

Basel, 23 September 2009

From inoperable disease to potentially life saving surgery - new Avastin data gives hope to colorectal cancer patients with liver metastases

New data from several studies presented at ECCO 15¹ and ESMO 34² confirm unique benefits of Avastin (bevacizumab) and Xeloda (capecitabine) in treatment of colon cancer:

- Combination of Avastin with standard chemotherapy resulted in shrinkage or disappearance of liver metastases in 78% of patients with advanced colon cancer. A third of patients with previously inoperable liver metastasis became eligible for a potentially life saving surgery (BOXER Study).
- Elderly patients derive similar benefits from Avastin based treatment as younger patients. Age should not preclude them from treatment (First BEAT study).
- Additional data show Xeloda combined with oxaliplatin offers superior three, four and five year disease-free survival in early colon cancer (NO16968 XELOXA).

Colorectal cancer is the second most common cause of death from cancer across all tumour types in Europe and is the third most commonly reported cancer in the world.

Avastin in combination with chemotherapy led to shrinkage or disappearance (overall response rate) of liver metastases (disease that has spread to the liver) in 78% of patients with advanced colorectal cancer. As a result, one third (33%) of patients who were initially unable to undergo surgery were eligible to undergo a potentially life saving surgery. Complete surgical removal of the metastases was achieved in 56% of all Avastin-treated patients.

The multicentre **phase II BOXER study** investigated the efficacy and safety of Avastin in combination with oral Xeloda and intravenous oxaliplatin (XELOX) in patients considered unsuitable for upfront resection (surgical removal) of their liver metastases.

“The data from BOXER shows that Avastin in combination with standard chemotherapy has the ability to shrink metastatic lesions which might allow surgical removal and therefore offer a potential for cure for

patients with advanced disease,” explained Professor David Cunningham, Head of the Gastrointestinal Unit at the Royal Marsden Hospital, UK.

Data from the large, observational **First BEAT study** showed that Avastin-based treatment delivers the same benefits to all patients including those aged above 65 years who represent the majority of people with advanced colorectal cancer. This is an important finding as older patients are often under-represented in clinical trials. The study results showed that the time patients lived without their disease advancing (PFS) was similar across age groups – 10.8 months for those below 65 years, 11.2 months for those between 65 and 74 years and 10 months for those 75 years and older.

Patients taking Xeloda with oxaliplatin immediately after surgery live disease free for longer compared to those treated with commonly used chemotherapy regimen:

New results for Xeloda in early colon cancer were also presented at ECCO ESMO. The pivotal **NO16968 (XELOXA) study**, the largest-ever study of patients with stage III colon cancer, showed that the three year disease-free survival (DFS) for patients receiving XELOX was 70.9%, superior to the 5-FU/LV arm (66.5%) (HR=0.80 (95% CI: 0.69-0.93), p=0.0045). The DFS result obtained with XELOX is similar to that shown in trials evaluating the use of FOLFOX in patients with stage III colon cancer.

“We know that XELOX helps keep patients free from recurrence of their cancer longer,” said Dr Dan Haller, Professor of Medicine, University of Pennsylvania. “These results now confirm that patients have an additional option for the treatment of stage III colon cancer. In these potentially curable patients, XELOX offers the additional benefit of an oral medication, Xeloda.”

“Colorectal cancer sadly claims more than 600,000 lives each year, despite the treatment advances made in the last decade” said William M. Burns, CEO of Roche’s Pharmaceuticals. “Today’s announcements about Avastin and Xeloda are therefore very welcome news for patients and their families as they offer more options for fighting this disease and hope that some patients may even have the potential to be cured” he added.

About the BOXER trial

BOXER is a single arm phase II study that assessed response rate in 45 patients treated with Avastin plus XELOX chemotherapy who were considered unsuitable for upfront resection of liver-only metastases. Response rates were measured by RECIST criteria. Secondary objectives of BOXER included complete resection rate, safety and feasibility of the regimen, PFS and overall survival.

About the First BEAT trial

The international First BEAT phase IV trial assessed the safety and efficacy of Avastin in almost 2,000 previously untreated patients with mCRC in combination with a variety of standard chemotherapies. The most common chemotherapy regimens combined with Avastin in First BEAT were: FOLFOX, XELOX, FOLFIRI (oxaliplatin, fluorouracil and irinotecan) and Xeloda. The primary endpoint of First BEAT was safety and secondary objectives were PFS and overall survival.

About the NO16968 study

The NO16968 trial (XELOXA) is an open-label, randomised, phase III study of XELOX (oral Xeloda in combination with intravenous oxaliplatin) versus 5-fluorouracil/leucovorin (5-FU/LV) as adjuvant therapy for patients with stage III colon cancer who have undergone surgery. It studied the use of XELOX for six months. The study included 1886 patients and was conducted at 226 study sites across 29 countries. The primary endpoint of the study was to demonstrate the superiority of XELOX versus 5-FU/LV in terms of disease-free survival. Secondary endpoints included overall survival, safety profiles and perceived treatment convenience between the treatment arms.

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, non-small cell lung cancer (NSCLC) 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 five tumour types: colorectal cancer, non-small cell lung cancer, breast cancer, glioblastoma, and renal cell carcinoma.

More than 500,000 patients have been treated with Avastin so far. A comprehensive clinical programme with over 450 clinical trials is investigating the use of Avastin in various tumour types (including colorectal, breast,

non-small cell lung, brain, gastric, ovarian, prostate and others) and different settings (advanced or early stage disease).

About Xeloda (capecitabine)

Xeloda is a highly effective targeted oral chemotherapy offering patients a survival advantage when taken on its own or in combination with other anticancer drugs. Xeloda is converted to the active cancer-killing agent 5-FU (5-fluorouracil) directly inside the cancer cells, thus reducing damage to healthy cells. Xeloda tablets can be taken by patients in their own home, reducing the number of hospital visits.

Licensed and marketed by Roche in more than 100 countries worldwide, Xeloda has more than ten years of proven clinical experience providing an effective and flexible treatment option to over 1.8 million people with cancer.

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:

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¹ European CanCer Organisation

² European Society for Medical Oncology