Study shows potential of anti-growth factor drugs for reducing complication of advanced ovarian cancer

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Blocking the action of vascular endothelial growth factor (VEGF) with the new anti-VEGF drug aflibercept can curb the development of malignant ascites (excessive fluid in the abdomen), a common and painful complication of advanced ovarian cancer, according to a new phase 2 randomised study published Online First in the *Lancet Oncology*.

"Anti-VEGF treatments such as aflibercept appear to reduce the formation of malignant ascites and could dramatically improve the quality of life for patients with this debilitating complication. But clinicians must exercise caution in their use of aflibercept because of the significantly increased risk of fatal bowel perforation", explains lead author Walter Gotlieb from Jewish General Hospital, McGill University, Montreal, Canada.

Two-thirds of ovarian cancer patients are diagnosed with late-stage disease, which is commonly associated with the abnormal build-up in the abdomen of fluid that contains cancer cells (malignant ascites). The cancer cells produce VEGF, which increases the permeability of capillaries, increasing the flow of fluids into the abdomen, and forming ascites. The usual treatment, paracentesis (using a needle to remove excess fluid from the abdomen), can provide temporary relief but is invasive and unpleasant for patients.

Aflibercept is a potent inhibitor of both VEGF and placental growth factor, and preclinical studies and a pilot study indicate that the drug might be effective in suppressing the development of malignant ascites.

Here, the researchers report the results of a phase 2 randomised study designed to investigate whether aflibercept might delay the time until paracentesis is needed and to examine the safety of VEGF inhibition in patients with advanced ovarian cancer and recurrent malignant ascites.

The study included 55 patients from six countries who had received at least two prior chemotherapy regimens and whose tumours had become chemoresistant. Participants were randomly assigned to intravenous aflibercept (29 patients) or placebo (26).

Patients treated with aflibercept more than doubled their time to repeat paracentesis compared with those given placebo (55 days vs 23 days).

Additionally, two patients receiving aflibercept did not require a repeat paracentesis during the 6 months of treatment. Patients in the aflibercept group also reported a greater improvement in symptoms of ascites than those in the placebo group.

The most common treatment related adverse events were dyspnoea (six [20%] aflibercept vs two [8%] placebo], fatigue or asthenia (four [13%] vs 11 [44%]), and dehydration (three [10%] vs three [12%]).

Three deaths from bowel perforations were recorded in the aflibercept group and one intestinal fistula leading to sepsis and death in the placebo group.

The authors say: "The trial clearly shows the effectiveness of VEGF blockade in the reduction of ascites formation…but confirms the significant clinical risk of fatal bowel perforation in this population of patients with very advanced cancer."

They conclude: "VEGF blockade should be used with caution in advanced ovarian cancer with

abdominal carcinomatosis, and the benefit-risk balance should be thoroughly discussed for each patient."

In an accompanying Comment, Dr Gerhild Becker and H E Blum from University Hospital Freiburg, Freiburg, Germany say: "Careful patient selection could reduce the incidence of gastrointestinal perforations. However, before a general recommendation of aflibercept for the treatment of malignant ascites can be made, further studies, including comparative effectiveness research, are needed to compare the effectiveness of the different therapeutic strategies in daily clinical practice."

More information: Paper online: www.thelancet.com/journals/lan … (11)70338-2/abstract

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