sample which might also be relevant to the lytic capacity against tumor cells) in a physiological setting. Accordingly, with the methods of the present invention it is possible to reduce the dose of the antibody to the minimal dose required for target cell lysis as determined by a CDC assay or a WBT. Furthermore, the methods of the invention allow to individually determine the effective antibody dose and thus, take into account the individual differences in anti-tumor responses of the patients. Another key aspect of the invention is that it is possible to reduce and manage the side effect of pain by determining the threshold dose of the anti-GD2 antibody to be administered to induce CDC and/or whole blood cytolytic activity. Another key finding of the invention is that the side effect of pain can be substantially reduced by administering the anti-GD2 antibody as a continuous infusion until the predetermined overall patient dose has been administered. Accordingly, with the methods according to the invention it is possible to substantially reduce the analgesic administration, especially the administration of strong analgesics such as morphine, during the antibody treatment, and thus, also substantially reduce the side effects of such analgesic administration.

Brief description

In one aspect of the present disclosure, there is provided a use of a preparation comprising a ch14.18 antibody in the manufacture of a medicament for treating a GD2 positive cancer, wherein said medicament is to be administered to a patient in a daily dose of 1 to 25 mg/m2 and in a dose of 50 to 150 mg/m2/cycle as a continuous intravenous infusion over 24 hours per day.

In one example, the present disclosure relates to a method for treating a GD2 positive cancer by administering a preparation comprising an anti-GD2 antibody to a patient as a continuous intravenous infusion over 24 hours per day. Said preparation comprising an anti-GD2 antibody may be administered by using a mini-pump, and may be administered for a treatment period until the predetermined overall patient dose has been administered.

In another example, the present disclosure relates to a method for treating a GD2 positive cancer by administering a preparation comprising an anti-GD2 antibody to a patient, wherein the preparation is administered in a dose sufficient to induce tumor cell lysis (cytolysis threshold dose), and wherein said cytolysis threshold dose is administered for a

treatment period until the predetermined overall patient dose has been administered.

In a related example the present disclosure provides an anti-GD2 antibody for use in said treatment. In a further related example the present disclosure provides the use of an anti-GD2 antibody in the preparation of a medicament for said treatment. The present disclosure is further defined by the claims. All preferred examples of the

Claims

1. Use of a preparation comprising a ch14.18 antibody in the manufacture of a medicament for treating a GD2 positive cancer, wherein said medicament is to be administered to a patient in a daily dose of 1 to 25 mg/m^2 and in a dose of 50 to 150 mg/m^2/cycle as a continuous intravenous infusion over 24 hours per day.

2. The use according to claim 1, wherein the preparation is to be administered to the patient in a dose of 50, 60, 75, 80, 100, 120, or 150 mg/m^2/cycle.

3. The use according to claim 1 or 2, wherein the preparation is to be administered to the patient in a daily dose of 1 to 20 mg/m^2 or 1 to 15 mg/m^2.

4. The use according to any one of claims 1 to 3, wherein the preparation comprising an anti-GD2 antibody is to be administered in in a daily dose of 1, 2, 3, 4, 5, 6, 7, 7.5, 8, 9, 10, 12, 15, 20, 25 mg/m^2.

5. The use according to any one of claims 1 to 3, wherein the preparation is to be administered to the patient in a daily dose of up to 7, 10, 15, or 20 mg/m^2.

6 The use according to any one of claims 1 to 5, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered for a treatment period until the predetermined overall patient dose has been administered.

7. The use according to any one of claims 1 to 6, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered for a treatment period until a certain therapeutic effect has been reached.

8. The use according to any one of claims 1 to 7, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered by using a mini-pump.

9. The use according to any one of claims 1 to 8, wherein the anti-GD2 antibody ch14.18 is ch14.18/CHO or ch14.18/SP2/0.

10. The use according to any one of claims 1 to 9, wherein the preparation comprising the anti-GD2 antibody ch14.18 is APN311 or APN301.

11. The use according to any one of claims 1 to 10, wherein the ch14.18 antibody has the light chain amino acid sequence of SEQ ID NO:3 and the heavy chain amino acid sequence of SEQ ID NO:4.

