

Claims

1. A CD20 and CD22 targeting antigen-binding molecule comprising at least three binding domains, wherein
 - (i.) the first binding domain comprises a paratope which immuno-specifically binds to CD20, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:
 - a) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 - 63,
 - b) CDR H1-3 of SEQ ID NO: 71 - 73 and CDR L1-3 of SEQ ID NO: 74 - 76,
 - c) CDR H1-3 of SEQ ID NO: 84 - 86 and CDR L1-3 of SEQ ID NO: 87 - 89, and
 - d) CDR H1-3 of SEQ ID NO: 97 - 99 and CDR L1-3 of SEQ ID NO: 100 - 102;
 - (ii.) the second binding domain comprises a paratope which immuno-specifically binds to CD22, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from
 - a) CDR H1-3 of SEQ ID NO: 138 - 140 and CDR L1-3 of SEQ ID NO: 141 - 143,
 - b) CDR H1-3 of SEQ ID NO: 151 - 153 and CDR L1-3 of SEQ ID NO: 154 - 156,
 - c) CDR H1-3 of SEQ ID NO: 164 - 166 and CDR L1-3 of SEQ ID NO: 167 - 169,
 - d) CDR H1-3 of SEQ ID NO: 177 - 179 and CDR L1-3 of SEQ ID NO: 180 - 182,
 - e) CDR H1-3 of SEQ ID NO: 190 - 192 and CDR L1-3 of SEQ ID NO: 193 - 195,
 - f) CDR H1-3 of SEQ ID NO: 203 - 205 and CDR L1-3 of SEQ ID NO: 206 - 208,
 - g) CDR H1-3 of SEQ ID NO: 125 - 127 and CDR L1-3 of SEQ ID NO: 128 - 130,
 - h) CDR H1-3 of SEQ ID NO: 216 - 218 and CDR L1-3 of SEQ ID NO: 219 - 221, and
 - i) CDR H1-3 of SEQ ID NO: 379 - 381 and CDR L1-3 of SEQ ID NO: 382 - 384;

and

 - (iii.) the third binding domain comprises a paratope which immune-specifically binds to an extracellular epitope of the human and/or the Macaca CD3 ϵ chain,

wherein the first, second and third binding domain are arranged in an amino to carboxyl order, and wherein the first binding domain and the second binding domain are linked by a peptide linker having a length of 5 to 24, preferably 18 amino acids.

2. The CD20 and CD22 targeting antigen-binding molecule of claim 1, wherein the antigen-binding molecule comprises a fourth domain which comprises two polypeptide monomers, each comprising a hinge, a CH2 and a CH3 domain, wherein said two polypeptide monomers are fused to each other via a peptide linker

wherein said forth domain preferably comprises in an amino to carboxyl order:

hinge-CH2-CH3-linker-hinge-CH2-CH3

and/or wherein preferably each of said polypeptide monomers in the fourth domain has an amino acid sequence that is at least 90% identical to a sequence selected from the group consisting of: SEQ ID NO: 17-24, wherein preferably each of said polypeptide monomers has an amino acid sequence selected from SEQ ID NO: 17-24,

and/or wherein preferably the CH2 domain comprises an intra domain cysteine disulfide bridge,

and/or wherein the first, second, third and fourth binding domain are arranged in an amino to carboxyl order.

3. The CD20 and CD22 targeting antigen-binding molecule of any of the preceding claims, wherein the antigen-binding molecule is a single chain antigen-binding molecule, preferably a CD20 and CD22 targeting scFv antigen-binding molecule.
4. The CD20 and CD22 targeting antigen-binding molecule of any of the preceding claims, wherein the peptide linker between the first binding domain and the second binding domain is selected from having a length of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 23, or 24 amino acids, preferably 5, 6, 7, 8, 9, 10, 11 or 12 amino acids, more preferably 6 amino acids.
5. The CD20 and CD22 targeting antigen-binding molecule of any of the preceding claims, wherein the peptide linker between the first binding domain and the second binding domain is selected from the group consisting of S(G₄S)_n, (G₄S)_n, G_{4n}, and G_{5n}, wherein n equals 1, 2, 3 or 4, preferably n equals 1 or 2, more preferably SG₄S.
6. The CD20 and CD22 targeting antigen-binding molecule of any of the preceding claims, wherein the first binding domain and the second binding domain each comprise a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:
 - a) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 138 - 140 and CDR L1-3 of SEQ ID NO: 141 – 143 of the second binding domain;

- b) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 151 - 153 and CDR L1-3 of SEQ ID NO: 154 – 156 of the second binding domain;
- c) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 164 - 166 and CDR L1-3 of SEQ ID NO: 167 - 169 of the second binding domain;
- d) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 177 - 179 and CDR L1-3 of SEQ ID NO: 180 – 182 of the second binding domain;
- e) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 190 - 192 and CDR L1-3 of SEQ ID NO: 193 – 195 of the second binding domain;
- f) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 203 - 205 and CDR L1-3 of SEQ ID NO: 206 - 208 of the second binding domain;
- g) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 125 - 127 and CDR L1-3 of SEQ ID NO: 128 – 130 of the second binding domain;
- h) CDR H1-3 of SEQ ID NO: 58 - 60 and CDR L1-3 of SEQ ID NO: 61 – 63 of the first binding domain and CDR H1-3 of SEQ ID NO: 216 - 218 and CDR L1-3 of SEQ ID NO: 219 – 221 of the second binding domain;
- i) CDR H1-3 of SEQ ID NO: 71 - 73 and CDR L1-3 of SEQ ID NO: 74 – 76 of the first binding domain and CDR H1-3 of SEQ ID NO: 379 - 381 and CDR L1-3 of SEQ ID NO: 382 – 384 of the second binding domain;
- j) CDR H1-3 of SEQ ID NO: 71 - 73 and CDR L1-3 of SEQ ID NO: 74 – 76 of the first binding domain and CDR H1-3 of SEQ ID NO: 203 - 205 and CDR L1-3 of SEQ ID NO: 206 - 208 of the second binding domain;
- k) CDR H1-3 of SEQ ID NO: 84 - 86 and CDR L1-3 of SEQ ID NO: 87 – 89 of the first binding domain and CDR H1-3 of SEQ ID NO: 164 - 166 and CDR L1-3 of SEQ ID NO: 167 – 169 of the second binding domain;

