

## 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 daily on a continuous basis, wherein serum phosphate levels of the cancer patient are to be monitored and when the serum phosphate are  $\leq 9$  mg/dL, the amount of erdafitinib to be administered is to be increased to 9 mg 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.

10 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.

20 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 daily on a continuous basis, wherein serum phosphate levels of the cancer patient are to be monitored and when the serum phosphate are  $\leq 9$  mg/dL, the amount of erdafitinib to be administered is to be increased to 9 mg daily on a continuous basis.
2. The use according to claim 1, wherein erdafitinib is to be administered in an amount of 8 mg daily on a continuous basis, 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  $\leq 9$  mg/dL and no early onset toxicity is shown, the amount of erdafitinib to be administered is to be increased to 9 mg daily on a continuous basis.
3. The use according to claim 1 or claim 2, wherein, when the serum phosphate levels range from and including 7 mg/dL to  $\leq 9$  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 and including  $> 9$  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  $\geq 10$  mg/dL for  $> 2$  weeks, the erdafitinib treatment is to be interrupted permanently.
7. The use according to claim 5 or claim 6, wherein the lower dose is 6 mg daily on a continuous basis.
8. The use according to any one of the preceding claims, wherein the amount of 8 mg 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 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  $14 \pm 2$  days 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 of erdafitinib administration.

12. The use according to any one of claims 1 to 9, wherein the serum phosphate levels of the cancer patient are to be measured at or around the 21<sup>st</sup> day of erdafitinib administration.

13. The use according to any one of the preceding claims, wherein the amount of 8 mg of erdafitinib is to be administered as 2 formulations.

14. The use according to claim 13, wherein the 2 formulations are 2 tablets, each comprising 4 mg of erdafitinib.

15. The use according to any one of the preceding claims, wherein the amount of 9 mg of erdafitinib is to be administered as 3 formulations.

16. The use according to claim 15, wherein the 3 formulations are 3 tablets, each comprising 3 mg of erdafitinib.

17. 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.

18. The use according to any one of claims 1-16, wherein the cancer is advanced or metastatic cholangiocarcinoma.

19. The use according to claim 17, wherein the cancer is urothelial cancer.

20. The use according to claim 19, wherein the cancer is metastatic or surgically unresectable urothelial cancer.

21. The use according to claim 17, wherein the cancer is bladder cancer.

22. The use according to claim 21, wherein the cancer is non-muscle-invasive bladder cancer.
23. The use according to claim 17, wherein the cancer is hepatocellular cancer.
- 5 24. The use according to claim 17, wherein the cancer is squamous cell carcinoma.
25. The use according to claim 17, wherein the cancer is lung cancer.
- 10 26. The use according to any one of the preceding claims, wherein the cancer is a cancer with at least one FGFR genetic alteration.
27. The use according to claim 19, wherein the cancer is advanced urothelial cancer with selected FGFR gene alterations.
- 15 28. The use according to claim 27, wherein the cancer is advanced urothelial cancer with selected FGFR gene alterations which has progressed on or after one prior treatment.
29. The use according to claim 26, wherein the alteration is a FGFR3-TACC3 fusion.
- 20 30. The use according to claim 21, wherein the cancer is bladder cancer with a FGFR3-TACC3 translocation.
31. The use according to claim 19, wherein the cancer is urothelial cancer with a
- 25 FGFR3-TACC3 translocation.
32. The use according to claim 20, wherein the cancer is metastatic or surgically unresectable urothelial cancer with a FGFR3-TACC3 translocation.
- 30 33. The use according to claim 26, 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.
- 35 34. The use according to claim 33, wherein the alteration is a FGFR3:TACC3 v1 fusion.

35. The use according to claim 33, wherein the alteration is a FGFR3:TACC3 v3 fusion.

36. The use according to claim 33, wherein the alteration is a FGFR3:BAIAP2L1 fusion.

37. The use according to claim 33, wherein the alteration is a FGFR2:BICC1 fusion.

38. The use according to claim 33, wherein the alteration is a FGFR2:CASP7 fusion.

39. The use according to claim 26, wherein the alteration is selected from the following FGFR3 gene mutations: FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

40. The use according to any one of claims 19 to 21, wherein the cancer harbors at least one of the following FGFR3 gene mutations: FGFR3 R248C, FGFR3 S249C, FGFR3 G370C, FGFR3 Y373C.

41. The use according to claim 40, wherein the mutation is a FGFR3 R248C mutation.

42. The use according to claim 40, wherein the mutation is a FGFR3 S249C mutation.

43. The use according to claim 40, wherein the mutation is a FGFR3 G370C mutation.

44. The use according to claim 40, wherein the mutation is a FGFR3 Y373C mutation.

45. The use according to any one of claims 1-16, 26-29 and 31-44, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the treatment provides for an objective response rate of at least 40%.

46. The use according to claim 45, wherein the treatment provides an objective response rate ranging from 40% to 45%.

47. The use according to any one of claims 1-16, 26-29 and 31-46, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the median duration of response is at least 5 months.

48. The use according to claim 47, wherein the median duration of response is at least 5.4 months.

49. The use according to any one of claims 1-16, 26-29 and 31-46, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the treatment provides a median duration of response ranging between 4 months and 7 months.

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50. The use according to any one of claims 1-16, 26-29 and 31-49, wherein the cancer is urothelial cancer, metastatic or surgically unresectable urothelial cancer and wherein the median time to response is around 1.4 months.

10 51. The use according to claim 2, or any one of claims 3 to 50 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.