Claims

1. A pharmaceutical composition comprising a monoclonal antibody with high affinity for the target antigen suitable for reducing the duration and/or severity of diarrhoea, morbidity and/or mortality in a patient with *Clostridium difficile* infection or at risk of said infection wherein the antibody is specific to: antigen TcdA and binds 3 or more times thereto with an EC50 in the range 0.1 to 10 ng/ml when toxin is used at an LD_{80} or higher.
2. A pharmaceutical composition according to claim 1, wherein the anti-TcdA antibody binds to the C-terminal cell binding portion of TcdA.
3. A pharmaceutical composition according to claim 2, wherein the anti-TcdA antibody binds to TcdA123 or TcdA456.
4. A pharmaceutical composition according to any one of claims 1 to 3, wherein the anti-TcdA antibody binds 12 times.
5. A pharmaceutical composition according to claim 4, wherein the antibody EC_{50} is between 1 and 10ng/ml when toxin is at an LD_{80} or higher.
6. A pharmaceutical composition according to claims 4 or claim 5 wherein the maximal inhibition of toxin is between 50 and 100% when toxin is used at an LD_{80} or higher.
7. A pharmaceutical composition according to any one of claims 1 to 6, further comprising a monoclonal antibody specific to TcdB.
8. A pharmaceutical composition according to claim 7, wherein the anti-TcdB antibody binds to the C-terminal cell binding portion of TcdB.
9. A pharmaceutical composition according to claim 8, wherein the anti-TcdB antibody binds to TcdB1234.
10. A pharmaceutical composition according to any one of claims 1 to 9, wherein the antibody to TcdB binds the target antigen 2 times.
11. A pharmaceutical composition according to claim 10, wherein the antibody binds the target antigen 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 times or more.
12. A pharmaceutical composition according to any one of claims 1 to 11, further comprising a monoclonal antibody specific to TcdB.

~~13. A pharmaceutical composition according to any one of claims 1 to 12, wherein the anti-TcdA and/or anti-TcdB antibody has an affinity in the range 50 to 600pM.~~

~~14. A pharmaceutical composition according to any one of claims 1 to 13, wherein one or more antibodies is a neutralizing antibody.~~

~~15.~~1. A ~~pharmaceutical composition according to claim 1 comprising a~~ monoclonal antibody specific to antigen TcdA wherein the antibody comprises ~~which specifically binds TcdA comprising~~ a heavy chain wherein the variable domain of the heavy chain comprises ~~at least one of a~~ 3 CDRs having the sequence given in SEQ ID NO:44 for CDR-H1, a CDR having the sequence given in SEQ ID NO:45 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:46 for CDR-H3~~.~~.

~~16.~~ ~~A pharmaceutical composition according to claim 15 wherein the monoclonal antibody further comprises~~ and a light chain wherein the variable domain of the light chain comprises at least ~~one of a~~ 3 CDRs having the sequence given in SEQ ID NO:41 for CDR-L1, a CDR having the sequence given in ~~in~~ SEQ ID NO:42 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:43 for CDR-L3.

~~17.~~2. A ~~pharmaceutical composition according to claim 16 wherein the~~ monoclonal antibody according to claim 1 having ~~has~~ a heavy chain comprising the sequence given in SEQ ID NO:49 and a light chain comprising the sequence given in SEQ ID NO:47.

3. A pharmaceutical composition comprising a monoclonal antibody as defined in any one of claim 1 or 2.

~~18.~~4. A pharmaceutical composition according to claim ~~1~~3 further comprising a monoclonal antibody which specifically binds TcdA comprising a heavy chain wherein the variable domain of the heavy chain comprises ~~at least one of a~~ 3 CDRs having the sequence given in SEQ ID NO:54 for CDR-H1, a CDR having the sequence given in SEQ ID NO:55 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:56 for CDR-H3~~.~~

~~19.~~ ~~A pharmaceutical composition according to claim 18 wherein the monoclonal antibody further comprises~~ and a light chain wherein the variable domain of the light chain comprises ~~at least one of a~~ 3 CDRs having the sequence given in SEQ ID NO:51 for CDR-L1, a CDR having the sequence given in ~~in~~ SEQ ID NO:52 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:53 for CDR-L3.

~~20.~~5. A pharmaceutical composition according to claim ~~19~~4 comprising a ~~wherein the~~ monoclonal antibody ~~has~~having a heavy chain comprising the sequence given in SEQ ID NO:59 and a light chain comprising the sequence given in SEQ ID NO:57.

~~21.~~6. A pharmaceutical composition according to any one of claims ~~7~~ 3 to 5 comprising a monoclonal antibody which specifically binds TcdB comprising a heavy chain wherein the variable domain of the heavy chain comprises at least one of a CDR having the sequence given in SEQ ID NO:124 for CDR-H1, a CDR having the sequence given in ~~in~~ SEQ ID NO:125 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:126 for CDR-H3~~.~~

~~22.~~ ~~A pharmaceutical composition according to claim 21 wherein the monoclonal antibody which specifically binds TcdB further comprises~~ and a light chain wherein the variable domain of the light chain comprises at least one of a CDR having the sequence given in SEQ ID NO:121 for CDR-L1, a CDR having the sequence given in ~~in~~ SEQ ID NO:122 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:123 for CDR-L3.

