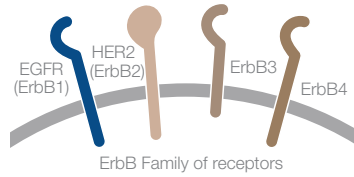


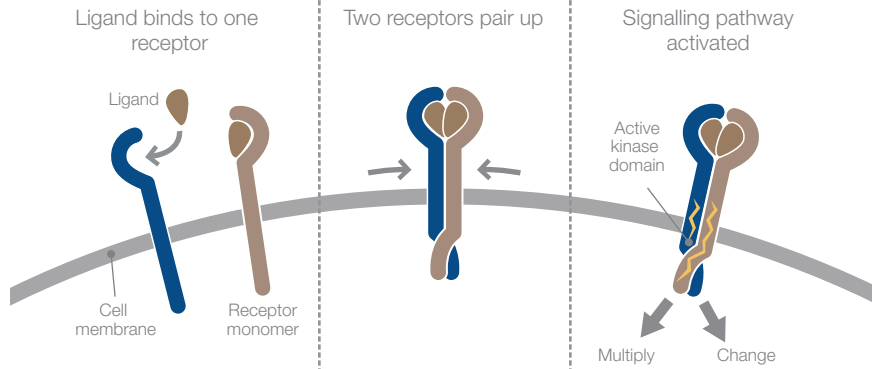
AFATINIB* – IRREVERSIBLE ERBB FAMILY BLOCKER

1. How does ErbB Family signalling work?

Signals from receptors of the ErbB Family tell cells to perform normal cell functions, such as multiply or change.

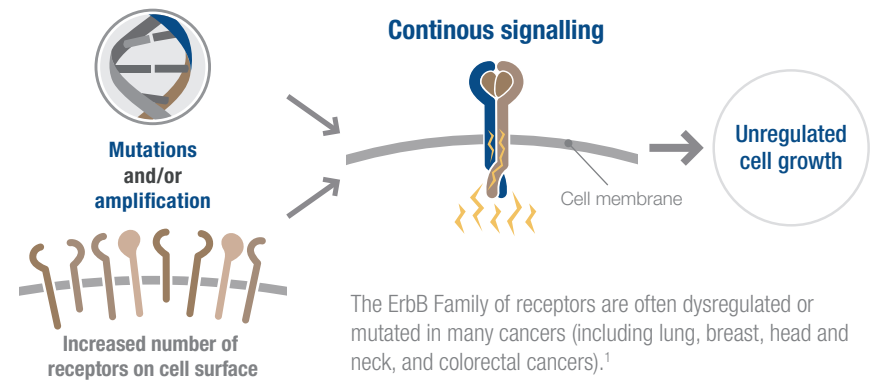


Activation of ErbB receptors in a normal cell



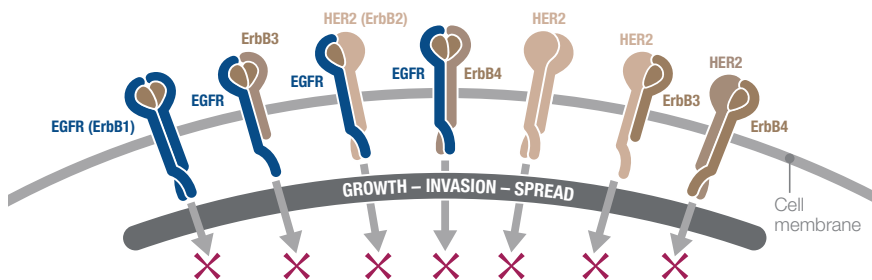
Dysregulated activation of ErbB signalling in cancer cells

The genes coding for ErbB receptors in cancer cells can mutate and/or amplify which leads to a disruption in the normal signalling process. This results in a higher rate of cell division and tumour growth.



2. Afatinib mode of action - targeting the ErbB Family²

Afatinib blocks the signalling of all ErbB Family receptors, therefore interfering with key pathways involved in cell growth.



