# Association of Anti-inflammatory Therapy Use With the Incidence of Parkinson's Disease: A Person-Time Analysis Among Patients With Autoimmune Disease

**Michele Potashman**[1], Jennifer S Haas[2], Ambrish Pandit[3], Dana Stafkey[3], Vlad Coric[1], Wolfgang Singer[4], Gil L'Italien[1]

1. Biohaven Pharmaceuticals, Inc., 215 Church St, New Haven, CT, USA; 2. Xcenda GmbH part of Cencora Inc., Lange Laube 31, 30159 Hannover, Germany; 3. Cencora Inc., 1 West First Avenue, Conshohocken, PA 19428, USA; 4. Department of Neurology, Mayo Clinic, Rochester, MN, USA

***Michele Potashman is an employee of and owns stocks/option in Biohaven Pharmaceuticals, Inc. This study was funded by Biohaven Pharmaceuticals, Inc.***

*Jennifer S Haas, Ambrish Pandit, and Dana Stafkey are employees of Cencora, which received consulting fees for the purpose of conducting this analysis. They do not have any financial interests or holdings in Biohaven Pharmaceuticals, Inc. Vlad Coric and Gil L'Italien are employees and own stocks/options in Biohaven Pharmaceuticals, Inc. Wolfgang Singer has nothing to disclose.*

# Introduction

- Autoimmune diseases are characterized by an immune response to self-antigens causing tissue damage[1]
- Previous studies have linked the development of Parkinson's disease (PD) with autoimmune disorders, suggesting shared pathophysiology[2]
- Seminal scientific publications suggest that reducing inflammatory processes can be a potential target for intervention in PD[3,4]
- To date, relatively little information is available regarding the potential benefit of anti-tumor necrosis factor (anti-TNFs), such as adalimumab, and anti-interleukin-17 (anti-IL-17) drugs, such as secukinumab and ixekizumab, on the development of PD

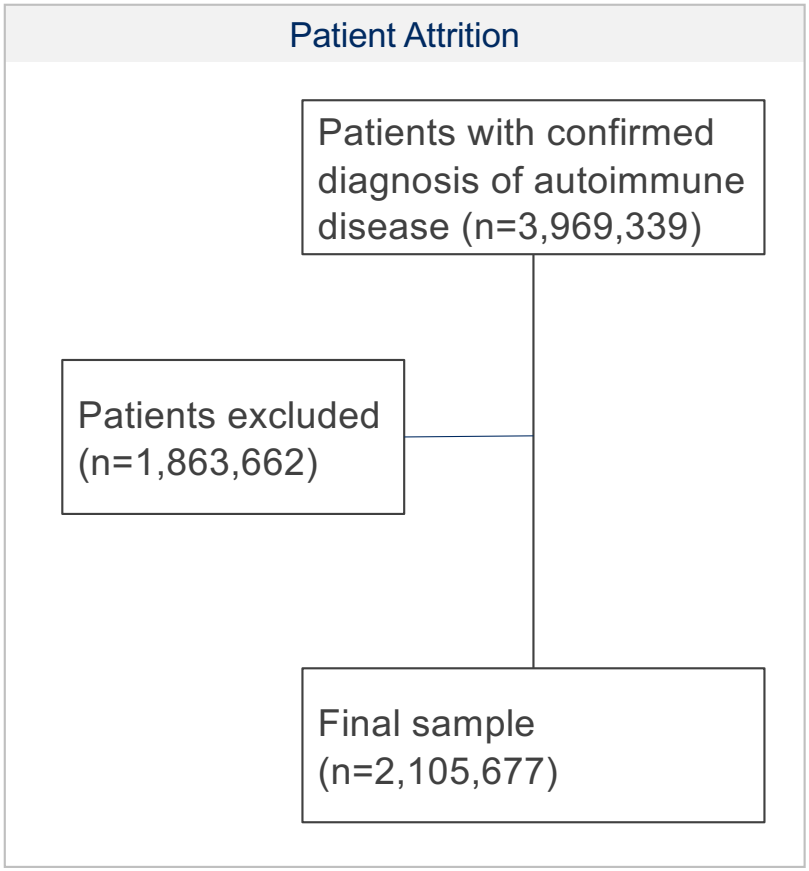
1. Ngo ST, Steyn FJ, McCombe PA. Gender differences in autoimmune disease. *Front Neuroendocrinol.* 2014;35(3):347-369. doi:10.1016/j.yfrne.2014.04.004. 2. Witoelar A, Jansen IE, Wang Y, et al. Genome-wide Pleiotropy Between Parkinson Disease and Autoimmune Diseases. *JAMA Neurol.* 2017;74(7):780-792. doi:10.1001/jamaneurol.2017.0469. 3. Wang Q, Liu Y, Zhou J. Neuroinflammation in Parkinson's disease and its potential as therapeutic target. *Transl Neurodegener.* 2015;4:19. Published 2015 Oct 12. doi:10.1186/s40035-015-0042-0. 4. Tansey MG, Goldberg MS. Neuroinflammation in Parkinson's disease: its role in neuronal death and implications for therapeutic intervention. *Neurobiol Dis.* 2010;37(3):510-518. doi:10.1016/j.nbd.2009.11.004.