~~23.~~7. A pharmaceutical composition according to claim ~~22~~6 comprising a ~~wherein the~~ monoclonal antibody having ~~which specifically binds TcdB has~~ a heavy chain comprising the sequence given in SEQ ID NO:129 and a light chain comprising the sequence given in SEQ ID NO:127.

~~24.~~8. A pharmaceutical composition according to any one of claims 3 to 7 comprising a monoclonal antibody which specifically binds TcdB comprising a heavy chain wherein the variable domain of the heavy chain comprises ~~at least one of a~~ 3 CDRs having the sequence

given in SEQ ID NO:154 for CDR-H1, a CDR having the sequence given in ~~in~~ SEQ ID NO:155 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:156 for CDR-H3~~.~~

~~25. A pharmaceutical composition according to claim 24 wherein the monoclonal antibody which specifically binds TcdB further comprises~~ and a light chain wherein the variable domain of the light chain comprises ~~at least one of a~~ 3 CDR~~s~~ having the sequence given in SEQ ID NO:151 for CDR-L1, a CDR having the sequence given in ~~in~~ SEQ ID NO:152 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:153 for CDR-L3.

~~26.~~9. A pharmaceutical composition according to claim ~~25~~8, comprising a ~~wherein the~~ monoclonal antibody having ~~which specifically binds TcdB has~~ a heavy chain comprising the sequence given in SEQ ID NO:159 and a light chain comprising the sequence given in SEQ ID NO:157.

~~27.~~10. A pharmaceutical composition according to any one of claim~~s~~ ~~1~~3 to 9 comprising a monoclonal antibody which specifically binds TcdA having a heavy chain and a light chain wherein the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NO:9, SEQ ID NO:19, SEQ ID NO:29 and SEQ ID NO:39 and the light chain variable region comprises a sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:17, SEQ ID NO:27 and SEQ ID NO:37.

~~28.~~11. A pharmaceutical composition according to any one of claim~~s~~ ~~7~~3 to 10 comprising a monoclonal antibody which specifically binds TcdB having a heavy chain and a light chain wherein the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NO:69, SEQ ID NO:79, SEQ ID NO:89, SEQ ID NO:99, SEQ ID NO:109, SEQ ID NO:119, SEQ ID NO:139, SEQ ID NO:149 and SEQ ID NO:159 and the light chain variable region comprises a sequence selected from the group consisting of SEQ ID NO:67, SEQ ID NO:77, SEQ ID NO:87, SEQ ID NO:97, SEQ ID NO:107, SEQ ID NO:117, SEQ ID NO:137, SEQ ID NO:147 and SEQ ID NO:157.

~~29. A pharmaceutical composition according to any one of claims 7 to 28, comprising two or more antibodies specific to TcdB.~~

~~30. A pharmaceutical composition according to any one of claims 1 to 28, comprising two or more antibodies specific to TcdA.~~

~~31.~~12. A pharmaceutical composition according to any one of claims ~~73~~ to ~~30~~11, wherein at least one antibody in the composition is specific to TcdA and at least one antibody in the composition is specific to TcdB.

~~32.~~13. A pharmaceutical composition according to claim ~~31~~12, wherein the composition further comprises at least a second antibody specific to TcdB.

~~33. A pharmaceutical composition according to claims 1 to 32, wherein the composition comprises 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 distinct antibodies to the target antigen or antigens, such as 2, 3, 4, or 5 antibodies.~~

~~34. A pharmaceutical composition or mixture comprising the antibodies of claims 17, 23 and 26.~~

~~35. A pharmaceutical composition according to any one of claims 1 to 34, which further comprises a pharmaceutically acceptable excipient.~~

~~36.~~14. Use of ~~a pharmaceutical composition comprising~~ a monoclonal antibody as defined in any one of claim 1 or 2, ~~with high affinity for the target antigen suitable for reducing the duration and/or severity of diarrhoea, morbidity and/or mortality in a patient with *Clostridium difficile* infection or at risk of said infection wherein the antibody is specific to: antigen TcdA and binds 3 or more times thereto with an EC50 in the range 1 to 10 ng/ml when toxin is used at an LD_{80} or higher,~~

in the manufacture of a medicament for the treatment ~~or prophylaxis~~ of *C. difficile* infection ~~or complications associated therewith~~.

~~37. Use according to claim 36, wherein the composition further comprises a monoclonal antibody specific to antigen TcdB.~~

~~38. Use according to claim 37, wherein the monoclonal antibody specific to antigen TcdB binds to TcdB with affinity of 600 pM.~~

~~39. Use according to any one of claims 36 to 38, wherein the complication is diarrhea, colitis, bloating, abdominal pain and toxic mega colon.~~

~~40. Use according to any one of claims 36 to 39, wherein the *C. difficile* infection is a secondary infections or re-infection.~~

~~41. Use according to any one of claims 36 to 40, wherein a composition comprising at least one TcdA antibody, and two TcdB antibodies is to be employed.~~

15. Use of a monoclonal antibody according to claim 14, wherein the *C. difficile* infection is a hypervirulent strain.

16. Use of a monoclonal antibody according to claim 15, wherein the hypervirulent strain is ribotype 027.