# Supplementary material

## Table 1: Published PopPK models for therapeutic mAbs

*Table 1:* ***Published mAb PopPK models included in the study****. SC: subcutaneous, IV: intravenous, WT: reference weight, N: study size, NonLinCL: Nonlinear clearnce included in the structural model (1: yes, 0: no).*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **mAb** | **Route** | **ka** | **V1** | **CL** | **Q** | **V2** | **Patients** | **WT** | **N** | **Number of model compartments** | **NonLinCL** | **Reference** |
| adalimumab | SC | 0.259 | 2.49 | 0.28 | 1.7 | 3.74 | Rheumatoid Arthritis | 70 | 1398 | 2 | 0 | [doi: 10.1111/bcp.14330](https://dx.doi.org/10.1111%2Fbcp.14330) |
| adalimumab | SC | 0.195 | 13.5 | 0.66 |  |  | Hidradenitis suppurativa | 94 | 1200 | 1 | 0 | [DOI: 10.1007/s40262-016-0502-4](https://doi.org/10.1007/s40262-016-0502-4) |
| adalimumab | SC | 0.28 | 10.8 | 0.32 |  |  | Rheumatoid Arthritis | 67 | 30 | 1 | 0 | DOI:10.1111/bcp.12509 |
| alemtuzumab | IV |  | 2.13 | 0.25 | 0.18 | 1.5 | Hematopoietic Cell Transplantation | 17 | 206 | 2 | 1 | [DOI: 10.1007/s40262-019-00782-0](https://doi.org/10.1007/s40262-019-00782-0) |
| alirocumab | SC/IV | 0.697 | 3.16 | 0.167 | 0.494 | 2.61 | Healthy, Patients | 81 | 527 | 2 | 1 | DOI 10.1007/s40262-016-0505-1 |
| alirocumab | SC/IV | 0.697 | 4.67 | 0.176 | 0.343 | 2.61 | Healthy, Patients | 85 | 2870 | 2 | 1 | DOI 10.1007/s40262-016-0505-1 |
| alirocumab | SC/IV | 0.309 | 3.63 | 0.2976 | 0.444 | 2.95 | Hypercholesterolemia, Healthy | 82.9 | 2799 | 2 | 1 | https://doi.org/10.1007/s40262-018-0669-y |
| atezolizumab | IV |  | 3.28 | 0.2 | 0.546 | 3.63 | Metastatic Urothelial Carcinoma | 77 | 906 | 2 | 0 | [DOI: 10.1002/cpt.587](https://doi.org/10.1002/cpt.587) |
| atezolizumab | IV |  | 3.01 | 0.217 | 0.183 | 1.36 | Cancer | 77 | 87 | 2 | 0 | [DOI: 10.1186/s40425-019-0791-x](https://doi.org/10.1186/s40425-019-0791-x) |
| atezolizumab | IV |  | 3.35 | 0.233 | 0.452 | 3.36 | Non-small cell Lung Cancer | 77 | 88 | 2 | 0 | [doi.org/10.1002/cpt.1198](https://doi.org/10.1002/cpt.1198) |
| avelumab | IV |  | 3.42 | 0.528 | 0.751 | 0.918 | Merkel Cell Carcinoma, Urothelial Carcinoma | 71 | 1827 | 2 | 1 | doi:10.1002/psp4.12406 |
| basiliximab | IV |  | 3.72 | 0.88 | 4.16 | 4.08 | Renal Transplantation | 72 | 46 | 2 | 0 | doi: 10.1023@a@1020658023774 |
| basiliximab | IV |  | 3.6 | 0.744 |  |  | Renal Transplantation |  | 169 | 2 | 0 | [DOI: 10.1097/00007890-200210150-00011](https://doi.org/10.1097/00007890-200210150-00011) |
| basiliximab | IV |  | 2.1 | 0.408 |  |  | Renal Transplantation |  | 39 | 2 | 0 | [DOI: 10.1097/00007890-200210150-00011](https://doi.org/10.1097/00007890-200210150-00011) |
| belimumab | SC | 0.235 | 2.3 | 0.204 | 0.698 | 2.65 | Systemic Lupus Erythematosus, Healthy | 67 | 688 | 2 | 0 | [DOI: 10.1007/s40262-017-0586-5](https://doi.org/10.1007/s40262-017-0586-5) |
| belimumab | IV |  | 2.56 | 0.215 | 0.459 | 2.73 | Systemic Lupus Erythematosus | 66 | 1464 | 2 | 0 | [DOI: 10.1002/jcph.104](https://doi.org/10.1002/jcph.104) |
| benralizumab | SC |  | 3.13 | 0.219 | 0.738 | 2.52 | Asthma | 70 | 3533 | 2 | 0 | [DOI: 10.1007/s40262-019-00738-4](https://doi.org/10.1007/s40262-019-00738-4) |
