CANCER TREATMENT

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.

The present invention provides a method for the treatment of cancer with erdafitinib in high-risk patients, in particular high-risk patients with advanced urothelial carcinoma.

Summary

In one aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, preferably once daily, on a continuous basis, or in an amount of 9 mg daily, preferably once daily, on a continuous basis, so that the levels of serum phosphate of the patient range from and including 5.5 mg/dL to < 7 mg/dL or range from and including 5.5 mg/dL to ≤9 mg/dL; and wherein the objective response rate is at least 50%.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, in particular once daily, on a continuous basis, wherein the amount of 8 mg is uptitrated to 9 mg daily, preferably once daily, on a continuous basis when the levels of serum phosphate of the patient are < 5.5 mg/dL, are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL, and wherein the objective response rate is at least 50%.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein

a) the medicament comprises erdafitinib in an amount of 8 mg and wherein the medicament is for daily, in particular once daily, administration on a continuous basis;

b) the serum phosphate levels of the patient are to be measured on a treatment day during the first cycle of erdafitinib treatment, in particular on day 14 ± 2 days, more in particular on day 14, of erdafitinib administration;

c-1) when the serum phosphate levels are <5.5 mg/dL, the amount of erdafitinib in the medicament for daily, in particular once daily, administration on a continuous basis is increased to 9 mg;

c-2) when the serum phosphate levels range from and including 5.5 mg/dL to < 7 mg/dL, the patient remains on the 8 mg daily, in particular once daily, continuous treatment;

c-3) when the serum phosphate levels are ≥ 7 mg/dL, the erdafitinib treatment is to be interrupted temporarily until serum phosphate levels are <5.5 mg/dL and then erdafitinib treatment is to be re-started with 8 mg daily, in particular once daily, on a continuous basis; and wherein the cancer patient is a patient aged ≥75 years; and wherein the objective response rate is at least 50%.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein

a) the medicament comprises erdafitinib in an amount of 8 mg and wherein the medicament is for daily, in particular once daily, administration on a continuous basis;

b) the serum phosphate levels of the patient are measured on a treatment day during the first cycle of erdafitinib treatment, in particular on day 14 ± 2 days, more in particular on day 14, of erdafitinib administration;

c-1) when the serum phosphate levels are < 7 mg/dL or when the serum phosphate levels range from and including 7 mg/dL to ≤ 9 mg/dL, the amount of erdafitinib in the medicament for daily, in particular once daily, administration on a continuous basis is increased to 9 mg; and when the serum phosphate levels range from and including 7 mg/dL to ≤ 9 mg/dL, concurrent treatment with a phosphate binder, such as for example sevelamer, is optionally initiated;

c-2) when the serum phosphate levels are > 9 mg/dL, the erdafitinib treatment is interrupted temporarily until serum phosphate levels are <7 mg/dL and then

erdafitinib treatment is re-started with 8 mg daily, in particular once daily, on a continuous basis;

wherein the cancer patient is a patient aged ≥75 years, and wherein the objective response rate is at least 50%.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient wherein the cancer is metastatic or surgically unresectable urothelial cancer harboring select FGFR genetic alterations (FGFR translocations or mutations), wherein the patient is a patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, in particular once daily, on a continuous basis and wherein the daily amount of erdafitinib is to be administered as two pharmaceutical compositions, in particular two tablets, each comprising 4 mg of erdafitinib, or as two pharmaceutical compositions, in particular two tablets, one comprising 3 mg of erdafitinib and one comprising 5 mg of erdafitinib; and wherein the objective response rate is at least 50%.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient wherein the cancer is metastatic or surgically unresectable urothelial cancer harboring select FGFR genetic alterations (FGFR translocations or mutations), wherein the patient is a patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 9 mg daily, in particular once daily, on a continuous basis, and wherein the daily amount of erdafitinib is to be administered as three pharmaceutical compositions, in particular three tablets, each comprising 3 mg of erdafitinib, or as two pharmaceutical compositions, in particular two tablets, one comprising 4 mg of erdafitinib and one comprising 5 mg of erdafitinib; and wherein the objective response rate is at least 50%.

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

Claims

1. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, preferably once daily, on a continuous basis, or in an amount of 9 mg daily, preferably once daily, on a continuous basis, so that the levels of serum phosphate of the patient range from and including 5.5 mg/dL to < 7 mg/dL or range from and including 5.5 mg/dL to ≤9 mg/dL; and wherein the objective response rate is at least 50%.

2. The use according to claim 1 wherein the levels of serum phosphate range from and including 5.5 mg/dL to < 7 mg/dL.

3. The use according to claim 1 wherein the levels of serum phosphate range from and including 5.5 mg/dL to ≤9 mg/dL.

4. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, in particular once daily, on a continuous basis, wherein the amount of 8 mg is uptitrated to 9 mg daily, preferably once daily, on a continuous basis when the levels of serum phosphate of the patient are < 5.5 mg/dL, are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL, and wherein the objective response rate is at least 50%..

5. The use according to claim 4 wherein the amount of 8 mg daily is uptitrated to 9 mg daily when the levels of serum phosphate are < 5.5 mg/dL.

6. The use according to claim 4 wherein the amount of 8 mg daily is uptitrated to 9 mg daily when the levels of serum phosphate are < 7 mg/dL.

