**Supplemental Material**

Supplemental Table 1. Protein names from Olink® CVDII panel sorted in alphabetical order

|  |  |  |
| --- | --- | --- |
| **Protein full name** | **Entry name** | **Uniprot ID\*\*** |
| Angiotensin-converting enzyme 2 | ACE2 | Q9BYF1 |
| Adisintegrin and metalloproteinase with thrombospondin motifs 13 | ADAMTS13 | Q76LX8 |
| ADM | ADM | P35318 |
| Agouti-related protein | AGRP | O00253 |
| Protein AMBP | AMBP | P02760 |
| Angiopoietin-1 | ANG1 | Q15389 |
| Bone morphogenetic protein 6 | BMP6 | P22004 |
| Natriuretic peptides B | BNP | P16860 |
| Carbonic anhydrase 5A, mitochondrial | CA5A | P35218 |
| C-C motif chemokine 17 | CCL17 | Q92583 |
| C-C motif chemokine 3 | CCL3 | P10147 |
| T-cell surface glycoprotein CD4 | CD4 | P01730 |
| CD40 ligand | CD40L | P29965 |
| SLAM family member 5 | CD84 | Q9UIB8 |
| Carcinoembryonic antigenrelated cell adhesion molecule 8 | CEACAM8 | P31997 |
| Chymotrypsin C | CTRC | Q99895 |
| Cathepsin L1 | CTSL1 | P07711 |
| C-X-C motif chemokine 1 (CVD2) | CXCL1 | P09341 |
| Decorin | DCN | P07585 |
| 2,4-dienoyl-CoA reductase, mitochondrial | DECR1 | Q16698 |
| Dickkopf-related protein 1 | DKK1 | O94907 |
| Fatty acid-binding protein, intestinal | FABP2 | P12104 |
| Fibroblast growth factor 21 (CVD2) | FGF21 | Q9NSA1 |
| Fibroblast growth factor 23 (CVD2) | FGF23 | Q9GZV9 |
| Follistatin | FS | P19883 |
| Galectin-9 | GAL9 | O00182 |
| Growth/differentiation factor 2 | GDF2 | Q9UK05 |
| Growth hormone | GH | P01241 |
| Gastric intrinsic factor | GIF | P27352 |
| Lactoylglutathione lyase | GLO1 | Q04760 |
| Gastrotropin | GT | P51161 |
| Hydroxyacid oxidase 1 | HAOX1 | Q9UJM8 |
| Proheparin-binding EGF-like growth factor | HBEGF | Q99075 |
| Heme oxygenase 1 | HO1 | P09601 |
| Osteoclast-associated immunoglobulin-like receptor | HOSCAR | Q8IYS5 |
| Heat shock 27 kDa protein | HSP27 | P04792 |
| Alpha-L-iduronidase | IDUA | P35475 |
| Low affinity immunoglobulin gamma Fc region receptor II-b | IGGFCRECEPTORIIB | P31994 |
| Pro-interleukin-16 | IL16 | Q14005 |
| Interleukin-17D | IL17D | Q8TAD2 |
| Interleukin-18 (CVD2) | IL18 | Q14116 |
| Interleukin-1 receptor antagonist protein | IL1RA | P18510 |
| Interleukin-1 receptor-like 2 | IL1RL2 | Q9HB29 |
| Interleukin-27 | IL27 | Q8NEV9 |
| Interleukin-4 receptor subunit alpha | IL4RA | P24394 |
| Interleukin-6 (CVD2) | IL6 | P05231 |
| Melusin | ITGB1BP2 | Q9UKP3 |
| Kidney injury molecule 1 | KIM1 | Q96D42 |
| Leptin | LEP | P41159 |
| Lectin-like oxidized LDL receptor 1 | LOX1 | P78380 |
| Lipoprotein lipase | LPL | P06858 |
| Macrophage receptor MARCO | MARCO | Q9UEW3 |
| Tyrosine-protein kinase Mer | MERTK | Q12866 |
| Matrix metalloproteinase-12 | MMP12 | P39900 |
| Matrix metalloproteinase-7 | MMP7 | P09237 |
| NF-kappa-B essential modulator | NEMO | Q9Y6K9 |
| Pappalysin-1 | PAPPA | Q13219 |
| Proteinase-activated receptor 1 | PAR1 | P25116 |
| Poly [ADP-ribose] polymerase 1 | PARP1 | P09874 |
| Platelet-derived growth factor subunit B | PDGFSUBUNITB | P01127 |
| Programmed cell death 1 ligand 2 | PDL2 | Q9BQ51 |
| Polymeric immunoglobulin receptor | PIGR | P01833 |
| Placenta growth factor | PLGF | P49763 |
| Prolargin | PRELP | P51888 |
| Brother of CDO | PROTEINBOC | Q9BWV1 |
| Serine protease 27 | PRSS27 | Q9BQR3 |
| Prostasin | PRSS8 | Q16651 |
| P-selectin glycoprotein ligand 1 | PSGL1 | Q14242 |
| Pentraxin-related protein PTX3 | PTX3 | P26022 |
| Receptor for advanced glycosylation end products | RAGE | Q15109 |
| Renin | REN | P00797 |
| Stem cell factor (CVD2) | SCF | P21583 |
| Serpin A12 | SERPINA12 | Q8IW75 |
| SLAM family member 7 | SLAMF7 | Q9NQ25 |
| Superoxide dismutase [Mn], mitochondrial | SOD2 | P04179 |
| Sortilin | SORT1 | Q99523 |
| Spondin-2 | SPON2 | Q9BUD6 |
| Proto-oncogene tyrosine-protein kinase Src | SRC | P12931 |
| Serine/threonine-protein kinase 4 | STK4 | Q13043 |
| Tissue factor | TF | P13726 |
| Protein-glutamine gamma-glutamyltransferase 2 | TGM2 | P21980 |
| Thrombospondin-2 | THBS2 | P35442 |
| Thrombopoietin | THPO | P40225 |
| Angiopoietin-1 receptor | TIE2 | Q02763 |
| Thrombomodulin | TM | P07204 |
| Tumor necrosis factor receptor superfamily member 10A | TNFRSF10A | O00220 |
| Tumor necrosis factor receptor superfamily member 11A | TNFRSF11A | Q9Y6Q6 |
| Tumor necrosis factor receptor superfamily member 13B | TNFRSF13B | O14836 |
| TNF-related apoptosis-inducing ligand receptor 2 | TRAILR2 | O14763 |
| Vascular endothelial growth factor D | VEGFD | O43915 |
| V-set and immunoglobulin domain-containing protein 2 | VSIG2 | Q96IQ7 |
| Lymphotactin | XCL1 | P47992 |