The signalling of ErbB3 is blocked indirectly through transphosphorylation

3. Approved indications

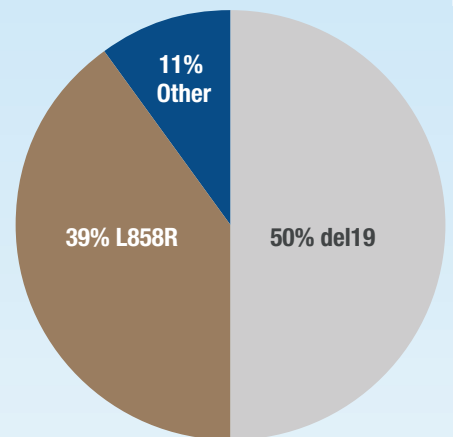
Afatinib* is approved for the first-line treatment of patients with EGFR mutation-positive non-small cell lung cancer (NSCLC) (under the brand names: GIOTRIF®/GILOTRIF®).

The prevalence of EGFR mutations in lung cancer is approximately

40-50%
among Asians³⁻⁶ and

10-15%
among Caucasians^{7,8}

Types of EGFR mutations in lung cancer^{9,10}



Afatinib is also approved in Europe, US and other markets for the treatment of patients with advanced squamous cell carcinoma (SqCC) of the lung whose disease has progressed (on or) after treatment with platinum-based chemotherapy (under the brand names: GIOTRIF®/ GILOTRIF®)

SqCC of the lung represents approximately

20-30%
of NSCLC cases^{11,12}

LET'S COLLABORATE ONCOLOGY FROM BOEHRINGER INGELHEIM

*Afatinib is approved in a number of markets, including the EU, Japan, Taiwan and Canada under the brand name Giotrif®, in the US under the brand name Gilotrif® and in India under the brand name Xovoltib® for use in patients with distinct types of EGFR mutation-positive NSCLC. Afatinib is also approved in the EU, US and other markets for the treatment of patients with advanced SqCC of the lung whose disease has progressed (on or) after treatment with platinum-based chemotherapy. Afatinib is under regulatory review by health authorities in other countries worldwide. Registration conditions differ internationally, please refer to locally approved prescribing information. Afatinib is under regulatory review by health authorities in other countries worldwide. 1. Hynes NE, MacDonald G. *Curr Opin Cell Biol* 2009;21:177-84. 2. BI Data on File. 3. Mitsudomi T *et al.* Mutations of the epidermal growth factor receptor gene predict prolonged survival after gefitinib treatment in patients with non-small cell lung cancer with postoperative. *J Clin Oncol* 2005;23:2513-2520 4. Chou TY *et al.* Mutation in the Tyrosine Kinase Domain of Epidermal Growth Factor Receptor is a Predictive and Prognostic Factor for Gefitinib Treatment in Patients with Non-Small Cell Lung Cancer. *Clin Cancer Res* 2005;11:3750-3757 5. Seo JS *et al.* The transcriptional landscape and mutational profile of lung adenocarcinoma. *Genome Res*. 2012;22:2109-2119 6. Yang SH *et al.* Mutations in the tyrosine kinase domain of the epidermal growth factor receptor in non-small cell lung cancer. *Clin Cancer Res* 2005;11:2106-2110 7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: non-small cell lung cancer, version 1, 2015. 8. Quest Diagnostics - Lung Cancer Mutation Panel (EGFR, KRAS, ALK); Available at: http://www.questdiagnostics.com/testcenter/testguide.action?dc=TS_LungCancerMutation_Panel. 9. Yang J *et al.* *J Clin Oncol* 2013;DOI: 10.1200/JCO.2012.46.1764. 10. Wu Y-L *et al.* *J Clin Oncol* 2014;DOI:10.1016/S1470-2045(13)70604-1. 11. Soria *et al.* *Lancet Oncol* 2015;16:8:897-907. 12. Travis WD. *Clin. Chest Med* 2011;32(4):669-692. ©2016 Boehringer Ingelheim International GmbH. All rights reserved | Last updated: December 2016