| benralizumab | SC |  | 3.16 | 0.323 | 0.939 | 2.83 | Asthma, healthy | 77 | 200 | 2 | 0 | [DOI: 10.1002/psp4.12160](https://doi.org/10.1002/psp4.12160) |
| bevacizumab | IV |  | 2.99 | 0.271 | 6.45 | 6.09 | Non-small cell Lung Cancer | 71 | 719 | 2 | 0 | [DOI: 10.1007/s00280-019-03946-8](https://doi.org/10.1007/s00280-019-03946-8) |
| bevacizumab | IV |  | 2.68 | 0.2064 | 0.4464 | 2.42 | Cancer | 70 | 1792 | 2 | 0 | [DOI: 10.1007/s00280-016-3079-6](https://doi.org/10.1007/s00280-016-3079-6) |
| bevacizumab | IV |  | 2.85 | 0.2376 | 0.672 | 2.56 | Paediatric Cancer | 70 | 232 | 2 | 0 | [DOI: 10.1111/bcp.12778](https://doi.org/10.1111/bcp.12778) |
| bevacizumab | IV |  | 3.14 | 0.17 | 0.36 | 2.63 | Colorectal Cancer | 70 | 19 | 2 | 1 | [DOI: 10.1007/s00280-015-2701-3](https://doi.org/10.1007/s00280-015-2701-3) |
| bevacizumab | IV |  | 4.389 | 0.361 | 0.974 | 2.9 | Oesteocarcoma (Cancer) | 70 | 27 | 2 | 0 | [DOI: 10.1158/1078-0432.CCR-13-2364](https://doi.org/10.1158/1078-0432.ccr-13-2364) |
| bevacizumab | IV |  | 2.83 | 0.231 | 0.636 | 2.49 | Colon Cancer | 80 | 1213 | 2 | 0 | [DOI: 10.1007/s00280-012-2031-7](https://doi.org/10.1007/s00280-012-2031-7) |
| bezlotoxumab | IV |  | 3.43 | 0.281 | 0.552 | 3.57 | Clostridium difficile | 72 | 2631 | 2 | 0 | [DOI: 10.1128/AAC.01971-18](https://doi.org/10.1128/aac.01971-18) |
| brodalumab | SC | 0.3 | 4.68 | 0.155 | 0.328 | 2.41 | Plaque Psoriasis | 87 | 622 | 2 | 1 | [DOI: 10.1111/bcpt.13202](https://doi.org/10.1111/bcpt.13202) |
| brodalumab | SC | 0.243 | 3.89 | 0.226 | 0.82 | 2.68 | Psoriasis, Healthy | 90 | 388 | 2 | 1 | [DOI: 10.1002/jcph.334](https://doi.org/10.1002/jcph.334) |
| burosumab | SC | 0.349 | 7.17 | 0.279 |  |  | X-linked Hypophosphatemia | 70 | 62 | 1 | 0 | [DOI: 10.1002/jcph.611](https://doi.org/10.1002/jcph.611) |
| cemiplimab | IV |  | 3.32 | 0.29 | 0.638 | 1.65 | Advanced Malignancies | 76 | 549 | 2 | 0 | [DOI: 10.1007/s10928-021-09739-y](https://doi.org/10.1007/s10928-021-09739-y) |
| cetuximab | IV |  | 4.4 | 0.456 | 0.665 | 8.1 | Advanced Head and Neck Carcinoma | 62 | 28 | 2 | 0 | [DOI: 10.1111/bcp.13907](https://doi.org/10.1111/bcp.13907) |
| cetuximab | IV |  | 2.96 | 0.497 | 0.836 | 4.65 | Metastatic Colorectal Cancer | 73 | 96 | 2 | 1 | doi: 10.1158/1078-0432.CCR-11-1081 |
| daclizumab | SC |  | 3.89 | 0.24 | 1.056 | 2.52 | Healthy | 70 | 71 | 2 | 0 | [DOI: 10.1007/s40262-014-0159-9](https://doi.org/10.1007/s40262-014-0159-9) |
| daratumumab | SC | 0.28 | 5.25 | 0.119 | 0.229 | 3.78 | Multiple Myeloma | 79 | 742 | 2 | 1 | [DOI: 10.1002/jcph.1771](https://doi.org/10.1002/jcph.1771) |
| daratumumab | IV |  | 4.4 | 0.117 | 0.207 | 3.3 | Multiple Myeloma | 76 | 694 | 2 | 1 | doi.org/10.1007/s12325-018-0815-9 |
| denosumab | SC | 0.2568 | 2.62 | 0.078 | 1.09 | 1.37 | Bone Metastases from Solid Tumours | 66 | 1076 | 2 | 1 | [DOI: 10.2165/11598090-000000000-00000](https://doi.org/10.2165/11598090-000000000-00000) |
| denosumab | SC | 0.25 | 2.59 | 0.072 | 0.96 | 1.29 | Osteopepenia/Osteoperosis, Healthy | 66 | 1564 | 2 | 1 | [DOI: 10.2165/11594240-000000000-00000](https://doi.org/10.2165/11594240-000000000-00000) |
| dinutuximab | IV |  | 1.4 | 0.709 | 0.857 | 3.85 | High-risk Neuroblastoma in myeloablative terapy | | 28 | 2 | 0 | DOI 10.1007/s00280-015-2955-9 | |