Legend: \*CVDII: cardiovascular II panel; \*\*UniProt ID from UniProt Knowledgebase

Supplemental Table 2. Clinical variables and their association with worsening kidney function

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Beta coef. (95%CI)** | **Z** | **P** |
| Anemia | 1.39 (0.96 to 1.82) | 6.4 | 0.00001 |
| Previous HFH | 0.79 (0.37 to 1.22) | 3.7 | 0.0002 |
| Diuretic use | 0.74 (0.31 to 1.16) | 3.4 | 0.001 |
| eGFR <60 | 0.42 (-0.02 to 0.85) | 1.9 | 0.06 |
| Hypertension | 0.43 (-0.03 to 0.88) | 1.9 | 0.065 |
| Alogliptin | 1.13 (-0.25 to 2.52) | 1.6 | 0.108 |
| Insulin | 0.37 (-0.08 to 0.82) | 1.6 | 0.111 |
| Female | 0.28 (-0.13 to 0.68) | 1.3 | 0.183 |
| Duration of diabetes >7yr | 0.17 (-0.26 to 0.60) | 0.8 | 0.447 |
| Smoker | -0.05 (-0.69 to 0.60) | -0.1 | 0.891 |
| Age >65yr | -0.32 (-0.74 to 0.10) | -1.5 | 0.136 |
| Metformin | -0.36 (-0.79 to 0.06) | -1.7 | 0.096 |
| Statin | -0.71 (-1.28 to -0.14) | -2.5 | 0.014 |

Legend: HFH, heart failure hospitalization; eGFR, estimated glomerular filtration rate.

