CANCER TREATMENT

The present invention provides use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein erdafitinib is to be administered in an amount of 8 mg erdafitinib base daily on a continuous basis or 8 mg base equivalent of a pharmaceutically acceptable salt of erdafitinib daily on a continuous basis, wherein serum phosphate levels of the cancer patient are to be monitored and when the serum phosphate are ≤9 mg/dL, the amount of erdafitinib to be administered is to be increased to 9 mg erdafitinib base daily on a continuous basis or 9 mg base equivalent of a pharmaceutically acceptable salt of erdafitinib daily on a continuous basis.

The present invention provides for the treatment of cancer with erdafitinib with a high potential for response while limiting potential toxicities such as for example nail toxicities.

The present invention provides for treatment of cancer with erdafitinib that maximizes erdafitinib exposure while limiting potential toxicities.

The present invention provides for treatment of cancer with erdafitinib with a high objective response rate, in particular with an objective response rate of at least 40%, in particular with an objective response rate of at least 40 % in chemo-naïve cancer patients, with an objective response rate of at least 40 % in cancer patients who had disease progression after one prior line of chemotherapy, with an objective response rate of at least 40 % in cancer patients who had disease progression after two or more prior lines of chemotherapy.

The present invention provides for treatment of cancer with erdafitinib with a short time to response, in particular with a median time to response less than 2 months.

Description of the Figures

Figure 1 represents the study scheme for the Phase 2, multicenter, open-label study to evaluate the efficacy and safety of erdafitinib in subjects with metastatic or surgically unresectable urothelial cancer harboring selected FGFR (fibroblast growth factor receptor) genetic alterations (FGFR translocations or mutations).

Figure 2 represents a Waterfall plot of maximum percentage reduction from baseline in sum of target lesion diameters among patients treated with the regimen of 8 mg continuous erdafitinib (Regimen 3 of the phase 2 study (Fig. 1)). M, *FGFR* mutation; T, *FGFR* translocation.

Detailed description of the invention

The present invention provides for the treatment of cancer with erdafitinib that maximizes erdafitinib exposure already within the first cycle of treatment (set at, for example, the first 28 days of treatment or the first 21 days of treatment, in particular with daily continuous dosing) as well as during further treatment cycles (set at, for example, 28 days/cycle or 21 days/cycle, in particular with daily continuous dosing) while limiting potential toxicities.

Claims

1. Use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein the erdafitinib is to be administered in an amount of 8 mg erdafitinib base daily on a continuous basis or 8 mg base equivalent of a pharmaceutically acceptable salt of erdafitinib daily on a continuous basis, wherein serum phosphate levels of the cancer patient are to be monitored and when the serum phosphate are ≤9 mg/dL, the amount of erdafitinib to be administered is to be increased to 9 mg erdafitinib base daily on a continuous basis or 9 mg base equivalent of a pharmaceutically acceptable salt of erdafitinib daily on a continuous basis.

2. The use according to claim 1, wherein the serum phosphate levels of the cancer patient and early onset toxicity are to be monitored, and wherein, when the serum phosphate levels are ≤9 mg/dL and no early onset toxicity is shown, the amount of erdafitinib to be administered is to be increased to 9 mg erdafitinib base daily on a continuous basis or 9 mg base equivalent of a pharmaceutically acceptable salt of erdafitinib daily on a continuous basis.

3. The use according to claim 1 or claim 2, wherein, when the serum phosphate levels range from and include 7 mg/dL to ≤ 9 mg/dL, concurrent treatment with a phosphate binder is to be initiated.

4. The use according to any one of the preceding claims, wherein, when the serum phosphate levels range from > 9 mg/dL to 10 mg/dL, the erdafitinib treatment is to be interrupted until serum phosphate levels are <7 mg/dL.

5. The use according to any one of the preceding claims, wherein, when the serum phosphate levels are >10 mg/dL, the erdafitinib treatment is to be interrupted temporarily until serum phosphate levels are <7 mg/dL and then erdafitinib treatment is to be re-started at a lower dose.

6. The use according to claim 5, wherein, when the serum phosphate levels are ≥10 mg/dL for >2 weeks, the erdafitinib treatment is to be interrupted permanently.

7. The use according to claim 5, wherein the lower dose is 6 mg erdafitinib base daily on a continuous basis or 6 mg base equivalent of the salt of erdafitinib daily on a continuous basis.

8. The use according to any one of the preceding claims, wherein the amount of 8 mg of erdafitinib base or 8 mg base equivalent of the salt of erdafitinib is to be administered once daily.

9. The use according to any one of the preceding claims, wherein the amount of 9 mg of erdafitinib base or 9 mg base equivalent of the salt of erdafitinib is to be administered once daily.

10. The use according to any one of the preceding claims, wherein the serum phosphate levels of the cancer patient are to be measured on day 14 ± 2 days to around day 21 of erdafitinib administration.

11. The use according to claim 10, wherein the serum phosphate levels of the cancer patient are to be measured on day 14 ± 2 days of erdafitinib administration.

12. The use according to claim 11, wherein the serum phosphate levels of the cancer patient are to be measured on day 14 of erdafitinib administration.