| dupilumab | SC | 0.306 | 2.74 | 0.131 | 0.583 | 1.86 | Atopic Dermatitis, Healthy | 75 | 2041 | 2 | 1 | DOI: 10.1002/cpdd.780 |
| dupilumab | SC | 0.254 | 2.74 | 0.126 | 0.179 | 1.38 | Atopic Dermatitis, Healthy | 75 | 197 | 2 | 1 | [DOI: 10.1002/psp4.12136](https://doi.org/10.1002/psp4.12136) |
| durvalumab | IV |  | 4.63 | 0.2568 | 0.9024 | 2.68 | Hematologic Malignancies | 75 | 267 | 2 | 0 | [DOI: 10.1007/s40262-019-00804-x](https://doi.org/10.1007/s40262-019-00804-x) |
| durvalumab | IV |  | 3.51 | 0.232 | 0.477 | 3.56 | Cancer | 70 | 1409 | 2 | 1 | [DOI: 10.1002/cpt.982](https://doi.org/10.1002/cpt.982) |
| efalizumab | SC | 0.19 | 9.13 | 1.29 |  |  | Psoriasis | 91 | 1504 | 1 | 0 | [DOI: 10.1177/0091270004272731](https://doi.org/10.1177/0091270004272731) |
| elotuzumab | IV |  | 3.94 | 0.0806 | 0.515 | 2.01 | Multiple Myeloma | 75 | 420 | 3 | 1 | [DOI: 10.1002/jcph.1698](https://doi.org/10.1002/jcph.1698) |
| elotuzumab | IV |  | 4.04 | 0.0895 | 0.676 | 2.22 | Multiple Myeloma | 75 | 375 | 3 | 1 | [DOI: 10.1007/s10928-016-9469-x](https://doi.org/10.1007/s10928-016-9469-x) |
| emicizumab | SC | 0.536 | 10.4 | 0.272 |  |  | Hemophilia A | 69 | 389 | 1 | 0 | [doi: 10.1007/s40262-020-00904-z](https://dx.doi.org/10.1007%2Fs40262-020-00904-z) |
| emicizumab | SC |  | 8.87 | 0.235 |  |  | Healthy | 60 | 16 | 1 | 0 | [doi: 10.1002/cpdd.805](https://dx.doi.org/10.1002%2Fcpdd.805) |
| emicizumab | SC | 0.44 | 10.2 | 0.222 |  |  | Hemophilia A | 65 | 60 | 1 | 0 | [doi: 10.1007/s40262-017-0616-3](https://dx.doi.org/10.1007%2Fs40262-017-0616-3) |
| eptinezumab | IV |  | 3.64 | 0.15 |  |  | Episodic and Chronic Migraine | 70 | 2123 | 2 | 0 | [DOI: 10.1002/prp2.567](https://doi.org/10.1002/prp2.567) |
| erenumab | SC |  | 4.27 | 0.214 | 3.34 | 2.73 | Migraine, Healthy | 70 | 108 | 2 | 1 | [DOI: 10.1007/s11095-017-2183-6](https://doi.org/10.1007/s11095-017-2183-6) |
| evolocumab | SC | 0.24 | 2.75 | 0.278 |  |  | Healthy, Hypercholesterolaemic | 67 | 143 | 1 | 1 | [DOI: 10.1111/bcp.13767](https://doi.org/10.1111/bcp.13767) |
| evolocumab | SC | 0.319 | 5.18 | 0.105 |  |  | Healthy, Hypercholesterolaemic | 84 | 3414 | 1 | 1 | [DOI: 10.1007/s10928-018-9592-y](https://doi.org/10.1007/s10928-018-9592-y) |
| fremanezumab | SC | 0.18 | 1.88 | 0.09 | 0.26 | 1.72 | Migraine, Healthy | 71 | 2546 | 2 | 0 | [DOI: 10.1111/bcp.14096](https://doi.org/10.1111/bcp.14096) |
| galcanezumab | SC | 0.45 | 7.33 | 0.1896 |  |  | Migraine, Healthy | 74 | 1889 | 1 | 0 | [DOI: 10.1002/jcph.1511](https://doi.org/10.1002/jcph.1511) |
| golimumab | SC | 0.908 | 24.9 | 1.38 |  |  | Psoriatic Arthritis | 70 | 337 | 1 | 0 | [DOI: 10.1177/0091270009339192](https://doi.org/10.1177/0091270009339192) |
| golimumab | SC | 0.125 | 6.6 | 1.41 | 0.486 | 12.7 | Rheumatoid Arthritis | 70 | 302 | 2 | 0 | [DOI: 10.1177/0091270010372520](https://doi.org/10.1177/0091270010372520) |
| golimumab | SC | 0.802 | 14 | 0.967 |  |  | Moderately to Severely Active Ulcerative Colitis | 70 | 1174 | 1 | 0 | [DOI: 10.1002/jcph.1353](https://doi.org/10.1002/jcph.1353) |
| golimumab | SC | 0.187 | 5.05 | 0.861 | 0.9 | 4.66 | Moderate to Severe Ulcerative Colitus | 76 | 20 | 2 | 0 | [DOI: 10.1080/00365521.2019.1619828](https://doi.org/10.1080/00365521.2019.1619828) |
| golimumab | SC | 0.495 | 8.82 | 0.417 | 0.469 | 4.48 | Ulcerative Colitus | 72 | 56 | 2 | 0 | [DOI: 10.1093/ibd/izz144](https://doi.org/10.1093/ibd/izz144) |
| golimumab | SC | 0.213 | 3.43 | 0.544 | 0.291 | 2.27 | Moderate to Severe Ulcerative Colitus | 70 | 1227 | 2 | 0 | [DOI: 10.1016/j.clinthera.2019.11.010](https://doi.org/10.1016/j.clinthera.2019.11.010) |
| guselkumab | SC | 0.09 | 13.5 | 0.513 |  |  | Moderate to Severe Plaque Psoriasis | 87 | 1454 | 1 | 0 | [DOI: 10.1002/jcph.1063](https://doi.org/10.1002/jcph.1063) |
| infliximab | IV |  | 2.37 | 0.381 | 0.122 | 1.37 | Inflammatory Bowel Disease | 70 | 169 | 2 | 0 | [DOI: 10.1097/MIB.0000000000000212](https://doi.org/10.1097/mib.0000000000000212) |
| infliximab | IV |  | 3.29 | 0.407 | 4.13 | 7.14 | Ulcerative Colitus | 79 | 482 | 2 | 0 | [DOI: 10.1007/s00228-009-0718-4](https://doi.org/10.1007/s00228-009-0718-4) |
| infliximab | IV |  | 2.3 | 0.288 | 0.129 | 1.9 | Inflammatory Bowel Disease | 67 | 33 | 2 | 0 | [DOI: 10.1097/FTD.0b013e318180e300](https://doi.org/10.1097/ftd.0b013e318180e300) |
| infliximab | IV |  | 3.06 | 0.273 | 1.72 | 2.94 | Ankylosing Spondylitis | 77 | 279 | 2 | 0 | [DOI: 10.1177/0091270008316886](https://doi.org/10.1177/0091270008316886) |
| ipilimumab | IV |  | 4.15 | 0.36 | 0.9864 | 3.11 | Advanced Melanoma | 80 | 499 | 2 | 0 | [DOI: 10.1111/bcp.12323](https://doi.org/10.1111/bcp.12323) |
| isatuximab | IV |  | 5.13 | 0.2292 | 1.03 | 3.62 | Multiple Myeloma | 76 | 476 | 2 | 1 | [DOI: 10.1002/psp4.12561](https://doi.org/10.1002/psp4.12561) |
| lanadelumab | SC |  | 14.9 | 0.74 |  |  | Hereditary Angioedema | 81 | 257 | 1 | 0 | [DOI: 10.1111/cts.12806](https://doi.org/10.1111/cts.12806) |
| mepolizumab | SC | 0.194 | 4.57 | 0.31 | 1.27 | 4.53 | Asthma (and stable ICS) | 75 | 59 | 2 | 0 | [DOI: 10.5414/CP202446](https://doi.org/10.5414/cp202446) |
| mepolizumab | IV |  | 3.6 | 0.21 | 1 | 3.56 | Asthma (and stable ICS) | 75 | 11 | 2 | 0 | [DOI: 10.5414/CP202446](https://doi.org/10.5414/cp202446) |
| mogamulizumab | IV |  | 3.65 | 0.3312 | 1.276 | 2.48 | T-Cell Lymphoma | 73 | 444 | 2 | 0 | [DOI: 10.1002/jcph.1564](https://doi.org/10.1002/jcph.1564) |
| natalizumab | IV |  | 3.76 | 0.15 | 0.4 | 1.82 | Multiple Sclerosis | 70 | 990 | 2 | 1 | [DOI: 10.1002/jcph.894](https://doi.org/10.1002/jcph.894) |
| necitumumab | IV |  | 3.41 | 0.27 | 0.439 | 3.29 | Cancer | 70 | 807 | 2 | 1 | [DOI: 10.1007/s40262-016-0452-x](https://doi.org/10.1007/s40262-016-0452-x) |
| nivolumab | IV |  | 3.46 | 0.211 | 0.48 | 3.46 | Metastatic non-small cell lung cancer, melanoma and renal cell cancer | 79 | 221 | 2 | 0 | [DOI: 10.1186/s40425-019-0669-y](https://doi.org/10.1186/s40425-019-0669-y) |
| nivolumab | IV |  | 4.46 | *0.211* | 0.624 | 2.52 | Gastic and Gastro-esophageal junction cancers | 80 | 1302 | 2 | 1 | [DOI: 10.1007/s00280-019-03771-z](https://doi.org/10.1007/s00280-019-03771-z) |
| nivolumab | IV |  | 4.13 | *0.187* | 0.746 | 2.5 | Classical Hodgkin Lymphoma | 80 | 1074 | 2 | 1 | [DOI: 10.1002/jcph.1324](https://doi.org/10.1002/jcph.1324) |
| nivolumab | IV |  | 3.63 | *0.169* | 0.77 | 2.78 | Solid Tumours | 80 | 1895 | 2 | 1 | [DOI: 10.1002/psp4.12143](https://doi.org/10.1002/psp4.12143) |
| obinutuzumab | IV |  | 2.76 | 0.0828 | 1.29 | 1.01 | CLL and Non-Hodgkin's Lymphoma | 75 | 678 | 2 | 1 | [DOI: 10.1038/psp.2014.42](https://doi.org/10.1038/psp.2014.42) |
| ocrelizumab | IV |  | 2.78 | 0.17 | 0.294 | 2.68 | Relapsing Multiple Sclerosis | 75 | 941 | 2 | 1 | [DOI: 10.1111/bcp.14658](https://doi.org/10.1111/bcp.14658) |
| ofatumumab | IV |  | 3.26 | 0.18 | 0.532 | 2.07 | CLL, Follicular Lymphoma and Rheumatoid Arthritis | 75 | 477 | 2 | 1 | [DOI: 10.1002/jcph.268](https://doi.org/10.1002/jcph.268) |
| olaratumab | IV |  | 4.16 | *0.483* | 0.756 | 3.58 | Advanced or Metastatic Cancer | 80 | 196 | 2 | 0 | [DOI: 10.1007/s40262-017-0562-0](https://doi.org/10.1007/s40262-017-0562-0) |
| omalizumab | SC |  | 8.12 | 0.202 |  |  | Allergic Asthma | 70 | 3229 | 3 | 1 | [DOI: 10.1016/j.dmpk.2015.12.003](https://doi.org/10.1016/j.dmpk.2015.12.003) |
| omalizumab | SC |  | 9.33 | 0.208 |  |  | Allergic Asthma | 70 | 1781 | 3 | 1 | [DOI: 10.1111/j.1365-2125.2009.03401.x](https://doi.org/10.1111/j.1365-2125.2009.03401.x) |
| omalizumab | SC |  | 5.9 | 0.175 |  |  | Atopic Asthma | 70 | 733 | 3 | 1 | [DOI: 10.1111/j.1365-2125.2006.02803.x](https://doi.org/10.1111/j.1365-2125.2006.02803.x) |
| palivizumab | IM | 1.01 | 4.09 | 0.198 | 0.879 | 2.23 | High risk Respiratory Syncytial Virus (RSV) | 70 | 1999 | 2 | 0 | [DOI: 10.1128/AAC.06446-11](https://doi.org/10.1128/aac.06446-11) |
| panitumumab | IV |  | 3.66 | 0.269 | 0.389 | 2.58 | Advanced Solid Tumors | 80 | 1200 | 2 | 1 | [DOI: 10.1177/0091270009344989](https://doi.org/10.1177/0091270009344989) |
| pembrolizumab | IV |  | 3.49 | 0.219 | 0.792 | 4 | Advanced Solid Tumors | 77 | 2195 | 2 | 0 | [DOI: 10.1007/s10928-017-9528-y / DOI: 10.1002/psp4.12139](https://doi.org/10.1007/s10928-017-9528-y) |
| pertuzumab | IV |  | 3.11 | 0.235 | 0.534 | 2.46 | Solid Tumours | 48 | 481 | 2 | 0 | [DOI: 10.1007/s00280-014-2560-3](https://doi.org/10.1007/s00280-014-2560-3) |
| pertuzumab | IV |  | 2.74 | 0.214 | 0.556 | 2.15 | Cancer | 69 | 1000 | 2 | 0 | [DOI: 10.1007/s11095-006-0205-x](https://doi.org/10.1007/s11095-006-0205-x) |
| ramucirumab | IV |  | 3.26 | 0.355 | 0.2448 | 2.04 | Cancer | 68 | 1639 | 2 | 0 | [DOI: 10.1111/bcp.13403](https://doi.org/10.1111/bcp.13403) |
| reslizumab | IV |  | 3.13 | 0.171 | 0.24 | 2.05 | Asthma, nasal polyposis | 73 | 804 | 2 | 0 | [DOI: 10.1002/jcph.1609](https://doi.org/10.1002/jcph.1609) |
| risankizumab | SC | 0.229 | 4.86 | 0.243 | 0.656 | 4.25 | Plaque Psoriasis, Healthy | 70 | 1899 | 2 | 0 | [DOI: 10.1007/s40262-019-00759-z](https://doi.org/10.1007/s40262-019-00759-z) |
| risankizumab | SC | 0.18 | 5.66 | 0.3 | 0.33 | 3.43 | Psoriasis, Chron's disease | 70 | 157 | 2 | 0 | [DOI: 10.1007/s40262-018-0704-z](https://doi.org/10.1007/s40262-018-0704-z) |
| rituximab | IV |  | 4.1 | 0.45 | 1.72 | 6.88 | Rheumatoid Arthritis |  | 64 | 2 | 0 | [DOI: 10.1111/bcp.13270](https://doi.org/10.1111/bcp.13270) |
| rituximab | IV |  | 2.48 | 0.159 | 0.94 | 2.54 | Kidney | 69 | 20 | 2 | 0 | [DOI: 10.1111/bcp.12098](https://doi.org/10.1111/bcp.12098) |
| rituximab | IV |  | 4.15 | 0.171 | 1.15 | 2.32 | Chronic Lymphocytic Leukemia | 80 | 21 | 2 | 1 | [DOI: 10.1177/0091270011430506](https://doi.org/10.1177/0091270011430506) |