- l) CDR H1-3 of SEQ ID NO: 97 - 99 and CDR L1-3 of SEQ ID NO: 100 – 102 of the first binding domain and CDR H1-3 of SEQ ID NO: 177 - 179 and CDR L1-3 of SEQ ID NO: 180 – 182 of the second binding domain;
 - m) CDR H1-3 of SEQ ID NO: 97 - 99 and CDR L1-3 of SEQ ID NO: 100 – 102 of the first binding domain and CDR H1-3 of SEQ ID NO: 190 - 192 and CDR L1-3 of SEQ ID NO: 193 – 195 of the second binding domain.
7. The CD20 and CD22 targeting antigen-binding molecule of any of the preceding claims, wherein the first binding domains is capable of binding to CD20 and the second binding domain is capable of binding to CD22 simultaneously, preferably wherein CD20 and CD22 are on the same target cell.
 8. The CD20 and CD22 targeting antigen-binding molecule of claim 1, wherein the third binding domain comprise a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:
 - a) CDR H1-3 of SEQ ID NO: 392 - 394 and CDR L1-3 of SEQ ID NO: 395 – 397; and
 - b) CDR H1-3 of SEQ ID NO: 401 - 403 and CDR L1-3 of SEQ ID NO: 404- 406.
 9. The CD20 and CD22 targeting antigen-binding molecule according to any of the preceding claims, wherein the antigen-binding molecule comprises in an amino to carboxyl order:
 - (a) the first domain;
 - (b) a peptide linker preferably having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-4 and 9-12, preferably 11;
 - (c) the second domain;
 - (d) a peptide linker preferably having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-3; and
 - (e) the third domain.
 10. The CD20 and CD22 targeting antigen-binding molecule according to claim 9, wherein the antigen-binding molecule further comprises in an amino to carboxyl order:
 - (f) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 9, 10, 11 and 12;

- (g) the first polypeptide monomer of the fourth domain;
 - (h) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 6, 7 and 8; and
 - (i) the second polypeptide monomer of the fourth domain.
11. The CD20 and CD22 targeting antigen-binding molecule according to any of the preceding claims, wherein the first binding domain comprises a VH region and a VL region selected from SEQ ID Nos: 64 as VH and 65 as L, 77 as VH and 78 as VL, 90 as VH and 91 as VL, 103 as VH and 104 as VL, respectively, and wherein the second binding domain comprises a VH region and a VL region selected from SEQ ID Nos: 144 as VH and 145 as VL, 157 and 158, 172 and 173, 183 and 184, 196 and 197, 209 and 210, 131 and 132, and 385 and 386, respectively.
 12. The CD20 and CD22 targeting antigen-binding molecule according to any of the preceding claims, wherein the first binding domain comprises a scFv sequence selected from the group consisting of SEQ ID Nos: 66, 79, 92, and 105, and wherein the second binding domain comprises a scFv sequence selected from the group consisting of SEQ ID Nos 146, 159, 172, 185, 198, 211, 133, 224 and 387, respectively.
 13. The CD20 and CD22 targeting antigen-binding molecule according to according to any of the preceding claims, wherein the antigen-binding molecule comprises a first (CD20) and second (CD22) target binding domain together with a third effector (CD3) binding domain and a fourth domain conferring extended half-life, the three binding domains and the forth domain linked together having a sequence selected from the group consisting of SEQ ID Nos: 238, 248, 258, 268, 278, 288, 308, 318, 328, 338, 348, 368 and 378.
 14. A polynucleotide encoding an antigen-binding molecule as defined in any one of the preceding claims.
 15. A vector comprising a polynucleotide as defined in claim 14.
 16. A host cell transformed or transfected with the polynucleotide as defined in claim 14 or with the vector as defined in claim 15.
 17. A process for the production of the CD20 and CD22 targeting antigen-binding molecule according to any of the preceding claims, said process comprising culturing a host cell as defined in claim 16 under conditions allowing the expression of the antigen-binding molecule as defined in any one of claims 1 to 13 and recovering the produced antigen-binding molecule from the culture.
 18. A pharmaceutical composition comprising the CD20 and CD22 targeting antigen-binding molecule according to any one of claims 1 to 13, or produced according to the process of claim 17,

which is preferably stable for at least four weeks at about -20°C.

19. The CD20 and CD22 targeting antigen-binding molecule according to any of the preceding claims, or produced according to the process of claim 17, for use in medicine.
20. Use of the CD20 and CD22 targeting antigen-binding molecule according to claim 1, or produced according to the process of claim 17 in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, wherein the disease preferably is Non-Hodgkin lymphoma (NHL), Non-small-cell lung carcinoma (NSCLC) and Colorectal cancer (CRC).