12. The use according to any one of claims 1 to 11, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered in a dose of 7, 10, 15, or 25 mg/m^2/day.

13. The use according to any one of claims 1 to 12, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered for 4, 10, 14, 15, or 21 consecutive days.

14. The use according to any one of claims 1 to 13, wherein the preparation comprising the ch14.18 antibody is to be administered to the patient for 2 or more treatment cycles.

15. The use according to claim 14, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered for 3, 4, 5, 6, 7, 8, 9, or 10 treatment cycles.

16. The use according to claim 15, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered for 3, 4, 5, or 6 treatment cycles.

17. The use according to any one of claims 1 to 16, wherein the preparation comprising the anti-GD2 antibody ch14.18 is APN311 and is to be administered in a dose of 10 mg/m^2/day for 10 consecutive days for 6 treatment cycles.

18. The use according to any one of claims 1 to 17, wherein the anti-GD2 antibody is ch14.18/SP2/0 and is to be administered in a dose of 25 mg/m^2/day for 4 consecutive days for 5 treatment cycles.

19. The use according to any one of claims 1 to 18, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered and preceded and/or accompanied by the administration of IL-2 and/or GM-CSF or another cytokine.

20. The use according to any one of claims 1 to 19, wherein the administration period of the preparation comprising the anti- GD2 antibody ch14.18 may be followed by an administration period of isotretinoin or another retinoid.

21. The use according to any one of claims 1 to 20, wherein the preparation comprising the anti-GD2 antibody ch14.18 is to be administered and accompanied by the administration of morphine and/or one or more other analgesics.

22. The use according to any one of claims 1 to 21, wherein the daily morphine dose during one or more days of continuous intravenous infusion of the anti-GD2 antibody ch14.18 and/or of all morphine treatment days is to be administered lower than the daily morphine dose during non-continuous administration of the antibody.

23. The use according to any one of claims 1 to 22, wherein morphine is to be administered only for some but not all days on which the antibody is administered.

24. The use according to any one of claims 1 to 23, wherein the morphine dose per treatment cycle during one or more treatment cycles comprising the continuous intravenous infusion of the antibody according to the invention is to be administered lower than the morphine dose per treatment cycle in a non-continuous infusion schedule.

25. The use according to any one of claims 1 to 24, wherein the morphine dose of the overall treatment time is lower than the morphine dose of the overall treatment time in a non- continuous infusion schedule.

26. The use according to any one of claims 1 to 25, wherein the morphine dose during one or more hours or days of continuous intravenous infusion of the anti-GD2 antibody ch14-18 and/or of all morphine treatment hours or days is to be administered lower than 50 mcg/kg/h, or lower than 30 mcg/kg/h.

27. The use according to any one of claims 1 to 20, wherein the daily morphine dose during one or more days of continuous intravenous infusion of the anti-GD2 antibody ch14.18 and/or of all morphine treatment days is to be administered lower than 0.9, 0.72, 0.48, 0.38, 0.4375, and/or 0.205 mg/kg/day.

28. The use according to any one of claims 1 to 21, wherein the dose of the one or more analgesics, especially morphine, is reduced within the overall treatment time, within a treatment cycle, during the antibody treatment period within a treatment cycle, from one antibody treatment day to the next antibody treatment day within a treatment cycle, and/or from one treatment cycle to the next.

29. The use according to any one of claims 1 to 22, wherein the morphine dose is continuously reduced within a treatment cycle, during the antibody treatment period within a treatment cycle, and/or from one antibody treatment day to the next antibody treatment day within a treatment cycle.

30. The use according to any one of claims 1 to 29, wherein the GD2 positive cancer is neuroblastoma, glioblastoma, medulloblastoma, astrocytoma, melanoma, small cell lung cancer, desmoplastic small round cell tumor, osteosarcoma, rhabdomyosarcoma, or another soft tissue sarcoma.

31. The use according to any one of claims 1 to 30, wherein the patient suffers from primary refractory or relapsed high risk-neuroblastoma, or from minimal residual disease in high- risk neuroblastoma.