Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes joint inflammation, which can manifest as stiffness, swelling, and pain.1 If untreated, RA may lead to considerable joint damage and an increased risk of comorbidities because of systemic inflammation.1 RA is estimated to affect approximately 0.46% of the global population2 and is associated with significant economic burden.3

Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), such as methotrexate (MTX; oral or parenteral), are typically the first-line treatment for RA; however, in patients who do not adequately respond to csDMARDs, American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) guidelines recommend the use of biologic DMARDs (bDMARDs), such as parental tumor necrosis factor inhibitors (TNFi) and targeted synthetic DMARDs (tsDMARDs).4,5 EULAR guidelines suggest that pertinent risk factors are considered for oral Janus kinase inhibitors (JAKi).5

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The efficacy and safety of the oral JAKi tofacitinib (TOF) in patients with RA have been demonstrated in phase III and phase IIIb/IV randomized controlled trials (RCTs). \(^6\)\(^-\)\(^12\) Oral Rheumatoid Arthritis Trial (ORAL) Surveillance, a postauthorization safety study of TOF in patients with RA aged ≥ 50 years with ≥ 1 additional cardiovascular (CV) risk factor, showed that risks of major adverse CV events and cancers were higher with TOF vs TNFi. \(^13\) This resulted in a US Food and Drug Administration (FDA) class label change indicating TOF and other JAKi for patients with RA who have had an inadequate response or intolerance to ≥ 1 TNFi. \(^14\)

Although RCTs remain the gold standard to determine treatment efficacy and safety, real-world studies can complement data gathered in RCTs and may be used to support regulatory decision-making. \(^15\) Previous analyses of US claims databases and registries of patients with RA have shown that TOF is commonly used as monotherapy, \(^16\) in later lines of therapy, \(^17\) and is effective in real-world settings, \(^17\)\(^,\)\(^18\) particularly when assessed at month 6 of therapy (per Clinical Disease Activity Index [CDAI] low disease activity [LDA] and remission rates). \(^19\) In addition, TOF as monotherapy or with MTX provided similar effectiveness at month 6 when used as third- or fourth-line therapy. \(^17\) Here, using data from the real-world US CorEvitas RA Registry, we expand on the results of Reed et al \(^17\) by reporting data following 12 months of treatment. Specifically, this retrospective observational study (ClinicalTrials.gov: NCT04721808) sought to evaluate the baseline demographics/characteristics and TOF treatment patterns and effectiveness in patients with RA initiating TOF in the CorEvitas RA Registry with 12 and/or 6 months of follow-up. All outcomes were stratified by TOF regimen (monotherapy vs combination therapy), line of therapy, time period of treatment initiation, and TOF dose, to assess how trends in prescribing may have changed over time since TOF approval.

**METHODS**

**Data source.** The CorEvitas RA Registry (ClinicalTrials.gov: NCT01402661; formerly known as Corrona), established in 2001, is one of the largest ongoing US registries for RA. The registry contains longitudinal follow-up data collected from patients and their treating rheumatologists during clinical encounters. As of December 31, 2020 (data available at time of analysis), the registry included data from 202 active private and academic clinical sites, provided by 857 physicians and 56,090 patients with RA across 42 states. Overall, 211,000 patient-years of data were available for analysis.

**Study population.** This study (ClinicalTrials.gov: NCT04721808) included patients aged ≥ 18 years enrolled in the CorEvitas RA Registry with rheumatologist-diagnosed RA, who initiated TOF on or after November 6, 2012 (date of TOF FDA approval), and had a 12-month (primary analysis) or 6-month (secondary analysis) follow-up visit on or before January 31, 2021 (before the 2021 update to TOF US label). \(^16\) Eligible patients for the 12-month visit had ≥ 1 visit that occurred 10-15 months after the index date (the date of first reported use of TOF in the CorEvitas RA Registry [baseline]). Eligible patients for the 6-month visit had ≥ 1 visit that occurred 3-9 months after baseline. If the patient had > 1 visit between 10-15 months or 3-9 months, the visit closest to the 12- or 6-month timepoint was selected. Patients could be included in both the 12-month and 6-month analysis groups if they had eligible visits.

