

**Association Between Surrogate Endpoints and Clinical Outcomes in  
Immunoglobulin A Nephropathy: A Systematic Literature Review**

**Supplementary Material**

Maria Lorenzi,<sup>1\*</sup> Sarah N. Ali,<sup>2</sup> Sarah Cadarette,<sup>1</sup> Stephen Ebohon,<sup>3</sup> Vakaramoko Diaby,<sup>2</sup> Mohit Mathur,<sup>4</sup>  
Ancilla W. Fernandes<sup>2</sup>

<sup>1</sup>Cencora, 1 West First Avenue, Conshohocken, Pennsylvania 19428, United States of America.

<sup>2</sup>Otsuka Pharmaceutical Development and Commercialization, Inc., 508 Carnegie Center Drive,  
Princeton, New Jersey 08540, United States of America.

<sup>3</sup>Cencora, 5<sup>th</sup> Floor, Bush House, North West Wing, London WC2B 4PJ, United Kingdom.

<sup>4</sup>Visterra, Inc., 275 Second Avenue, Fourth Floor, Waltham, Massachusetts 02451, United States of  
America.

**\*Corresponding Author**

Maria Lorenzi

[maria.lorenzi@cencora.com](mailto:maria.lorenzi@cencora.com)

**Table S1. Embase, MEDLINE, and CENTRAL search strategies: Initial search – February 2022**

| #  | Search string                                                                | Number of hits (23 February 2022) |
|----|------------------------------------------------------------------------------|-----------------------------------|
| 1  | (IGA nephro\$ or igan).ti,ab.                                                | 19,885                            |
| 2  | Berger's disease.mp.                                                         | 453                               |
| 3  | (nephropathy adj3 (immunoglobulin or Ig)).ti,ab.                             | 3,356                             |
| 4  | *Glomerulonephritis, IGA/ use medall                                         | 5,700                             |
| 5  | *Glomerulonephritis, IGA/ use cctr                                           | 169                               |
| 6  | *immunoglobulin A nephropathy/ use oomezd                                    | 7,877                             |
| 7  | 1 or 2 or 3 or 4 or 5 or 6                                                   | 22,070                            |
| 8  | Clinical trial/                                                              | 1,562,498                         |
| 9  | exp Randomized controlled trial/                                             | 1,259,435                         |
| 10 | Randomization/ use oomezd                                                    | 93,117                            |
| 11 | Prospective study/ use oomezd                                                | 747,397                           |
| 12 | Single blind procedure/ use oomezd                                           | 45,265                            |
| 13 | Double blind procedure/ use oomezd                                           | 192,620                           |
| 14 | Crossover procedure/ use oomezd                                              | 69,519                            |
| 15 | Placebo/ use oomezd                                                          | 377,287                           |
| 16 | Random allocation/ use medall                                                | 106,628                           |
| 17 | Double blind method/ use medall                                              | 170,217                           |
| 18 | Single blind method/ use medall                                              | 31,637                            |
| 19 | Random allocation/ use cctr                                                  | 20,704                            |
| 20 | Double blind method/ use cctr                                                | 146,049                           |
| 21 | Single blind method/ use cctr                                                | 22,792                            |
| 22 | Controlled clinical trial/ use oomezd                                        | 465,055                           |
| 23 | Placebos/ use medall                                                         | 35,896                            |
| 24 | Placebos/ use cctr                                                           | 24,478                            |
| 25 | (allocated adj2 random).ti,ab.                                               | 2,837                             |
| 26 | Placebo\$.ti,ab.                                                             | 906,473                           |
| 27 | (clinic\$ adj trial\$1).ti,ab.                                               | 1,239,970                         |
| 28 | ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab. | 749,479                           |
| 29 | Randomi?ed controlled trial\$.ti,ab.                                         | 710,335                           |
| 30 | comparative study/ use medall                                                | 1,909,254                         |
| 31 | follow-up studies/ use medall                                                | 682,002                           |
| 32 | time factors/ use medall                                                     | 1,225,258                         |
| 33 | comparative study/ use cctr                                                  | 9                                 |
| 34 | follow-up studies/ use cctr                                                  | 62,662                            |
| 35 | time factors/ use cctr                                                       | 67,119                            |

