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Avastin could play an important role in improving the daily lives of patients with the most aggressive form of brain cancer

Analysis of BRAIN study shows that patients may have a stabilisation or improvement in neurocognitive function and a reduction in steroid use.

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that an analysis of the phase II BRAIN study of Avastin (bevacizumab) alone or in combination with irinotecan chemotherapy for the treatment of relapsed or progressive glioblastoma (GBM) demonstrated that in addition to increasing the chance of patients being alive without worsening of their disease at six months (progression free survival; PFS-6*)¹, Avastin-based therapy may also lead to additional positive impact on patients' daily lives². Adverse events in the BRAIN study were consistent with those previously seen with Avastin and no new safety signals were reported.

The analysis presented today at Europe's largest scientific meeting for cancer specialists, the joint 15th ECCO and 34th ESMO, showed that those patients who responded to Avastin-based therapy may also have a stabilisation or improvement in neurocognitive function and a reduction in their dose of steroids².

"Stabilising neurocognitive function and reducing reliance on steroids can improve day to day life for patients with recurrent GBM which, given the poor prognosis, is a key aim of treatment," said Professor James Vredenburgh, Medical Director, Adult Clinical Service, Duke University Medical Center, Durham, USA. "This analysis suggests that Avastin-based therapy which has already demonstrated PFS benefits may also have a positive impact on patients' daily lives and should offer hope to physicians, patients and their caregivers alike."

Neurocognitive function includes the ability to think and reason, to make judgements and remember things. A decline in this function, a common consequence of GBM, can be distressing for both patients and their families. Avastin based treatment was also associated with lower use of steroids in some patients. Steroids are

* In the BRAIN Study, PFS-6 was defined as the percentage of patients who remained alive and progression free at 24 weeks

an important part of managing symptoms in many patients with GBM but they can lead to complications such as weight gain, insomnia and behavioural changes. Reduction in steroid dose means that physicians may be able to reduce the side effects of long term steroid use.

GBM is the most common and the most aggressive type of primary malignant brain tumour and most patients experience relapse or progression of their disease following initial treatment^{3,4}. When the disease returns, prognosis is particularly poor and improving day to day life for patients is a component of the treatment aim.

“Avastin continues to demonstrate its benefits as a treatment for an increasing variety of cancers,” said William M. Burns, CEO of Roche’s Pharmaceuticals Division. “Avastin based therapy has the potential to make a real difference for patients with glioblastoma.”

Avastin precisely inhibits vascular endothelial growth factor (VEGF) a key mediator of angiogenesis, the growth of new blood vessels, which is essential for tumour growth and spread. GBM has very high VEGF expression. By controlling angiogenesis, Avastin controls tumour growth.

In May 2009, Avastin was granted accelerated approval for the treatment of GBM patients with progressive disease following prior therapy from the US Food and Drug Administration (FDA) based on data from the BRAIN study (AVF3708g) which was recently published in the Journal of Clinical Oncology¹ and an NCI study (NCI 06-C-0064E). The data is currently being discussed with regulators in Europe and has led to approvals in Switzerland, Albania, Dominican Republic, India, Moldova and the Ukraine.

A large, over 900 patient phase III study of Avastin, for the treatment of newly diagnosed GBM patients (AVAGLIO) is underway.⁵

About the BRAIN study

The BRAIN study was a US based open-label, multicentre, non-comparative phase II study including 167 patients with histologically confirmed GBM that had progressed following initial treatment with temozolomide and radiation. The primary endpoints of the BRAIN trial were progression free survival-6 (PFS-6), (defined as the percentage of patients who remained alive and progression free at 24 weeks) and objective response rate (ORR), (defined as a complete or partial response on two consecutive MRIs obtained 4 weeks apart). Secondary endpoints explored included OS, PFS, duration of response to treatment and safety. The BRAIN study evaluated Avastin at a dose of 10mg/kg every two weeks, as a single agent (BEV), or

in combination with irinotecan chemotherapy (BEV-IRI).

This latest analysis of the BRAIN study demonstrated that²:

Steroid use

Of the patients not requiring corticosteroids at baseline, more than 75% Avastin and 65% Avastin plus chemotherapy patients did not use corticosteroids post-baseline.

