Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N. Engl. J. Med. 354, 34-43 (2006); McGuire,W.P. et al. *Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer.* N. Engl. J. Med. 334, 1-6 (1996); Muggia,F.M. et al. *Phase III randomized study of cisplatin versus paclitaxel versus cisplatin and paclitaxel in patients with suboptimal stage III or IV ovarian cancer: a gynecologic oncology group study.* J. Clin. Oncol. 18, 106-115 (2000); Piccart,M.J. et al. *Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: three-year results.* J. Natl. Cancer Inst. 92, 699-708 (2000)).

The majority of patients who achieve a CR with first-line chemotherapy ultimately develop recurrent disease. These patients can be subdivided into platinum-sensitive or platinum-resistant groups.12 In platinum-sensitive patients, disease recurrence occurs more than 6 months after cessation of initial platinum-containing chemotherapy.12 Platinum-based therapies are typically used to retreat these patients, in light of clinically meaningful responses observed in these patients following a second platinum-based treatment. 13 Currently, there is no optimal treatment strategy for platinum-resistant patients whose disease recurs within 6 months of completing initial platinum-based chemotherapy.12,14 Despite a wide range of available treatments, prolonged survival has not been shown in this setting, and ORR is generally less than 20%.12,15 As resistant-disease is not curable, the goals of treatment for these patients include palliation of symptoms, prolonged survival and improvements in quality of life.13,15,16

Platinum-resistance is therefore a significant clinical problem for which improved treatment regimens are needed. In particular, bevacizumab (Avastin®), a monoclonal antibody targeted against the pro-angiogenic vascular endothelial growth factor (VEGF), holds significant therapeutic potential.

SUMMARY

The present disclosure contemplates a method of treating a patient diagnosed with a platinum-resistant ovarian cancer comprising administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said treatment prolongs said patient's median progression-free survival time as compared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone. According to a first aspect, there is provided use of an anti-VEGF antibody in the manufacture of a medicament for the treatment of a patient diagnosed with a platinum-resistant epithelial ovarian cancer (EOC), fallopian tube carcinoma (FTC), or primary peritoneal carcinoma (PPC), wherein an effective amount of said anti-VEGF antibody and a chemotherapeutic is to be administered to said patient, wherein said patient received two or fewer

prior anti-cancer regimens, wherein said chemotherapeutic is paclitaxel, wherein said anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1, and wherein said treatment prolongs said patient's median progression-free survival time as compared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone~~an anti-VEGF antibody for use in a method of treating a patient diagnosed with a platinum-resistant ovarian cancer, wherein the method comprising administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said chemotherapeutic is selected from the group consisting of paclitaxel, topotecan or a pegylated liposomal doxorubicin (PLD), wherein said treatment prolongs said patient's median progression-free survival time as compared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone~~. In one embodiment, the platinum-resistant ovarian cancer is an epithelial ovarian cancer (EOC), a fallopian tube carcinoma (FTC), or a primary peritoneal carcinoma (PPC). In another embodiment, the patient is not refractory to previous platinum

We claim:

1. Use of ~~An~~ an anti-VEGF antibody in the manufacture of a medicament for the treatment of ~~for use in a method of treating~~ a patient diagnosed with a platinum-resistant ~~ovarian cancer~~ epithelial ovarian cancer (EOC), fallopian tube carcinoma (FTC), or primary peritoneal carcinoma (PPC), wherein ~~the method comprising administering to said patient~~ an effective amount of ~~an~~ said anti-VEGF antibody and a chemotherapeutic is to be administered to said patient, wherein said patient received two or fewer prior anti-cancer regimens, wherein said chemotherapeutic is ~~selected from the group consisting of~~ paclitaxel~~, topotecan or a pegylated liposomal doxorubicin (PLD)~~, wherein said anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1, and wherein said treatment prolongs said patient's median progression-free survival time as compared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone.

~~2. The anti-VEGF antibody of claim 1, wherein said platinum-resistant ovarian cancer is an epithelial ovarian cancer (EOC), a fallopian tube carcinoma (FTC), or a primary peritoneal carcinoma (PPC).~~

~~3.~~2. The use ~~anti-VEGF antibody~~ of claim 1, wherein said patient is not refractory to previous platinum treatment.

~~4.~~3. The use ~~anti-VEGF antibody~~ of claim 1, wherein said patient has measurable disease according to RECIST 1.0 or CA-125 assessable disease according to the GCIG criteria.

~~5.~~4. The use ~~anti-VEGF antibody~~ of claim 1, wherein said patient has an ECOG performance status of 0-2 and a life expectancy of at least 12 weeks.

~~6.~~5. The use ~~anti-VEGF antibody~~ of claim 1, wherein said effective amount of said paclitaxel is to be administered at 80 mg/m2 as a 1 hour intravenous infusion on days 1, 8, 15 and 22 ~~q4w~~every four weeks.

~~7. The anti-VEGF antibody of claim 1, wherein said effective amount of said topotecan is administered at 4 mg/m2 as a 30 minute intravenous infusion on days 1, 8 and 15 q4w or at 1.25 mg/m2 as a 30 minute intravenous infusion on days 1 to 5 every three weeks.~~

~~8. The anti-VEGF antibody of claim 1, wherein said effective amount of said PLD is administered at 40 mg/m2 as a 1 mg/min intravenous infusion on day 1 only, then as a 1 hour infusion thereafter, q4w.~~

~~9.~~6. The use ~~anti-VEGF antibody~~ of claim 1, wherein said anti-VEGF antibody binds the A4.6.1 epitope.

~~10.~~7. The use ~~anti-VEGF antibody~~ of claim 1, wherein said anti-VEGF antibody is bevacizumab.

~~11. The anti-VEGF antibody of claim 1, wherein said anti-VEGF antibody comprises a variable heavy chain (VH) and a variable light chain (VL), wherein said VH has an amino acid sequence of SEQ ID NO:2 and said VL has an amino acid sequence of SEQ ID NO:1.~~

~~12.~~8. The use ~~anti-VEGF antibody~~ of claim 1, wherein said effective amount of said anti-VEGF antibody is 10 mg/kg intravenously every two weeks or 15 mg/kg intravenously every three weeks.

~~13.~~9. The use ~~anti-VEGF antibody~~ of claim ~~12~~8, wherein said effective amount of said anti-VEGF antibody is to be administered initially intravenously over 90 minutes, with subsequent infusions over 60 minutes and then 30 minutes.

~~14.~~10. The use ~~anti-VEGF antibody~~ of claim 1, wherein said patient has a platinum free interval (PFI) of less than 3 months.

~~15.~~11. The use ~~anti-VEGF antibody~~ of claim 1, wherein said patient has abdominal ascites.

~~16.~~12. The use ~~anti-VEGF antibody~~ of claim 1, wherein said treatment further improves said patient's objective response rate (ORR) as compared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone.