rearrangements, bcr/abl transcripts or t(4;11) translocations), and that this treatment is well tolerated. In light of this, the administration of the CD19xCD3 bispecific single chain antibody described herein provides an alternative treatment option especially for adult acute lymphoblastic leukemia (ALL), in particular to ALL refractory to conventional ALL therapy, such as chemotherapy and/or HSCT. Treatment with the CD19xCD3 bispecific single chain antibody is especially advantageous for the treatment of MRD-positive ALL.

CLAIMS

1. A method for the treatment, amelioration or elimination of acute lymphoblastic leukemia (ALL), the method comprising the administration of a pharmaceutical composition comprising a CD19xCD3 bispecific single chain antibody construct to an adult patient in the need thereof.

2. The method of claim 1, wherein said acute lymphoblastic leukemia (ALL) is B-lineage acute lymphoblastic leukemia, preferably B-precursor acute lymphoblastic leukemia.

3. The method of claim 1 or 2, wherein said acute lymphoblastic leukemia (ALL) is refractory to chemotherapy in patients non-eligible for allogeneic hematopoietic stem cell transplantation.

4. The method of claim 1 or 2, followed by allogeneic hematopoietic stem cell transplantation or wherein said method replaces allogeneic hematopoietic stem cell transplantation in patients eligible for allogeneic hematopoietic stem cell transplantation.

5. The method of any of claims 1 to 4, wherein the method is for the treatment, amelioration or elimination of minimal residual disease (MRD) in a patient with acute lymphoblastic leukemia (ALL).

6. The method of claim 5, wherein said patient is MRD-positive in complete hematological remission.

7. The method of claim 5 or 6, wherein the administration of said pharmaceutical composition results in stable disease or converts MRD positive acute lymphoblastic leukemia (ALL) into an MRD negative status.

8. The method of any of claims 5 to 7, wherein MRD is measured with quantitative detection of individual rearrangements of immunoglobulin genes or T-cell receptor (TCR) rearrangements, or by bcr/abl fusion transcripts, or by t(4;11) translocations using PCR or FACS analysis.

9. The method of claim 8, wherein the ALL patient shows a bcr/abl or a t(4;11) translocation signal above detection limit and/or at least one marker by rearrangement with a sensitivity of $\geq 10^{-4}$.

10. The method of any of claims 1 to 9, wherein the time to molecular relapse detectable by the method of claim 8 is more than 4 months.

11. The method of any of claims 1 to 10, wherein the corresponding variable heavy chain regions (V_H) and the corresponding variable light chain regions (V_L) regions in said CD19xCD3 bispecific single chain antibody construct are arranged, from N-terminus to C-terminus, in the order, V_L(CD19)-V_H(CD19)-V_H(CD3)-V_L(CD3).

12. The method of claim 11, wherein said CD19xCD3 bispecific single chain antibody construct comprises an amino acid sequence as set forth in SEQ ID NO. 1, or an amino acid sequence at least 90%, preferably 95% identical to SEQ ID NO. 1.

13. The method of any of claims 1 to 12, wherein one treatment cycle is a 4-week continuous infusion, followed by repeated cycles after a 2-week treatment-free interval.

14. The method of claim 13, wherein the treatment cycle is repeated at least three times, after determination of a MRD negative status (consolidation).

15. The method of any of claims 1 to 14, wherein the CD19xCD3 bispecific single chain antibody construct is to be administered in a daily dose of 10µg to 100µg per square meter patient body surface area.

16. The method of claim 15, wherein the CD19xCD3 bispecific single chain antibody construct is to be administered in a daily dose of 15µg to 30µg per square meter patient body surface area.

17. A CD19xCD3 bispecific single chain antibody construct for the treatment, amelioration or elimination of adult acute lymphoblastic leukemia (ALL).

rearrangements, bcr/abl transcripts or t(4;11) translocations), and that this treatment is well tolerated. In light of this, the administration of the CD19xCD3 bispecific single chain antibody described herein provides an alternative treatment option especially for adult acute lymphoblastic leukemia (ALL), in particular to ALL refractory to conventional ALL therapy, such as chemotherapy and/or HSCT. Treatment with the CD19xCD3 bispecific single chain antibody is especially advantageous for the treatment of MRD-positive ALL.

