FDA approves Roche’s Avastin (bevacizumab) plus chemotherapy as a treatment for women with advanced ovarian cancer following initial surgery

Avastin is now approved for ten distinct uses across six different types of cancer in the United States

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved Avastin® (bevacizumab) in combination with chemotherapy (carboplatin and paclitaxel), followed by Avastin as a single agent, for the treatment of women with advanced (stage III or IV) ovarian cancer following initial surgical resection.¹

“Today’s approval is an important advance for women newly diagnosed with this type of ovarian cancer,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We’re committed to advancing medicines in areas of unmet need and this FDA approval of Avastin plus chemotherapy gives women with advanced ovarian cancer a new treatment option that has been shown to significantly delay disease progression or death.”

The approval for Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for the treatment of women with stage III or stage IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection, is based on data from the pivotal phase III GOG-0218 trial. Women who received Avastin in combination with chemotherapy, and continued use of Avastin alone, had a median progression-free survival (PFS) of 18.2 months compared to 12.0 months in women who received chemotherapy alone (HR=0.62; 95% CI 0.52 - 0.75, p<0.0001). This PFS benefit was achieved with a fixed-duration treatment (up to 22 cycles of Avastin total).¹

Avastin is now approved for ten distinct uses across six different types of cancer in the United States. This indication represents Avastin’s fourth gynaecologic oncology indication in four years, including advanced cervical cancer and two different forms of ovarian cancer that recurred after platinum-based chemotherapy.
### About the GOG-0218 Study

GOG-0218 (NCT00262847) is a multi-centre, randomised, double-blind, placebo-controlled, phase III study in 1,873 women with previously untreated stage III or IV epithelial ovarian, primary peritoneal, or fallopian tube carcinoma who already had surgery to remove as much of the tumour as possible. Participants were randomised into one of three treatment arms: chemotherapy alone (carboplatin and paclitaxel), Avastin (15 mg/kg) plus chemotherapy followed by placebo alone, or Avastin plus chemotherapy followed by Avastin alone for a total of up to 22 cycles. The primary endpoint of the study was investigator-assessed PFS and secondary endpoints included overall survival (OS). The study was conducted by the Gynecologic Oncology Group (GOG) and initial results were previously published in the New England Journal of Medicine.²

### GOG-0218 Study Results¹

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Avastin with chemotherapy followed by Avastin alone (N=623)</th>
<th>Avastin with chemotherapy (N= 625)</th>
<th>Chemotherapy alone (N= 625)</th>
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<tbody>
<tr>
<td><strong>Progression-free survival (PFS, primary endpoint)</strong></td>
<td></td>
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<tr>
<td>Median PFS (months)</td>
<td>18.2</td>
<td>12.8</td>
<td>12.0</td>
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<tr>
<td>Hazard ratio (95% CI)²</td>
<td>0.62 (0.52, 0.75)</td>
<td>0.83 (0.70, 0.98)</td>
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<tr>
<td>p-value²</td>
<td>&lt; 0.0001</td>
<td>Not significant</td>
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<tr>
<td>**Overall survival (OS, secondary endpoint)**³</td>
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<tr>
<td>Median OS (months)</td>
<td>43.8</td>
<td>38.8</td>
<td>40.6</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)²</td>
<td>0.89 (0.76, 1.05)</td>
<td>1.06 (0.90, 1.24)</td>
<td></td>
</tr>
</tbody>
</table>

### Safety

Grade 3-4 adverse events occurring more often (≥2%) in the Avastin with chemotherapy followed by Avastin alone arm or the Avastin with chemotherapy arm versus the chemotherapy alone arm were fatigue (9%, 6%, 6%, respectively), high blood pressure (10%, 6%, 2%), decreased platelet count (21%, 20%, 15%) and decreased white blood cell count (51%, 53%, 50%).

¹Relative to the control arm; stratified hazard ratio
²Two-sided p-value based on re-randomisation test
³Final overall survival analysis
About Ovarian Cancer

Ovarian cancer causes more deaths among women than any other gynaecologic cancer in the United States. In 2018, more than 22,000 women will be diagnosed with ovarian cancer in the US and about 14,000 will die from the disease. About 80% of ovarian cancer cases are found at an advanced stage, when the cancer has spread beyond the ovaries. Early ovarian cancer often does not have any symptoms and when symptoms, such as abdominal swelling, bloating, abdominal pain, difficulty eating or feeling full quickly and/or frequent urination, are present, they can be associated by other less serious conditions. Five-year survival rates worsen dramatically based on stage of diagnosis.3

About Avastin

With the initial approval in the United States for advanced colorectal cancer in 2004, Avastin became the first anti-angiogenic therapy made widely available for the treatment of patients with an advanced cancer. Today, Avastin is continuing to transform cancer care through its proven survival benefit (overall survival and/or progression free survival) across several types of cancer. Avastin is approved in Europe for the treatment of advanced stages of breast cancer, colorectal cancer, non-small cell lung cancer, kidney cancer, ovarian cancer and cervical cancer, and is available in the United States for the treatment of colorectal cancer, non-small cell lung cancer, kidney cancer, cervical cancer, recurrent, platinum-resistant and platinum-sensitive ovarian cancer, and recurrent glioblastoma. In addition, Avastin is approved in over 70 other countries worldwide for the treatment of patients with progressive glioblastoma following prior therapy. Avastin is approved in Japan for the treatment of the advanced stages of colorectal cancer, non-small cell lung cancer, cervical cancer, breast cancer, ovarian cancer and malignant glioma, including newly diagnosed glioblastoma.

Avastin has made anti-angiogenic therapy a fundamental pillar of cancer treatment today. Over 2.7 million patients have been treated with Avastin so far. A comprehensive clinical programme has investigated Avastin in over 50 tumour types.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people’s lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare - a strategy that aims to fit the right treatment to each patient in the best way possible.
Roche is the world’s largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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References
1) GOG-0218 Filing Package (Roche data on file).