# Objective

To assess the comparative incidence of PD among patients with autoimmune diseases who are exposed to anti-TNF/anti-IL-17 drugs vs those without exposure

# Methods: Study Population and Data Source

- **Study design:** Retrospective cohort study
- **Data:** Closed claims data from the Komodo Health database (2014–2022)
- **Patient eligibility criteria:**
  - ≥18 years of age
  - ≥1 inpatient claim or ≥2 outpatient claims for rheumatoid arthritis (RA), ulcerative colitis (UC), Crohn's disease (CD), ankylosing spondylitis (AS), psoriasis (PS) or psoriatic arthritis (PsA) identified by ICD-9-CM or ICD-10 diagnosis code
  - Subjects with PD diagnosis or prescription claim prior to the index diagnosis date were excluded
- **Index diagnosis date:** Date of first confirmed autoimmune diagnosis (6-month baseline period required)
  - Variable follow-up
- **Exposure window:**
  - Start date of anti-TNF/anti-IL-17 to end of enrollment or PD event
  - "Not treated" patients index date is start date (to end of enrollment, PD event or initiation of anti-TNF/anti-IL-17 therapy )



# Methods

## Outcomes

Primary outcome -- Person-time incidence

- PD events
- Person-time (in years) with anti-TNF/anti-IL-17 treatment (exposure time).
  - Observation time for “not treated” patient

Additional key outcomes captured (cohort description, multivariate adjustments):

- Quan-enhanced Charlson Comorbidity Index (CCI)
- Anti-inflammatory comedications:
  - Included conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs), corticosteroids, and nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Identified from National Drug Codes and Healthcare Common Procedure Coding System codes

## Statistical analysis

- Descriptive statistics
  - Unadjusted PD event rate
- Adjusted findings : Poisson regression
  - Assessed association between anti-TNF and/or anti-IL-17 therapies and PD incidence
  - Adjusts for individual-specific times at risk
  - Adjustment covariates: age, gender, baseline CCI, exposure-time and post-index date anti-inflammatory medications (DMARDs, csDMARDs, corticosteroids and NSAIDs [binary])
  - *Preferred method to evaluate data with rare events*
  - Findings reported as incidence rate ratios (IRRs) and 95% confidence intervals (95% CIs)

# Results: Demographic and Clinical Characteristics

- Overall study population consisted of 2,105,677 subjects, 114,082 (18.5%) received either anti-TNF/anti-IL-17

| | Not treated with anti-TNF/anti-IL-17 (n, %) N = 1,991,595 | Anti-TNF/anti-IL-17 n (%) N = 114,082 | Anti-TNF only n (%) N = 106,314 | Anti-IL-17 only n (%) N = 5,672 |
|---|---|---|---|---|
| Age, mean (SD) | 54.2 (16.2) | 46.9 (14.9) | 46.9 (15.1) | 46.9 (13.2) |
| Female | 1,263,892 (63.5%) | 71,254 (62.5%) | 66,766 (62.8%) | 3,135 (55.3%) |
| CCI, mean (SD) | 1.25 (1.90) | 0.70 (1.26) | 0.70 (1.25) | 0.71 (1.30) |
| Chronic pulmonary disease (%) | 28.8% | 23.3% | 23.1% | 24.2% |
| Diabetes, without chronic complications (%) | 24.1% | 16.0% | 15.9% | 18.2% |
| Cerebrovascular disease (%) | 17.6% | 10.9% | 9.9% | 11.3% |
| csDMARDs | 566,357 (28.4%) | 58,748 (51.5%) | 56,254 (52.9%) | 1,524 (26.9%) |
| Corticosteroids | 1,451,034 (72.9%) | 98,353 (86.2%) | 92,028 (86.6%) | 4,502 (79.4%) |
| NSAIDs | 1,194,730 (60%) | 74,466 (65.3%) | 69,490 (65.4%) | 3,404 (60.0%) |
| Follow-up time (in days), mean (SD) | 969.5 (820.7) | 1392.8 (870.8) | 1411.5 (878.8) | 1153.4 (722.9) |

# Results: Clinical Characteristics

- Overall study population predominantly consists of subjects with RA (39%) and Ps/PsA (32%)
- Anti-IL-17 population predominantly subjects with Ps/PsA (88%)

## Distribution of Patients Across Exposure Groups and Autoimmune Disease Cohorts

| | Not treated with anti-TNF/anti-IL-17 (n, %) N = 1,991,595 | Anti-TNF/anti-IL-17 n (%) N = 114,082 | Anti-TNF only n (%) N = 106,314 | Anti-IL-17 only n (%) N = 5,672 |
|---|---|---|---|---|
| RA | 769,062 (39) | 41,728 (37) | 41,357 (39) | 198 (3) |
| UC | 273,556 (14) | 11,911 (10) | 11,908 (11) | 2 (0) |
| CD | 171,026 (9) | 17,266 (15) | 17,263 (16) | 2 (0) |
| AS | 41,729 (2) | 7,014 (6) | 6,376 (6) | 275 (5) |
| Ps/PsA | 645,912 (32) | 29,714 (26) | 23,332 (22) | 4,993 (88) |
| ≥1 autoimmune disease | 90,310 (5) | 6,449 (6) | 6,078 (6) | 202 (4) |

