SUMMARY ~~OF THE INVENTION~~

[0005] The present ~~invention~~ disclosure provides methods and kits for treating patients diagnosed with glioblastoma, including patients newly diagnosed with glioblastoma.

In one aspect, there is provided use of an effective amount of an anti-VEGF antibody in the manufacture of a medicament for treating a patient diagnosed with a glioblastoma, wherein the antibody is to be administered with an effective amount of a chemotherapeutic and an effective amount of radiotherapy, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without an anti-VEGF antibody.

[0006] One embodiment of the ~~invention~~ disclosure provides methods of treating a patient diagnosed with a glioblastoma comprising administering to said patient a therapy comprising an effective amount of an anti-VEGF antibody, an effective amount of a chemotherapeutic, and radiotherapy wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody. In one embodiment, the patient has a WHO performance status of ≤ 2. In some embodiments, the chemotherapeutic is temozolomide. In some embodiments, the effective amount of the temozolomide is 150 mg/m^2 administered orally. In some embodiments, the effective amount of the temozolomide is 200 mg/m^2 administered orally. In some embodiments, the anti-VEGF antibody binds the A4.6.1 epitope. In some embodiments, the anti-VEGF antibody is bevacizumab. In some embodiments, the anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1. In some embodiments, the effective amount of said anti-VEGF antibody is 10 mg/kg intravenously every two weeks, administered, for example, initially intravenously over 90 minutes, with subsequent infusions over 60 minutes and then 30 minutes. In some embodiments, the effective amount of said anti-VEGF antibody is 15 mg/kg intravenously every three weeks administered, for example, initially intravenously over 90 minutes, with subsequent infusions over 60 minutes and then 30 minutes. In the methods described above, the anti-VEGF antibody is administered first to said patient at the first cycle and then subsequent administrations of said anti-VEGF antibody are either prior to or after said chemotherapeutic. In another embodiment, the anti-VEGF antibody is administered concurrently with said chemotherapeutic and radiotherapy. In some embodiments, administration of steroid to the patient is discontinued.

[0007] In the methods described above for treating a patient diagnosed with a glioblastoma, the median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient

receiving said chemotherapeutic without the anti-VEGF antibody . In another embodiment, the median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody . In another embodiment, the median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody . In another embodiment, the median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody . In yet another embodiment in the methods described above, the patient is less than 65 years old. In yet another embodiment in the methods described above, the patient is equal to or greater than 65 years old. In one embodiment in the methods described above, the patient has a treatment free interval (TFI) of about 4 weeks.

[0008] ~~Another embodiment of the invention provides~~ In one aspect there is provided a kits comprising an anti-VEGF antibody binding essentially to epitope A4.6.1, a chemotherapeutic and a package insert or label with instructions to treat a patient diagnosed with glioblastoma comprising administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody . In ~~another~~ one embodiment of the kit described above, the anti-VEGF antibody is bevacizumab and said chemotherapeutic is temozolomide.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] Figure 1 shows the two-arm Phase III study design treatment sequence as disclosed in more detail in Example 1. Study treatment started between 4 and 7 weeks after debulking surgery or biopsy of the glioblastoma and included 3 different phases: A Concurrent Phase during which 10 mg/kg bevacizumab or placebo was administered every two weeks in combination with temozolomide and radiotherapy followed by a treatment break of 28 days, a Maintenance Phase during which 10

What is claimed is:

1. A method of treating a patient diagnosed with a glioblastoma comprising administering to said patient a therapy comprising an effective amount of an anti-VEGF antibody, an effective amount of a chemotherapeutic and an effective amount of radiotherapy, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without an anti-VEGF antibody.
2. The method of claim 1, wherein said patient has a WHO performance status of ≤ 2.
3. The method of claim 1, wherein the chemotherapeutic is temozolomide.
4. The method of clam 3, wherein the temozolomide is administered at 150 mg/m^2.
5. The method of clam 3, wherein the temozolomide is administered at 200 mg/m^2.
6. The method of claim 1, wherein said anti-VEGF antibody binds the A4.6.1 epitope.
7. The method of claim 1, wherein said anti-VEGF antibody is bevacizumab.
8. The method of claim 1, wherein said anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1.
9. The method of claim 1, wherein said effective amount of said anti-VEGF antibody is 10 mg/kg intravenously every two weeks.
10. The method of claim 1, wherein said effective amount of said anti-VEGF antibody is 15 mg/kg intravenously every three weeks.
11. The method of claim 1, wherein said effective amount of said anti-VEGF antibody is administered initially intravenously over 90 minutes, with subsequent infusions over 60 minutes and then 30 minutes.
12. The method of claim 1, wherein said anti-VEGF antibody is administered first to said patient at the first cycle.