Light Green: variables with P-value ≤0.0001

Supplemental Table 3. Biomarkers associated with worsening kidney function ≥40% from baseline in a mixed random effects logistic regression model

|  |  |  |  |
| --- | --- | --- | --- |
| **Biomarker** | **Beta coef. (95%CI)** | **Z** | **P** |
| kim1 | 0.84 (0.66-1.03) | 9.1 | 0.00001 |
| pgf | 1.81 (1.31-2.32) | 7.1 | 0.00001 |
| trailr2 | 1.06 (0.76-1.36) | 6.9 | 0.00001 |
| tnfrsf11a | 1.26 (0.89-1.63) | 6.6 | 0.00001 |
| tm | 2.07 (1.46-2.68) | 6.6 | 0.00001 |
| tnfrsf10a | 1.49 (1.03-1.95) | 6.4 | 0.00001 |
| il4ra | 1.29 (0.88-1.69) | 6.2 | 0.00001 |
| uNGAL | 0.33 (0.22-0.44) | 6 | 0.00001 |
| tf | 1.82 (1.22-2.43) | 5.9 | 0.00001 |
| vsig2 | 0.9 (0.56-1.24) | 5.1 | 0.00001 |
| rage | 1.02 (0.6-1.45) | 4.7 | 0.00001 |
| ambp | 2.19 (1.25-3.13) | 4.6 | 0.00001 |
| vegfd | 1.21 (0.69-1.73) | 4.5 | 0.00001 |
| xcl1 | 0.61 (0.31-0.9) | 4 | 0.0001 |
| agrp | 0.66 (0.34-0.98) | 4 | 0.0001 |
| bnp | 0.2 (0.1-0.3) | 4 | 0.0001 |
| cd4 | 1.18 (0.61-1.75) | 4 | 0.0001 |
| spon2 | 2.11 (1.02-3.21) | 3.8 | 0.0001 |
| mertk | 0.86 (0.4-1.32) | 3.7 | 0.0003 |
| boc | 1.21 (0.55-1.88) | 3.6 | 0.0003 |
| gal9 | 1.02 (0.46-1.57) | 3.6 | 0.0004 |
| prss8 | 1.22 (0.54-1.91) | 3.5 | 0.0004 |
| mmp7 | 0.29 (0.12-0.47) | 3.3 | 0.001 |
| prelp | 1.43 (0.55-2.31) | 3.2 | 0.0014 |
| v-gt | 0.37 (0.15-0.6) | 3.2 | 0.0013 |
| prss27 | 0.54 (0.19-0.88) | 3.1 | 0.0022 |
| dcn | 1.23 (0.45-2.02) | 3.1 | 0.002 |
| tnfrsf13b | 0.65 (0.23-1.06) | 3.1 | 0.0022 |
| ca5a | 0.29 (0.1-0.47) | 3.1 | 0.0022 |
| uKIM1 | 0.24 (0.08-0.39) | 2.9 | 0.0034 |
| par1 | 0.44 (0.15-0.74) | 2.9 | 0.0034 |
| scf | 0.68 (0.22-1.14) | 2.9 | 0.0037 |
| il16 | 0.4 (0.12-0.68) | 2.8 | 0.005 |
| lpl | 0.55 (0.16-0.93) | 2.8 | 0.0051 |
| ceacam8 | 0.3 (0.07-0.52) | 2.6 | 0.0089 |
| fabp2 | 0.35 (0.09-0.61) | 2.6 | 0.0084 |
| hoscar | 1.15 (0.28-2.03) | 2.6 | 0.0097 |
| troponin i | 0.12 (0.02-0.21) | 2.4 | 0.0181 |
| il17d | 0.51 (0.09-0.93) | 2.4 | 0.0172 |
| ptx3 | 0.43 (0.08-0.78) | 2.4 | 0.0165 |
| mmp12 | 0.33 (0.06-0.59) | 2.4 | 0.0153 |
| ren | 0.28 (0.04-0.51) | 2.3 | 0.0205 |
| ccl3 | 0.3 (0.04-0.56) | 2.3 | 0.0232 |
| ho1 | 0.44 (0.05-0.82) | 2.2 | 0.0257 |
| hsp27 | 0.35 (0.04-0.67) | 2.2 | 0.0278 |