| #  | Search string                                                                                     | Number of hits (23 February 2022) |
|----|---------------------------------------------------------------------------------------------------|-----------------------------------|
| 36 | Treatment outcome/ use oomezd                                                                     | 911,451                           |
| 37 | major clinical study/ use oomezd                                                                  | 4,384,402                         |
| 38 | controlled study/ use oomezd                                                                      | 8,663,479                         |
| 39 | clinical trial/ use oomezd                                                                        | 1,028,476                         |
| 40 | ((prospective\$ or retrospective\$) adj1 (study or studies)).tw.                                  | 1,022,532                         |
| 41 | (cohort\$ or case series).tw.                                                                     | 2,235,114                         |
| 42 | ((compare\$ or compara\$) adj1 (study or studies)).tw.                                            | 465,138                           |
| 43 | Meta-Analysis as Topic/ use medall                                                                | 20,906                            |
| 44 | Meta-Analysis as Topic/ use cctr                                                                  | 286                               |
| 45 | ((meta adj analy\$) or metaanalys\$).tw.                                                          | 534,696                           |
| 46 | (systematic adj (review\$1 or overview\$1)).tw.                                                   | 530,442                           |
| 47 | exp Review Literature as Topic/ use medall                                                        | 18,926                            |
| 48 | exp Review Literature as Topic/ use cctr                                                          | 51                                |
| 49 | or/8-48                                                                                           | 19,933,214                        |
| 50 | exp kidney failure/ use oomezd                                                                    | 423,867                           |
| 51 | exp end stage renal disease/ use oomezd                                                           | 42,582                            |
| 52 | Kidney Failure, Chronic/ use medall                                                               | 98,050                            |
| 53 | Kidney Failure, Chronic/ use cctr                                                                 | 4,876                             |
| 54 | (ESKF or ESKF or “end stage kidney disease” or “end stage renal disease” or “kidney failure”).tw. | 137,795                           |
| 55 | exp renal replacement therapy/ use oomezd                                                         | 210,874                           |
| 56 | exp Renal Replacement Therapy/ use medall                                                         | 224,203                           |
| 57 | exp Renal Replacement Therapy/ use cctr                                                           | 9,427                             |
| 58 | (“renal replacement” or dialysis).tw.                                                             | 323,868                           |
| 59 | Mortality/                                                                                        | 868,173                           |
| 60 | (mortal* or death).tw.                                                                            | 3,824,554                         |
| 61 | creatinine blood level/ use oomezd                                                                | 129,103                           |
| 62 | creatinine.tw.                                                                                    | 355,018                           |
| 63 | exp glomerulus filtration rate/ use oomezd                                                        | 124,966                           |
| 64 | Glomerular Filtration Rate/ use medall                                                            | 48,158                            |
| 65 | Glomerular Filtration Rate/ use cctr                                                              | 2,948                             |
| 66 | (eGFR or “glomerular filtration rate”).tw.                                                        | 298,923                           |
| 67 | or/50-66                                                                                          | 5,262,724                         |
| 68 | 7 and 49 and 67                                                                                   | 5,405                             |
| 69 | exp animals/ not humans/                                                                          | 17,061,302                        |
| 70 | letter/ or editorial/ or case report/                                                             | 8,110,792                         |
| 71 | (letter or editorial or comment\$ or note or conference\$).pt.                                    | 9,981,757                         |

| #  | Search string                  | Number of hits (23 February 2022) |
|----|--------------------------------|-----------------------------------|
| 72 | or/69-71                       | 27,632,428                        |
| 73 | 68 not 72                      | 3,135                             |
| 74 | conference abstract.pt.        | 4,343,208                         |
| 75 | limit 74 to yr="1974 – 2018"   | 3,405,808                         |
| 76 | 73 not 75                      | 3,135                             |
| 77 | limit 76 to yr="2006 -Current" | 2,128                             |
| 78 | limit 77 to 4edal4h language   | 1,994                             |
| 79 | remove duplicates from 78      | 1,479                             |

Key: ab – abstract; adj – adjacent; cctr – controlled vocabulary search of CENTRAL; CENTRAL – Cochrane Central Register of Controlled Trials; exp – explode; 4edal – controlled vocabulary search of MEDLINE; mp – multipurpose; oomezd – controlled vocabulary search of Embase; pt – publication type; ti – title; tw – text word; yr – year.