# Results: PD Incidence (Unadjusted)

Summary of PD Incidence Among Anti-TNF/ Anti-IL-17 Treated vs No Exposure

| Variable | PD event | Person Year |
|---|---|---|
| **Anti-TNF/anti-IL-17 treatment** | | |
| **Yes** | 2,597 | 393,114.3 |
| **No** | 50,562 | 5,328,307.4 |

- PD incidence rates:
  - Exposed cohort: 0.661 per 100-person year (PY)
    - 0.661 (95% CI: 0.634, 0.687)
  - Unexposed cohort: 0.949 per 100 PY
    - 0.949 (95% CI: 0.949, 0.957)

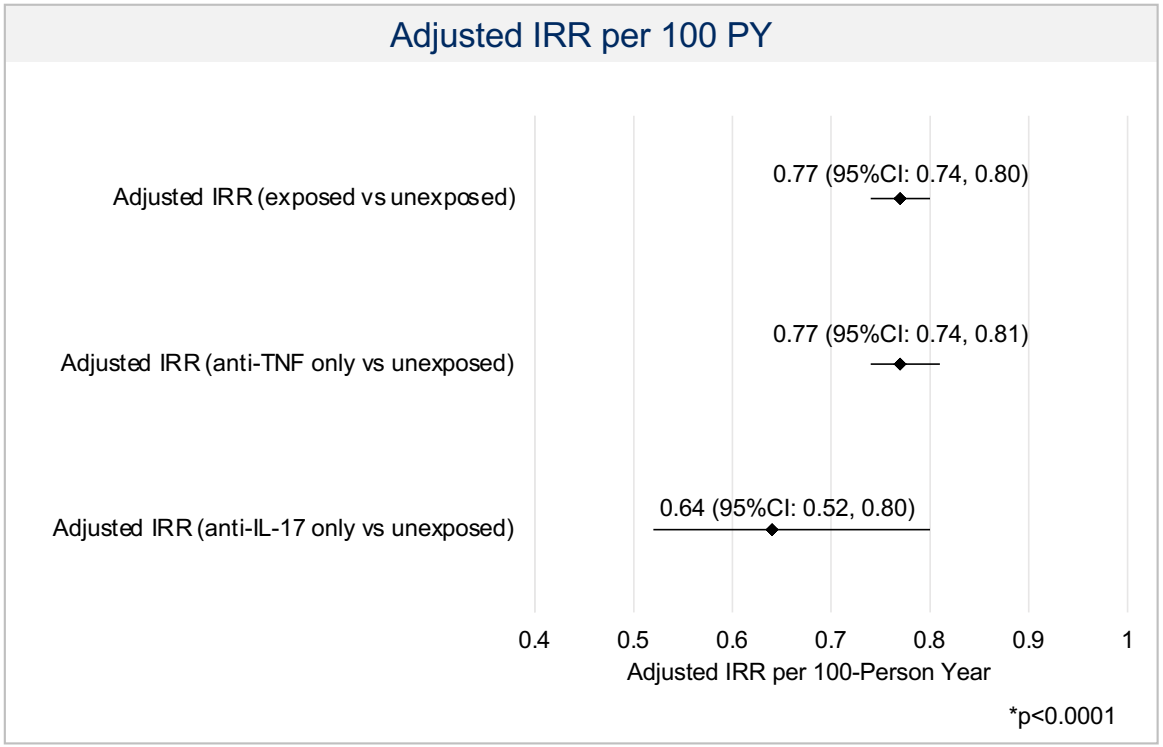
- Unadjusted IRR: 0.696 (95% CI: 0669, 0.724)

**Crude analysis indicates reduced incidence of PD associated with treatment**

# Results: PD Incidence (Adjusted)

Summary of PD Incidence Among Anti-TNF/ Anti-IL-17 Treated vs No Exposure

| Variable | PD event | Person Year |
|---|---|---|
| **Anti-TNF/anti-IL-17 treatment** | | |
| **Yes** | 2,597 | 393,114.3 |
| **No** | 50,562 | 5,328,307.4 |
| **Anti-TNF only treatment** | | |
| **Yes** | 2,471 | 371,667.4 |
| **No** | 50,562 | 5,328,307.4 |
| **Anti-IL-17 only treatment** | | |
| **Yes** | 81 | 15,598.3 |
| **No** | 50,562 | 5,328,307.4 |




**Results suggested use of either anti-TNF and anti-IL-17 may be associated with a reduction in PD incidence**

# Conclusions

- Among individuals with autoimmune conditions and targeted anti-inflammatory treatment, specifically anti-TNF and anti-IL-17, a lower PD incidence rate was observed in comparison to those not treated (unadjusted and adjusted)

- Lowering the levels of systemic inflammation may be associated with a reduced risk of PD

# Thank you!