

# Genentech **Firsts** in Targeted Cancer Therapy: Translating Science into Life

1987

Dennis Slamon at UCLA and Genentech scientists discover **first** link between the excessive production of human epidermal growth factor receptor 2 (HER2) and the progression of breast cancer<sup>1</sup>

1990

Genentech scientists are the **first** to humanize a monoclonal antibody directed at the HER2 gene<sup>4,5</sup>

1998

Herceptin® becomes the **first** FDA-approved monoclonal antibody for the first-line treatment of HER2-positive metastatic breast cancer, in combination with chemotherapy, and as a single agent for second- and third-line treatment<sup>8</sup>

2004

Avastin® becomes the **first** FDA-approved anti-angiogenic therapy proven to extend survival, in combination with intravenous (IV) chemotherapy, in patients with first-line metastatic colorectal cancer<sup>9</sup>

Tarceva® becomes the **first** and only FDA-approved EGFR-targeted therapy to improve survival in previously treated, locally advanced or metastatic, non-small cell lung cancer (NSCLC)<sup>10</sup>

2006

Herceptin® becomes the **first** FDA-approved targeted therapy, in combination with chemotherapy, for the adjuvant treatment of HER2-positive, node-positive breast cancer<sup>9</sup>

1989

Napoleone Ferrara and Genentech scientists are the **first** to identify and clone the gene for vascular endothelial growth factor (VEGF), a key mediator of angiogenesis<sup>2,3</sup>

1997

Rituxan® becomes the **first** FDA-approved therapeutic antibody for treating cancer in the U.S. and the **first** biologic therapy for the treatment of relapsed or refractory, low-grade or follicular CD20-positive, B-cell non-Hodgkin's lymphoma (NHL)<sup>6</sup>  
Genentech scientists are the **first** to develop a humanized monoclonal antibody directed at VEGF<sup>7</sup>

2001

Herceptin, in combination with chemotherapy, becomes the **first** targeted therapy to improve survival in advanced HER2-positive breast cancer patients<sup>8</sup>

2005

Tarceva becomes the **first** and only FDA-approved EGFR-targeted therapy to improve survival, in combination with chemotherapy, for first-line advanced pancreatic cancer<sup>10</sup>

2006

Avastin® becomes the **first** FDA-approved targeted therapy, in combination with IV chemotherapy, to extend median survival beyond one year in patients with first-line unresectable, locally advanced, recurrent or metastatic non-squamous, NSCLC<sup>9</sup>

Rituxan plus CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) becomes the **first** treatment to improve survival for patients with first-line, diffuse large B-cell, CD20-positive, non-Hodgkin's lymphoma since the introduction of the CHOP chemotherapeutic regimen more than 25 years ago<sup>6,11</sup>

## **Rituxan**

### **Indications**

RITUXAN is indicated for the first-line treatment of follicular, CD20+, B-cell non-Hodgkin's lymphoma (NHL) in combination with CVP chemotherapy.

RITUXAN is indicated for the treatment of low-grade, CD20+, B-cell NHL in patients with stable disease or who achieve a partial or complete response following first-line treatment with CVP chemotherapy.

RITUXAN is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20+, B-cell NHL.

RITUXAN is indicated for the first-line treatment of diffuse, large B-cell, CD20+ non-Hodgkin's lymphoma (DLBCL) in combination with CHOP or other anthracycline-based chemotherapy regimens.

### **Boxed WARNINGS and Additional Important Safety Information**

RITUXAN has been associated with **fatal infusion reactions, tumor lysis syndrome, severe mucocutaneous reactions, progressive multifocal leukoencephalopathy (PML)**, hepatitis B reactivation with related fulminant hepatitis and other serious viral infections, cardiovascular events, renal toxicity, and bowel obstruction and perforation. The most common adverse events were infusion-related symptoms, including fever (53%), chills/rigors (33%), nausea (23%), asthenia (26%), and headache (19%). The incidence of infusion reactions was highest during the first infusion and decreased with each subsequent infusion. These reactions generally have resolved with slowing or interruption of the infusion and with supportive care.

