

SUPPLEMENTARY MATERIALS

Improved Health Outcomes in Patients With Systemic Lupus Erythematosus Following Early Belimumab Initiation Without Prior Immunosuppressant Use: A Real-World Descriptive Study

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Table S1. SLE disease severity algorithm

| Severity of disease | Criteria |
|----------------------------|--|
| Severe | ≥1 filled prescription for cyclophosphamide, rituximab, or OGC with a prednisone-equivalent dose of ≥60 mg/day |
| | ≥1 non-laboratory claims ^a with a diagnosis listed as 'severe,' where the diagnosis occurs in any position on the claim ^b |
| Moderate | No filled prescriptions for cyclophosphamide, rituximab, or OGC with ≥60 mg/day of prednisone-equivalent dose |
| | No claims with a diagnosis of a 'severe' condition |
| | Met at least one of the following criteria at any time during the follow-up period: <ul style="list-style-type: none"> • ≥1 non-laboratory claims with a diagnosis of a condition listed as 'moderate,' where the diagnosis occurs in any position on the claim^b • ≥1 filled prescription for OGC with a prednisone-equivalent dose of ≥7.5 mg/day and <60 mg/day, or a prescription or for an immunosuppressive agent (other than cyclophosphamide) |
| Mild | Did not meet the criteria for moderate or severe disease |

^aLaboratory claims were defined as claims with a Place of Service value of 81 (independent laboratory); ^ba list of moderate and severe diagnoses and their associated disease codes are listed in

Table S2.

OGC, oral glucocorticoid; SLE, systemic lupus erythematosus.

Table S2. List of moderate and severe SLE diagnoses and associated disease codes

| Severity of disease | Diagnosis | ICD-9-CM | ICD-10-CM |
|---------------------|-----------------------------------|---|---|
| Severe | Acute confusional state/psychosis | 290.11, 290.3, 290.41, 293.0, 293.1, 298.2 | F03.90, F03.90, F01.51, F05, F44.89 |
| | Aortitis | 447.6 | I77.6 |
| | Arterial/venous thrombosis | 444.xx, 445.xx, 452.x, 453.xx, 362.30, 362.31, 362.32, 362.33, 362.35, 362.36 | I81, I82.0, I82.1, I82.210, I82.211, I82.220, I82.221, I82.290, I82.291, I82.3, I82.401, I82.402, I82.403, I82.409, I82.411, I82.412, I82.413, I82.419, I82.421, I82.422, I82.423, I82.429, I82.431, I82.432, I82.433, I82.439, I82.441, I82.442, I82.443, I82.449, I82.491, I82.492, I82.493, I82.499, I82.4Y1, I82.4Y2, I82.4Y3, I82.4Y9, I82.4Z1, I82.4Z2, I82.4Z3, I82.4Z9, I82.501, I82.502, I82.503, I82.509, I82.511, I82.512, I82.513, I82.519, I82.521, I82.522, I82.523, I82.529, I82.531, I82.532, I82.533, I82.539, I82.541, I82.542, I82.543, I82.549, I82.591, I82.592, I82.593, I82.599, I82.5Y1, I82.5Y2, I82.5Y3, I82.5Y9, I82.5Z1, I82.5Z2, I82.5Z3, I82.5Z9, I82.601, I82.602, I82.603, I82.609, I82.611, I82.612, I82.613, I82.619, I82.621, I82.622, I82.623, I82.629, I82.701, I82.702, I82.703, I82.709, I82.711, I82.712, I82.713, I82.719, I82.721, I82.722, I82.723, I82.729, I82.811, I82.812, I82.813, I82.819, I82.890, I82.891, I82.90, I82.91, I82.A11, I82.A12, I82.A13, I82.A19, I82.A21, I82.A22, I82.A23, I82.A29, I82.B11, I82.B12, I82.B13, I82.B19, I82.B21, I82.B22, I82.B23, I82.B29, I82.C11, I82.C12, I82.C13, I82.C19, I82.C21, I82.C22, I82.C23, I82.C29, K64.5, I67.6, N48.81, I63.6, G08, I26.01, I26.02, I26.09, I26.90, I26.92, |

