Neoadjuvant Chemotherapy for Ovarian Cancer: The Debate Reconsidered

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The question of a well-defined role for the use of neoadjuvant chemotherapy in the treatment of ovarian cancer is recognized to be one of the most hotly debated issues in the management of female pelvic malignancies.[1-3] One group of oncologists would argue that it should be the rare patient (eg, with severe comorbidity) who is not a candidate for an initial attempt at maximal cytoreduction.[1] A second group, including the team headed by Dr. Peter Schwartz at Yale, have proposed (and provided data to support the concept) that the delivery of cytotoxic chemotherapy to women with known or suspected ovarian cancer prior to considering an attempt at surgical resection is a rational therapeutic alternative.[2,3]

The space allowed for this brief commentary does not permit a thorough review of the arguments for and against the “neoadjuvant chemotherapeutic approach” to ovarian cancer management, but the major points can reasonably be summarized as follows:

**Against**

(a) Extensive retrospective data have clearly demonstrated the major favorable impact on survival associated with successful primary surgical cytoreduction that leaves an ovarian cancer patient with no, or only minimal, macroscopic disease prior to the initiation of cytotoxic chemotherapy.[4]
(b) There is concern that the delivery of chemotherapy in the presence of large-volume cancer will increase the risk for the development of chemotherapy-resistant cells, or reduce the ability of drugs to eliminate cells that are only modestly sensitive to the available antineoplastic agents.
(c) Existing data reveal that the large majority of women presenting with advanced-stage ovarian cancer are able to successfully and safely undergo an attempt at primary aggressive surgical cytoreduction when the procedure is performed by a qualified gynecologic oncologist.

**In Favor**

(a) The neoadjuvant chemotherapy approach is associated with reduced treatment-related morbidity.[2,3]
(b) The neoadjuvant chemotherapy approach may permit a larger percentage of patients to become free of gross macroscopic cancer after surgery (performed following two to six cycles of systemic drug treatment). Considering the fact that some of the residual tumors masses may have contained poorly vascularized cancer cells that are not inherently chemoresistant, continuation of active chemotherapy following surgery may have legitimate potential to improve the overall effectiveness of the multimodality management program.
(c) The neoadjuvant chemotherapy approach will define the 20% to 40% of the ovarian cancer patient population with inherently chemotherapy-resistant disease (no or minimal response to the initial drug therapy) for whom a subsequent aggressive surgical procedure would not appear to be justified.[5] (Carefully considered surgery performed for palliation of cancer-related symptoms may still be an appropriate option even in the setting of chemoresistant disease.).

**Need for Evidence-Based Data**

As is often the case in cancer medicine, it is not possible to know which of these groups of arguments is “correct,” in the absence of data from well-designed, well-conducted phase III randomized trials. Today, most oncologists would quite reasonably limit their own use of neoadjuvant chemotherapy, based on the extensive series of retrospective reports dealing with primary surgical cytoreduction, and long-standing teaching and clinical experience, rather than on the availability of data generated from evidence-based clinical trials. Fortunately, it is appropriate to
anticipate that the results of the phase III trials noted by Dr. Schwartz will provide critically important objective information that can enlighten the ongoing debate regarding this management paradigm. It is relevant to acknowledge here that use of the term “neoadjuvant chemotherapy” in the management of a patient with ovarian cancer should only be employed in the setting where there is the legitimate intent to subsequently perform surgical cytoreduction, assuming a reasonable response to the initial drug program. There are clearly patients for whom it is believed that surgery is not warranted (eg, the very elderly, a patient with severe symptomatic coronary artery disease), and where chemotherapy may serve as the primary therapeutic modality. In this situation, the cytotoxic drugs would not be delivered as a component of a “neoadjuvant approach.”

**Concluding Thought**

Finally, a comment should be made regarding the suggestion in Dr. Schwartz’s excellent review that aggressive surgery might be considered in nonperitoneal cavity sites (eg, thoracic cavity) for ovarian cancer patients with stage IV disease. This author has previously questioned the routine use of this therapeutic approach in the absence of data from randomized phase III clinical trials.[6] I reiterate my statement here—that the documented ability of individual surgeons to safely perform a complex and costly surgical procedure should be considered, by itself, insufficient justification to routinely do so, except in the setting of a well-designed and well-conducted clinical trial. This arena is in desperate need of such a trial.[6]

—Maurie Markman, MD

The main article can be found [here](http://www.physicianspractice.com/articles/neoadjuvant-chemotherapy-ovarian-cancer-debate-reconsidered).

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