| rituximab | IV |  | 2.98 | 0.257 | 0.6556 | 3.64 | Rheumatoid Arthritis | 66 | 102 | 2 | 0 | [DOI: 10.1177/0091270005277075](https://doi.org/10.1177/0091270005277075) |
| romosozumab | SC | 0.45 | 3.92 | 0.2352 |  |  | Postmenopausal Osteoperosis |  | 72 | 1 | 1 | [DOI: 10.1016/j.bone.2020.115223](https://doi.org/10.1016/j.bone.2020.115223) |
| sarilumab | SC | 0.136 | 2.08 | 0.26 | 0.156 | 5.23 | Rheumatoid Arthritis | 71 | 1935 | 2 | 1 | [doi: 10.1007/s40262-019-00765-1](https://dx.doi.org/10.1007%2Fs40262-019-00765-1) |
| secukinumab | SC | 0.18 | 3.61 | 0.19 | 0.39 | 2.87 | Psoriasis | 90 | 1233 | 2 | 0 | [DOI: 10.1002/jcph.876](https://doi.org/10.1002/jcph.876) |
| siltuximab | IV |  | 3.66 | 0.214 | 0.624 | 3.13 |  | 73 | 460 | 2 | 0 | [DOI: 10.1007/s00280-019-03939-7](https://doi.org/10.1007/s00280-019-03939-7) |
| siltuximab | IV |  | 4.5 | 0.315 | 3.64 | 1.9 | Metastatic Renal Carcinoma | 80 | 36 | 2 | 0 | [DOI: 10.1158/1078-0432.CCR-09-2581](https://doi.org/10.1158/1078-0432.ccr-09-2581) |
| tildrakizumab | SC | 0.458 | 10.7 | 0.297 |  |  | Psoriasis, Healthy | 85 | 2098 | 1 | 0 | [DOI: 10.1007/s40262-019-00743-7](https://doi.org/10.1007/s40262-019-00743-7) |
| tocilizumab | IV |  | 4.83 | 0.2496 |  |  | Rheumatid Arthritis | 63 | 35 | 1 | 1 | [DOI: 10.1111/bcp.13500](https://doi.org/10.1111/bcp.13500) |
| tocilizumab | IV/SC | 0.23 | 4.5 | 0.216 | 0.274 | 2.8 | Rheumatoid Arthritis | 70 | 1699 | 2 | 1 | [DOI: 10.1002/jcph.826](https://doi.org/10.1002/jcph.826) |
| tocilizumab | IV |  | 3.5 | 0.3 | 0.2 | 2.9 | Rheumatoid Arthritis | 70 | 1793 | 2 | 1 | [DOI: 10.1177/0091270009350623](https://doi.org/10.1177/0091270009350623) |
| trastuzumab | IV |  | 3.15 | 0.2496 | 0.47 | 5.55 | Her2+ metastatic breast cancer | 67 | 702 | 2 | 0 | [DOI: 10.1007/s00280-019-03850-1](https://doi.org/10.1007/s00280-019-03850-1) |
| trastuzumab | IV |  | 2.62 | 0.127 | 0.544 | 2.97 | Solid Tumours | 60 | 1582 | 2 | 1 | [DOI: 10.1007/s00280-018-3728-z](https://doi.org/10.1007/s00280-018-3728-z) |
| trastuzumab | SC/IV | 0.404 | 2.91 | 0.111 | 0.445 | 3.06 | Her2+ early breast cancer | 68 | 595 | 2 | 1 | [DOI: 10.1007/s00280-015-2922-5](https://doi.org/10.1007/s00280-015-2922-5) |
| trastuzumab | IV |  | 3.63 | 0.23 | 0.366 | 3.74 | Gastric cancer | 62 | 266 | 2 | 1 | [DOI: 10.1007/s00280-014-2400-5](https://doi.org/10.1007/s00280-014-2400-5) |
| trastuzumab | IV |  | 2.95 | 0.225 | 0.4838 | 4.79 | Her2+ metastatic breast cancer | 70 | 476 | 2 | 0 | [DOI: 10.1007/s00280-005-1026-z](https://doi.org/10.1007/s00280-005-1026-z) |
| ustekinumab | SC | 0.23 | 10.2 | 0.44 |  |  | Psoriasis | 92 | 491 | 1 | 0 | [doi: 10.1111/cts.12725](https://dx.doi.org/10.1111%2Fcts.12725) |
| ustekinumab | SC | 0.142 | 3.01 | 0.186 | 0.157 | 1.43 | Moderate and Severe Active Ulcerative Colitis | 71 | 823 | 2 | 0 | [DOI: 10.1002/jcph.1582](https://doi.org/10.1002/jcph.1582) |
| vedolizumab | IV |  | 3.19 | 0.159 | 0.12 | 1.65 | Ulcerative Colitis & Chron's Disease | 70 | 2554 | 2 | 1 | [DOI: 10.1111/apt.13243](https://doi.org/10.1111/apt.13243) |
| vedolizumab | IV |  | 3.16 | 0.165 | 0.161 | 1.84 | Ulcerative Colitis & Chron's Disease | 70 | 1933 | 2 | 1 | [DOI: 10.5217/ir.2019.09167](https://doi.org/10.5217/ir.2019.09167) |
| teprotumumab | IV |  | 3.26 | 0.27 | 0.74 | 4.32 |  |  | 40 |  | 0 | **FDA** |