**Table S2. Embase, MEDLINE, and CENTRAL search strategies: Update search – September 2023**

| #  | Search string                                                                | Results from 1 Sep 2023 |
|----|------------------------------------------------------------------------------|-------------------------|
| 1  | (IGA nephro\$ or igan).ti,ab.                                                | 22,468                  |
| 2  | Berger's disease.mp.                                                         | 465                     |
| 3  | (nephropathy adj3 (immunoglobulin or Ig)).ti,ab.                             | 4,016                   |
| 4  | *Glomerulonephritis, IGA/ use medall                                         | 6,277                   |
| 5  | *Glomerulonephritis, IGA/ use cctr                                           | 1                       |
| 6  | *immunoglobulin A nephropathy/ use oomezd                                    | 8,949                   |
| 7  | 1 or 2 or 3 or 4 or 5 or 6                                                   | 24,836                  |
| 8  | Clinical trial/                                                              | 1,627,777               |
| 9  | exp Randomized controlled trial/                                             | 1,409,305               |
| 10 | Randomization/ use oomezd                                                    | 98,322                  |
| 11 | Prospective study/ use oomezd                                                | 875,296                 |
| 12 | Single blind procedure/ use oomezd                                           | 51,580                  |
| 13 | Double blind procedure/ use oomezd                                           | 210,178                 |
| 14 | Crossover procedure/ use oomezd                                              | 75,184                  |
| 15 | Placebo/ use oomezd                                                          | 401,648                 |
| 16 | Random allocation/ use medall                                                | 106,957                 |
| 17 | Double blind method/ use medall                                              | 176,045                 |
| 18 | Single blind method/ use medall                                              | 32,894                  |
| 19 | Random allocation/ use cctr                                                  | 23,363                  |
| 20 | Double blind method/ use cctr                                                | 154,864                 |
| 21 | Single blind method/ use cctr                                                | 24,574                  |
| 22 | Controlled clinical trial/ use oomezd                                        | 470,841                 |
| 23 | Placebos/ use medall                                                         | 35,932                  |
| 24 | Placebos/ use cctr                                                           | 25,480                  |
| 25 | (allocated adj2 random).ti,ab.                                               | 2,742                   |
| 26 | Placebo\$.ti,ab.                                                             | 969,259                 |
| 27 | (clinic\$ adj trial\$1).ti,ab.                                               | 1,399,317               |
| 28 | ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).ti,ab. | 799,972                 |
| 29 | Randomi?ed controlled trial\$.ti,ab.                                         | 804,023                 |
| 30 | comparative study/ use medall                                                | 1,912,994               |
| 31 | follow-up studies/ use medall                                                | 692,986                 |
| 32 | time factors/ use medall                                                     | 1,230,391               |
| 33 | comparative study/ use cctr                                                  | 3,444                   |
| 34 | follow-up studies/ use cctr                                                  | 67,326                  |
| 35 | time factors/ use cctr                                                       | 72,566                  |

| #  | Search string                                                                                     | Results from 1 Sep 2023 |
|----|---------------------------------------------------------------------------------------------------|-------------------------|
| 36 | Treatment outcome/ use oomezd                                                                     | 966,757                 |
| 37 | major clinical study/ use oomezd                                                                  | 4,983,347               |
| 38 | controlled study/ use oomezd                                                                      | 9,839,401               |
| 39 | clinical trial/ use oomezd                                                                        | 1,069,782               |
| 40 | ((prospective\$ or retrospective\$) adj1 (study or studies)).tw.                                  | 1,149,382               |
| 41 | (cohort\$ or case series).tw.                                                                     | 2,634,804               |
| 42 | ((compare\$ or compara\$) adj1 (study or studies)).tw.                                            | 458,591                 |
| 43 | Meta-Analysis as Topic/ use medall                                                                | 22,846                  |
| 44 | Meta-Analysis as Topic/ use cctr                                                                  | 1,307                   |
| 45 | ((meta adj analy\$) or metaanalys\$).tw.                                                          | 644,242                 |
| 46 | (systematic adj (review\$1 or overview\$1)).tw.                                                   | 661,976                 |
| 47 | exp Review Literature as Topic/ use medall                                                        | 22,982                  |
| 48 | exp Review Literature as Topic/ use cctr                                                          | 343                     |
| 49 | or/8-48                                                                                           | 21,914,425              |
| 50 | exp kidney failure/ use oomezd                                                                    | 487,271                 |
| 51 | exp end stage renal disease/ use oomezd                                                           | 52,364                  |
| 52 | Kidney Failure, Chronic/ use medall                                                               | 101,127                 |
| 53 | Kidney Failure, Chronic/ use cctr                                                                 | 5,482                   |
| 54 | (ESKF or ESKF or "end stage kidney disease" or "end stage renal disease" or "kidney failure").tw. | 138,890                 |
| 55 | exp renal replacement therapy/ use oomezd                                                         | 235,634                 |
| 56 | exp Renal Replacement Therapy/ use medall                                                         | 234,364                 |
| 57 | exp Renal Replacement Therapy/ use cctr                                                           | 11,581                  |
| 58 | ("renal replacement" or dialysis).tw.                                                             | 351,623                 |
| 59 | Mortality/                                                                                        | 951,312                 |
| 60 | (mortal* or death).tw.                                                                            | 4,272,179               |
| 61 | creatinine blood level/ use oomezd                                                                | 147,727                 |
| 62 | creatinine.tw.                                                                                    | 389,745                 |
| 63 | exp glomerulus filtration rate/ use oomezd                                                        | 150,230                 |
| 64 | Glomerular Filtration Rate/ use medall                                                            | 50,130                  |
| 65 | Glomerular Filtration Rate/ use cctr                                                              | 3,343                   |
| 66 | (eGFR or "glomerular filtration rate").tw.                                                        | 337,088                 |
| 67 | or/50-66                                                                                          | 5,838,479               |
| 68 | 7 and 49 and 67                                                                                   | 6,488                   |
| 69 | exp animals/ not humans/                                                                          | 16,814,313              |
| 70 | letter/ or editorial/ or case report/                                                             | 6,518,142               |
| 71 | (letter or editorial or comment\$ or note or conference\$).pt.                                    | 11,111,632              |