The study was performed in accordance with the guidelines for Good Pharmacoepidemiology Practice. All participating investigators were required to obtain full institutional review board (IRB) approval for conducting research involving human patients with a limited dataset. Sponsor approval and continuing review were obtained through the New England Independent Review Board (no. 120160610). All sites had undergone annual IRB review processes, and documentation of approval was submitted to CorEvitas, LLC, prior to the initiation of any study procedures. All patients in the registry were required to provide written informed consent and authorization prior to participating in the study.

**Outcomes.** Outcomes were assessed in patients with a 12-month visit and/or 6-month visit.

Data collected at baseline included patient demographics, lifestyle characteristics, history of comorbidities, RA-related characteristics, disease activity, patient-reported outcomes [PROs], RA treatment history, concomitant therapies, and reasons for TOF initiation.

Reasons for discontinuing TOF (among patients who discontinued at/ prior to month 12 and/or month 6) were documented, and TOF effectiveness (disease activity and PROs) at month 12 and/or month 6 were assessed.

Continuous effectiveness outcomes were mean change from baseline in CDAI (0-76), Health Assessment Questionnaire (HAQ; 0-3), patient global assessment (PtGA; 0-100 mm visual analog scale [VAS]), patient pain (0-100 mm VAS), and patient fatigue (0-100 mm VAS).

Binary effectiveness outcomes were the proportions of patients achieving CDAI LDA (CDAI ≤ 10, among patients with baseline CDAI > 10 [primary effectiveness outcome]), CDAI remission (CDAI ≤ 2.8, among patients with baseline CDAI > 2.8), and ≥ 20%, ≥ 50%, or ≥ 70% improvement in modified ACR response criteria (mACR20/50/70). The mACR20/50/70 response criteria use the same components of the ACR20/50/70 response criteria, but without acute phase reactant values, to allow for the use of these measures in the absence of laboratory reports. \(^19\)

**Statistical analyses.** All outcomes were stratified by (1) the use of TOF as monotherapy vs combination therapy (TOF + hydroxychloroquine, leflunomide, MTX, or sulfasalazine); (2) the use of TOF as second-line (prior use of ≥ 1 csDMARD and no prior use of a bDMARD), third-line (prior use of ≥ 1 csDMARD and 1 bDMARD), and fourth-line (prior use of ≥ 1 csDMARD and ≥ 2 bDMARDs) therapy; (3) the time period of TOF initiation from 2012 to 2014, 2015 to 2017, and 2018 to 2020; and (4) TOF dose of 5 mg twice daily (BID) or 11 mg once daily (QD).

For patient baseline demographics/characteristics, TOF treatment patterns, reasons for TOF initiation/discontinuation, and continuous effectiveness outcomes, summary statistics were calculated. Binary effectiveness outcomes were presented as response rates (%) with corresponding 95% CIs.

For all effectiveness outcomes, if a patient discontinued TOF but did not switch to a bDMARD, the value at the 12- or 6-month visit was used. If a patient discontinued TOF and switched to a bDMARD or another JAKi, the value at the switch visit was used. If no value was available at the switch visit, the outcome was set to missing. The number of patients in each category is provided.

**RESULTS**

**Baseline demographics and characteristics.** In total, 2874 patients with RA initiated TOF on or after November 6, 2012. Of these, 1298 and 1712 patients had a qualifying 12-month and 6-month follow-up visit, respectively, and were included in the analysis (Supplementary Figure S1A and S1B, available with the online version of this article).

At baseline, most TOF initiators with a 12-month visit were female (79.9%) and White (86.6%), with a mean age of 59.6 years and mean disease duration of 13.5 years; most patients had moderate (34.6%) or high (35.1%) disease activity based on CDAI (Table 1). Slightly less than half of patients (43.1%)...
Table 1. Baseline demographics and characteristics of patients with a 12-month visit stratified by TOF regimen, TOF line of therapy, and time period of TOF initiation.

