Avastin® in ovarian cancer: Summary of clinical data

Ovarian cancer is the sixth most commonly diagnosed cancer in women and the eighth leading cause of cancer death among women worldwide. Annually, an estimated 230,000 women will be diagnosed with ovarian cancer around the world and approximately 140,000 will die from the disease[1]. The vast majority of cases of ovarian cancer are diagnosed after the cancer has spread beyond the primary site to other parts of the body (metastasised)[2].

Avastin (bevacizumab) could potentially be an important new therapy for ovarian cancer - phase II studies have demonstrated Avastin's activity in this disease[3,4] and highlighted an association between high levels of VEGF (vascular endothelial growth factor) and poor survival in women with ovarian cancer[5]. Furthermore, VEGF appears to be an important mediator of ascites formation[6,7,8] (cancer-related accumulation of fluid in the abdomen) which can cause symptoms for ovarian cancer patients.

Avastin is an antibody that specifically binds and blocks VEGF. 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 to other parts of the body[9,10]. Avastin's precise mode of action helps control tumour growth and metastases with only a limited impact on side effects of chemotherapy[11,12].

Today, Avastin is transforming cancer care through its proven survival benefit (overall survival and / or progression free survival) across several types of cancer[12-17], making anti-angiogenic therapy a fundamental pillar of cancer treatment. Over half a million patients have been treated with Avastin so far[18].

A comprehensive clinical program with more than 500 clinical trials is investigating the use of Avastin in over 50 tumour types (including colorectal, breast, non small cell lung, brain, gastric, ovarian and others) and different settings (advanced or early stage disease)[19]. Roche has developed an extensive research and clinical trial programme in order to improve treatment outcomes for patients with ovarian cancer both in the front-line setting (in newly diagnosed patients following surgery) and in the second-line setting (when the cancer has returned after initial therapy).

Outlined overleaf is key information from clinical trials of Avastin in ovarian cancer.

Avastin in front-line ovarian cancer

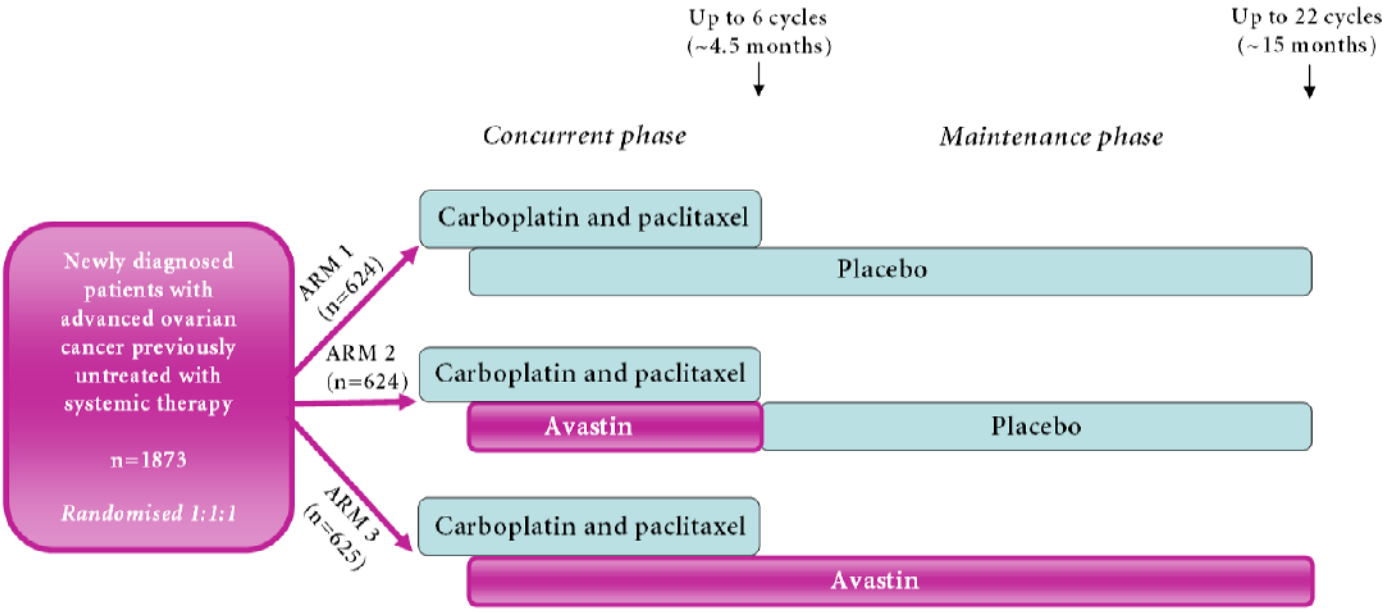
GOG 0218

The GOG 0218 trial was an international, double-blind, placebo-controlled study conducted by a network of researchers led by the Gynecologic Oncology Group (GOG) that enrolled more than 1,800 patients with previously untreated advanced ovarian cancer who already had surgery to remove as much of the tumour as possible. Patients were randomised to one of three treatment arms:

Key findings

- Women who continued Avastin alone, after receiving Avastin in combination with chemotherapy lived longer without the disease worsening compared to those who received chemotherapy alone.
- Full data to be presented at ASCO 2010.

