

## **SUPPLEMENTARY MATERIAL**

**Title: Burden of glucocorticoid use and risk of toxicities among patients with immunoglobulin-G4-related disease – A retrospective US-based claims study**

### **Author list:**

Author 1<sup>1</sup>: Zachary S. Wallace, MD, MSc

Author 2<sup>2</sup>: Jenny Y. Park, PharmD, MS

Author 3<sup>3</sup>: Elizabeth Serra, MScPH

Author 4<sup>3</sup>: Patrick Gagnon-Sanschagrin, MS

Author 5<sup>3</sup>: Annie Guérin, MSc

Author 6<sup>2</sup>: Kristina Patterson, MD, PhD

Author 7<sup>2</sup>: Haridarshan Patel, PharmD, PhD

Author 8<sup>4</sup>: Vikesh K. Singh<sup>4</sup>, MD, MSc

### **Affiliations:**

<sup>1</sup> Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Rheumatology and Allergy Clinical Epidemiology Research Center, 100 Cambridge Street, 16th Floor, Boston, MA 02114, USA

<sup>2</sup> Amgen Inc, 1 Amgen Center Drive, Thousand Oaks, CA 91320, USA

<sup>3</sup> Analysis Group, Inc., 1190 avenue des Canadiens-de-Montréal, Tour Deloitte, Suite 1500, Montréal, QC, H3C 1B3, Canada

<sup>4</sup> Division of Gastroenterology, Johns Hopkins Medical Institutions, 1830 E. Monument St, Room 436, Baltimore, MD 21287

### **Corresponding author**

Jenny Y. Park, PharmD, MS

Amgen Inc, 1 Amgen Center Drive, Thousand Oaks, CA 91320, USA

*Email:* [jenpark217@gmail.com](mailto:jenpark217@gmail.com)

**Supplementary Table 1. Patient demographic characteristics in the subgroup analysis**

| Patient characteristics <sup>1</sup>   | Among patients with pancreatic or biliary manifestations |                       |
|----------------------------------------|----------------------------------------------------------|-----------------------|
|                                        | Low GC use<br>N = 36                                     | High GC use<br>N = 74 |
| <b>Age, mean ± SD [median]</b>         | 50.9 ± 12.4 [54.5]                                       | 52.8 ± 13.0 [57.5]    |
| <b>Female, N (%)</b>                   | 19 (52.8%)                                               | 29 (39.2%)            |
| <b>Region of residence, N (%)</b>      |                                                          |                       |
| South                                  | 11 (30.6%)                                               | 25 (33.8%)            |
| Midwest                                | 12 (33.3%)                                               | 24 (32.4%)            |
| Northeast                              | < 5                                                      | 14 (18.9%)            |
| West                                   | 9 (25.0%)                                                | 10 (13.5%)            |
| Unknown                                | < 5                                                      | < 5                   |
| <b>Primary health plan type, N (%)</b> |                                                          |                       |
| Preferred Provider Organization        | 24 (66.7%)                                               | 55 (74.3%)            |
| Health Maintenance Organization        | < 5                                                      | 9 (12.2%)             |
| Point of Service                       | < 5                                                      | 6 (8.1%)              |
| Consumer Directed Health Care          | < 5                                                      | < 5                   |
| Indemnity/Traditional                  | < 5                                                      | < 5                   |
| Other/Unknown                          | < 5                                                      | < 5                   |