The invention is defined in the independent claim. Some optional features of the invention are defined in the dependent claims.

This description may contain subject matter that falls outside the scope of the claims. This subject matter is included to aid understanding of the invention.

CLAIMS

1. Use of a CD19xCD3 bispecific single chain antibody construct for the manufacture of a medicament for the treatment, amelioration or elimination of acute lymphoblastic leukemia (ALL).

2. The use of claim 1, wherein said acute lymphoblastic leukemia (ALL) is B-lineage acute lymphoblastic leukemia.

3. The use of claim 2, wherein said B-lineage acute lymphoblastic leukemia is B-precursor acute lymphoblastic leukemia.

4. The use of any one of claims 1 to 3, wherein said acute lymphoblastic leukemia (ALL) is refractory to chemotherapy in patients non-eligible for allogeneic hematopoietic stem cell transplantation.

5. The use of any one of claims 1 to 4, wherein the medicament is formulated to be followed by allogeneic hematopoietic stem cell transplantation or wherein said use replaces allogeneic hematopoietic stem cell transplantation in a patient eligible for allogeneic hematopoietic stem cell transplantation.

6. The use of any of claims 1 to 5, wherein the medicament is for the treatment, amelioration or elimination of minimal residual disease (MRD) in a patient with acute lymphoblastic leukemia (ALL).

7. The use of claim 6, wherein said patient is MRD-positive in complete hematological remission.

8. The use of claim 6 or 7, wherein the medicament is formulated to result in stable disease or converts MRD positive acute lymphoblastic leukemia (ALL) into an MRD negative status.

9. The use of any one of claims 6 to 8, wherein MRD is measured with quantitative detection of individual rearrangements of immunoglobulin genes or T-cell receptor (TCR) rearrangements, or by bcr/abl fusion transcripts, or by t(4;11) translocations using PCR or FACS analysis.

10. The use of claim 9, wherein the patient shows a bcr/abl or a t(4;11) translocation signal above detection limit and/or at least one marker by rearrangement with a sensitivity of $\geq 10^{-4}$.

11. The use of any one of claims 1 to 10, wherein the time to molecular relapse detectable by quantitative detection of individual rearrangements of immunoglobulin genes or T-cell receptor (TCR) rearrangements, or by bcr/abl fusion transcripts, or by t(4;11) translocations using PCR or FACS analysis is more than 4 months.

12. The use of any one of claims 1 to 11, wherein the corresponding variable heavy chain regions (V_H) and the corresponding variable light chain regions (V_L) regions in said CD19xCD3 bispecific single chain antibody construct are arranged, from N-terminus to C-terminus, in the order, V_L(CD19)-V_H(CD19)-V_H(CD3)-V_L(CD3).

13. The use of claim 12, wherein said CD19xCD3 bispecific single chain antibody construct comprises an amino acid sequence as set forth in SEQ ID NO. 1.

14. The use of claim 12, wherein said CD19xCD3 bispecific single chain antibody construct comprises an amino acid sequence at least 90% identical to SEQ ID NO. 1.

15. The use of claim 12, wherein said CD19xCD3 bispecific single chain antibody construct comprises an amino acid sequence at least 95% identical to SEQ ID NO. 1.

16. The use of any one of claims 1 to 15, wherein the medicament is formulated such that one treatment cycle is a 4-week continuous administration.

17. The use of claim 16, wherein said treatment cycle is followed by repeated treatment cycles after a 2 week treatment-free interval.

18. The use of claim 17, wherein said treatment cycle is to be repeated at least two, three, four, five, six, seven, eight, nine or ten times.

19. The use of any one of claims 16 to 18, wherein the treatment cycle is repeated at least three times, after determination of a MRD negative status.

20. The use of any one of claims 1 to 19, wherein the medicament is formulated for administration of the CD19xCD3 bispecific single chain antibody construct in a daily dose of 5 µg to 100 µg per square meter patient body surface area.

21. The use of claim 20, wherein the medicament is formulated for administration of the CD19xCD3 bispecific single chain antibody construct in a daily dose of 15 µg to 30 µg per square meter patient body surface area.