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| | | I26.99, Z86.718, I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.4, I22.0, I22.1, I22.2, I22.8, I22.9, I24.0, I26.01, I26.02, I26.09, I26.90, I26.92, I26.99, I63.00, I63.011, I63.012, I63.013, I63.019, I63.02, I63.031, I63.032, I63.033, I63.039, I63.09, I63.30, I63.311, I63.312, I63.313, I63.319, I63.321, I63.322, I63.323, I63.329, I63.331, I63.332, I63.333, I63.339, I63.341, I63.342, I63.343, I63.349, I63.39, I65.01, I65.02, I65.03, I65.09, I65.1, I65.21, I65.22, I65.23, I65.29, I65.8, I65.9, I66.01, I66.02, I66.03, I66.09, I66.11, I66.12, I66.13, I66.19, I66.21, I66.22, I66.23, I66.29, I66.3, I66.8, I66.9, I74.01, I74.09, I74.10, I74.11, I74.19, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, G95.11, H34.00, H34.01, H34.02, H34.03, H34.10, H34.11, H34.12, H34.13, H34.211, H34.212, H34.213, H34.219, K55.0, K55.069, M31.1, N28.0 |
| Aseptic meningitis | 322.0 | G03.0 |
| Cardiac tamponade | 423.3, 423.0 | I31.4 |
| Cranial neuropathy | 350.x, 351.x, 352.x | G50.x, G51.x, G52.x, G53 |
| End stage renal disease | 458.21, 585.6, 792.5, 996.56, 996.73, 996.81, V42.0, V45.1x, V56.0, V56.1, V56.2, V56.3x, V56.8 | I95.3, N18.6, R88.0, T85.691A, T82.818A, T82.828A, T82.838A, T82.848A, T82.858A, T82.868A, T82.898A, T86.10, T86.11, T86.12, Z94.0, Z99.2, Z91.15, Z49.31, Z49.01, Z49.02, Z49.31, Z49.32 |
| Intestinal pseudo-obstruction | 569.89 | K59.8 |
| Optic neuritis | 377.3x | H46.x |
| Pulmonary hemorrhage | 786.3, 446.21 | R04.2, R04.9, R04.89, M31.0 |
| Stroke/transient ischemic attack | 430, 431, 432.x, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, | I60.x, I61.x I62.x, I63.00, I63.011, I63.012, I63.019, I63.02, I63.031, I63.032, I63.039, I63.09, I63.10, I63.111, I63.112, I63.119, I63.12, I63.131, I63.132, I63.139, I63.19, I63.20, I63.211, I63.212, I63.219, I63.22, I63.231, I63.232, I63.239, I63.29, I63.30, I63.311, I63.312, I63.319, I63.321, I63.322, |

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| | | 434.91, 437.1, 362.34, 435.x | I63.329, I63.331, I63.332, I63.339, I63.341, I63.342, I63.349, I63.39, I63.40, I63.411, I63.412, I63.419, I63.421, I63.422, I63.429, I63.431, I63.432, I63.439, I63.441, I63.442, I63.449, I63.49, I63.50, I63.511, I63.512, I63.519, I63.521, I63.522, I63.529, I63.531, I63.532, I63.539, I63.541, I63.542, I63.549, I63.59, I63.6, I63.8, I63.9, I97.810, I97.811, I97.820, I97.821, G45.0, G45.1, G45.2, G45.8, G45.9, G46.0, G46.1, G46.2, I67.841, I67.848 |
| Moderate | Acute pancreatitis | 577.0 | B25.2, K85.00, K85.01, K85.02, K85.10, K85.11, K85.12, K85.20, K85.21, K85.22, K85.30, K85.31, K85.32, K85.80, K85.81, K85.82, K85.90, K85.91, K85.92 |
| | Chorioretinitis | 363.0x, 363.10, 363.11, 363.12, 363.13, 363.20 | H30.001, H30.002, H30.003, H30.009, H30.011, H30.012, H30.013, H30.019, H30.021, H30.022, H30.023, H30.029, H30.031, H30.032, H30.033, H30.039, H30.041, H30.042, H30.043, H30.049, H30.101, H30.102, H30.103, H30.109, H30.111, H30.112, H30.113, H30.119, H30.121, H30.122, H30.123, H30.129, A18.53, H30.131, H30.132, H30.133, H30.139, H30.891, H30.892, H30.893, H30.899, H30.90, H30.91, H30.92, H30.93 |
| | Demyelinating syndrome/acute inflammatory demyelinating polyradiculoneuropathy | 357.81, 357.82, 341.8, 341.9 | G61.81, G62.81, G36.1, G36.8, G37.1, G37.2, G3.4, G37.8, G36.9, G37.9 |
| | Episcleritis/scleritis | 379.0x | H15.001, H15.002, H15.003, H15.009, H15.101, H15.102, H15.103, H15.109, H15.111, H15.112, H15.113, H15.119, H15.121, H15.122, H15.123, H15.129, H15.011, H15.012, H15.013, H15.019, H15.051, H15.052, H15.053, H15.059, H15.041, H15.042, H15.043, H15.049, H15.021, H15.022, H15.023, H15.029, H15.031, |

