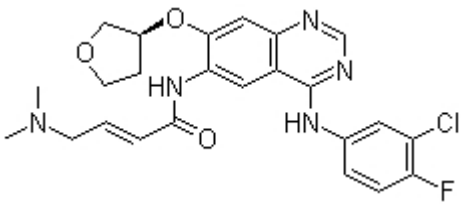
Product Introduction

Afatinib (BIBW2992)

Afatinib (BIBW2992) irreversibly inhibits EGFR/HER2 including **EGFR(wt)**, **EGFR(L858R)**, EGFR(L858R/T790M) and HER2 with **IC50** of 0.5 nM, 0.4 nM, 10 nM and 14 nM, respectively; 100-fold more active against Gefitinib-resistant L858R-T790M EGFR mutant. Phase 3.

Technical Data:

Molecular Weight (MW):	485.94	
Formula:	$C_{24}H_{25}ClFN_5O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 97 mg/mL	
	Water <1 mg/mL	
	Ethanol 15 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	439081-18-2	

Biological Activity

BIBW2992 shows potent activity against both wild-type and mutant forms of EGFR and HER2. It is similar to Gefitinib in potency against L858R EGFR, but about 100-fold more active against the Gefitinib resistant L858R-T790M EGFR double mutant. BIBW2992 exhibits potent effects on both EGFR and HER2 phosphorylation in vivo. It compares favorably to reference compounds (such as Lapatinib et al.) in all cell

types tested, such as human epidermoid carcinoma cell line A431 expressing wt EGFR, murine NIH-3T3 cells transfected with wt HER2, as well as breast cancer cell line BT-474 and gastric cancer cell line NCI-N87, which express endogenous HER2. [1]

Daily oral administration of BIBW2992 at 20 mg/kg for 25 days results in dramatic tumor regression with a cumulative treated/control tumor volume ratio (T/C ratio) of 2%. Reduced phosphorylation of EGFR and AKT is confirmed by immunohistochemical staining of tissue sections. Therefore, like lapatinib and neratinib, BIBW2992 is a next generation tyrosine kinase inhibitor (TKI) that inhibits human epidermal growth factor receptor 2 (Her2) and epidermal growth factor receptor (EGFR) kinases irreversibly. BIBW2992 is not only active against EGFR mutations targeted by first generation TKIs like Erlotinib or Gefitinib, but also against those insensitive to these standard therapies. [1]

References

[1] Li D, et al. Oncogene, 2008, 27(34), 4702-4711.

[2] Hickish T, et al. 2010 ASCO Annual Meeting, Abst 1065.

[3] Yasuda H, et al. Lancet Oncol, 2012, 13(1), e23-31.

[4] De Grève J, et al. Lung Cancer, 2012, 76(1), 123-127

[5] Awada AH, et al. Invest New Drugs, 2012, 17.