Gynecologic Oncology 130 (2013) 9–11

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Meeting Report

Ovarian cancer national alliance: A report of the 2012 Consensus Conference on Current Challenges in ovarian cancer

Ovarian cancer continues to be one of the most challenging cancers to diagnose and to treat, and remains the deadliest of gynecologic cancers. Since the war on Cancer was declared 40 years ago women with ovarian cancer are living significantly longer, but cure rates are only slightly better. [1]. While no one could attempt to address the totality of difficult issues in ovarian cancer, the Ovarian Cancer National Alliance convened a groundbreaking meeting last year which focused on three of the most challenging topics facing the ovarian cancer community: patient reported outcomes (PROs), access to clinical trials at the community level and personalized medicine.

To be clear, many of the questions we addressed at the conference have no easy answers: how can more women be treated where they live; how can we facilitate increased awareness and use of PROs by regulatory authorities and payers; and what can we expect from personalized medicine in the next few years for women with ovarian and other gynecologic cancers—does the hype outweigh the reality? However, through a facilitated discussion, a diverse group of researchers, gynecologic oncologists, medical oncologists, regulatory experts (including the FDA), advocates and industry representatives came to some consensus (Table 1—Supplemental material). We identified key problems, opportunities and recommendations to help shape the Alliance's future policy positions, with the ultimate goal to improve ovarian cancer patient outcomes.

Patient reported outcomes

Within the cancer community, there is increasing evidence that PROs are essential to assessing the overall burden of cancer and treatment efficacy [2]. Ovarian cancer, with its high rate of recurrence and multi-therapy treatment regimens, makes a compelling case for PROs. While most current clinical trials are beginning to integrate PROs into study design, patients and physicians often differ as to which PROs they deem important, and reports of qualitative issues—such as energy level, neuropathy, and "chemobrain".—can vary widely from patient to patient. PROs also require complex measurement processes, and are often stigmatized as unscientific or tacked on at the end of studies as "soft endpoints," such that it is challenging to implement and use PROs as the basis for policy or decision making.

Recommendations

Our consensus is that we must first define the ovarian cancer PROs and put patients at the center of that discussion. Currently there is no firm answer to what the ovarian cancer-specific PROs are or should be. In addition, PRO-related research should be integral to the trial design process for all clinical trials, both in public and private settings. To achieve this, we must first come to an agreement on a simpler way to measure and objectively validate PROs.

PROs must also be included in FDA approval standards and the payer process. While it would be a sea change for the FDA to require PRO data pre-approval, this would mean increased burden on data collectors and manufacturers, and could result in the rejection of certain drugs because they are not appealing enough from a reimbursement standpoint. Given that the issue of PROs in ovarian cancer involves science, practice and payment, it would be fruitful to convene a broader group of cancer patients, across all diseases, along with the National Cancer Institute, payers, advocates and organizations such as the American Society of Clinical Oncology and Society of Gynecologic Oncology for a PRO summit. As PROs are essential to improve patient care and outcomes, they should be incorporated into the standard of care for all patients with ovarian and other types of cancer. To that end, the group agreed that we should financially incentivize providers to ask patients about and report PROs, regardless of clinical trial status. These PROs can become part of quality outcome measures which are used to determine provider payment.

Patient access to clinical trials at the community level

Fewer than 10% of adults diagnosed with cancer participate in clinical trials [3]. While organizations such as the National Cancer Institute have made efforts to increase clinical trial enrollment, the medical community does not view clinical trial participation as a high priority. We have a fundamental problem of substandard, decentralized care in ovarian cancer, and studies bear this out. For example, studies show that while approximately 78% of people live within 50 miles of an academic center, many are not treated in these centers. A recent study of SEER-Medicare patients found that only 39% of women treated for ovarian cancer receive even the baseline care of surgery and six cycles of chemotherapy in any order [4,5].

Far too many physicians are not referring to clinical trials or wait to tell their patients about trials only when they have no other treatment options to offer, in part because they don't want to lose these patients and the financial reimbursement. Then there are the financial considerations of clinic trial research: an abstract that presented the Society of Gynecologic Oncology's 2010 Annual Meeting on Women's Cancer detailed the current costs of conducting a phase-3 Gynecologic Oncology Group (GOG) study compared with the amount of reimbursement provided by the GOG. The study found that participants are only

0090-8258/$ – see front matter.
http://dx.doi.org/10.1016/j.ygyno.2013.04.006

reimbursed for about 30% of their costs of conducting a clinical trial [3]. This factor alone can be highly disincentivizing to physicians to have their practice and patients participate in clinical trials. For patients, late diagnosis (just 15% of patients are diagnosed in the early stages of disease) [5], makes proactive disease management more difficult, and far too many patients wrongly assume that clinical trials are solely for rare cancers, or are a last resort for the sickest patients.

Recommendations

Clearly, we must raise patient awareness about the role of clinical trials in disease management, and reach these patients before they start making treatment decisions. This could be achieved in part through the sharing of educational materials, many of which currently exist and are easily transferrable. Additionally, the online patient community could significantly boost patient recruitment and education, allowing patients to hear from trial participants or those who are alive because of others' participation in clinical trials. Social networks that link geographically diverse patients have the potential to drive research participation and clinical trial accrual.