<table>
<thead>
<tr>
<th>TOF Regimen</th>
<th>TOF Line of Therapy</th>
<th>Time Period of TOF Initiation</th>
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<tbody>
<tr>
<td>Overall, N = 1298</td>
<td>Overall, N = 1265¹</td>
<td>Overall, N = 1298</td>
</tr>
<tr>
<td>Monotherapy, n = 560</td>
<td>Second-Line, n = 172</td>
<td>2012-2014, n = 354</td>
</tr>
<tr>
<td>Combination Therapy, n = 738</td>
<td>Third-Line, n = 236</td>
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<td>Fourth-Line, n = 841</td>
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<td>2018-2020, n = 341</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Age, yrs, mean (SD)</th>
<th>59.6 (11.9)</th>
<th>59.6 (11.9)</th>
<th>59.6 (11.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>59.5 (12.3)</td>
<td>59.5 (12.3)</td>
<td>59.5 (12.3)</td>
</tr>
<tr>
<td>White</td>
<td>59.7 (11.7)</td>
<td>60.3 (11.8)</td>
<td>58.8 (11.5)</td>
</tr>
<tr>
<td></td>
<td>59.6 (11.9)</td>
<td>62.7 (12.7)</td>
<td>55.6 (11.5)</td>
</tr>
</tbody>
</table>
| Mean age was lowest in patients who initiated TOF as monotherapy, and most (66.5%) initiated TOF as fourth-line therapy (Table 1). Approximately half of patients (46.5%) initiated TOF between 2015 and 2017 (Table 1) and at a dose of 5 mg BID (53.9%; Supplementary Table S1, available with the online version of this article).

Baseline demographics and characteristics in patients with a 12-month visit were generally similar across TOF regimens, lines of therapy, time periods of initiation, and doses (Table 1; Supplementary Table S1, available with the online version of this article). However, mean age was lowest in patients who initiated TOF as fourth-line therapy (58.8 yrs vs 62.7 yrs and 60.3 yrs in fourth- vs second- and third-line initiators, respectively); current smoking was lowest in second-line initiators (16% vs 23.4% and 20.4% in second- vs third- and fourth-line initiators, respectively), whereas mean RA duration was longest in fourth-line initiators (15.0 yrs vs 7.7 yrs and 12.1 yrs in fourth vs second- and third-line initiators, respectively). A lower proportion of patients initiating TOF as third-line therapy had high disease activity vs those who initiated as fourth-line therapy (27.1% vs 38.5%, respectively), whereas PROs, such as HAQ...
scores, increased with later lines of therapy (HAQ scores 0.8-1.2 from second- to fourth-line therapy; Table 1).

Current smoking was lowest in patients who initiated TOF between 2012-2014 vs 2015-2017 and 2018-2020 (16.4% vs 20.6% and 23.7%, respectively); mean RA duration was longer in patients who initiated TOF between 2012-2014 and 2015-2017 vs 2018-2020 (13.7 vs 12.7 yrs, respectively), whereas mean CDAI was higher in patients who initiated TOF between 2012-2014 vs 2015-2017 and 2018-2020 (21.1 vs 18.4 and 17.7, respectively; Table 1).

Baseline demographics and characteristics of patients with a 6-month visit (Supplementary Table S2, available with the online version of this article) were generally similar to patients with a 12-month visit.

Treatment patterns.

1. **Overall TOF initiators.** Of the 1298 patients with a 12-month visit, most had previously received a csDMARD (96.2%) or a bDMARD/tsDMARD (85.5%). The most common treatment received immediately prior to TOF was a TNFi (40.8% TNFi only; 2.5% TNFi + csDMARD); 0.1% had previously received a csDMARD. Additionally, 28.7% were receiving concomitant prednisone at the time of TOF initiation (Table 2).

   With increasing line of therapy, the proportion of patients initiating TOF as monotherapy increased (26.2-46% from second- to fourth-line therapy). The proportion of patients with concomitant prednisone use increased with increasing line of therapy (22.1%-30.8% from second- to fourth-line therapy). Most TOF third-line initiators received TNFi immediately prior to TOF (68.6% TNFi only, 5.1% TNFi + csDMARD), whereas less than half of TOF fourth-line initiators received TNFi immediately prior to TOF (41.5% TNFi only, 2.5% TNFi + csDMARD; Table 2).

   Treatment patterns in patients with a 12-month visit were generally similar across time periods of TOF initiation and TOF doses (Table 2; Supplementary Table S3, available with the online version of this article). Of note, a higher percentage of patients were bDMARD-naïve when they initiated TOF between 2018-2020 vs 2012-2014 and 2015-2017 (19.1% vs 12.2% and 13.3%, respectively; Table 2).