**Abbreviations:** GC, glucocorticoid; N, number; SD, standard deviation

**Note:**

1. Patient characteristics were assessed as of the index date.

**Supplementary Table 2. Patient clinical characteristics in the subgroup analysis**

| Clinical characteristics <sup>1</sup>                                      | Among patients with pancreatic or biliary manifestations |                             |
|----------------------------------------------------------------------------|----------------------------------------------------------|-----------------------------|
|                                                                            | Low GC use<br>N = 36                                     | High GC use<br>N = 74       |
| <b>PED summary</b>                                                         |                                                          |                             |
| Patients with any GC use <sup>2</sup> , N (%)                              | 26 (72.2%)                                               | 74 (100.0%)                 |
| Number of GC prescription fills, mean ± SD [median]                        | 1.8 ± 2.4 [1.0]                                          | 5.8 ± 3.6 [5.0]             |
| PEDD (mg), mean ± SD [median]                                              | 1.6 ± 1.6 [1.2]                                          | 12.2 ± 6.4 [10.0]           |
| Cumulative PED (mg), mean ± SD [median]                                    | 592.7 ± 585.3 [422.3]                                    | 4,448.4 ± 2,350.6 [3,632.5] |
| Cumulative days of supply, mean ± SD [median]                              | 39.5 ± 69.8 [22.5]                                       | 176.8 ± 110.7 [132.5]       |
| <b>IgG4-RD treatments, N (%)</b>                                           |                                                          |                             |
| <i>GC</i>                                                                  | 26 (72.2%)                                               | 74 (100.0%)                 |
| Prednisone                                                                 | 19 (52.8%)                                               | 71 (95.9%)                  |
| Dexamethasone                                                              | 5 (13.9%)                                                | 7 (9.5%)                    |
| Methylprednisolone                                                         | 7 (19.4%)                                                | < 5                         |
| Prednisolone                                                               | < 5                                                      | < 5                         |
| <i>Non-steroidal</i>                                                       | 17 (47.2%)                                               | 35 (47.3%)                  |
| Azathioprine                                                               | 5 (13.9%)                                                | 26 (35.1%)                  |
| Methotrexate                                                               | < 5                                                      | < 5                         |
| Mycophenolate mofetil                                                      | < 5                                                      | 5 (6.8%)                    |
| Rituximab                                                                  | 9 (25.0%)                                                | 11 (14.9%)                  |
| Mycophenolic acid                                                          | < 5                                                      | < 5                         |
| <b>Manifestation of IgG4-RD, N (%)</b>                                     |                                                          |                             |
| Pancreas                                                                   | 29 (80.6%)                                               | 68 (91.9%)                  |
| Biliary                                                                    | 25 (69.4%)                                               | 57 (77.0%)                  |
| Sialadenitis                                                               | < 5                                                      | 7 (9.5%)                    |
| Lacrimal                                                                   | < 5                                                      | < 5                         |
| Retroperitoneum                                                            | < 5                                                      | < 5                         |
| Mesenteritis                                                               | < 5                                                      | < 5                         |
| Orbit                                                                      | < 5                                                      | < 5                         |
| Aortitis                                                                   | < 5                                                      | < 5                         |
| <b>Top 5 most frequent specialists involved in care<sup>3</sup>, N (%)</b> |                                                          |                             |
| Internal medicine                                                          | 17 (47.2%)                                               | 29 (39.2%)                  |
| Gastroenterology                                                           | 24 (66.7%)                                               | 44 (59.5%)                  |
| Rheumatology                                                               | 9 (25.0%)                                                | 13 (17.6%)                  |
| Ophthalmology                                                              | < 5                                                      | 14 (18.9%)                  |
| Cardiology                                                                 | 6 (16.7%)                                                | 15 (20.3%)                  |
| <b>CCI, mean ± SD [median]</b>                                             | <b>2.5 ± 2.5 [2.0]</b>                                   | <b>2.7 ± 2.3 [2.0]</b>      |

**Comorbidities, N (%)**

|                                   |            |            |
|-----------------------------------|------------|------------|
| Hypertension                      | 11 (30.6%) | 29 (39.2%) |
| Hyperlipidemia                    | 13 (36.1%) | 26 (35.1%) |
| Gastro-esophageal reflux          | 10 (27.8%) | 12 (16.2%) |
| Malignant neoplasms               | 8 (22.2%)  | 11 (14.9%) |
| Type 2 diabetes mellitus          | 7 (19.4%)  | 24 (32.4%) |
| Muscle weakness                   | < 5        | < 5        |
| Cardiac arrhythmias               | < 5        | 5 (6.8%)   |
| Chronic kidney disease            | < 5        | < 5        |
| Congestive heart failure          | < 5        | < 5        |
| Glaucoma                          | < 5        | < 5        |
| Exocrine pancreatic insufficiency | < 5        | 12 (16.2%) |
| Any pneumonia                     | < 5        | < 5        |
| Osteoporosis                      | < 5        | 6 (8.1%)   |
| Atrial fibrillation               | < 5        | < 5        |
| Cataract                          | < 5        | < 5        |
| Hyperglycemia                     | < 5        | < 5        |
| Stroke (cerebral infarction)      | < 5        | < 5        |

**Abbreviations:** CCI, Charlson Comorbidity Index; GC, glucocorticoid; IgG4-RD, immunoglobulin G4-related disease; mg, milligram; N, number; PEDD, prednisone equivalent daily dose; SD, standard deviation

**Notes:**

1. Clinical characteristics were assessed during the study period.
2. Glucocorticoids used in PED calculations included systemic (oral, injection, or intravenous) prednisone, prednisolone, methylprednisolone, and dexamethasone. Medical claims were not used since dose could not be reliably assessed (i.e., only pharmacy claims contained required strength and quantity information).
3. Specialist involved in care was defined as the billing provider, as reported in IQVIA PharMetrics® Plus, observed in any outpatient visit claim(s) for each patient.

