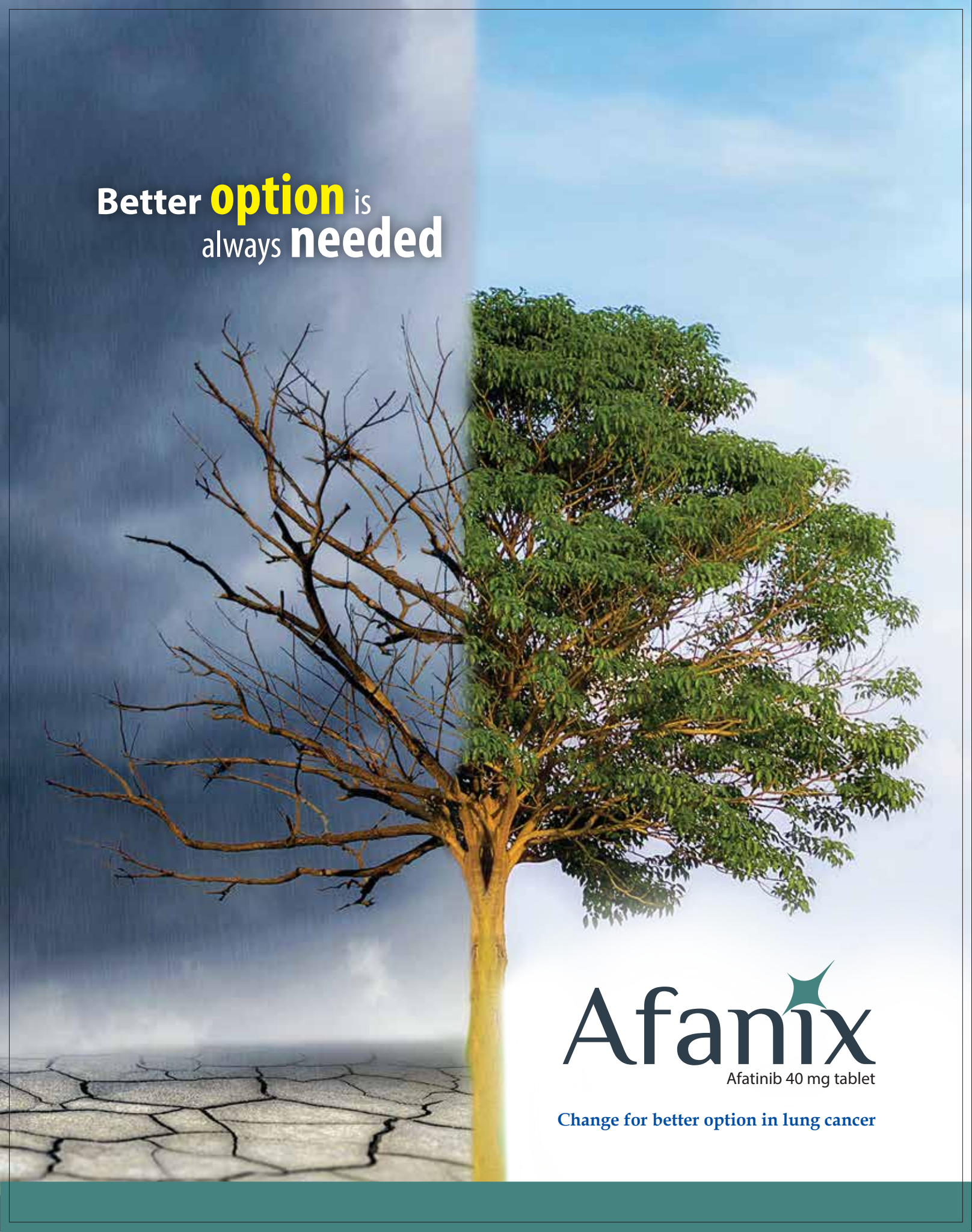

Better option is
always needed
Afanix
Afatinib 40 mg tablet
Change for better option in lung cancer

Afatinib met the unmet need for effective treatment in patient with non-small cell lung cancer. Manageable safety and convenience oral administration suggest that Afatinib is better option compared to Erlotinib & Gefitinib.