| #  | Search string                  | Results from 1 Sep 2023 |
|----|--------------------------------|-------------------------|
| 72 | or/69-71                       | 26,811,719              |
| 73 | 68 not 72                      | 3,772                   |
| 74 | conference abstract.pt.        | 4,870,997               |
| 75 | limit 74 to yr="1974 - 2018"   | 3,417,713               |
| 76 | 73 not 75                      | 3,772                   |
| 77 | limit 76 to yr="2022 -Current" | 610                     |
| 78 | limit 77 to English language   | 598                     |
| 79 | remove duplicates from 78      | 420                     |

Key: ab – abstract; adj – adjacent; cctr – controlled vocabulary search of CENTRAL; CENTRAL – Cochrane Central Register of Controlled Trials; exp – explode; medall – controlled vocabulary search of MEDLINE; mp – multipurpose; oomezd – controlled vocabulary search of Embase; pt – publication type; ti – title; tw – text word; yr – year.

**Table S3. PICOS criteria for study selection**

|                     | <b>Inclusion criteria</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <b>Exclusion criteria</b>                                                                                                                   |
|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Population</b>   | <ul style="list-style-type: none"> <li>Adults or children with IgAN</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                      | <ul style="list-style-type: none"> <li>Patients without IgAN</li> </ul>                                                                     |
| <b>Intervention</b> | <ul style="list-style-type: none"> <li>Any</li> <li>None</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                             |
| <b>Comparator</b>   | <ul style="list-style-type: none"> <li>Any</li> <li>None</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                             |
| <b>Outcomes</b>     | <ul style="list-style-type: none"> <li>Relationship between clinical surrogate endpoints of disease progression and the following hard clinical outcomes: <ul style="list-style-type: none"> <li>kidney failure</li> <li>mortality</li> <li>time to kidney replacement therapy</li> <li>time to doubling of SCr</li> <li>percentage decline in eGFR</li> </ul> </li> </ul> <p><i>Note:</i> These outcomes could be measured as correlation, HR, OR, proportion achieving an event, p-value of association test.</p> | Studies that do not report an association outcome between a surrogate endpoint and standard clinical outcome.                               |
| <b>Study Design</b> | <p>Interventional studies</p> <ul style="list-style-type: none"> <li>RCTs</li> <li>single-arm trials</li> <li>pragmatic trials</li> <li>non-randomized trials</li> </ul> <p>Observational studies</p> <ul style="list-style-type: none"> <li>Prospective cohort studies</li> <li>Prospective database studies</li> <li>Registries</li> </ul> <p>Systematic literature reviews and meta-analyses<sup>a</sup></p>                                                                                                     | <ul style="list-style-type: none"> <li>Editorials, letters</li> <li>Narrative reviews</li> <li>Case reports</li> <li>Case series</li> </ul> |
| <b>Language</b>     | English language only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Non-English publications <sup>b</sup>                                                                                                       |
| <b>Time Horizon</b> | 2006-2023 for articles; 2019-2023 for conference abstracts                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Conference abstracts published prior to 2019                                                                                                |

<sup>a</sup>Reference lists of relevant SLRs and meta-analyses, including those excluded for no outcome of interest, were hand-searched for relevant studies.

<sup>b</sup>The search was not restricted by language, but any studies identified that were not published in English were excluded during title/abstract screening.

Key: eGFR – estimated glomerular filtration rate; HR – hazard ratio; IgAN – immunoglobulin A nephropathy; OR – odds ratio; PICOS – population, intervention, comparison, outcomes and study; RCT – randomized controlled trial; SCr – serum creatinine; SLR – systematic literature review.