**Supplementary Table 3. Incident GC-related toxicities in the subgroup analysis**

| Incident GC-related toxicities <sup>1</sup>                                   | Among patients with pancreatic or biliary manifestations |                       | P-value     |
|-------------------------------------------------------------------------------|----------------------------------------------------------|-----------------------|-------------|
|                                                                               | Low GC use<br>N = 36                                     | High GC use<br>N = 74 |             |
| <b>Any incident GC-related toxicity, N (%)</b>                                | <b>30 (83.3%)</b>                                        | <b>62 (83.8%)</b>     | <b>0.95</b> |
| Number of distinct GC-related toxicities <sup>2</sup> ,<br>mean ± SD [median] | 1.7 ± 1.6 [1.0]                                          | 2.0 ± 1.5 [2.0]       | 0.27        |
| No GC-related toxicities                                                      | 6 (16.7%)                                                | 12 (16.2%)            | 0.95        |
| 1 GC-related toxicity                                                         | 15 (41.7%)                                               | 17 (23.0%)            | 0.04        |
| 2 GC-related toxicities                                                       | 7 (19.4%)                                                | 18 (24.3%)            | 0.57        |
| ≥ 3 GC-related toxicities                                                     | 8 (22.2%)                                                | 27 (36.5%)            | 0.13        |
| <b>Cardiovascular, N (%)</b>                                                  | <b>10 (27.8%)</b>                                        | <b>24 (32.4%)</b>     | <b>0.62</b> |
| Cardiac arrhythmias                                                           | < 5                                                      | 7 (9.5%)              | 0.72        |
| Hypertension                                                                  | < 5                                                      | 9 (12.2%)             | 0.34        |
| Myocardial infarction                                                         | < 5                                                      | 7 (9.5%)              | 0.27        |
| Dyslipidemia                                                                  | 5 (13.9%)                                                | 7 (9.5%)              | 0.52        |
| <b>Gastrointestinal, N (%)</b>                                                | <b>12 (33.3%)</b>                                        | <b>30 (40.5%)</b>     | <b>0.47</b> |
| Nausea and vomiting                                                           | 8 (22.2%)                                                | 18 (24.3%)            | 0.81        |
| Gastrointestinal ulcers and bleeds                                            | 7 (19.4%)                                                | 17 (23.0%)            | 0.67        |
| <b>Infections, N (%)</b>                                                      | <b>9 (25.0%)</b>                                         | <b>25 (33.8%)</b>     | <b>0.35</b> |
| Fungal infections                                                             | 5 (13.9%)                                                | 6 (8.1%)              | 0.50        |
| Urinary tract infection                                                       | < 5                                                      | 8 (10.8%)             | 0.27        |
| Pneumonia                                                                     | < 5                                                      | 6 (8.1%)              | 1.00        |
| Sepsis                                                                        | < 5                                                      | 8 (10.8%)             | 0.49        |
| <b>Metabolic/Endocrine, N (%)</b>                                             | <b>&lt; 5</b>                                            | <b>16 (21.6%)</b>     | <b>0.18</b> |
| Type 2 diabetes mellitus                                                      | < 5                                                      | 7 (9.5%)              | 0.72        |
| Obesity                                                                       | < 5                                                      | 9 (12.2%)             | 0.34        |
| <b>Musculoskeletal, N (%)</b>                                                 | <b>7 (19.4%)</b>                                         | <b>13 (17.6%)</b>     | <b>0.81</b> |
| Osteoporosis                                                                  | < 5                                                      | 7 (9.5%)              | 0.27        |
| Myopathy, paralysis, and other muscle weakness                                | 5 (13.9%)                                                | 8 (10.8%)             | 0.75        |
| <b>Neuropsychiatric, N (%)</b>                                                | <b>11 (30.6%)</b>                                        | <b>13 (17.6%)</b>     | <b>0.12</b> |
| Anxiety                                                                       | < 5                                                      | 10 (13.5%)            | 0.54        |
| <b>Ophthalmologic, N (%)</b>                                                  | <b>&lt; 5</b>                                            | <b>7 (9.5%)</b>       | <b>0.27</b> |
| Cataract                                                                      | < 5                                                      | 7 (9.5%)              | 0.27        |

**Abbreviations:** GC, glucocorticoid; N, number; SD, standard deviation

**Notes:**

- Individual toxicities with a frequency of < 5 in both groups are not displayed (i.e., bipolar disorder, depression, fractures, herpes zoster, metabolic syndrome, migraine, osteonecrosis, psychosis, sleep disturbances, tuberculosis).
- Number of distinct GC-related toxicities was defined as the count of GC-related toxicities for which a patient had ≥ 1 claim with the respective diagnosis code(s).