   Typically, treatment patterns for patients with a 6-month visit were similar (Supplementary Table S4, available with the online version of this article) to those with a 12-month visit.

2. **Stratified by TOF regimen, line of TOF therapy, time period of TOF initiation, and TOF dose (12-month visit).** A higher proportion of patients receiving TOF as combination therapy, approximately half (54.9%) received MTX only as a concomitant therapy (Table 2).

Effectiveness of TOF.

3. **Overall TOF initiators.** Of the 1298 patients with a qualifying 12-month visit, improvements from baseline in CDAI, HAQ, PtGA, patient pain, and patient fatigue were observed at month 12 (Figure 1A). At month 12, 31.9% achieved the primary effectiveness outcome: CDAI LDA (CDAI ≤ 10, 95% CI 29-35%). In addition, 10.1% achieved CDAI remission (CDAI ≤ 2.8), and 22.4%/10.4%/5% achieved mACR20/50/70 (Figure 1B).

4. **Overall TOF initiators.** Of the 1298 patients with a qualifying 12-month visit, improvements from baseline in CDAI, HAQ, PtGA, patient pain, and patient fatigue were observed at month 12 (Figure 1A). At month 12, 31.9% achieved the primary effectiveness outcome: CDAI LDA (CDAI ≤ 10, 95% CI 29-35%). In addition, 10.1% achieved CDAI remission (CDAI ≤ 2.8), and 22.4%/10.4%/5% achieved mACR20/50/70 (Figure 1B).

   - **Stratified by TOF regimen, line of TOF therapy, time period of TOF initiation, and TOF dose (12-month visit).** Effectiveness was generally similar across TOF regimens, lines of TOF therapy, time periods of TOF initiation, and TOF doses (Figures 1-3; Supplementary Table S8, available with the online version of this article).

   Of note, a mean increase from baseline was recorded for patient fatigue at month 12 in third-line initiators, whereas a mean decrease from baseline was noted in second-
DISCUSSION

This observational study evaluated baseline demographics/clinical characteristics and TOF treatment patterns and effectiveness in patients with RA initiating TOF in the US CorEvitas RA Registry. Although TOF treatment patterns and effectiveness have been described previously using real-world RA databases and registries, we have expanded on these studies, by providing an updated analysis (observation period: November 2012–January 2021) of TOF real-world outcomes using data from a large cohort of patients with RA (2874 patients) at 12 months and 6 months of follow-up. We also had the opportunity to evaluate how trends in TOF prescribing changed in different time periods, as more studies about TOF were published and TOF and JAKi class US product labeling changed. This analysis showed that TOF is used as early (13.6% as second-line treatment) and more commonly as later (66.5% as fourth-line treatment) lines of therapy in real-world settings of patients with RA. Similar to previous studies, most patients had failed multiple bDMARDs prior to TOF initiation, and patients often had treatment (or non-MTX) lines of therapy in real-world settings of patients with RA.

Table 2. Treatment patterns prior to TOF initiation, and concurrent therapies at TOF initiation for patients with a 12-month visit, stratified by TOF regimen, TOF line of therapy, and time period of TOF initiation.

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</table>

RA treatment history

History of prior csDMARD use

- None: 49 (3.8)
- 1: 425 (32.7)
- ≥ 2: 824 (63.5)

History of prior bDMARD/csDMARD use

- None: 188 (14.5)
- 1: 248 (19.1)
- ≥ 2: 862 (66.4)

MOA history

Immediately previous treatment

- TNFi only: 530 (40.8)
- TNFi + csDMARD: 33 (2.5)
- Non-TNFi bDMARD only: 384 (29.6)
- Non-TNFi + csDMARD: 31 (2.4)
- csDMARD only: 148 (11.4)
- tsDMARD only: 1 (0.1)
- Indeterminant: 171 (13.2)

Concomitant therapies at TOF initiation

- None: 560 (43.1)
- MTX only: 405 (31.2)
- Non-MTX csDMARD only: 246 (19)
- MTX and non-MTX csDMARD: 87 (6.7)

Prednisone use at TOF initiation

- Current prednisone use: 372 (28.7)
- Dose, mg/d, mean (SD): 7.2 (5.0)