| ace2 | 0.28 (0.02-0.54) | 2.1 | 0.0355 |
| adm | 0.25 (0.01-0.49) | 2 | 0.0415 |
| il27 | 0.44 (0.01-0.88) | 2 | 0.0438 |
| idua | 0.31 (-0.02-0.64) | 1.8 | 0.0663 |
| fgf21 | 0.12 (-0.01-0.26) | 1.8 | 0.0751 |
| ctsl1 | 0.51 (-0.04-1.06) | 1.8 | 0.071 |
| pappa | 0.26 (-0.06-0.58) | 1.6 | 0.1078 |
| il6 | 0.15 (-0.05-0.34) | 1.5 | 0.1414 |
| lox1 | 0.17 (-0.06-0.4) | 1.5 | 0.1383 |
| pdl2 | 0.3 (-0.11-0.71) | 1.4 | 0.1533 |
| tgm2 | 0.16 (-0.07-0.4) | 1.4 | 0.1678 |
| gh | 0.07 (-0.03-0.17) | 1.3 | 0.183 |
| il18 | 0.19 (-0.12-0.5) | 1.2 | 0.2218 |
| glo1 | 0.12 (-0.08-0.32) | 1.2 | 0.236 |
| iggfcreceptoriib | 0.12 (-0.08-0.32) | 1.2 | 0.2382 |
| bmp6 | 0.16 (-0.13-0.45) | 1.1 | 0.2696 |
| thpo | 0.21 (-0.16-0.58) | 1.1 | 0.2614 |
| slamf7 | 0.14 (-0.14-0.42) | 1 | 0.3367 |
| fs | 0.2 (-0.18-0.57) | 1 | 0.3099 |
| pigr | 0.65 (-0.7-1.99) | 0.9 | 0.3461 |
| fgf23 | 0.08 (-0.12-0.27) | 0.8 | 0.429 |
| ccl17 | 0.06 (-0.08-0.2) | 0.8 | 0.4116 |
| thbs2 | 0.3 (-0.52-1.11) | 0.7 | 0.4745 |
| dkk1 | 0.06 (-0.15-0.28) | 0.6 | 0.5562 |
| src | 0.03 (-0.1-0.16) | 0.4 | 0.6677 |
| gif | 0.03 (-0.13-0.2) | 0.4 | 0.6746 |
| sort1 | 0.07 (-0.4-0.54) | 0.3 | 0.7721 |
| nemo | 0.02 (-0.12-0.16) | 0.3 | 0.738 |
| stk4 | 0.01 (-0.08-0.1) | 0.2 | 0.8733 |
| gdf2 | 0.03 (-0.27-0.34) | 0.2 | 0.8313 |
| il1rl2 | 0.03 (-0.42-0.48) | 0.1 | 0.8948 |
| ang1 | 0 (-0.13-0.13) | 0 | 0.9866 |
| pdgfsubunitb | 0 (-0.12-0.13) | 0 | 0.9929 |
| cd84 | 0 (-0.31-0.31) | 0 | 0.9953 |
| cd40l | 0 (-0.12-0.12) | -0.1 | 0.956 |
| il1ra | -0.01 (-0.26-0.24) | -0.1 | 0.9485 |
| marco | -0.02 (-0.58-0.54) | -0.1 | 0.9463 |
| haox1 | 0 (-0.13-0.12) | -0.1 | 0.9506 |
| sod2 | -0.22 (-1.45-1.02) | -0.3 | 0.7319 |
| itgb1bp2 | -0.01 (-0.1-0.07) | -0.3 | 0.7759 |
| hbegf | -0.04 (-0.25-0.16) | -0.4 | 0.6745 |
| decr1 | -0.05 (-0.18-0.08) | -0.7 | 0.4748 |
| tie2 | -0.26 (-0.9-0.38) | -0.8 | 0.4195 |
| serpina12 | -0.06 (-0.2-0.08) | -0.8 | 0.3957 |
| psgl1 | -0.34 (-0.94-0.27) | -1.1 | 0.2742 |
| lep | -0.11 (-0.3-0.09) | -1.1 | 0.289 |
| parp1 | -0.1 (-0.28-0.07) | -1.1 | 0.2508 |
| ctrc | -0.13 (-0.35-0.08) | -1.2 | 0.2115 |
| cxcl1 | -0.08 (-0.2-0.04) | -1.3 | 0.2024 |
| adamts13 | -0.59 (-1.35-0.17) | -1.5 | 0.1307 |

