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, in an amount so that the levels of serum phosphate 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a ECOG PS of 2, in an amount so that the levels of serum phosphate 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a hemoglobin level <10 g/dL, in an amount so that the levels of serum phosphate 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having visceral metastases, in an amount so that the levels of serum phosphate 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having 2 or 3 Bellmunt risk factors, in an amount so that the levels of serum phosphate 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.

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 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a ECOG PS of 2, wherein 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.

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a hemoglobin level <10 g/dL, wherein 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.

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

In another aspect, there is provided use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having 2 or 3 Bellmunt risk factors, wherein 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.

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 meeting one or more of the following criteria : : age ≥75 years; ECOG PS 2; hemoglobin <10 g/dL; visceral metastases, in particular of the liver, lung and/or bone; and 2 or 3 Bellmunt risk factors.

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.

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.

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 having visceral metastases, 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.

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 having visceral metastases, 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.

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 $\geq$ 75 years and having visceral metastases, 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.

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 $\geq$ 75 years and having visceral metastases, 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.

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, in an amount so that the levels of serum phosphate 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.

2. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a ECOG PS of 2, in an amount so that the levels of serum phosphate 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.

3. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a hemoglobin level <10 g/dL, in an amount so that the levels of serum phosphate 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.

4. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having visceral metastases, in an amount so that the levels of serum phosphate 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.

5. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having 2 or 3 Bellmunt risk factors, in an amount so that the levels of serum phosphate 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.

6. The use according to any one of claims 1 to 5 wherein the levels of serum phosphate range from and including 5.5 mg/dL to < 7 mg/dL.

7. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient aged ≥ 75 years, wherein 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.

8. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a ECOG PS of 2, wherein 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.

9. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having a hemoglobin level <10 g/dL, wherein 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.

10. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having visceral metastases, wherein 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.

11. The use of erdafitinib in the manufacture of a medicament for the treatment of cancer in a cancer patient having 2 or 3 Bellmunt risk factors, wherein 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.

12. 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.

13. The use according to claim 12 wherein the cancer is metastatic or surgically unresectable urothelial cancer.

14. The use according to claim 12 wherein the cancer is advanced or metastatic cholangiocarcinoma.

15. 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;

and wherein the cancer patient, is a patient meeting one or more of the following criteria : : age ≥75 years; ECOG PS 2; hemoglobin <10 g/dL; visceral metastases, in particular of the liver, lung and/or bone; and 2 or 3 Bellmunt risk factors.

16. 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.

17. 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.

18. 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 having visceral metastases, 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.

19. 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 having visceral metastases, 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.

20. 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 and having visceral metastases, 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.

21. 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 and having visceral metastases, 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.