| No               | 195 (42.9%) | 108 (40.4%) | .579    |
| Yes              | 260 (57.1%) | 159 (59.6%) |

**Number TNF antagonist exposed**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| 0                | 195 (42.9%) | 108 (40.4%) | .930    |
| 1                | 186 (40.9%) | 115 (43.1%) |
| 2                | 65 (14.3%)  | 39 (14.6%)  |
| 3                | 9 (2.0%)   | 5 (1.9%)   |

**TNF antagonist failure (Yes/No)**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| No               | 246 (54.1%) | 155 (58.1%) | .336    |
| Yes              | 209 (45.9%) | 112 (41.9%) |

**Ever PNR TNF antagonist? (Yes/No)**

|                  | n = 260 | n = 159   |
|------------------|---------|-----------|
| No               | 185 (71.2%) | 110 (69.2%) | .750    |
| Yes              | 75 (28.8%)  | 49 (30.8%)  |

**TNF antagonist vs VDZ**

|                  | n = 455 | n = 267   |
|------------------|---------|-----------|
| Anti-TNF         | 187 (41.1%) | 81 (30.3%) | .005    |
| Vedolizumab      | 268 (58.9%) | 186 (69.7%) |

**Infliximab vs VDZ**

|                  | n = 392 | n = 227   |
|------------------|---------|-----------|
| Infliximab       | 124 (31.6%) | 41 (18.1%) | <.001   |
| Vedolizumab      | 268 (68.4%) | 186 (81.9%) |

**Subcutaneous TNF Antagonist vs VDZ**

|                  | n = 331 | n = 226   |
|------------------|---------|-----------|
| Subcutaneous anti-TNF | 63 (19.0%) | 40 (17.7%) | .774    |
| Vedolizumab      | 268 (81.0%) | 186 (82.3%) |

Values are mean (SD) or n (%).
BMI, body mass index; CRP, C-reactive protein; EIM, extraintestinal manifestation; IM, immunomodulator; PNR, primary nonresponse; SD, standard deviation; TNF, tumor necrosis factor; VDZ, vedolizumab.
**Supplemental Table 2**: Baseline Characteristics of Vedolizumab-Treated UC Patients Stratified by Prior Anti-TNF Exposure

| Prior anti-TNF exposure | No (n = 143) | Prior anti-TNF exposure | Yes (n = 311) |
|-------------------------|-------------|-------------------------|--------------|
| Age (biol.)             | 42.80 (18.85) | 41.75 (16.30) |
| Age (Dx)                | 33.79 (17.09) | 32.22 (15.30) |
| Sex (female)            | 86 (60.1%) | 140 (45.0%) |
| BMI                     | 25.77 (6.20) | 25.75 (5.83) |
| Smoking status          |             |                         |
| Current                 | 4 (2.8%) | 7 (2.3%) |
| Former                  | 43 (30.1%) | 70 (22.5%) |
| Never                   | 96 (67.1%) | 234 (75.2%) |
| Disease duration        | 6 (11.5) | 6 (10) |
| Ever hospitalized?      |             |                         |
| Never                   | 77 (53.8%) | 136 (43.7%) |
| Yes (in the last year)  | 36 (25.2%) | 78 (25.1%) |
| Yes (not in the last year) | 30 (21.0%) | 97 (31.2%) |
| CRP                     | 1 (4.1) | 2.4 (7.89) |
| Albumin                 | 3.99 (0.46) | 3.88 (0.58) |
| Rheumatic EIM (Yes)     | 19 (13.3%) | 60 (19.3%) |
| Ophthal EIM (Yes)       | 0 (0.0%) | 3 (1.0%) |
| Derm EIM (Yes)          | 5 (3.5%) | 12 (3.9%) |
| Hepatic EIM (Yes)       | 7 (4.9%) | 13 (4.2%) |
| Disease extent          |             |                         |
| E1                      | 8 (5.6%) | 14 (4.5%) |
| E2                      | 61 (42.7%) | 100 (32.3%) |
| E3                      | 74 (51.7%) | 196 (63.2%) |
| Disease severity        |             |                         |
| Mild                    | 20 (14.0%) | 32 (10.3%) |
| Moderate                | 93 (65.0%) | 160 (51.4%) |
| Severe                  | 30 (21.0%) | 119 (38.3%) |
| Endoscopic severity     |             |                         |
| Mild                    | 11 (10.6%) | 37 (14.9%) |
| Moderate                | 66 (63.5%) | 100 (40.3%) |
| Severe                  | 27 (26.0%) | 111 (44.8%) |
| Combo. IM (Yes)         | 33 (23.1%) | 116 (37.3%) |
| Combo. steroids (Yes)   | 74 (51.7%) | 169 (54.3%) |
| Steroid dependency (Yes)| 64 (44.8%) | 152 (48.9%) |