Caption: Models adjusted on all variables depicted in the Supplemental Table 2 plus visit by treatment interaction.

Light Green: variables with P-value ≤0.0001

Supplemental Table 4. Biomarkers associated with eGFR slope in a mixed random effects linear regression model

|  |  |  |  |
| --- | --- | --- | --- |
| **Biomarker** | **Beta coef. (95%CI)** | **Z** | **P** |
| pgf | -4.77 (-5.4--4.15) | -15 | 0.00001 |
| kim1 | -1.35 (-1.58--1.12) | -11.5 | 0.00001 |
| tnfrsf11a | -2.54 (-3--2.08) | -10.8 | 0.00001 |
| tm | -3.71 (-4.39--3.02) | -10.6 | 0.00001 |
| trailr2 | -2.62 (-3.12--2.12) | -10.2 | 0.00001 |
| spon2 | -5.85 (-7.02--4.69) | -9.9 | 0.00001 |
| tf | -3.61 (-4.35--2.87) | -9.6 | 0.00001 |
| rage | -2.34 (-2.83--1.85) | -9.4 | 0.00001 |
| il4ra | -2.59 (-3.16--2.02) | -8.9 | 0.00001 |
| ambp | -4.82 (-5.93--3.7) | -8.5 | 0.00001 |
| tnfrsf10a | -2.45 (-3.04--1.86) | -8.1 | 0.00001 |
| prss8 | -3.19 (-3.96--2.42) | -8.1 | 0.00001 |
| vsig2 | -1.52 (-1.93--1.11) | -7.3 | 0.00001 |
| bnp | -0.45 (-0.57--0.33) | -7.2 | 0.00001 |
| vegfd | -1.67 (-2.17--1.18) | -6.6 | 0.00001 |
| mmp7 | -0.67 (-0.88--0.46) | -6.4 | 0.00001 |
| boc | -2.35 (-3.08--1.62) | -6.3 | 0.00001 |
| cd4 | -2.16 (-2.83--1.48) | -6.3 | 0.00001 |
| gal9 | -2.12 (-2.8--1.44) | -6.1 | 0.00001 |
| mertk | -1.71 (-2.26--1.16) | -6.1 | 0.00001 |
| fabp2 | -0.86 (-1.15--0.57) | -5.8 | 0.00001 |
| scf | -1.46 (-1.96--0.96) | -5.7 | 0.00001 |
| prss27 | -1.19 (-1.6--0.77) | -5.6 | 0.00001 |
| mmp12 | -0.91 (-1.23--0.59) | -5.5 | 0.00001 |
| dcn | -2.51 (-3.45--1.57) | -5.2 | 0.00001 |
| agrp | -1.04 (-1.44--0.65) | -5.2 | 0.00001 |
| il17d | -1.55 (-2.15--0.95) | -5.1 | 0.00001 |
| pdl2 | -1.2 (-1.69--0.72) | -4.9 | 0.00001 |
| prelp | -1.72 (-2.48--0.96) | -4.4 | 0.00001 |
| xcl1 | -0.73 (-1.06--0.4) | -4.4 | 0.00001 |
| adm | -0.51 (-0.75--0.28) | -4.2 | 0.00001 |
| uNGAL | -0.3 (-0.44--0.16) | -4.1 | 0.00001 |
| Troponin i | -0.24 (-0.36--0.12) | -4 | 0.0001 |
| lpl | -0.68 (-1.03--0.32) | -3.8 | 0.0002 |
| ctsl1 | -1.26 (-1.92--0.6) | -3.8 | 0.0002 |
| pigr | -2.84 (-4.34--1.34) | -3.7 | 0.0002 |
| fgf21 | -0.3 (-0.46--0.14) | -3.6 | 0.0003 |
| v-gt | -0.51 (-0.78--0.23) | -3.6 | 0.0003 |
| il16 | -0.6 (-0.93--0.27) | -3.6 | 0.0004 |
| hoscar | -1 (-1.65--0.34) | -3 | 0.0029 |
| ccl3 | -0.47 (-0.79--0.15) | -2.9 | 0.0039 |
| gdf2 | -0.54 (-0.91--0.17) | -2.9 | 0.0041 |
