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## INTERVIEW

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“My overall impression from the ovarian cancer sessions at ASCO in 2012 is that we continue to advance our understanding of the malignancy and continue to make small but clinically relevant and meaningful advances.”

# American Society of Clinical Oncology 2012 annual meeting: new optimism for fighting platinum-resistant ovarian cancer

**Maurie Markman\***

**Maurie Markman speaks to Alice O’Hare, Commissioning Editor, about the 2012 annual meeting of the American Society of Clinical Oncology (ASCO) held in Chicago (IL, USA) on 1–5 June 2012.**

Maurie Markman is Senior Vice President for Clinical Affairs and National Director for Medical Oncology, for the Cancer Treatment Centers of America. For more than 25 years Markman has been engaged in clinical research in the area of gynecologic malignancies, with a particular focus on new drug development and exploring novel management strategies in female pelvic cancers. Prior to assuming his current position, Markman served as Vice President for Clinical Research at the University of Texas MD Anderson Cancer Center (TX, USA). Additional previous positions include Director of the Cleveland Clinic Cancer Center, as well as Chairman at the Department of Hematology/Medical Oncology at the Cleveland Clinic (OH, USA), and Vice-Chairman at the Department of Medicine, Memorial Sloan-Kettering Cancer Center (NY, USA). Markman has been the primary author or co-author on more than 1000 published peer-reviewed manuscripts, reviews, book chapters, editorials or abstracts, and he has written, edited or co-edited 16 books on various topics in the management of malignant disease, including *Atlas of Cancer* and the most recent edition of *Principles and Practice of Gynecologic Oncology*. In addition, Markman has served on numerous editorial boards, including *Clinical Investigation*, the *Journal of Clinical Oncology* and *Gynecologic Oncology*; and he is currently Editor-in-Chief of *Oncology* and *Case Reports in Oncology* (Karger Press).

Q Prior to the American Society of Clinical Oncology (ASCO) 2012 annual meeting, what have been the major research advances in the field of platinum-resistant ovarian cancer and the problems this presents?

Prior to ASCO 2012, there had been a number of Phase III trials conducted and reported in platinum-resistant ovarian cancer (recurrence within 6 months of completing the last platinum-based regimen) but the universal results had been negative; no evidence of a favorable impact on a clinically relevant end point, including higher objective response rate, progression-free survival or overall survival.

Q In light of recent advances, would you say that platinum-based chemotherapy still has a part to play in the treatment of ovarian cancer?

Absolutely! Platinum drugs are the cornerstone of the management of ovarian cancer

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and it is difficult for me to imagine this will ever change. The large majority of patients with advanced ovarian cancer achieve a meaningful clinical response to platinum-based chemotherapy. The issue is that in most patients the disease ultimately recurs. Thus, the goal should be to improve the effectiveness of platinum-based therapy, and not to replace it.

Q What special considerations need to be taken into account in clinical trials against platinum-resistant tumors?

Platinum-resistant ovarian cancer consists of a heterogeneous group of patients and includes individuals who never respond to a platinum-based regimen, individuals who initially respond but then rapidly progress, and patients who achieve a relatively long time before disease progression but the cancer ultimately develops resistance. Further, it is increasingly recognized that there are multiple mechanisms for resistance that may be operative in individual tumors. In the future, it is highly likely that molecular profiling will change the manner in which we view 'platinum-resistance', which will mandate a major alteration in the clinical trials paradigm for drug development.

Q One study at ASCO 2012 suggested that administering bevacizumab with standard chemotherapy doubled the time it took for platinum-resistant ovarian cancers to worsen – what implications would you say this study presents?

The AURELIA trial demonstrated a quite unexpected but impressive improvement in both the objective response rate and progression-free survival associated with adding bevacizumab with one of three single-agent chemotherapy strategies in the management of platinum-resistant ovarian cancer [1]. While the study results remain preliminary (not yet published in the peer-reviewed literature) the data suggest a highly relevant impact associated with combining this antiangiogenic agent with chemotherapy on meaningful clinical events in this difficult clinical setting. To the best of my knowledge, this has been the only study to date to demonstrate a favorable impact on a meaningful clinical outcome in platinum-resistant ovarian cancer.

Q Looking at platinum-sensitive ovarian cancer, a PARP blocker was presented at ASCO 2012 for the treatment of ovarian cancer [2] – what promise would you say this type of targeted therapy holds?

PARP inhibitors are quite interesting agents in ovarian cancer, and it is absolutely clear that some patients achieve

considerable clinical benefit when treated with such class of drugs. Unfortunately, the optimal candidates to receive treatment (e.g., patients with *BRCA1* or *BRCA2* documented mutation versus any patient with a high-grade serous ovarian cancer) have yet to be defined. It can be anticipated that future research in this area will resolve this important issue.

Q Apart from platinum resistance, what would you say are the biggest challenges still faced in the field of ovarian cancer treatment?

As stated earlier, the majority of patients respond to initial treatment, but ultimately experience recurrence of the disease process. Therefore, the establishment of an effective, relatively nontoxic, easy to administer, and cost-effective 'maintenance' strategy could be a major advance in this clinical arena.

Q Looking to the future, which novel therapeutics against ovarian cancer do you believe hold most promise?

There are a number of approaches currently being examined in the clinical trials setting that hold promise for producing a favorable clinical effect in ovarian cancer. What we have learned over the past several decades is that preclinical data or early-stage testing are poor predictors of what will be seen in Phase III randomized trials. However, it is highly likely that in the future small subsets of patients with particular molecular abnormalities will be identified, for whom it will not be realistically possible to define the clinical utility of a therapeutic through the 'traditional' Phase II trial mechanisms.

Q In light of this, are there any areas of ovarian cancer treatment that you feel require further research?

Angiogenesis appears to be a very important area in ovarian cancer progression and symptoms. It will be important to attempt to define molecular markers or clinical criteria that predict which patients are most likely to respond, or not respond to such therapy. This is relevant not only because of the toxicity of such strategies, but also because of increasingly recognized cost considerations. PARP inhibitors should also continue to be aggressively examined in this malignancy.

Q Overall, how would you summarize the events at ASCO in relation to ovarian cancer treatment?

My overall impression from the ovarian cancer sessions at ASCO in 2012 is that we continue to advance our

understanding of the malignancy and continue to make small but clinically relevant and meaningful advances.

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**Financial & competing interests disclosure**

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