- Arm 1: Placebo in combination with paclitaxel and carboplatin chemotherapy followed by placebo alone for a total of up to 15 months of therapy.
- Arm 2: Avastin in combination with paclitaxel and carboplatin chemotherapy followed by placebo alone for a total of up to 15 months of therapy.
- Arm 3: Avastin in combination with paclitaxel and carboplatin chemotherapy followed by the continuation of Avastin alone for a total of up to 15 months of Avastin-based therapy.



Avastin: 15mg/kg every 3 weeks
carboplatin: AUC6
paclitaxel: 175 mg/m² every 3 weeks

Women who continued Avastin alone, after receiving Avastin in combination with chemotherapy, (Arm 3) lived longer without the disease worsening (progression-free survival, or PFS) compared to those who received chemotherapy alone. The study also investigated Avastin in combination with chemotherapy but without the continuation of Avastin alone. Women who received this shorter

duration of Avastin did not have a statistically significant increase in PFS compared with chemotherapy alone.

A preliminary assessment of safety noted adverse events previously observed in pivotal trials of Avastin.

Full study results of this significant trial will be presented at the American Society of Clinical Oncology (ASCO) 2010 Annual Meeting at the plenary session on Sunday 6 June, 13.45pm CST by Dr. Robert Burger, M.D., Fox-Chase Cancer Center in Philadelphia and lead investigator of the study (Abstract LBA001).

ICON-7

The ICON-7 study is an international open-label study investigating the efficacy of Avastin as front-line treatment in combination with commonly-used chemotherapy (carboplatin and paclitaxel) in approximately 1,500 women with advanced ovarian cancer. The aim of the study is to demonstrate that Avastin in combination with chemotherapy improves the time patients live without the disease worsening compared to chemotherapy alone. The ICON-7 study differs from the GOG 0218 study in terms of patient population (includes patients with earlier stage disease) and the dosing and duration of Avastin therapy (Avastin used at a dose of 7.5mg/kg for a maximum treatment duration of 12 months).

GOG 0252

GOG 0252 is a US based, multicentre study that investigates Avastin in combination with carboplatin and paclitaxel chemotherapy and is comparing two ways of administering chemotherapy - intravenous versus intraperitoneal* and whether this makes a difference to the time that patients with advanced ovarian cancer previously untreated with systemic therapy live compared to chemotherapy alone. An estimated 1,200 patients will be enrolled in the study.

Second line trials

The time between receiving the last dose of platinum-based chemotherapy and disease recurrence determines the choice of chemotherapy used second-line. Patients are said to have 'platinum-sensitive' disease if disease recurrence occurred more than 6 months after completing their initial platinum-based chemotherapy, and 'platinum-resistant' disease if recurrence occurred within 6 months. Avastin is being investigated as a second-line therapy in combination with both non-platinum- and platinum-based chemotherapies.

Avastin in platinum sensitive ovarian cancer

OCEANS

OCEANS is a US based, multicentre trial of approximately 480 patients with platinum sensitive ovarian cancer who will receive Avastin or placebo, in combination with gemcitabine and carboplatin

chemotherapy followed by continued use of Avastin as maintenance therapy or placebo alone until progression of disease. The aim of the study is to demonstrate that Avastin based therapy can extend the time that patients with platinum sensitive ovarian cancer live without their disease getting worse, compared to chemotherapy alone.

GOG 0213

GOG 0213 is an international trial involving nearly 700 patients with platinum sensitive ovarian cancer. Initially, patients are assessed to determine whether they are candidates for surgical resection of their tumours and if appropriate, patients will undergo surgery. All patients will then receive treatment with carboplatin and paclitaxel chemotherapy in combination with Avastin followed by continued use of Avastin alone as maintenance therapy, or chemotherapy alone as second line treatment for their disease. The main objective of the study is to demonstrate that Avastin based therapy can prolong survival (also known as overall survival, OS) of patients with platinum sensitive ovarian cancer. Additionally, participants enrolled in this trial can have received Avastin as part of their front line treatment for their ovarian cancer.

Avastin in platinum resistant ovarian cancer

AURELIA

AURELIA is an international trial investigating the efficacy and safety of Avastin in combination with a range of chemotherapies (including paclitaxel, topotecan and liposomal doxorubicin) in over 300 patients with platinum resistant ovarian cancer. The aim of AURELIA is to demonstrate that Avastin based therapy can improve the time that patients live without their disease getting worse compared to chemotherapy alone.

Summary

GOG218 is the first positive phase III study of an anti-angiogenic therapy in advanced ovarian cancer and continues to support Avastin and anti-angiogenesis as a fundamental pillar of cancer treatment today. Currently, advanced ovarian cancer is a disease with a poor prognosis and patients are in great need of new effective therapies. Avastin has shown potential to become a new treatment option for physicians, and offers hope to patients and their families.

* Intraperitoneal chemotherapy refers to chemotherapy that is administered directly into the abdomen, so that more chemotherapy may reach the tumour than would do via the bloodstream.

End

To download images and videos relating to Avastin please visit: www.thenewsmarket.com

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