Real-World Prescribing Patterns of Certolizumab in the Treatment of Crohn's Disease

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Abstract

Background: Certolizumab (CZP) is a pegylated anti-tumor necrosis factor (TNF) agent approved for the treatment of moderate-to-severe Crohn's disease (CD). CZP therapy has proven effective and well-tolerated for biologic-naïve patients, as well as anti-TNF-experienced patients with secondary non-response or intolerance. CZP is also the preferred anti-TNF during pregnancy. We sought to describe real-world prescribing patterns of CZP in the treatment of CD.

Methods: We performed a retrospective cohort study of CD patients treated with CZP at a large multicenter gastroenterology private practice since drug approval in 2008. Data collection included demographics, diagnosis, treatment history, and reason for CZP use. CZP use was classified as one of the following: first-line anti-TNF, prior anti-TNF non-response or intolerance, payor requirements, and/or pregnancy considerations.

Results: A total of 59 patients receiving CZP for the treatment of CD were identified. Mean age was 48±16.1 years, and 42 (71%) were female. Median CZP treatment duration was 26 [IQR 9-50] months. Forty-six (78%) patients had private insurance, 12 (20%) were enrolled in Medicare or Medicaid, and 1 was uninsured. Nine (15%) patients were bio-naive. Of the 50 (85%) biologic-experienced patients, 22 were previously treated with 1 agent, 23 received 2 previous agents, and 5 patients received 3 or more previous agents. Reasons for CZP use were as follows: prior biologic non-response or intolerance in 39 (66%), pregnancy considerations in 8 (14%), payor requirements or cost considerations in 6 (10%), first-line anti-TNF in 4 (7%), and other reasons in 2 (3%). To date, 26 (44%) patients remain on CZP with a median treatment duration of 48 [IQR 31-59] months.

Conclusions: We described real-world utilization of CZP. In our cohort, CZP was most commonly prescribed to biologic-experienced patients with prior anti-TNF non-response or intolerance.

Background

Treatment with anti-tumor necrosis factor (TNF) agents has become a mainstay of therapy for patients with Crohn's disease (CD) who are unresponsive to conventional medical management. Certolizumab (CZP), the only humanized pegylated anti-TNF agent, was FDA approved for the treatment of moderate-to-severe CD in 2008.[1] Compared to alternative agents, infliximab (IFX) and adalimumab (ADA), CZP has a higher binding affinity for TNF. Similar to ADA, CZP also gives patients an option for subcutaneous self-administration, and its longer half-life allows for less frequent dosing once monthly compared to weekly with ADA.[2-3]

Evidence supports the use of CZP for biologic-naïve patients, as well as anti-TNF-experienced patients with secondary non-response or intolerance.[4-5] CZP is also a safe anti-TNF option during pregnancy.[6-8] In clinical practice CZP is rarely first-line therapy compared to IFX and ADA, and is more commonly prescribed to special populations and/or to patients with confounding factors. We sought to describe real-world prescribing patterns of CZP in the treatment of CD.

Methods

Retrospective cohort study of CD patients initiated on CZP therapy with available records at a large multicenter gastroenterology private practice since FDA approval in 2008.

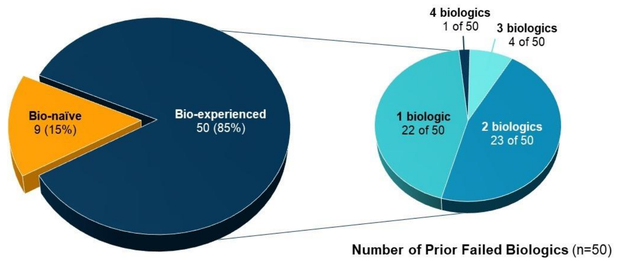
- Data collection included demographics, diagnosis, treatment history, insurance coverage, and reason for CZP use
  - CZP use was classified as one of the following: first-line anti-TNF, prior anti-TNF non-response or intolerance, payor requirements, and/or pregnancy considerations
- Descriptive data were reported as frequencies and proportions for categorical variables, and as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables. The Kaplan Meier Log Rank test was used to assess CZP treatment duration.

Results

Patient Demographics

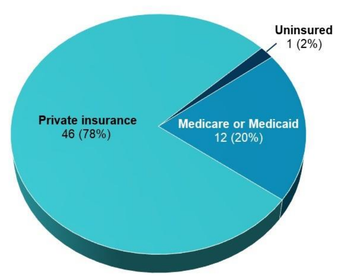
	CD patients n=59
Age in years, mean ± SD	48.4 ± 16.1
Female gender, n (%)	42 (71%)
Disease duration in years, median (IQR)	9.6 (4.5 - 15.8)

Prior Biologic Therapies



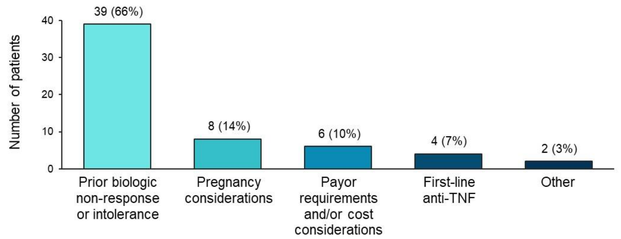
- The majority of CD patients initiated on CZP therapy were bio-experienced.
- The most common prior biologics included IFX (n=39) and ADA (n=36). Vedolizumab and ustekinumab had been previously used in 4 patients each.