7. The use according to claim 4 wherein the amount of 8 mg daily is uptitrated to 9 mg daily when the levels of serum phosphate range from and include 7 mg/dL to ≤9 mg/dL.

8. The use according to claim 4 wherein the amount of 8 mg daily is uptitrated to 9 mg daily when the levels of serum phosphate are ≤9 mg/dL.

9. The use according to any one of claims 4 to 8 wherein the levels of serum phosphate for determining whether or not to uptitrate are measured on day 14 ± 2 days of erdafitinib administration.

10. The use according to claim 9 wherein the levels of serum phosphate for determining whether or not to uptitrate are measured on day 14 of erdafitinib administration.

11. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein

a) the medicament comprises erdafitinib in an amount of 8 mg and wherein the medicament is for daily, in particular once daily, administration on a continuous basis;

b) the serum phosphate levels of the patient are to be measured on a treatment day during the first cycle of erdafitinib treatment, in particular on day 14 ± 2 days, more in particular on day 14, of erdafitinib administration;

c-1) when the serum phosphate levels are <5.5 mg/dL, the amount of erdafitinib in the medicament for daily, in particular once daily, administration on a continuous basis is increased to 9 mg;

c-2) when the serum phosphate levels range from and including 5.5 mg/dL to < 7 mg/dL, the patient remains on the 8 mg daily, in particular once daily, continuous treatment;

c-3) when the serum phosphate levels are ≥ 7 mg/dL, the erdafitinib treatment is to be interrupted temporarily until serum phosphate levels are <5.5 mg/dL and then erdafitinib treatment is to be re-started with 8 mg daily, in particular once daily, on a continuous basis;

wherein the cancer patient is a patient aged ≥75 years; and wherein the objective response rate is at least 50%.

12. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient, wherein

a) the medicament comprises erdafitinib in an amount of 8 mg and wherein the medicament is for daily, in particular once daily, administration on a continuous basis;

b) the serum phosphate levels of the patient are measured on a treatment day during the first cycle of erdafitinib treatment, in particular on day 14 ± 2 days, more in particular on day 14, of erdafitinib administration;

c-1) when the serum phosphate levels are < 7 mg/dL or when the serum phosphate levels range from and including 7 mg/dL to ≤ 9 mg/dL, the amount of erdafitinib in the medicament for daily, in particular once daily, administration on a continuous basis is increased to 9 mg; and when the serum phosphate levels range

from and including 7 mg/dL to ≤ 9 mg/dL, concurrent treatment with a phosphate binder, such as for example sevelamer, is optionally initiated;

c-2) when the serum phosphate levels are > 9 mg/dL, the erdafitinib treatment is interrupted temporarily until serum phosphate levels are <7 mg/dL and then erdafitinib treatment is re-started with 8 mg daily, in particular once daily, on a continuous basis;

wherein the cancer patient is a patient aged ≥75 years, and wherein the objective response rate is at least 50%.

13. The use according to claim 11 or 12 wherein the serum phosphate levels of the patient are measured on day 14 ± 2 days of erdafitinib administration.

14. The use according to claim 13 wherein the serum phosphate levels of the patient are measured on day 14 of erdafitinib administration.

15. The use according to any one of claims 1 to 14 wherein erdafitinib is administered once daily.

16. 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.

17. The use according to claim 16 wherein the cancer is metastatic or surgically unresectable urothelial cancer.

18. The use according to claim 16 wherein the cancer is advanced or metastatic cholangiocarcinoma.

19. The use according to any one of the preceding claims wherein the cancer harbors an alteration 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.

20. The use according to any one of claims 1 to 15 wherein the cancer is bladder cancer with FGFR3-TACC3 translocation, or urothelial cancer with FGFR3-TACC3 translocation, or metastatic or surgically unresectable urothelial cancer with FGFR3-TACC3 translocation.

21. The use according to any one of claims 1 to 18 wherein the cancer harbors an alteration selected from the following FGFR3 gene mutations : FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

22. The use according to any one of claims 1 to 15 wherein the cancer is bladder cancer or urothelial cancer or metastatic or surgically unresectable urothelial cancer harboring at least one of the following FGFR3 gene mutations : FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

23. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient wherein the cancer is metastatic or surgically unresectable urothelial cancer harboring select FGFR genetic alterations (FGFR translocations or mutations), wherein the patient is a patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 8 mg daily, in particular once daily, on a continuous basis and wherein the daily amount of erdafitinib is to be administered as two pharmaceutical compositions, in particular two tablets, each comprising 4 mg of erdafitinib, or as two pharmaceutical compositions, in particular two tablets, one comprising 3 mg of erdafitinib and one comprising 5 mg of erdafitinib; and wherein the objective response rate is at least 50%.

24. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient wherein the cancer is metastatic or surgically unresectable urothelial cancer harboring select FGFR genetic alterations (FGFR translocations or mutations), wherein the patient is a patient aged ≥ 75 years, wherein erdafitinib is to be administered in an amount of 9 mg daily, in particular once daily, on a continuous basis, and wherein the daily amount of erdafitinib is to be administered as three pharmaceutical compositions, in particular three tablets, each comprising 3 mg of erdafitinib, or as two pharmaceutical compositions, in particular two tablets, one comprising 4 mg of erdafitinib and one comprising 5 mg of erdafitinib; and wherein the objective response rate is at least 50%.

25. The use according to any one of the preceding claims wherein the objective response rate is about 50%.