BEACON Pharma Introduces

Afanix

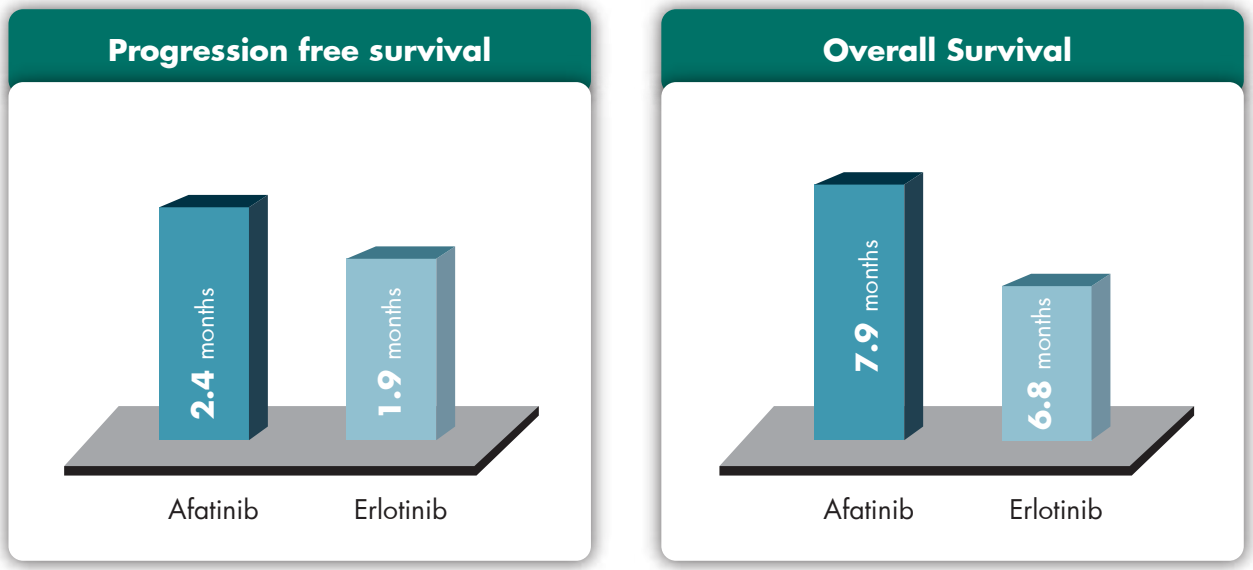
Afatinib 40 mg tablet

Change for better option in lung cancer

Superior improvement than Erlotinib

In an open label phase 3 trials at 183 cancer centers in 23 countries, patients enrolled with stage 3 or 4 squamous cell carcinoma of the lung who had progressed after at least four cycles of platinum based chemotherapy. And patients were randomly assigned to receive Afatinib and Erlotinib.

Result



Ensures significant improvement

Afanix

Afatinib 40 mg tablet

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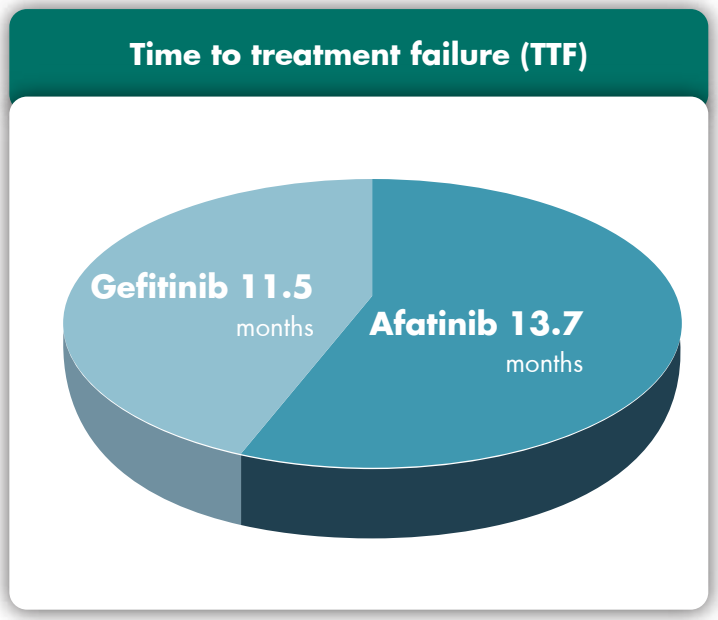
Supreme efficacious than Gefitinib

In randomised controlled phase 2B trial was done at 64 centres in 13 countries. total 319 patients with satge IIIB and IV NSCLC and a common EGFR mutation were randomly assigned to receive Afatinib and Gefitinib as first line therapy.