| ca5a | -0.34 (-0.57--0.1) | -2.8 | 0.0059 |
| ace2 | -0.44 (-0.76--0.12) | -2.7 | 0.0076 |
| tnfrsf13b | -0.69 (-1.2--0.18) | -2.7 | 0.0076 |
| lep | -0.31 (-0.55--0.07) | -2.5 | 0.0124 |
| ho1 | -0.4 (-0.82-0.02) | -1.9 | 0.059 |
| fgf23 | -0.23 (-0.49-0.04) | -1.7 | 0.0945 |
| thbs2 | -0.71 (-1.67-0.24) | -1.5 | 0.143 |
| ctrc | -0.18 (-0.44-0.08) | -1.4 | 0.1706 |
| slamf7 | -0.24 (-0.57-0.1) | -1.4 | 0.1718 |
| par1 | -0.13 (-0.41-0.14) | -1 | 0.3401 |
| il18 | -0.18 (-0.55-0.19) | -0.9 | 0.3469 |
| pappa | -0.16 (-0.55-0.22) | -0.8 | 0.4084 |
| uKIM1 | -0.07 (-0.24-0.11) | -0.7 | 0.4573 |
| il6 | -0.09 (-0.34-0.16) | -0.7 | 0.476 |
| iggfcreceptoriib | -0.08 (-0.31-0.15) | -0.7 | 0.5002 |
| thpo | -0.14 (-0.56-0.29) | -0.6 | 0.5252 |
| il27 | -0.12 (-0.64-0.4) | -0.5 | 0.6453 |
| bmp6 | -0.06 (-0.36-0.25) | -0.4 | 0.7195 |
| ceacam8 | -0.03 (-0.31-0.25) | -0.2 | 0.8334 |
| marco | -0.07 (-0.76-0.61) | -0.2 | 0.8364 |
| fs | -0.03 (-0.47-0.41) | -0.1 | 0.8865 |
| serpina12 | 0.02 (-0.15-0.18) | 0.2 | 0.8366 |
| gh | 0.01 (-0.11-0.13) | 0.2 | 0.8484 |
| adamts13 | 0.18 (-0.61-0.97) | 0.4 | 0.6576 |
| ren | 0.06 (-0.21-0.32) | 0.4 | 0.6814 |
| idua | 0.07 (-0.31-0.46) | 0.4 | 0.7057 |
| hsp27 | 0.06 (-0.27-0.39) | 0.4 | 0.7197 |
| gif | 0.07 (-0.12-0.27) | 0.7 | 0.4775 |
| ptx3 | 0.17 (-0.25-0.59) | 0.8 | 0.4406 |
| il1rl2 | 0.25 (-0.29-0.78) | 0.9 | 0.3651 |
| dkk1 | 0.11 (-0.13-0.35) | 0.9 | 0.3724 |
| sort1 | 0.29 (-0.23-0.82) | 1.1 | 0.277 |
| lox1 | 0.15 (-0.12-0.41) | 1.1 | 0.2855 |
| il1ra | 0.17 (-0.14-0.47) | 1.1 | 0.2875 |
| tgm2 | 0.17 (-0.1-0.45) | 1.2 | 0.2175 |
| haox1 | 0.11 (-0.05-0.26) | 1.3 | 0.1822 |
| ang1 | 0.12 (-0.02-0.27) | 1.6 | 0.1004 |
| tie2 | 0.65 (-0.13-1.44) | 1.6 | 0.1041 |
| psgl1 | 0.62 (-0.13-1.37) | 1.6 | 0.1047 |
| ccl17 | 0.13 (-0.03-0.29) | 1.6 | 0.1211 |
| pdgfsubunitb | 0.13 (-0.01-0.27) | 1.8 | 0.0691 |
| sod2 | 1.53 (-0.02-3.07) | 1.9 | 0.0532 |
| src | 0.15 (0-0.3) | 1.9 | 0.0563 |
| glo1 | 0.25 (0.01-0.48) | 2.1 | 0.0388 |
| parp1 | 0.24 (0.05-0.42) | 2.5 | 0.0113 |
| cxcl1 | 0.18 (0.04-0.33) | 2.5 | 0.0117 |
| hbegf | 0.3 (0.08-0.53) | 2.6 | 0.0089 |
| nemo | 0.25 (0.1-0.41) | 3.2 | 0.0015 |
| cd84 | 0.57 (0.24-0.91) | 3.3 | 0.0009 |
| stk4 | 0.19 (0.08-0.29) | 3.4 | 0.0006 |
| cd40l | 0.24 (0.1-0.38) | 3.5 | 0.0005 |
| itgb1bp2 | 0.2 (0.1-0.29) | 4.1 | 0.00001 |
| decr1 | 0.31 (0.17-0.46) | 4.2 | 0.00001 |