Biol, Biologic; Dx, Diagnosis; BMI, body mass index; CRP, C-reactive protein; Dx, diagnosis; EIM, extraintestinal manifestation; IM, immunomodulator; TNF, tumor necrosis factor.
### Supplemental Table 3: Baseline Characteristics of Anti-TNF–Treated UC Patients Stratified by Prior Anti-TNF Exposure

|                           | Prior anti-TNF exposure | Prior anti-TNF exposure |
|---------------------------|-------------------------|-------------------------|
|                           | No (n = 160)            | Yes (n = 108)           |
| Age (biol.)               | 39.26 (15.91)           | 38.85 (15.45)           |
| Age (Dx)                  | 31.83 (15.10)           | 32.21 (15.07)           |
| Sex (female)              | 78 (48.8%)              | 57 (52.8%)              |
| BMI                       | 25.29 (6.67)            | 25.40 (6.33)            |
| Smoking status            |                         |                         |
| Current                   | 8 (5.0%)                | 4 (3.7%)                |
| Former                    | 42 (26.2%)              | 33 (30.6%)              |
| Never                     | 110 (68.8%)             | 71 (65.7%)              |
| Disease duration          |                         |                         |
| Never                     | 72 (45.0%)              | 57 (52.8%)              |
| Yes (in the last year)    | 61 (38.1%)              | 27 (25.0%)              |
| Yes (not in the last year)| 27 (16.9%)              | 24 (22.2%)              |
| CRP                       | 1.95 (15.375)           | 0.7 (3.85)              |
| Albumin                   | 3.80 (0.65)             | 3.92 (0.62)             |
| Rheumatic EIM (Yes)       | 26 (16.2%)              | 16 (14.8%)              |
| Ophthal EIM (Yes)         | 2 (1.2%)                | 3 (2.8%)                |
| Derm EIM (Yes)            | 5 (3.1%)                | 6 (5.6%)                |
| Hepatic EIM (Yes)         | 4 (2.5%)                | 4 (3.7%)                |
| Disease extent            |                         |                         |
| E1                        | 9 (5.7%)                | 2 (1.9%)                |
| E2                        | 52 (32.9%)              | 41 (38.0%)              |
| E3                        | 97 (61.4%)              | 65 (60.2%)              |
| Disease severity          |                         |                         |
| Mild                      | 4 (2.5%)                | 9 (8.3%)                |
| Moderate                  | 89 (55.6%)              | 50 (46.3%)              |
| Severe                    | 67 (41.9%)              | 49 (45.4%)              |
| Endoscopic severity       |                         |                         |
| Mild                      | 11 (9.4%)               | 13 (15.7%)              |
| Moderate                  | 42 (35.9%)              | 34 (41.0%)              |
| Severe                    | 64 (54.7%)              | 36 (43.4%)              |
| Combo. IM (Yes)           | 69 (43.1%)              | 45 (41.7%)              |
| Combo. steroids (Yes)     | 84 (52.5%)              | 61 (56.5%)              |
| Steroid dependency (Yes)  | 60 (37.5%)              | 23 (21.3%)              |

Biol, Biologic; Dx, Diagnosis; BMI, body mass index; CRP, C-reactive protein; Dx, diagnosis; EIM, extraintestinal manifestation; IM, immunomodulator; TNF, tumor necrosis factor.
### Supplemental Table 4: Event Rates

|                     | Overall cohort | VDZ vs anti-TNF | VDZ vs SQ TNF naïve (VDZ vs. TNF antagonist) | TNF-antagonist–exposed (VDZ vs. TNF antagonist) |
|---------------------|----------------|-----------------|---------------------------------------------|-----------------------------------------------|
| **Clinical remission** |                |                 |                                             |                                               |
| 187/453 vs 100/266 | 187/453 vs 61/163 | 187/453 vs 39/103 | 74/143 vs 65/158 | 113/310 vs 35/108 |
| **Deep remission**  |                |                 |                                             |                                               |
| 40/169 vs 30/124   | 40/169 vs 21/86  | 40/169 vs 9/38   | 16/44 vs 22/82 | 24/125 vs 8/42 |
| **Steroid-free clinical remission** | 72/243 vs 37/143 | 72/243 vs 28/97 | 72/243 vs 9/46 | 25/74 vs 25/82 | 47/169 vs 12/61 |
| 24/150 vs 15/92    | 24/150 vs 11/67  | 24/150 vs 4/25   | 9/43 vs 9/57  | 15/107 vs 6/35 |
| **Serious Infection** |                |                 |                                             |                                               |
| 21/453 vs 27/266   | 21/453 vs 19/163 | 21/453 vs 8/103  | 3/143 vs 20/158 | 18/310 vs 7/108 |
| 26/453 vs 45/266   | 26/453 vs 31/163 | 26/453 vs 14/103 | 3/143 vs 32/158 | 23/310 vs 13/108 |

