Lapatinib → breast and lung cancer. It was approved by the FDA on March 13, 2007, for use in patients with advanced metastatic breast cancer in conjunction with Xeloda. Lapatinib is a once-daily oral drug indicated for women who have received prior treatment with Herceptin and cancer drugs called taxanes and anthracyclines.

Lapatinib is an epidermal growth factor receptor (EGFR) and HER2/neu (ErbB-2) dual tyrosine kinase inhibitor. It binds to the intracellular phosphorylation domain to prevent receptor autophospohorylation upon ligand binding.

Route of administration→ Oral

Erlotinib→ Like gefitinib, erlotinib has shown a survival benefit in the treatment of lung cancer in phase III trials. It has been approved for the treatment of locally advanced or metastatic non-small cell lung cancer that has failed at least one prior chemotherapy regimen. In November 2005, the FDA approved the use of erlotinib in combination with gemcitabine for treatment of locally advanced, unresectable, or metastatic pancreatic cancer.

Erlotinib specifically targets the epidermal growth factor receptor tyrosine kinase and binds in a reversible fashion to the ATP binding site of the receptor. For the signal to be transmitted, two members of the EGFR family need to come together to form a homodimer. These then use the molecule of ATP to autophosphorylate each other, which causes a conformational change in their intracellular structure, exposing a further binding site for binding proteins that cause a signal cascade to the nucleus. By inhibiting the ATP, autophosphorylation is not possible and the signal is stopped.

Route of administration→Oral tablets

Common side effects include:

- Diarrhea
- Rash occurs in the majority of patients. This resembles acne and primarily involves the face and neck. It is self-limited and resolves in the majority of cases, even with continued use. Some clinical studies have indicated a correlation between the severity of the skin reactions and increased survival though this has not been quantatively assessed.
- Loss of appetite
- Fatigue
- Rarely, interstitial pneumonitis, which is characterized by cough and increased dyspnea. This may be severe and must be considered among those patients whose breathing acutely worsens.

Sorafenib → advanced renal cell cancer. It is a small molecular inhibitor of Raf kinase, PDGF (platelet-derived growth factor) and VEGF receptor kinase.

Sorafenib was approved by the U.S. Food and Drug Administration (FDA) on December 20, 2005.

Route of administration→ Oral

Metabolism→ Liver

Side effects→ skin rash, hand-foot skin reactions, diarrhea, and hypertension

Sunitinib is a small molecule receptor tyrosine kinase inhibitor that is approved for the treatment of gastrointestinal stromal tumor (GIST) and renal cell carcinoma (RCC).

Sunitinib inhibits signaling through multiple receptor tyrosine kinases, including platelet-derived growth factor receptor and vascular endothelial growth factor receptor. GIST is driven by a mutationally activated kit kinase, and this is also inhibited by Sunitinib.

Sunitinib is primarily being used in patients with GIST who have disease progression during prior treatment with imatinib (another kit inhibitor) or those who did not tolerate imatinib. In one clinical trial of this patient population, the time to progression was significantly longer in the sunitinib arm than the placebo arm (27 v 6 weeks). Data on overall survival are not mature yet.

Notable side effects included diarrhea, hypertension, skin discoloration, mucositis, fatigue, and hypothyroidism. Neutropenia, thrombocytopenia, and decreases in left ventricular ejection fraction have also been seen with sunitinib.

Efficacy in renal cell carcinoma is probably through inhibition of vascular endothelial growth factor receptor. RCC is one of the most highly vascularized of tumors and is also being targeted by other angiogenesis inhibitors. These inhibitors in theory should have efficacy against many solid tumors, and sunitinib is currently in trials for breast, colon and lung cancers. A clinical trial reported in January 2007 on the *New England Journal of Medicine* showed significant benefit of sunitinib over interferon alpha (median progression free survival 11 months for patients on sunitinib versus 5 months for those on interferon alpha). It also reported significantly fewer side effects with sunitinib as compared to interferon alpha.

Nilotinib is a tyrosine kinase inhibitor under investigation as a possible treatment for chronic myelogenous leukemia (CML).

Dasatinib is an oral dual BCR/ABL and Src family tyrosine kinases inhibitor approved for use in patients with chronic myelogenous leukemia (CML) and Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL). The drug is named after

the inventor chemist, Jagabandhu Das, who codiscovered it while working at Bristol Myers Squibb.

Nimotozumab→ Humanised monoclonal antiboday against EGFR. Very low incidence of infusion reactions, rash, mucositis. Active (in combination with CT/RT) in SCCHN,NSCLC, HGG, Ca. pancreas.

Panitumumab→ Entirely human monoclonal antibody against EGFR. Main toxicity is skin rash. Used in refractory colorectal cancer.

Tipifarnib, Lonafarnib→ Farnesyl transferase inhibitors.

Temsirolimus→ mTOR kinase inhibitor