13. The method of claim 9, wherein subsequent administrations of said anti-VEGF antibody are either prior to or after said chemotherapeutic.
14. The method of claim 1, wherein said anti-VEGF antibody is administered concurrently with said chemotherapeutic.
15. The method of claim 1, wherein said median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
16. The method of claim 1, wherein said median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
17. The method of claim 1, wherein said median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
18. The method of claim 1, wherein said median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
19. The method of claim 15, 16, 17, or 18, wherein said patient is less than 65 years old.
20. The method of claim 15, 16, 17, or 18, wherein said patient is equal to or greater than 65 years old.
21. A kit comprising an anti-VEGF antibody binding essentially to epitope A4.6.1, a chemotherapeutic and a package insert or label with instructions to treat a patient diagnosed with a glioblastoma comprising administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.

22. The kit in claim 21, wherein said anti-VEGF antibody is bevacizumab.

What is claimed is:

1. Use of an effective amount of an anti-VEGF antibody in the manufacture of a medicament for treating a patient diagnosed with a glioblastoma, wherein the antibody is to be administered with an effective amount of a chemotherapeutic and an effective amount of radiotherapy, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without an anti-VEGF antibody.
2. The use of claim 1, wherein said patient has a WHO performance status of ≤ 2.
3. The use of claim 1, wherein the chemotherapeutic is temozolomide.
4. The use of claim 3, wherein the temozolomide is to be administered at 150 mg/m^2.
5. The use of claim 3, wherein the temozolomide is to be administered at 200 mg/m^2.
6. The use of claim 1, wherein said anti-VEGF antibody binds the A4.6.1 epitope.
7. The use of claim 1, wherein said anti-VEGF antibody is bevacizumab.
8. The use of claim 1, wherein said anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1.
9. The use of claim 1, wherein said effective amount of said anti-VEGF antibody is 10 mg/kg intravenously every two weeks.
10. The use of claim 1, wherein said effective amount of said anti-VEGF antibody is 15 mg/kg intravenously every three weeks.
11. The use of claim 1, wherein said effective amount of said anti-VEGF antibody is to be administered initially intravenously over 90 minutes, with subsequent infusions over 60 minutes and then 30 minutes.
12. The use of claim 1, wherein said anti-VEGF antibody is to be administered first to said patient at the first cycle.

13. The use of claim 9, wherein subsequent administrations of said anti-VEGF antibody are either prior to or after said chemotherapeutic.
14. The use of claim 1, wherein said anti-VEGF antibody is to be administered concurrently with said chemotherapeutic.
15. The use of claim 1, wherein said median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
16. The use of claim 1, wherein said median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) equal to 0.64, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
17. The use of claim 1, wherein said median progression-free survival time is prolonged by about 4.4 months with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
18. The use of claim 1, wherein said median progression-free survival time is prolonged by at least 4 months or greater with a hazard ratio (HR) from about 0.55 to about 0.74, as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.
19. The use of claim 15, 16, 17, or 18, wherein said patient is less than 65 years old.
20. The use of claim 15, 16, 17, or 18, wherein said patient is equal to or greater than 65 years old.
21. A kit comprising an anti-VEGF antibody binding essentially to epitope A4.6.1, a chemotherapeutic and a package insert or label with instructions to treat a patient diagnosed with a glioblastoma comprising administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said treatment prolongs said patient's median progression-free survival time as compared to a glioblastoma patient receiving said chemotherapeutic without the anti-VEGF antibody.

22. The kit in claim 21, wherein said anti-VEGF antibody is bevacizumab.