IFX, infliximab; SQ, subcutaneous; TNF, tumor necrosis factor; VDZ, vedolizumab.
**Supplemental Table 5:** Comparative Safety (HR) and Effectiveness (HR) of Vedolizumab vs Tumor Necrosis Factor Antagonists in Ulcerative Colitis

|                          | Overall cohort                                      | Clinical remission                                                                 |
|--------------------------|-----------------------------------------------------|--------------------------------------------------------------------------------------|
|                          | VDZ vs anti-TNF                                     | VDZ vs IFX                                                                           |
| Unweighted               | 1.435 (1.118, 1.843)                                | 1.410 (1.050, 1.893)                                                               |
|                          | 1.543 (1.077, 2.212)                                | 1.659 (1.180, 2.333)                                                               |
|                          | 1.644 (1.101, 2.455)                                |                                                                                     |
| IPW ATE                  | 1.651 (1.229, 2.217)                                | 1.810 (1.225, 2.675)                                                               |
|                          | 1.693 (1.091, 2.627)                                | 1.676 (1.157, 2.428)                                                               |
|                          | 1.689 (1.507, 2.700)                                |                                                                                     |
| Full match               | 2.156 (1.381, 3.366)                                | 2.091 (0.936, 4.673)                                                               |
|                          | 2.066 (1.299, 3.286)                                | 2.282 (1.102, 4.726)                                                               |
| Deep remission           | 1.541 (1.024, 2.317)                                | 1.576 (1.055, 2.747)                                                               |
| Steroid-free clinical remission | 1.828 (1.315, 2.944)                              | 1.899 (1.105, 3.847)                                                               |
| Steroid-free deep remission | 2.268 (1.226, 4.195)                              | 2.224 (1.017, 4.866)                                                               |
| Serious infection        | 2.469 (1.209, 5.045)                                | 2.579 (0.757, 8.789)                                                               |
|                          | 2.363 (1.081, 5.165)                                | 2.054 (0.738, 5.714)                                                               |
|                          | 2.045 (1.078, 4.546)                                | 2.738 (0.969, 7.997)                                                               |
| IPW ATE                  | 2.819 (1.496, 5.310)                                | 2.286 (0.977, 5.346)                                                               |
|                          | 2.908 (1.393, 6.070)                                | 2.571 (1.008, 6.557)                                                               |
|                          | 2.754 (1.232, 6.160)                                |                                                                                     |
| Full match               | 2.718 (1.412, 5.235)                                | 3.748 (1.641, 8.562)                                                               |
|                          | 5.811 (1.916, 17.625)                               | 4.203 (1.435, 12.306)                                                              |
|                          | 2.432 (0.932, 6.345)                                |                                                                                     |
| Serious adverse event    | 1.822 (0.638, 2.188)                                | 0.919 (0.476, 1.776)                                                               |
|                          | 2.448 (0.974, 6.152)                                | 0.355 (0.103, 1.227)                                                               |
| IPW ATE                  | 1.235 (0.608, 2.511)                                | 2.116 (0.776, 5.764)                                                               |
|                          | 0.964 (0.413, 2.248)                                | 0.320 (0.078, 1.322)                                                               |
|                          | 2.243 (0.282, 17.833)                               | 0.518 (0.133, 2.019)                                                               |
|                          | 3.006 (0.653, 13.839)                               |                                                                                     |
| Full match               | 1.481 (0.506, 4.334)                                | 3.225 (1.027, 10.130)                                                             |
|                          | 2.243 (0.282, 17.833)                               | 0.518 (0.133, 2.019)                                                               |
|                          | 3.006 (0.653, 13.839)                               |                                                                                     |
|                          | 0.844 (0.504, 1.414)                                | 0.694 (0.400, 1.206)                                                               |
|                          | 1.537 (0.741, 3.187)                                | 0.214 (0.064, 0.711)                                                               |
| IPW ATE                  | 0.899 (0.502, 1.612)                                | 0.739 (0.375, 1.456)                                                               |
|                          | 1.564 (0.691, 3.540)                                | 0.192 (0.049, 0.754)                                                               |
|                          | 2.495 (0.988, 6.301)                                |                                                                                     |
| Full match               | 0.992 (0.461, 2.135)                                | 1.356 (0.501, 3.673)                                                               |
|                          | 2.010 (0.410, 9.857)                                | 0.227 (0.060, 0.861)                                                               |
|                          | 1.936 (0.733, 5.113)                                |                                                                                     |

Bolded numbers are statistically significant. ATE, average treatment effect; IFX, infliximab; IPW, inverse probability weighting; SQ, subcutaneous; TNF, tumor necrosis factor; VD, vedolizumab. Data in parentheses are 95% confidence intervals.