Insurance Coverage



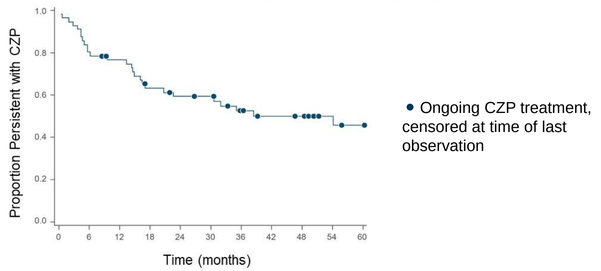
- 46 of 59 patients had private insurance, including Blue Cross Blue Shield (n=19), United Healthcare (n=14), Cigna (n=3), Aetna (n=3), Anthem (n=2), and other (n=5).
- Criteria for pharmacy coverage policies are described below.

Reasons for Certolizumab Use



- The most common reasons for CZP were prior biologic non-response or intolerance, pregnancy considerations and payor/cost considerations.
- Of 9 bio-naïve patients, CZP was selected as first-line anti-TNF biologic in 4. The remaining patients were started on CZP for pregnancy considerations (n=4) or payor/cost requirements (n=1).

Certolizumab Treatment Duration



- Treatment persistence rates at 6 weeks, 26 weeks, 52 weeks, and 104 weeks were as follows: 54/56 (96%), 44/56 (79%), 40/53 (75%), and 29/51 (57%).
- Overall median CZP treatment duration was 26 [IQR 9-50] months.
- To date, 26 (44%) patients remain on CZP with a median treatment duration of 48 [IQR 31-59] months.
  - 16 patients have been on CZP for >3 years, and 7 for >5 years. The longest ongoing treatment duration to date is 115 months.
- CZP discontinuations occurred in 30 patients at a median time of 14 [IQR 5-29] months, most commonly for lack or loss of response (n=22) and intolerance (n=6).
- Similar data were observed between bio-naïve and bio-experienced patients (median treatment duration 30 [IQR 5-75] vs 29 [IQR 10-49] months).
- Two patients that transferred care and one patient lost to follow-up were excluded.

Payor Specific Criteria for Use of Certolizumab

Payor	Certolizumab Use	Detailed Criteria for Use in Crohn's Disease
Aetna	Allowed	**Crohn's Disease:** Patient must have failed 6-MP, AZA OR CS and have signs and symptoms of active disease **Fistulizing Crohn's Disease:** Fistula must be present for at least three (3) months
Anthem	Allowed	Patient must have failed conventional therapy
Blue Cross Blue Shield of Texas	Allowed	Patient must have inadequate response to conventional therapy
Cigna (Employer Group Plans)	Non-preferred to ADA and UST	Patient must have documented failure or inadequate response, contraindication per FDA label, intolerance or is not a candidate for the TWO preferred products: ADA and UST
Cigna (Individual and Family Plans)	Non-preferred to ADA, IFX and VDZ	Patient must have documented failure or inadequate response, contraindication per FDA label, intolerance or is not a candidate for ALL preferred products: ADA, IFX, and VDZ
Humana	Allowed	Patient must have prior therapy, contraindication or intolerance with a CS OR an IMM
United Healthcare	Allowed	Patient must have inadequate response to conventional therapy AND not receiving a biologic DMARD or JAK inhibitor
Medicare	Allowed	Patient must have inadequate response to conventional therapy

*Medical benefit coverage policies for corresponding insurance payor. Accessed December 3, 2019.
Abbreviations: 6-MP, 6-mercaptopurine; ADA, adalimumab; AZA, azathioprine; CS, corticosteroid; DMARD, disease-modifying antirheumatic drugs; IFX, infliximab; IMM, immunomodulator; JAK, Janus kinase; UST, ustekinumab; VDZ, vedolizumab

Discussion

- We reported patient characteristics and associated indications for certolizumab prescribing at a large multicenter gastroenterology private practice.
- 50 of 59 patients in our cohort were bio-experienced. Of these, more than half (28 of 50, 56%) had been previously treated with two or more biologics prior to certolizumab.
- Over three-fourths of patients (46 of 59, 78%) in our cohort had private insurance.
  - Per private insurance coverage policies, certolizumab use is generally restricted to Crohn's patients who have documented failure to conventional oral therapy along with preferred biologics.
  - Consistent with private insurance coverage policies, the most common reason for certolizumab use was prior biologic non-response or intolerance (39 of 59, 66%).
  - These data suggest that in patients with private insurance, anti-TNF selection may be driven by payor-specific criteria.
- The second most common reason for certolizumab use was pregnancy considerations (8 of 59, 14%).
  - Certolizumab is the only anti-TNF agent that does not actively cross the placenta.
  - Moreover, certolizumab is the only biologic that may be continued throughout the entirety of a pregnancy without dose interruption or modification in the third trimester.[6-8]
- Our cohort experienced high treatment persistence rates throughout follow-up.
- Overall median certolizumab treatment duration was over two years.
- 44% patients have continued on certolizumab with a median treatment duration of four years, including one patient receiving therapy for almost ten years.

Conclusion

- We described real-world utilization of certolizumab. In our cohort, certolizumab was most commonly prescribed to biologic-experienced patients with prior anti-TNF non-response or intolerance.
- Our data indicate that patients treated with certolizumab have high treatment persistence, and may successfully remain on therapy long-term.

References

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