Health Technology Briefing
December 2021

Erdafitinib for treating advanced solid tumours with an FGFR mutation in people aged 6 years and older

Company/Developer	Janssen-Cilag Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 28381	NICE ID: 10577	UKPS ID: 659521

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Erdafitinib is intended for the treatment of advanced solid tumours with a mutation in receptors which bind to the fibroblast growth factor family of proteins, called fibroblast growth factor receptors (FGFR), in patients 6 years and older, who have failed at least one previous treatment and children or adolescent patients who are newly diagnosed and have no suitable treatment options. Approximately 5 – 30% of patients who have a solid tumour will have such a mutation, depending on tumour type and site and there are currently no treatments available in the EU/UK which reduce the activity of all four FGFRs so this product represents a new treatment approach in an area of unmet need.

Erdafitinib is an orally administered bioavailable tablet which reduces the activity of all four FGFRs, and has the potential to attack cancer cells in the tumour. Upon administration, erdafitinib binds to and inhibits FGFR 1 - 4, which may result in the interruption of FGFR-related signals in the cell and so stop tumour cell growth in cells which have too much FGFR.

Proposed Indication

Treatment of adults and paediatric patients with advanced, unresectable solid tumours with fibroblast growth factor receptor (FGFR) alterations (mutations or gene fusions), or child or adolescent patients with a newly-diagnosed solid tumor and no acceptable standard therapies.[1]

Technology

Description

Erdafitinib (Balversa, JNJ-42756493) is an orally bioavailable, pan FGFR inhibitor with potential antineoplastic activity. Upon administration, erdafitinib binds to and inhibits FGFR 1 - 4, which may result in the inhibition of FGFR-related signal transduction pathways and thus the inhibition of tumour cell proliferation and tumour cell death in FGFR-overexpressing tumour cells. FGFR, upregulated in many tumour cell types, is a receptor tyrosine kinase essential to tumour cell proliferation, differentiation and survival.[2]

Erdafitinib is in clinical development for the treatment of patients aged 6 years and older with solid tumours with a fibroblast growth factor receptor (FGFR) alteration. In the phase II clinical trial (NCT04083976), participants will receive a dose of erdafitinib oral tablets until disease progression, intolerable toxicity, withdrawal of consent, or decision by the investigator to discontinue treatment.[1]

Key Innovation

The use of erdafitinib has been associated with successful clinical activity in patients with urothelial cancer and cholangiocarcinoma with FGFR alterations.[3,4] The proposed indication will expand availability of this product to patients with other types of solid tumour who also have FGFR alterations and have failed or progressed on at least one prior systemic treatment.[1]

Regulatory & Development Status

Erdafitinib does not currently have a Marketing Authorisation in the EU/UK for any indication.

Erdafitinib is in phase III/II clinical development for the following indications:[5]

- Bladder cancer
- Lung cancer
- Urothelial cancer
- Oesophageal cancer
- Cholangiocarcinoma
- Prostate cancer
- Non-Hodgkin lymphoma
- Histiocytic disorders with FGFR mutations
- Hepatocellular carcinoma
- Multiple myeloma

Patient Group

Disease Area and Clinical Need

Solid tumours are defined as abnormal masses of tissue that usually do not contain cysts or liquid areas, and may be benign or malignant. Examples of solid tumours are sarcomas, carcinomas, and lymphomas. Solid tumours represent approximately 90% of all cancer diagnoses.[6]

FGFR alterations are present in 5 – 10% of all human cancers, although this frequency increases to 10 – 30% in urothelial carcinoma and intrahepatic cholangiocarcinoma.[7] Signs and symptoms, and prognosis of solid tumours can depend on where the tumour is located, its size, and how much it affects nearby organs and tissues.

In 2019, there were 453,741 incident tumours of all types in England. Using the data above, we could suggest that around 408,367 would be classed as solid tumours, and further that approximately 20,418 to 40,836 would be FGFR driven tumours.[8]

Recommended Treatment Options

There are multiple treatment options currently available for treatment of solid tumours which include surgery, chemotherapy, radiotherapy, hormone therapy, immunotherapies and targeted cancer drugs. The treatment provided will vary according to type of cancer, how big the cancer it, how it has spread and according to the patients' general health.[9]

There is no pan-FGFR treatment available in the UK/EU at this time.[10]

Clinical Trial Information

Trial	NCT04083976; 2019-002113-19; A phase 2 study of erdafitinib in subjects with advanced solid tumors and FGFR gene alterations. **Phase II –** recruiting **Locations –** Five EU countries, UK, USA, and other countries. **Primary Completion data (estimated) –** June 2022
Trial Design	Single group assignment, open label
Population	N=336 (planned). Adult and paediatric patients with advanced solid tumour with FGFR alteration who have received at least one prior line of systemic therapy in the advanced, unresectable, or metastatic setting, or is a child or adolescent patient with a newly diagnosed solid tumour and no acceptable standard therapies.
Intervention(s)	Erdafitinib oral tablets until disease progression, intolerable toxicity, withdrawal of consent or decision by the investigator to discontinue treatment. The company expect the dose to be 8mg erdafitinib every day (QD) with titration to 9mg on day 15 if phosphate still below target 7.0mg/dL.
Comparator(s)	N/A
Outcome(s)	Overall response rate as assessed by independent review committee (defined as the percentage of participants who achieve a complete response or partial response). See trial record for full list of other outcomes.
Results (efficacy)	-

Results (safety)	-

Estimated Cost

The cost of erdafitinib is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer [ID1333]. Expected date of issue to be confirmed.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 Standard Contract for Paediatric Oncology.
- NHS England. 2013/14 Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 Standard Contract for Cancer: Chemotherapy (Children, Teenagers and Young Adults). B15/S/b.
- NHS England. 2013/14 Standard Contract for Cancer: Teenagers & Young Adults. B17/S/a.
- NHS England. Standard Contract for Paediatric Medicine: Palliative Care. E03/S/h.

Other Guidance

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Additional Information

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References

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7 Krook M, Reeser J, Ernst G, Barker H, Wilberding M, Li G, et al. Fibroblast growth factor receptiors in cancer: genetic alterations, diagnostics, therapeutic targets and mechanisms of resistance. *British Journal of Cancer*. 2021;124:880 - 92. Available from: https://doi.org/10.1038/s41416-020-01157-0.

8 CancerData. *Cancer Incidence.* 2021. Available from: https://www.cancerdata.nhs.uk/incidence_and_mortality [Accessed 22 November 2021].

9 Cancer Research UK. *Treatment for cancer.* 2021. Available from: https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment [Accessed 16 November 2021].

10 Facchinetti F, Hollebecque A, Bahleda R, Loriot Y, Olausson K, Massard C, et al. Facts and new hopes on selective FGFR inhibitors in solid tumours. *Clinical Cancer Research*. 2020;26(4):764 - 74. Available from: https://doi.org/10.1158/1078-0432.CCR-19-2035.

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