## Table 2: Mann-Whitney significance test results

*Table 2:* ***Mann-Whitney significance test p-values of pairwise comparisons between parameter values V1, V2, Q and CL in predefined clusters.***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mann-Whitney p-values** | V1 | V2 | Q | CL |
| Pediatric/non-pediatric models | 0.45 | 0.27 | 0.32 | **0.012** |
| Nonlinear CL incorporation | 0.073 | 0.1 | **0.011** | **0.0013** |
| Autoimmune diseased study pop. | 0.21 | 0.61 | 0.25 | 0.77 |
| Human vs Humanized | **0.015** | 0.93 | 0.61 | 0.35 |
| Human vs Chimeric | 0.35 | 0.18 | **0.0052** | **0.037** |
| Humanized vs Chimeric | 0.88 | 0.16 | **0.0066** | **0.0022** |
| Cardiovascular vs Gastroenterology | 0.75 | 0.75 | 0.75 | 0.75 |
| Cardiovascular vs Neurology | 1.0 | 0.67 | 0.67 | 0.67 |
| Cardiovascular vs Oncology | 0.73 | 1.0 | 0.39 | 0.54 |
| Cardiovascular vs Other | 0.67 | 1.0 | 0.67 | 0.33 |
| Cardiovascular vs Rheumatology | 0.75 | 0.75 | 0.66 | 0.75 |
| Cardiovascular vs Transplantation | 0.67 | 0.67 | 0.67 | 0.67 |
| Cardiovascular vs Respiratory | 0.67 | 1.0 | 1.0 | 0.67 |
| Gastroenterology vs Neurology | 1.0 | 1.0 | 0.67 | 0.11 |
| Gastroenterology vs Oncology | 0.38 | 0.24 | **0.024** | 0.87 |
| Gastroenterology vs Other | 0.68 | 0.35 | 0.22 | 0.22 |
| Gastroenterology vs Rheumatology | 0.62 | 0.21 | 0.16 | 0.80 |
| Gastroenterology vs Transplantation | 0.22 | 0.33 | 0.22 | 0.056 |
| Gastroenterology vs Respiratory | 1.0 | 0.67 | 0.5 | 0.67 |
| Neurology vs Oncology | 0.67 | 0.23 | 0.070 | 0.070 |
| Neurology vs Other | 1.0 | 0.079 | 0.19 | 0.38 |
| Neurology vs Rheumatology | 0.67 | 0.11 | 0.46 | 0.056 |
| Neurology vs Transplantation | 0.67 | 0.33 | 0.33 | 0.33 |
| Neurology vs Respiratory | 1.0 | 0.67 | 1.0 | 0.33 |
| Oncology vs Other | 0.82 | 0.90 | 0.64 | 0.13 |
| Oncology vs Rheumatology | 0.99 | 0.69 | 0.70 | 0.51 |
| Oncology vs Transplantation | 0.15 | 0.23 | 0.49 | **0.014** |
| Oncology vs Respiratory | 0.93 | 0.81 | 0.88 | 0.26 |
| Other vs Rheumatology | 1.0 | 0.52 | 1.0 | 0.07 |
| Other vs Transplantation | 0.19 | 0.17 | 0.57 | 0.095 |
| Other vs Respiratory | 1.0 | 1.0 | 1.0 | 0.86 |
| Rheumatology vs Transplantation | 0.22 | 0.33 | 0.46 | 0.056 |
| Rheumatology vs Respiratory | 1.0 | 0.67 | 0.88 | 0.11 |
| Transplantation vs Respiratory | 0.33 | 0.67 | 0.67 | 0.33 |
| IgG1 vs IgG2 | 0.78 | 0.59 | 0.40 | 0.97 |
| IgG1 vs IgG4 | 0.46 | 0.20 | 0.92 | **0.028** |
| IgG2 vs IgG4 | 1.0 | 0.89 | 0.44 | 0.44 |

## Table 3: IIV meta-analysis

*Table 3:* ***Meta-analysis IIV characteristics.***

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Parameter** | **Median CV%** | **Counts** |
| 0 | V1 IIV | 25.7 | 23 |
| 1 | V2 IIV | 48.12 | 18 |
| 2 | Q IIV | 50.4 | 8 |
| 3 | CL IIV | 34.3 | 25 |
| 4 | VM IIV | 54 | 5 |
| 5 | KM IIV | 79.7 | 5 |

## Fig 1: IIV compensation

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*Figure 1****: Eta frequency distribution for V1 in the Tocilizumab dataset when model parameter V1 is fixed  
 to an extremely low value (1L).*** *The frequency (y-axis) is plotted against the eta on V1 values (x-axis). The   
distribution only takes on positive values and loses its normality assumption.*

## Table 4: Strict covariate combinations for the final model selection: subset 2 (n=22)

*Table 4:* ***Distinct covariate combinations and their respective counts found in data subset 2 (two-compartment models, IV administrated mAbs,   
nonlinear clearance incorporated) after exclusion of models containing no covariates at all.*** *Albumin covariates are highlighted in grey as these   
covariates are not included in this study due to unavailability I n the validation datasets. Covariates are represented as “parameter”\_”covariate”  
 (e.g. V1\_WT: covariate WT on V1). WT: body weight, Sx: sex, Alb: albumin content.*

|  |  |
| --- | --- |
| Covariate inclusions | Number of models containing strictly this combination of covariates |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx' | 2 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Alb' | 2 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'V1\_Sx' | 2 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'CL\_Alb' | 2 |
| 'V1\_Sx' | 1 |
| 'CL\_Alb' | 1 |
| 'V1\_WT', 'CL\_WT' | 1 |
| 'CL\_WT', 'V2\_WT' | 1 |
| 'CL\_WT', 'CL\_Alb' | 1 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT' | 1 |
| 'V1\_WT', 'CL\_WT', 'V2\_WT' | 1 |
| 'V1\_WT', 'CL\_WT', 'CL\_Alb' | 1 |
| 'CL\_Sx', 'V1\_Alb', 'CL\_Alb' | 1 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT' | 1 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx', 'CL\_Alb' | 1 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'V1\_Sx', 'CL\_Sx' | 1 |