Result



Ensures Longer treatment

Afanix

- Ensures significant result than Erlotinib and Gefitinib
- Efficacious treatment option for squamous cell carcinoma of the lung
- First line treatment for EGFR mutation-positive NSCLC
- Indicated in previously treated, metastatic squamous NSCLC

Afanix

Afatinib 40 mg tablet

Change for better option in lung cancer

Prescribing information

COMPOSITION: ***Afanix 40 Tablet:*** Each film coated tablet contains Afatinib Dimaleate INN 59.12 mg equivalent to Afatinib 40 mg. **CLINICAL PHARMACOLOGY:** ***Mechanism of Action:*** Afatinib covalently binds to the kinase domains of EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4) and irreversibly inhibits tyrosine kinase autophosphorylation, resulting in downregulation of ErbB signaling. Afatinib demonstrated inhibition of autophosphorylation and *in vitro* proliferation of cell lines expressing wild-type EGFR or those expressing selected EGFR exon 19 deletion mutations or exon 21 L858R mutations, including some with a secondary T790M mutation, at Afatinib concentrations achieved, at least transiently, in patients. In addition, Afatinib inhibited in vitro proliferation of cell lines overexpressing HER2. Treatment with Afatinib resulted in inhibition of tumor growth in nude mice implanted with tumors either overexpressing wild type EGFR or HER2 or in an EGFR L858R/T790M double mutant model. **Pharmacodynamics:** ***Cardiac Electrophysiology:*** The effect of multiple doses of Afatinib (50 mg once daily) on the QTc interval was evaluated in an open-label, single-arm study in patients with relapsed or refractory solid tumors. No large changes in the mean QTc interval (i.e., >20 ms) were detected. **Pharmacokinetics: Absorption and Distribution:** Following oral administration of Afatinib tablets, time to peak Afatinib plasma concentrations (T_{max}) is 2 to 5 hours. Maximum concentration (C_{max}) and area under the concentration-time curve from time zero to infinity ($AUC_{0-\infty}$) values increased slightly more than dose proportional in the range of 20 to 50 mg. The geometric mean relative bioavailability of 20 mg Afatinib tablets was 92% as compared to an oral solution. In vitro binding of Afatinib to human plasma proteins is approximately 95%. A high-fat meal decreased Cmax by 50% and $AUC_{0-\infty}$ by 39% relative to the fasted condition. **Metabolism and Elimination:** Covalent adducts to proteins are the major circulating metabolites of Afatinib and enzymatic metabolism of Afatinib is minimal. In humans, excretion of Afatinib is primarily via the feces (85%) with 4% recovered in the urine following a single oral dose of [$_{14}$C]-labeled Afatinib solution. The parent compound accounted for 88% of the recovered dose. The elimination half-life of Afatinib is 37 hours after repeat dosing in cancer patients. Steady-state plasma concentrations are achieved within 8 days of repeat dosing of Afatinib resulting in an accumulation of 2.8-fold for AUC and 2.1-fold for C_{max}. **Specific populations:** ***Renal Impairment:*** The median trough Afatinib plasma concentrations in patients with mild (CLcr 60-89 mL/min) and moderate (CLcr 30-59 mL/min) renal impairment were 27% and 85% higher than those in patients with normal renal function (CLcr≥90 mL/min). Afatinib has not been studied in patients with severely impaired renal function (CLcr <30 mL/min). ***Hepatic Impairment:*** Afatinib is eliminated mainly by biliary/fecal excretion. Mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment had no influence on the Afatinib exposure following a single dose of Afatinib. Subjects with severe (Child Pugh C) hepatic dysfunction have not been studied. ***Body Weight, Gender, Age, and Race:*** Based on the population pharmacokinetic analysis, weight, gender, age, and race do not have a clinically important effect on exposure of Afatinib. **INDICATIONS:** Afatinib is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. Limitation of Use: Safety and efficacy of Afatinib have not been established in patients whose tumors have other EGFR mutations. Afatinib is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy. **DOSAGE AND ADMINISTRATION:** ***Recommended Dose:*** The recommended dose of Afatinib is 40 mg orally once daily until disease progression or no longer tolerated by the patient. Afatinib should be taken at least 1 hour before or 2 hours after a meal. Patient should not take a missed dose within 12 hours of the next dose. ***Dosage Modification:*** *Withhold Afatinib for any drug-related adverse reactions of:* • NCI CTCAE* Grade 3 or higher • Diarrhea of Grade 2 or higher persisting for 2 or more consecutive days while taking anti-diarrheal medication • Cutaneous reactions of Grade 2 that are prolonged (lasting more than 7 days) or intolerable • enal dysfunction of Grade 2 or higher: Resume treatment when the adverse reaction fully resolves, returns to baseline, or improves to Grade 1. Reinstitute Afatinib at a reduced dose, i.e., 10 mg per day less than the dose at which the adverse reaction occurred. *Permanently discontinue Afatinib for:* • Life-threatening bullous, blistering, or exfoliative skin lesions • Confirmed interstitial lung disease (ILD) • Severe drug-induced hepatic impairment • Persistent ulcerative keratitis • Symptomatic left ventricular dysfunction • Severe or intolerable adverse reaction occurring at a dose of 20 mg per day ***P-gp Inhibitors:*** For patients who require therapy with a P-glycoprotein (P-gp) inhibitor, reduce Afatinib daily dose by 10 mg if not tolerated. Resume the previous dose after discontinuation of the P-gp inhibitor as tolerated. ***P-gp Inducers:*** For patients who require chronic therapy with a P-gp inducer, increase Afatinib daily dose by 10 mg as tolerated. Resume the previous dose 2 to 3 days after discontinuation of the P-gp inducer. **USE IN SPECIFIC POPULATIONS**: **Pregnancy**: Pregnancy Category D **Risk Summary:** Based on its mechanism of action, Afatinib can cause fetal harm when administered to a pregnant woman. Afatinib was embryotoxic and, in animals with maternal toxicity, led to abortions at late gestational stages in rabbits at doses of 5 mg/kg (approximately 0.2 times the exposure by AUC at the recommended human dose of 40 mg daily) or greater. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. **Nursing Mothers:** It is not known whether Afatinib is present in human milk. Afatinib was present in the milk of lactating rats at concentrations 80-150 times higher than those found in plasma from 1 to 6 hours after administration. Because many drugs are present in human milk and because of the potential for serious adverse reactions in nursing infants from Afatinib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness of Afatinib in pediatric patients have not been established. **Geriatric Use:** Of the 3865 patients in the clinical studies of Afatinib, 32% of patients were 65 years and older, while 7% were 75 years and older. No overall differences in safety were observed between patients 65 years and over and younger patients. 39% of the 345 patients were 65 years of age or older and 4% were 75 years or older. No overall differences in effectiveness were observed between patients 65 years and older and younger patients. **OVERDOSAGE:** Overdose was reported in 2 healthy adolescents each of whom ingested 360 mg of Afatinib (as part of a mixed-drug ingestion) resulting in nausea, vomiting, asthenia, dizziness, headache, abdominal pain, and elevated amylase (<1.5 times upper limit of normal [ULN]). Both subjects recovered. **CONTRAINDICATIONS:** None. **ADVERSE EFFECT:** Most common adverse reactions (≥20%) are diarrhea, rash/dermatitis acneiform, stomatitis, paronychia, dry skin, decreased appetite, pruritus. **DRUG INTERACTION:** ***Effect of P-glycoprotein (P-gp) Inhibitors and Inducers:*** Oral administration of a P-gp inhibitor (Ritonavir at 200 mg twice daily) 1 hour before administration of Afatinib increased systemic exposure to Afatinib by 48%. There was no change in Afatinib exposure when Ritonavir was administered simultaneously with or 6 hours after Afatinib. Concomitant taking of P-gp inhibitors (including but not limited to Ritonavir, Cyclosporine A, Ketoconazole, Itraconazole, Erythromycin, Verapamil, Quinidine, Tacrolimus, Nelfinavir, Saquinavir, and Amiodarone) with Afatinib can increase exposure to Afatinib. Co-administration with oral dose of a P-gp inducer (Rifampicin at 600 mg once daily for 7 days) decreased exposure to Afatinib by 34%. Concomitant taking of P-gp inducers (including but not limited to Rifampicin, Carbamazepine, Phenytoin, Phenobarbital, and St. John's wort) with Afatinib can decrease exposure to Afatinib. **PHARMACEUTICAL INFORMATION: Storage Conditinons:** Store in a cool and dry place, away from light. Keep out of the reach of children. **Presentation & Packaging:** ***Afanix 40 Tablet:*** Each commercial box contains 30 tablets in Alu-Alu blister pack.

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Pharmaceuticals Limited
Light for life

Ref: dx.doi.org/10.1016/ S1470-2045(15)00006-6, doi.org/10.1016/S1470-2045(16)30033-X