## **REFERENCES**

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4. Carter P, Presta L, Gorman CM, et al. Humanization of an anti-p185HER2 antibody for human cancer therapy. *Proc Natl Acad Sci USA* 1992; 89:4285-4289.
5. Shalaby MR, Shepard HM, Presta L, et al. Development of humanized bispecific antibodies reactive with cytotoxic lymphocytes and tumor cells overexpressing the HER2 protooncogene. *J Exp Med.* 1992; 175:217-225.
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9. Avastin prescribing information.
10. Tarceva prescribing information.
11. Portlock CS, Qin J, Schaindlin P, et al. The NHL-15 protocol for aggressive non-Hodgkin's lymphomas: a sequential dose-dense, dose-intense regimen of doxorubicin, vincristine and high-dose cyclophosphamide. *Ann Oncol.* 2004;15:1495-1503.

Please see accompanying full prescribing information for Rituxan, Herceptin, Tarceva and Avastin

Rituxan® with Biogen Idec, Inc. Tarceva® with OSI Pharmaceuticals, Inc.

## **Herceptin**

### **Indications**

Herceptin in combination with paclitaxel is indicated for treatment of patients with metastatic breast cancer whose tumors overexpress the HER2 protein and who have not received chemotherapy for their metastatic disease.

Herceptin as a single agent is indicated for the treatment of patients with metastatic breast cancer whose tumors overexpress the HER2 protein and who have received one or more chemotherapy regimens for their metastatic disease.

Herceptin, as part of a treatment regimen containing doxorubicin, cyclophosphamide, and paclitaxel, is indicated for the adjuvant treatment of patients with HER2-overexpressing, node-positive breast cancer.

### **Boxed WARNINGS and Additional Important Safety Information**

**Herceptin administration can result in left ventricular dysfunction and congestive heart failure. Serious infusion reactions and pulmonary toxicity have occurred;** rarely these have been fatal. Exacerbation of chemotherapy-induced neutropenia has also occurred. The most common adverse reactions associated with Herceptin use were fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, dyspnea, rash, neutropenia, anemia, and myalgia.

## **Tarceva**

### **Indication**

Tarceva monotherapy is indicated for the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

Results from two multicenter, placebo-controlled, randomized, Phase III trials conducted in first-line patients with locally advanced or metastatic NSCLC showed no clinical benefit with the concurrent administration of Tarceva with platinum-based chemotherapy, and its use is not recommended in that setting.

### **Important Safety Information**

Severe and potential fatal adverse events included Interstitial Lung Disease-like events, myocardial infarction or ischemia, cerebrovascular accident, and micro-angiopathic hemolytic anemia with thrombocytopenia. While receiving Tarceva therapy, women should be advised against becoming pregnant or breastfeeding. The most common side effects in patients with NSCLC receiving Tarceva monotherapy 150 mg were mild to moderate rash and diarrhea. The most common adverse reactions in patients with pancreatic cancer receiving Tarceva 100 mg plus gemcitabine were fatigue, rash, nausea, anorexia, and diarrhea.

## **Avastin**

### **Indications**

Avastin, in combination with intravenous 5-fluorouracil-based chemotherapy, is indicated for first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum.

Avastin, in combination with carboplatin and paclitaxel, is indicated for first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous, non-small cell lung cancer.

### **Boxed WARNINGS and Additional Important Safety Information**

The most serious adverse events associate with Avastin across all trials were **GI perforation, wound healing complication, hemorrhage**, arterial thromboembolic events, hypertensive crisis, reversible posterior leukoencephalopathy syndrome, neutropenia and infection, nephrotic syndrome, and congestive heart failure. The most common adverse events seen in patients receiving Avastin across all studies were asthenia, pain, abdominal pain, headache, hypertension, diarrhea, nausea, vomiting, anorexia, stomatitis, constipation, upper respiratory infection, epistaxis, dyspnea, exfoliative dermatitis, and proteinuria.