## Table 5: Strict covariate combinations for subset 1 (n=52)

*Table 5:* ***Distinct covariate combinations and their respective counts found in the data subset 1 (two-compartment models, IV administrated   
mAbs) after exclusion of models containing no covariates at all.*** *Albumin covariates are highlighted in grey as these covariates are not included   
in this study due to unavailability I n the validation datasets. Covariates are represented as “parameter”\_”covariate” (e.g. V1\_WT: covariate WT   
on V1). WT: body weight, Sx: sex, Alb: albumin content.*

|  |  |
| --- | --- |
| Covariate inclusions | Number of models containing strictly this combination of covariates |
| 'V1\_WT', 'CL\_WT' | 7 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'CL\_Alb' | 4 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx' | 3 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx', 'V1\_Alb', 'CL\_Alb' | 3 |
| 'CL\_WT' | 2 |
| ‘V1\_Sx’ | 2 |
| 'CL\_WT', 'CL\_Alb' | 2 |
| 'V1\_WT', 'CL\_WT', 'CL\_Alb' | 2 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Alb' | 2 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'V1\_Sx' | 2 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'V2\_Sx', 'V1\_Alb', 'CL\_Alb' | 2 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'V1\_Sx', 'CL\_Sx', 'CL\_Alb' | 2 |

## Table 6: Strict covariate combinations for the initial model list (n=96)

*Table 6:* ***Distinct covariate combinations and their respective counts found in the initial model selection after exclusion of models containing   
no covariates at all.*** *Albumin covariates are highlighted in grey as these covariates are not included in this study due to unavailability I n the   
validation datasets. Covariates are represented as “parameter”\_”covariate” (e.g. V1\_WT: covariate WT on V1). WT: body weight, Sx: sex, Alb:   
albumin content.*

|  |  |
| --- | --- |
| Covariate inclusions | Number of models containing strictly this combination of covariates |
| 'V1\_WT', 'CL\_WT' | 20 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT' | 8 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', ‘CL\_Alb’ | 7 |
| 'CL\_WT' | 7 |
| 'V1\_WT', 'CL\_WT', 'CL\_Alb' | 5 |
| 'V1\_WT', 'CL\_WT', 'Q\_WT', 'V2\_WT', 'V1\_Sx' | 4 |
| 'V1\_WT', 'CL\_WT', 'V2\_WT' | 3 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx' | 3 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Alb' | 3 |
| 'V1\_WT', 'CL\_WT', 'V1\_Sx', 'CL\_Sx', 'V1\_Alb', 'CL\_Alb' | 3 |

## Fig 2: GOF population prediction plots for covariate models in Natalizumab data.

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Description automatically generated with medium confidence1 A graph with blue dots

Description automatically generated2A graph with blue dots

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A graph with blue dots and a red line

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A graph with a line and a red line

Description automatically generated with medium confidence9

*Figure 2:* ***GOF plots for covariate model population predictions in the Natalizumab dataset.*** *The y-axis presents the logarithmically transferred population predicted concentration values and the x-axis presents the logarithmically transformed actual measured concentrations. The covariate model number is specified in the lower right corner and the corresponding MAPE is shown below the plot.*

## Fig 3: GOF population prediction plots for covariate models in Tocilizumab data.

A graph with red lines and white text

Description automatically generated0 A graph of a graph with a red line

Description automatically generated with medium confidence1 A graph of a graph with a red line

Description automatically generated with medium confidence2A graph with red lines and white text

Description automatically generated3

A graph with a red line

Description automatically generated4 A graph with a red line

Description automatically generated5 A graph with a red line

Description automatically generated6 A graph with a red line and blue dots

Description automatically generated7 A graph of a graph with a red line and white text

Description automatically generated with medium confidence8 A graph with a red line

Description automatically generated9

*Figure 3:* ***GOF plots for covariate model population predictions in the Tocilizumab dataset****. The y-axis presents the logarithmically transferred population predicted concentration values and the x-axis presents the logarithmically transformed actual measured concentrations. The covariate model number is specified in the lower right corner and the corresponding MAPE is shown below the plot.*

## Fig 4: GOF population prediction plots for covariate models in Guselkumab data.

A graph with a red line

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Description automatically generated1A graph with red line and blue dots

Description automatically generated2A graph with a red line and blue dots

Description automatically generated3 A graph with a red line and blue dots

Description automatically generated4A screen shot of a graph

Description automatically generated5A graph with a red line

Description automatically generated6 A graph with a red line and blue dots

Description automatically generated7A graph with a red line and blue dots

Description automatically generated8 A graph with red lines and white text

Description automatically generated 9

*Figure 4:* ***GOF plots for covariate model population predictions in the Guselkumab dataset.*** *The y-axis presents the logarithmically transferred population predicted concentration values and the x-axis presents the logarithmically transformed actual measured concentrations. The covariate model number is specified in the lower right corner and the corresponding MAPE is shown below the plot.*