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Maintenance treatment with Avastin and Tarceva in combination helps lung cancer patients live longer without their disease worsening

Phase III ATLAS study achieves a new milestone in treating advanced lung cancer

Roche announced today that the Phase III ATLAS study showed patients with advanced non-small cell lung cancer (NSCLC) who received Avastin (bevacizumab) and Tarceva (erlotinib) as combined first-line maintenance treatment had a 39 percent improvement in the time they lived without the disease advancing (progression-free survival or PFS, the primary endpoint of the study), compared with those who received Avastin aloneⁱ. The ATLAS study was stopped early because of the superior efficacy for patients in the combined treatment group.

Avastin-based therapy is already proven to offer patients with advanced NSCLC over 12 month survival - the longest survival time ever demonstratedⁱⁱⁱⁱ. Now results from the ATLAS study show that after initial treatment with Avastin and chemotherapy, combined maintenance treatment with Avastin and Tarceva extends the time patients live without their disease getting worse to 4.8 months compared to 3.7 months with Avastin maintenance therapy alone. Advanced NSCLC progresses rapidly and this benefit represents a new milestone in the treatment of the disease. Importantly, this improvement was achieved without the need for continued chemotherapy.

The value of Tarceva for maintenance treatment in advanced NSCLC was confirmed in a second Phase III study - SATURN^{iv}, also presented today at ASCO. Patients in the SATURN trial received maintenance treatment with Tarceva if their cancer had not progressed on initial chemotherapy. The data showed a significant 41% improvement in the length of time patients lived without their disease getting worse compared to placebo. The improvement was seen in both squamous cell and non-squamous cell lung cancer patients.

Commenting on the two studies Professor Federico Cappuzzo, principal investigator on the SATURN study from the Istituto Clinico Humanitas IRCCS, Milan said, "ATLAS and SATURN bring welcome news for patients and their physicians since extending the time patients live without their disease advancing is a key

goal of treatment in lung cancer. Stopping the cancer growing for as long possible reduces symptoms and helps improve the patient's life. Being able to achieve these benefits without the need for chemotherapy is important since the side effects of chemotherapy add considerably to the physical and psychological burden of cancer for many patients.”

Lung cancer is the most common cancer worldwide with 1.5 million new cases annually^y and NSCLC accounts for almost 85 percent of all lung cancers^{vi}. NSCLC progresses rapidly. Less than 5% of advanced NSCLC patients survive for five years^{vi}. Extending the time patients live without their disease progressing and managing side effects are key treatment goals. Each day, more than 3,000 people die from lung cancer worldwide^v.

Results of the ATLAS study were featured today during a press briefing at the 45th annual meeting of the American Society of Clinical Oncology (ASCO). Full results will be presented tomorrow by Dr. Vincent A. Miller, M.D., lead investigator of the ATLAS study, and Associate Attending Physician, Memorial Sloan-Kettering Cancer Center (Abstract #LBA8002 – Sunday, May 31, 2009, 9:30 a.m. – 9:45 a.m. EST, West Hall E1). Full results of SATURN will also be presented tomorrow (Abstract #8001 – Sunday, May 31, 2009, 9:15 a.m. – 9:30 a.m. EST, West Hall E1).

Study background and key results

ATLAS

A global multicentre, randomised, double blind, placebo controlled study that enrolled 1,160 patients with locally advanced, recurrent or metastatic NSCLC. Patients were initially given first line treatment of four cycles of Avastin in combination with investigators' choice of multiple platinum-based chemotherapy regimens. If their cancer did not progress patients were then randomised (n=743 ITT) to receive maintenance therapy with Avastin in combination with Tarceva or Avastin plus placebo, until disease progression.

- The ATLAS study met its primary endpoint with a statistically significant extension in the time patients live without their disease worsening; 39 % improvement compared to those who received maintenance therapy with Avastin alone. Median progression free survival (PFS) was 4.8 months for the combination compared to 3.7 months for Avastin maintenance therapy alone with a highly significant hazard ratio of 0.722 (p-value=0.0012).

SATURN

A global multicentre, double blind, randomised, prospective phase III study to evaluate the efficacy of Tarceva or placebo in patients with advanced, recurrent or metastatic NSCLC who had not progressed following first line platinum based chemotherapy. The study involved more than 880 patients from approximately 160 centres; 438 received Tarceva and 451 placebo.

- The study met its primary endpoint demonstrating a statistically significant extension of the time patients live without their disease worsening; there was a 41% increase compared with placebo (hazard ratio= 0.71. p-value <0.0001).

Adverse events in both the ATLAS and SATURN studies were consistent with previous Avastin or Tarceva studies, as well as with trials evaluating the two medicines together, and no new safety signals were observed.

About Avastin

Avastin is an antibody that specifically binds and blocks VEGF (vascular endothelial growth factor). VEGF is the key driver of tumour angiogenesis – an essential process of development and maintenance of blood vessels which is required for a tumour to grow and to spread (metastasize) to other parts of the body. Avastin's precise mode of action helps control tumour growth and metastases with only a limited impact on side effects of chemotherapy.

Avastin has proven survival benefits across multiple tumour types. Avastin is approved in Europe for the treatment of the advanced stages of four common types of cancer: colorectal cancer, breast cancer, lung cancer and kidney cancer. These types of cancer collectively cause nearly 3 million deaths each year. In the US, Avastin was the first anti-angiogenesis therapy approved by the FDA and is now approved for the treatment of four tumour types: breast, colorectal, glioblastoma, and non-small cell lung cancer (NSCLC)."

More than 500,000 patients have been treated with Avastin so far. A comprehensive clinical programme with more than 450 clinical trials is investigating the use of Avastin in various tumour types (including colorectal, breast, lung, brain, gastric, ovarian, prostate and other cancers) and different settings (advanced or early stage disease).

About Tarceva

Tarceva is different from conventional chemotherapies and has been shown to potently inhibit EGFR. It is the first and only EGFR oral targeted agent in second line with a proven and significant survival and symptom benefit in a broad range of patients with advanced lung cancer without the side effects associated

with chemotherapy. Tarceva has been approved in the EU since September 2005 and in the US since November 2004 for the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

Furthermore, Tarceva in combination with chemotherapy is the first treatment in over a decade to have shown a significant survival benefit in treating patients with pancreatic cancer. It is approved in the US in combination with gemcitabine for the first line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer and in the EU for treatment of metastatic pancreatic cancer. Since its initial launch three years ago, Tarceva has been used to treat more than 250,000 patients and has been approved in over 80 countries worldwide.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2008, Roche had over 80'000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The Group posted sales of 45.6 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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- Backgrounder Oncology: www.roche.com/media_backgrounder/media_oncology.htm
- Roche at ASCO: <http://www.roche.com/media/events/med-asco2009.htm>
- Videoclips, of broadcast standard: www.thenewsmarket.com

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References

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- ⁱ Miller V et al. Abstract LBA8002 presented at ASCO 2009 Annual Meeting, Orlando, US
 - ⁱⁱ Sandler A, et al. N Engl J Med. 2006;355; 2542-50.
 - ⁱⁱⁱ Sandler AB et al. J Thor Oncol 2008; 3 (1) Supplement 4, S283.
 - ^{iv} Cappuzzo F et al., Abstract 8001 presented at ASCO 2009 Annual Meeting, Orlando, US.
 - ^v Garcia M et al. Global Cancer Facts & Figures. Atlanta, GA: American Cancer Society, 2007.
 - ^{vi} Allen J et al. J Natl Compr Canc Netw 2008; 6(3): 285-93.