13. The use according to claim 10, wherein the serum phosphate levels of the cancer patient are to be measured at or around day 21 of erdafitinib administration.

14. The use according to any one of the preceding claims, wherein the amount of 8 mg of erdafitinib base or 8 mg base equivalent of the salt of erdafitinib is to be administered as 2 formulations.

15. The use according to claim 14, wherein the 2 formulations are 2 tablets, each comprising 4 mg of erdafitinib base or 4 mg base equivalent of the salt of erdafitinib.

16. The use according to any one of the preceding claims, wherein the amount of 9 mg of erdafitinib base or 9 mg base equivalent of the salt of erdafitinib is to be administered as 3 formulations.

17. The use according to claim 16, wherein the 3 formulations are 3 tablets, each comprising 3 mg of erdafitinib base or 3 mg base equivalent of the salt of erdafitinib.

18. The use according to any one of the preceding claims, wherein the cancer is urothelial cancer, bladder cancer, hepatocellular cancer, squamous cell carcinoma, or lung cancer.

19. The use according to any one of claims 1-17, wherein the cancer is advanced or metastatic cholangiocarcinoma.

20. The use according to claim 18, wherein the cancer is urothelial cancer.

21. The use according to claim 20, wherein the cancer is metastatic or surgically unresectable urothelial cancer.

22. The use according to claim 18, wherein the cancer is bladder cancer.

23. The use according to claim 22, wherein the cancer is non-muscle-invasive bladder cancer.

24. The use according to claim 18, wherein the cancer is hepatocellular cancer.

25. The use according to claim 18, wherein the cancer is squamous cell carcinoma.

26. The use according to claim 18, wherein the cancer is lung cancer.

27. The use according to any one of the preceding claims, wherein the cancer has progressed on or after one prior treatment.

28. The use according to any one of the preceding claims, wherein the cancer is a cancer with at least one FGFR genetic alteration.

29. The use according to claim 20, wherein the cancer is advanced urothelial cancer with selected FGFR gene alterations.

30. The use according to claim 29, wherein the cancer is advanced urothelial cancer with selected FGFR gene alterations which has progressed on or after one prior treatment.

31. The use according to claim 28, wherein the cancer is metastatic or surgically unresectable urothelial cancer with at least one FGFR2/FGFR3 alteration.

32. The use according to claim 31, wherein the cancer is metastatic or surgically unresectable urothelial cancer with at least one FGFR3 alteration.

33. The use according to claim 31 or 32, wherein the cancer has received prior immunotherapy with a PD-L1 or PD-1 inhibitor.

34. The use according to any one of claims 28-33, wherein the alteration is a FGFR3-TACC3 fusion.

35. The use according to claim 22, wherein the cancer is bladder cancer with a FGFR3-TACC3 translocation.

36. The use according to claim 20, wherein the cancer is urothelial cancer with a FGFR3-TACC3 translocation.

37. The use according to any one of claims 31-33, wherein the cancer is metastatic or surgically unresectable urothelial cancer with a FGFR3-TACC3 translocation.

38. The use according to any one of claims 28-31, wherein the alteration is selected from the following fusions: FGFR3:TACC3 v1; FGFR3:TACC3 v3; FGFR3:TACC3 Intron; FGFR3:BAIAP2L1; FGFR2:AFF3; FGFR2:BICC1; FGFR2:CASP7; FGFR2:CCDC6 and FGFR2:OFD1.

39. The use according to claim 38, wherein the alteration is a FGFR3:TACC3 v1 fusion.

40. The use according to claim 38, wherein the alteration is a FGFR3:TACC3 v3 fusion.

41. The use according to claim 38, wherein the alteration is a FGFR3:BAIAP2L1 fusion.

42. The use according to any one of claims 28-33, wherein the alteration is selected from the following FGFR3 gene mutations: FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

43. The use according to any one of claims 20 to 22, wherein the cancer harbors at least one of the following FGFR3 gene mutations: FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

44. The use according to claim 43, wherein the mutation is a FGFR3 R248C mutation.

45. The use according to claim 43, wherein the mutation is a FGFR3 S249C mutation.

46. The use according to claim 43, wherein the mutation is a FGFR3 G370C mutation.

47. The use according to claim 43, wherein the mutation is a FGFR3 Y373C mutation.

48. The use according to any one of claims 1-17, 27-34 and 36-47, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the erdafitinib treatment provides for an objective response rate of at least 35%.

49. The use according to any one of claims 1-17, 27-34 and 36-48, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the erdafitinib treatment provides a median progression free survival of at least 5 months.

50. The use according to any one of claims 1-17, 27-34 and 36-48, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the erdafitinib treatment provides a median progression free survival ranging between 4 months and 7 months.

51. The use according to any one of claims 1-17, 27-34 and 36-50, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the erdafitinib treatment provides a median duration of response ranging between 4 months and 7 months.

52. The use according to claim 2, or any one of claims 3 to 51 when dependent on claim 2, wherein early onset toxicity comprises grade 3 or higher xerostomia or stomatitis/mucositis, dry skin, dry eye, nail toxicity or grade 2 or higher eye toxicity.

53. The use according to any one of the preceding claims, wherein erdafitinib is erdafitinib base.