Legend: eGFR, estimated glomerular filtration rate.

Caption: Models adjusted on all variables depicted in the Supplemental Table 2 plus visit by treatment interaction.

Light Green: variables with P-value ≤0.0001

Dark Green: variables common from the logistic model presented in the Supplemental Table 3.

Supplemental Table 5. Association of KIM-1 with total WKF events among patients with available UACR (n =2999) and after multiple imputation (n =5380)

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Beta coef. (95%CI)** | **Z-score** | **P-value** |
| Complete case n =2999 |
| KIM1 (per doubling concentration) | 0.55 (0.35 to 0.75) | 5.3 | <0.0001 |
| Age (per year) | -0.01 (-0.03 to 0.01) | -0.9 | 0.37 |
| Male sex | 0.15 (-0.23 to 0.53) | 0.8 | 0.44 |
| eGFR (per 10 ml/min) | 0.04 (-0.05 to 0.14) | 0.9 | 0.39 |
| UACR (per doubling concentration) | 0.17 (0.08 to 0.27) | 3.7 | <0.0001 |
| Multiple imputation n =5380 |
| KIM1 (per doubling concentration) | 0.62 (0.44 to 0.79) | 6.9 | <0.0001 |
| Age (per year) | -0.01 (-0.01 to 0.02) | 0.5 | 0.62 |
| Male sex | 0.25 (-0.09 to 0.59) | 1.4 | 0.15 |
| eGFR (per 10 ml/min) | 0.01 (-0.01 to 0.01) | 1.7 | 0.10 |
| UACR (per doubling concentration) | 0.17 (0.09 to 0.26) | 3.9 | <0.0001 |

Legend: KIM-1, kidney injury molecule-1; eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio.

Model adjusted for the Kidney Failure Risk Equation (KFRE) including age, sex, eGFR, and UACR.

AUC of the KFRE model alone is =0.68. The AUC of KFRE+KIM-1 is =0.75. The p-value for the difference between the nested models is <0.0001.

Note: further adjustment on age, sex, baseline eGFR, anemia, diabetes duration, smoking, hypertension, prior HF hospitalization, use of diuretics, ACE/ARBs, insulin, metformin, statins, randomized treatment, diuretics, UACR, race, glycated hemoglobin, and time since acute coronary syndrome does not change the results: KIM-1 Beta per doubling concentration =0.53, Z-score =6.0.

Supplemental Figure 1. Effect of alogliptin (vs. placebo) on eGFR over time.



Legend: eGFR, estimated glomerular filtration rate.

eGFR slope of change (alogliptin vs. placebo) = -1.11 (-2.55 to 0.33), P =0.13.