INTERVIEW

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Tracks 1-13

Track 1 **Case discussion:** A 54-year-old Ashkenazi Jew with a family history of breast cancer and OC undergoes complete resection of Stage III OC followed by IP chemotherapy and IV bevacizumab on a Phase III GOG trial

Track 2 Epidemiology of histopathologic subtypes of OC and correlation with staging

Track 3 Postoperative treatment options after optimal debulking for Stage III OC

Track 4 BRCA testing in OC with family history of breast cancer/OC

Track 5 Activity of PARP inhibitors in high-grade serous OC with or without BRCA mutation

Track 6 GOG-0252: First-line bevacizumab with IV chemotherapy including weekly paclitaxel versus IP chemotherapy for Stages II, III and IV OC

Track 7 Safety and efficacy of bevacizumab in the initial management of OC

Track 8 Approach to minimizing complications associated with IP chemotherapy in OC

Track 9 Activity of bevacizumab monotherapy in relapsed/refractory OC

Track 10 Role of CA125 and ultrasound for OC risk assessment screening

Track 11 Liposomal doxorubicin with trabectedin for platinum-sensitive, recurrent OC

Track 12 Nonplatinum doublets for platinum-sensitive, recurrent OC

Track 13 GOG-262: A Phase III trial of three-weekly paclitaxel versus dose-dense weekly paclitaxel in combination with carboplatin with or without bevacizumab for OC with bulky residual disease after surgery

Select Excerpts from the Interview

Track 5

DR LOVE: What are your thoughts on PARP inhibitors in ovarian cancer?

DR MONK: From my perspective, PARP inhibition is a breakthrough in targeted therapy for ovarian cancer (Audeh 2010; [2.1]).

Data have recently been presented providing evidence that PARP inhibitors have activity not only in patients with BRCA mutations but also in patients who are BRCA germline normal (Gelmon 2010). It is interesting that the phenotype of high-grade serous tumors, without germline BRCA mutations, correlates with considerable BRCA dysfunction. In fact, the level of BRCA dysfunction may be greater in the high-grade serous ovarian cancer setting than in the triple-negative breast cancer phenotype.

2.1

Efficacy and Safety of Olaparib in Chemotherapy-Refractory Ovarian Cancer with BRCA1/BRCA2 Germline Mutation

RECIST response rate[1]	Clinical benefit rate[1,2]	Grade 3/4 nausea[1]	Grade 3/4 fatigue[1]
33%	52%	6%	3%

[1] Response rates, benefit rates and toxicities are with olaparib 400 mg PO BID (n = 33);
[2] Clinical benefit rate: RECIST response of complete response, partial response or stable disease for ≥8 weeks

Audeh MW et al. *Lancet* 2010;376(9737):245-51.

Tracks 7, 9

DR LOVE: What are your thoughts about the results of the GOG-0218 study of bevacizumab?

DR MONK: It has been almost six years since I began using bevacizumab for patients with recurrent ovarian cancer. I believe that anti-angiogenic therapy is effective in ovarian cancer and is the first real breakthrough of targeted agents in this cancer type. GOG-0218 is a positive trial, and I recommend up-front incorporation of bevacizumab to my patients and have seen this agent work in this setting.

DR LOVE: What are your thoughts on bevacizumab toxicity, particularly in patients with GI resections?

DR MONK: The incidence of bowel resection is decreasing overall in ovarian cancer. It probably occurs in 10 to 15 percent of patients. I am fine with using bevacizumab for patients who have undergone GI resections, as we have a lot of data on the safety of bevacizumab after bowel resection in colon cancer. A paper on this issue will be published from the GOG-0218 trial data also.

I always counsel my patients that proteinuria and hypertension are common and almost always occur with bevacizumab. However, they are not life threatening. The GOG-0218 study confirmed that the rates of potentially life-threatening complications such as thromboembolism are not very high (Burger 2010; [2.2]).

DR LOVE: What has been your experience using bevacizumab in later lines of treatment for ovarian cancer?

DR MONK: Bevacizumab provides a durable tumor control rate for patients with relapsed ovarian cancer. In the GOG Phase II trial, approximately 40 percent of patients remained progression free for six months, with an objective response rate of approximately 20 percent.

This is a major breakthrough because only four other drugs have shown response rates in this range as single agents in platinum-resistant ovarian cancer: docetaxel, paclitaxel, pemetrexed and nanoparticle albumin-bound (*nab*) paclitaxel. ■

2.2

GOG-0218 Study: Select Adverse Events

Adverse event	Arm I CP (n = 601)	Arm II CP + bev (n = 607)	Arm III CP + bev → bev (n = 608)
GI events (Grade ≥2)*	1.2%	2.8%	2.6%
Hypertension (Grade ≥2)	7.2%	16.5%	22.9%
Proteinuria (Grade ≥3)	0.7%	0.7%	1.6%
Venous thromboembolism	5.8%	5.3%	6.7%
Arterial thromboembolism	0.8%	0.7%	0.7%
CNS bleeding	0%	0%	0.3%
Non-CNS bleeding (Grade ≥3)	0.8%	1.3%	2.1%

* GI events include perforation, fistula, necrosis and leak.
CP = carboplatin/paclitaxel; bev = bevacizumab

Burger RA et al. *Proc ASCO* 2010;**Abstract LBA1**.

SELECT PUBLICATIONS

Abaid LN et al. **Bevacizumab, paclitaxel and carboplatin for advanced ovarian cancer: Low risk of gastrointestinal and cardiovascular toxicity.** *Eur J Gynaecol Oncol* 2010;31(3):308-11.

Audeh MW et al. **Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and recurrent ovarian cancer: A proof-of-concept trial.** *Lancet* 2010;376(9737):245-51.

Burger RA et al. **Phase III trial of bevacizumab (BEV) in the primary treatment of advanced epithelial ovarian cancer (EOC), primary peritoneal cancer (PPC), or fallopian tube cancer (FTC): A Gynecologic Oncology Group study.** *Proc ASCO* 2010;**Abstract LBA1**.

Fong PC et al. **Poly(ADP)-ribose polymerase inhibition: Frequent durable responses in BRCA carrier ovarian cancer correlating with platinum-free interval.** *J Clin Oncol* 2010;28(15):2512-9.

Penson RT et al. **Phase II study of carboplatin, paclitaxel, and bevacizumab with maintenance bevacizumab as first-line chemotherapy for advanced mullerian tumors.** *J Clin Oncol* 2010;28(1):154-9.

Randall LM, Monk BJ. **Bevacizumab toxicities and their management in ovarian cancer.** *Gynecol Oncol* 2010;117(3):497-504.

Richardson DL et al. **Which factors predict bowel complications in patients with recurrent epithelial ovarian cancer being treated with bevacizumab?** *Gynecol Oncol* 2010;118(1):47-51.