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| | | | H15.032, H15.033, H15.039, A18.51, H15.091, H15.092, H15.093, H15.099 |
| | Hemolytic anemia | 283.0, 283.9 | D59.0, D59.1, D59.9 |
| | Hepatitis (non-viral) | 571.4x | K73.9, K73.0, K75.4, K73.1, K73.2, K73.8 |
| | Ischemic necrosis of bone | 733.4x | M87.x, M90.5x |
| | Lupus enteritis/colitis | 558.9 | K52.29, K52.3, K52.831, K52.832, K52.838, K52.839, K52.89, K52.9 |
| | Mononeuropathy/polyneuropathy | 354.x, 355.x, 357.1, 357.4 | G56.x, G57.x, G58.7, G58.0, G58.8, G58.9, G59, E08.41, E09.41, E10.41, E11.41, E13.41, G63, M05.5x, A52.15, G63, G65.0, G65.1, G65.2, M34.83 |
| | Myelopathy | 336.3, 323.82, 341.20, 341.21 | G99.2, G04.89, G37.3 |
| | Myocarditis | 422.0, 422.90, 422.99 | A18.84, I41, I40.9, I40.8 |
| | Nephritis | 580.xx, 582.xx, 583.xx, 581.xx | N00.x, N01.x, N03.x, N08, N05.2, N06.2, N07.2, N05.3, N05.4, N05.5, N06.3, N06.4, N06.5, N07.3, N07.4, N07.5, N05.9, N17.1, N17.2, E09.21, E09.22, E09.29, M32.14, M32.15, M35.04, N16, N05.0, N05.1, N05.6, N05.7, N05.8, N06.0, N06.1, N06.6, N06.7, N06.8, N07.0, N07.1, N07.6, N07.7, N07.8, N14.0, N14.1, N14.2, N14.3, N14.4, N15.0, N15.8, N06.9, N07.9, N15.9, N04.4, N02.1, N02.2, N02.3, N04.1, N04.2, N02.4, N02.5, N02.6, N02.7, N04.3, N04.4, N04.5, N04.6, N02.0, N04.0, B52.0, E08.21, E08.22, E08.29, E09.21, E09.22, E09.29, N02.8, N04.7, N04.8, N02.9, N04.9 |
| | Pericarditis | 420.0, 420.90, 423.2 | A18.84, I32, M32.12, I30.1, I30.9, I31.1 |
| | Pleurisy/pleural effusion | 511.0, 511.89, 511.9 | J86.9, J92.0, J92.9, J94.1, J94.8, J94.9, R09.1, J90, J94.0, J94.2, |

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| | | | J94.8, J91.8 |
| | Pseudotumor cerebri | 377.01 | H47.11 |
| | Renal impairment other than nephritis or end stage renal disease (other renal impairment) | 285.21, 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 584.x, 585, 585.1, 585.2, 585.3, 585.4, 585.5, 585.9, 588.xx, 593.71, 593.72, 593.73, E879.1 | D63.1, I12.0, I13.11, I13.2, I13.11, I13.2, N17.0, N17.1, N17.2, N17.8, N17.9, N18.1, N18.2, N18.3, N18.4, N18.5, N18.9, N25.0, N25.1, N25.81, N25.89, N25.9, N13.721, N13.731, N13.722, N13.732, N13.729, N13.739, N13.9, Y84.1 |
| | Seizure | 780.3, 780.39 | R56.00, R56.01, R56.1, R56.9 |
| | Uveitis | 364.00, 364.01, 364.02, 364.04, 364.05, 364.10, 364.11, 364.3 | H20.00, H20.011, H20.012, H20.013, H20.019, H20.021, H20.022, H20.023, H20.029, H20.041, H20.042, H20.043, H20.049, H20.051, H20.052, H20.053, H20.059, H20.10, H20.11, H20.12, H20.13, A18.54, H20.9 |
| | Vasculitis (excluding aortitis) | 362.18, 437.4, 446.20, 446.29 | H35.061, H35.062, H35.069, I67.7, I68.2, M31.0 |

ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; SLE, systemic lupus erythematosus.

Table S3. Definition of SLE flares by severity

| Severity of disease | Criteria |
|---------------------|---|
| Severe | <p>Meets <u>≥1</u> of the following criteria:</p> <ul style="list-style-type: none"> • Initiation^a of <i>either</i> an OGC with prednisone-equivalent dose of >40 mg/day or cyclophosphamide • Admission for an inpatient stay with a primary diagnosis of SLE • Admission for an inpatient stay with a severe SLE-related condition: <ul style="list-style-type: none"> ○ Acute confusional state/psychosis, arthritis/arthralgia^b, aortitis, arterial/venous thrombosis, aseptic meningitis, cardiac tamponade, cranial neuropathy, dry eye/tear film insufficiency, intestinal pseudo- |

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|-----------------|---|
| | obstruction, end stage renal disease, low white blood cell count (leukopenia, neutropenia, lymphocytopenia) ^b , lymph node enlargement ^b , myalgia/myositis ^b , optic neuritis, pulmonary hemorrhage, rash ^b , stroke/transient ischemic attack, urticaria ^b |
| Moderate | <p>Meets <u>≥1</u> of the following criteria:</p> <ul style="list-style-type: none"> • Initiation^a of either an OGC with a prednisone-equivalent dose of ≥7.5 mg/day and ≤40 mg/day, or a prescription for an immunosuppressive agent (other than cyclophosphamide) • A claim for an emergency department visit with a primary diagnosis of SLE with no inpatient admission within 1 day • A claim for an emergency department or office visit (excluding visits associated with belimumab administration) with a primary or secondary diagnosis for the following moderate SLE-related conditions: <ul style="list-style-type: none"> ○ Arthritis/arthritis^b, chorioretinitis, demyelinating syndrome/acute inflammatory demyelinating polyradiculoneuropathy, dry eye/tear film insufficiency^b, episcleritis/scleritis, hemolytic anemia, hepatitis (non-viral), ischemic necrosis of bone, nephritis, other renal impairment, low white blood cell count (leukopenia, neutropenia, lymphocytopenia)^b, lupus enteritis/colitis, lymph node enlargement^b, mononeuropathy/polyneuropathy, myalgia/myositis^b, myelopathy, myocarditis, pericarditis, pleurisy/pleural effusion, pseudotumor cerebri, rash^b, seizure, urticaria^b, uveitis, vasculitis (excluding aortitis) |
| Mild | <p>Initiation^a of any of the following:</p> <ul style="list-style-type: none"> • Hydroxychloroquine or another antimalarial • OGC with prednisone-equivalent dose^b of ≤7.5 mg/day • Non-immunosuppressive therapy (e.g., NSAIDs, androgens) |

^aInitiation was categorized as filling of a prescription >60 days after the previous prescription fill date (the modified definition of flare categorized initiation of an immunosuppressant as filling of a prescription for an immunosuppressant >60 days after the supply of the former prescription ended);

^bincluded in both 'moderate' and 'severe' flare severity definitions.

NSAIDs, non-steroidal anti-inflammatory drugs; OGC, oral glucocorticoid; SLE, systemic lupus erythematosus.

Table S4. Medical conditions included in the definition of organ damage [1]

| System organ class | Medical condition |
|----------------------------|--|
| Cardiovascular | Valvular disease |
| | Cardiomyopathy (ventricular dysfunction) |
| | Angina or coronary artery bypass |
| | Myocardial infarction |
| | Pericarditis or pericardiectomy |
| Gastrointestinal | Any history of stricture or upper gastrointestinal tract surgery |
| | Mesenteric insufficiency |
| | Pancreatic insufficiency requiring enzyme replacement or with pseudocyst |
| | Chronic peritonitis |
| | Any history of infarction or resection of bowel below duodenum, spleen, liver, or gallbladder of any cause |
| General | Diabetes |
| | Malignancy (excluding dysplasia) |
| Musculoskeletal | Avascular necrosis |
| | Osteoporosis with fracture or vertebral collapse |
| | Muscle atrophy or weakness |
| | Osteomyelitis |
| | Ruptured tendon |
| | Deforming or erosive arthritis (including reducible deformities) |
| Neuropsychiatric | Cranial or peripheral neuropathy excluding optic |
| | Seizures |
| | Any history of cerebrovascular accident |
| | Cognitive impairment or major psychosis |
| | Transverse myelitis |
| Ocular | Cataract glaucoma |
| | Retinal damage or optic atrophy |
| Peripheral vascular | Venous thrombosis with swelling, ulceration, or venous stasis |
| | Minor tissue loss (pulp space) |
| | Significant tissue loss |
| | Claudication |
| Reproductive | Premature gonadal failure |
| Pulmonary | Pleural fibrosis |
| | Pulmonary hypertension |
| | Pulmonary fibrosis |
| | Pulmonary infarction |
| Renal | Chronic kidney disease |
| | End-stage renal disease |
| | Nephrotic syndrome |
| Skin | Scarring chronic alopecia |
| | Skin ulceration |
| | Extensive scarring of panniculus other than scalp and pulp space |

SUPPLEMENTARY REFERENCES

1. Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. *Arthritis Rheum.* 1996;39(3):363-9.