- The majority of patients with an objective response or who were alive and without progression at 24 weeks had sustained reduction in steroid dose when receiving Avastin based therapy.
 - At baseline, over half of the patients (50.6% BEV and 52.4% BEV-IRI pts) took systemic corticosteroids. Of these patients receiving steroids at baseline:
 - In patients that responded (complete or partial) to Avastin-based therapy, 57% and 64% of patients receiving Avastin and Avastin + chemotherapy, respectively had a sustained reduction in steroid use (defined as able to at least halve their steroid dose for at least half the time they were on treatment)
 - In patients who were alive and without progression of disease at 24 weeks 58% and 86% demonstrated a sustained reduction in steroid dose (defined as being able to at least halve steroid dose for at least half the time on treatment) when receiving Avastin or Avastin + chemotherapy, respectively.

Neurocognitive function

The majority of patients with an objective response or alive and without progression at 24 weeks^{**} had improved or stable neurocognitive function compared to baseline.

- Of the patients with an objective response, 75% and 60.7% of patients receiving Avastin and Avastin + chemotherapy, respectively experienced stable or improved neurocognitive function at time of their response relative to baseline
- Of the patients with PFS greater than 6 months, 70.4% and 70% had stable or improved neurocognitive function at week 24 relative to baseline, when receiving Avastin or Avastin + chemotherapy, respectively.

^{**} Objective Response rate (Avastin 28.2%, Avastin plus chemotherapy 37.8%) and 6m-PFS (Avastin 42.6%, Avastin plus chemotherapy 50.3%).

The BRAIN study previously demonstrated¹:

- When Avastin was evaluated as a single agent, the study showed that at six months almost half (42.6%) of patients lived without their disease advancing, as defined by progression-free survival (PFS). When Avastin was combined with irinotecan, this figure increased to 50.3%.
- In the study, nearly a third (28%) of patients responded to Avastin as a single agent, meaning tumours decreased in size by at least 50%. When Avastin was combined with irinotecan, 38% of patients responded to Avastin.
- Patients receiving Avastin alone had a median overall survival of 9.2 months compared to 8.7 months for those receiving Avastin in combination with irinotecan, which was a secondary endpoint in the study. Most adverse events related to Avastin in this trial appeared to be similar to those previously reported in other Avastin studies¹.

About Glioblastoma

Glioma (cancer of the glial cells) is the most common type of malignant primary brain tumour (a tumour that originates in the brain), accounting for approximately one third of all cases diagnosed³. Glioblastoma (or glioblastoma multiforme; GBM) is the most common and the most aggressive type of glioma³. The prognosis for patients with GBM is poor, and generally depends on the success of surgery to remove the tumour.

Glioblastoma affects approximately 13,000 people per year in the EU³. Following initial treatment, glioblastoma tumours nearly always return and currently, there are limited treatment options for patients when these relapses occur⁴. According to historical estimates, less than 10 percent of patients with recurrent GBM respond to treatment and approximately 15 percent will live six months without their disease getting worse^{1,5}. GBM is a compelling therapeutic target for Avastin as these tumours have among the highest levels of vascular endothelial growth factor (VEGF) of any solid tumour.

About Avastin

Avastin is an antibody that specifically binds and blocks the biological effects of VEGF (vascular endothelial growth factor). VEGF is a key driver of tumour angiogenesis – an essential process required for a tumour to grow and to spread (metastasize) to other parts of the body. Avastin's precise mode of action allows it to be combined effectively with a broad range of chemotherapies and other anti-cancer treatments. Avastin helps to control tumour growth and extend survival with only a limited impact on the side effects of chemotherapy.

Avastin has proven survival benefits across several types of cancer. It 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 over 2.5 million deaths each year^{6,7,8}. In the US, Avastin was the first anti-angiogenesis therapy approved by the FDA and it is now approved for the treatment of five tumour types: colorectal cancer, non-small cell lung cancer, breast cancer, brain (glioblastoma) and kidney (renal cell carcinoma).

Over half a million 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 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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