Data are n (%) unless otherwise stated. The total number of patients may vary for each outcome based on available data. *-12-month visit occurred 10-15 months after the index date. †-Combination therapy refers to TOF plus hydroxychloroquine, leflunomide, MTX, or sulfasalazine. ‡-First-line initiators (n = 16) were excluded from the analysis. bDMARD: biologic disease-modifying antirheumatic drug; csDMARD: conventional synthetic DMARD; MOA: mechanism of action; MTX: methotrexate; RA: rheumatoid arthritis; TNFi: tumor necrosis factor inhibitor; TOF: tofacitinib; tsDMARD: targeted synthetic DMARD.

fourth-line initiators (95% Cs overlapped; Figure 2A). CDAI LDA (CDAI ≤ 10) was achieved in a lower proportion of fourth-line initiators vs second- and third-line initiators at month 12. The proportion of patients achieving CDAI remission (CDAI ≤ 2.8) and mACR50 and mACR70 responses was greater in second-line initiators vs third- and fourth-line initiators at month 12 (Figure 2B).

Generally, effectiveness outcomes for patients with a 6-month visit (Supplementary Table S9, available with the online version of this article) were similar to those with a 12-month visit.

Pappas et al
mens, lines of therapy (including fourth-line treatment), time periods of initiation, and doses.

Here, in patients with a 12-month visit, 43.1% of patients with RA initiated TOF as monotherapy. This generally aligned with results from a real-world study of Australian patients with RA, which showed that 43.4% of patients initiated TOF as monotherapy,23 as well as results from a US claims database (November 2012–October 2014), which revealed that 53.1% of patients initiated TOF as monotherapy.16 We found that TOF monotherapy was more common in later lines of therapy. Additionally, a higher percentage of patients were bDMARD-naive when they initiated TOF between 2018 and 2020 vs earlier time periods of initiation. Overall, approximately 46% of patients with a 12-month visit discontinued TOF, which

Figure 1. Effectiveness of TOF based on (A) continuous and (B) binary efficacy and patient-reported outcomes at month 12 in patients with a 12-month visit, stratified by TOF regimen. *12-month visit occurred 10-15 months after the index date. **Combination therapy refers to TOF + hydroxychloroquine, leflunomide, methotrexate, or sulfasalazine. †Calculated among those patients with moderate or high disease activity (CDAI > 10) at baseline. ‡Calculated among those patients with LDA, moderate or high disease activity (CDAI > 2.8) at baseline. CDAI: Clinical Disease Activity Index; HAQ: Health Assessment Questionnaire; LDA: low disease activity; mACR20/50/70: modified American College of Rheumatology response criteria ≥20%, ≥50%, or ≥70%; TOF: tofacitinib; VAS: visual analog scale.
is in line with 12-month discontinuation rates for etanercept and adalimumab (43.3-46.7%) in the RA CorEvitas Registry. Although the discontinuation rate is high, given the increasing number of available therapies for RA, this may reflect a willingness to adjust therapies if target responses are not achieved.

Effectiveness of TOF at month 12 was demonstrated regardless of treatment regimen, line of therapy, time of initiation, and dose, which expands on previous analyses of TOF in the CorEvitas RA Registry at month 6. Similarly, a pooled analysis of TOF RA phase III RCTs revealed no significant differences in efficacy (eg, ACR20/50/70 and HAQ improvement ≥ 0.22) at month 3 between monotherapy and combination therapy. It should be noted that the mACR20/50/70 response criteria in this analysis use the same components of the ACR20/50/70 response criteria, but without acute phase reactant values. CorEvitas has validated the mACR measures against the ACR

Figure 2. Effectiveness of TOF based on (A) continuous and (B) binary efficacy and patient-reported outcomes at month 12 in patients with a 12-month visit, stratified by TOF line of therapy. a 12-month visit occurred 10-15 months after the index date. b Calculated among those patients with moderate or high disease activity (CDAI > 10) at baseline. c Calculated among those patients with LDA, moderate or high disease activity (CDAI > 2.8) at baseline. CDAI: Clinical Disease Activity Index; HAQ: Health Assessment Questionnaire; LDA: low disease activity; mACR20/50/70: modified American College of Rheumatology response criteria ≥ 20%, ≥ 50%, or ≥ 70%; TOF: tofacitinib; VAS: visual analog scale.
measures, and they have been shown to be close in value.26 The proportions of overall TOF initiators achieving CDAI LDA/remission and mACR20/50/70 were lower than those in a TOF RA phase III RCT at month 1211; however, there are differences between RCT populations and this real-world population (eg, differences in patient characteristics and treatment histories)27,28 and comparisons between RCTs and real-world data should therefore be interpreted with caution. In contrast with second- and fourth-line initiators, a slight mean increase from baseline in fatigue was noted in third-line initiators (95% CIs overlapped); the reasons underpinning this result are not understood.

In a separate analysis of the CorEvitas RA Registry of patients with RA initiating TNFi therapy, at month 12 improvements from baseline with TNFi were observed, as in this analysis of TOF, for CDAI (–6.8 vs –3.5 for TNFi vs TOF, respectively)

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Figure 3. Effectiveness of TOF based on (A) continuous and (B) binary efficacy and patient-reported outcomes at month 12 in patients with a 12-month visit, stratified by time period of TOF initiation. 12-month visit occurred 10-15 months after the index date. Calculated among those patients with moderate or high disease activity (CDAI > 10) at baseline. Calculated among those patients with LDA, moderate or high disease activity (CDAI > 2.8) at baseline. CDAI: Clinical Disease Activity Index; HAQ: Health Assessment Questionnaire; LDA: low disease activity; mACR20/50/70: modified American College of Rheumatology response criteria ≥ 20%, ≥ 50%, or ≥ 70%; TOF: tofacitinib; VAS: visual analog scale.
and patient fatigue (−4.7 vs −3.4 for TNFi vs TOF, respectively). In addition, at month 12 an increased proportion of patients who initiated TNFi, and of those who initiated TOF in this analysis, achieved CDAI LDA (CDAI ≤ 10: 39.9% vs 31.9% for TNFi vs TOF, respectively) and CDAI remission (CDAI ≤ 2.8: 17.6% vs 10.1% for TNFi vs TOF, respectively). This was despite the fact that TOF in the present study was initiated in later lines of therapy vs TNFi (second- to fourth-line vs first-line treatment, respectively).28

Collectively, these data resemble those of other analyses of the CorEvitas RA Registry of patients with RA. For instance, in analyses of patients with RA initiating tocilizumab (anti–interleukin 6 therapy) monotherapy or rituximab (B-cell–depleting therapy approved in combination with MTX), at month 12, improvements from baseline in CDAI and PROs were observed and were generally similar between patients who were TNFi-naive and TNFi-experienced.29,30

Overall, rheumatologists and patients with RA have many advanced therapies available for use. Data from real-world registries provide insights for patients who are not represented in clinical trials. Therefore, understanding TOF treatment patterns and effectiveness in real-world settings can inform daily practice and/or medical decision-making.

The analysis was strengthened by the fact that longitudinal data were collected for up to 12 months of follow-up in the largest US RA registry. The registry follows patients throughout the US in both academic and community-based practices,31 representing a diverse population. The study analyzed several patient-reported and physician-reported measures of wellbeing and disease activity, which may not be accessed through other data sources, such as health insurance claims data. The study period covered the period of TOF FDA approval (2012) up until January 31, 2021.

Limitations of this analysis should be considered. This is a descriptive study, without a comparator arm, presenting outcomes as observed in the registry. The CorEvitas RA Registry only includes a small proportion of patients from the US; therefore, it may not be representative of all adults with RA in the US, the rest of the world, or of those choosing not to participate. Not all patients provided a reason for initiating or discontinuing TOF. Missingness in real-world data also limited this study. Although CorEvitas has thorough training for sites, health-care providers, and quality control procedures, data are not always complete. Registry reporting is not based on a fixed-visit schedule; thus, a time window was used to determine eligible visits. Therefore, not all visits necessarily occurred at 6 months (time window: 3 to 9 months) or 12 months (time window: 10 to 15 months). This is one explanation for the lower number of patients with follow-up compared with the number of initiators. In addition, some of the patients initiating TOF may not have had the opportunity to accumulate the necessary follow-up time (ie, 6 or 12 months). It should be noted that prescribing patterns may have changed over time as more advanced therapies become available, which may have influenced the analysis of TOF treatment patterns and effectiveness by time period of initiation.

To the best of our knowledge, this is the most recent and comprehensive study that describes the patient baseline demo-