Centralizing ovarian cancer care is another much-needed change. With new care models that provide all-around, centralized patient care, incentives are changing. Under these models, all of the medical professionals who work with a given patient have a vested interest in shared accountability, such that physicians don't "win" by not referring to clinical trials. Ultimately, it must become easier for physicians to perform trials. To that end, financial incentives should compensate physicians for the additional time and paperwork required for clinical trial participation.

Finally, linking tumor registries to clinical trials would provide an optimal reporting mechanism through which doctors can participate. The current Surveillance, Epidemiology and End Results (SEER) Program's population-based cancer registries, a premier source for cancer statistics, have limitations—namely, the average two-year delay from diagnosis to data availability [6]. The Society of Gynecologic Oncology is working to create a registry/database that can link the PROs to physicians' trial reports, which could make clinical trial participation far less burdensome for physicians.

Personalized medicine

Though personalized medicine has the potential to improve outcomes, decrease side effects and lead to more effective treatments for specific cancer subpopulations, there are limited targeted treatments in ovarian cancer. The results of The Cancer Genome Atlas—a large project by the National Institutes of Health to examine genetic abnormalities in cancer—showed that there are no common drugable mutations for ovarian cancers that can be targeted for therapy [7]. Thus, the current treatment protocol is to try one drug after another, based in large part on guesswork. Gene-based studies are difficult to do in ovarian cancer in part because of its small patient population. In fact, a key challenge with gene-based research as a whole is the small number of people or tumors that may carry a specific genetic mutation, such that if patients are divided into studies by their gene mutations, there are typically too few patients for a study [7].

Recommendations

Advocacy groups should press the National Cancer Institute to develop the infrastructure needed for smaller, smarter, gene-based or pathway targeted studies with multiple disease sites, rather than continuing to fund organ-based large-scale trials. Once a pathway is identified, we should allow any type of tumor with that pathway to participate in the same trial. This is the way to determine, for example, if breast cancer responds differently to a drug than ovarian cancer.

The key to these smaller trials is synthesized research via consortia and collaborative work. For example, in a consortium of medical centers, each center directs one or more studies of one mutation and one drug that might act on that mutation. While just a small percentage of cancer patients would have a specific mutation, patients across the country with that mutation could participate in a clinical trial of a targeted drug. The medical center directing the trial could then analyze the data in partnership with the drug's manufacturer [7].

Another way to advance personalized medicine for ovarian cancer is to include a bio bank, for example, a sample of each patient's tumor, on every major clinical trial. Biological specimens could then be made available to researchers to determine, among other things, why specific drugs work in patients with specific genetic pathways.

We must also work with patients so they understand what is feasible. Many patients are excited by chemo-resistance and sensitivity assays, but we do not currently have data to support their widespread clinical use. Tumor response tests vary in their ability to predict sensitivity, and assays for sensitivity and resistance are less developed in ovarian cancer than in breast cancer [8]. Validating these tests through clinical trials is a crucial next step and we are looking forward to seeing the emerging science.

Finally, we must find a sharper, more targeted use of tax dollars for research, making better use of available money versus requesting more. We unfortunately are not seeing sufficient progress in our clinical trials, so we should consider different mechanisms for obtaining information, such as registries. As each patient is treated, patient outcomes and DNA samples could all be linked to the registry to determine which approaches are the most cost effective. Instead of conducting a clinical trial for $10 million, we can redirect the money by investing in the registry, allowing researchers to share information.

Ultimately, "redirecting" turned out to be a key theme of the conference: in order to reduce ovarian cancer mortality rates, we must redirect not only resources but also our energy and a lot of our current thinking. The barriers that we face are numerous. Some of these barriers are unique to the subculture of ovarian cancer, including the prevalence of late diagnosis, high rate of recurrence, decentralized care, and "missing pieces" such as the lack of defined PROs and validated biomarker assays. Other barriers are more general, and include socioeconomic factors, patient and physician burden, deeply imbedded attitudes and protocols within the research community, and low patient and physician awareness about the importance and availability of clinical trials. Coming out of the conference, we are recommending a number of action steps to inform future policy of the Alliance, centered around a few key themes:

- Cost effectiveness and getting "the biggest bang for the existing buck"
- Education for better advocacy and highly informed patients
- Model programs and how to emulate their success
- Centralized care and research to increase patient access to clinical studies

These recommendations are be highlighted in the white paper, *A Conversation about Ovarian Cancer*: *Outcomes*, *Opportunities and Recommendations*, available at http://www.ovariancancer.org/conversation/.

The conference achieved on a smaller scale is what we hope to bring to fruition in ovarian cancer care: namely, collaboration among the spectrum of stakeholders in the ovarian cancer community. In turn, the greater cancer community must work together, and break away from its current siloed structure based on cancer type. Most importantly, patients must have a seat at the table when and wherever policy decisions are made. It is time that we truly deliver patient-centered care.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2013.04.006.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

References

[1] Ovarian Cancer National Alliance statistics. Available from: http//www.ovariancancer.org/about-ovariancancer/statistics/.

[2] Lipscomb J, Gotay CC, Snyder CF. Patient reported outcomes in cancer: a review of recent research and policy initiatives. CA Cancer J Clin 2007;57:278–300.

[3] Experts discuss the current state of cancer clinical trials. HemOnc Today. May 25, 2010. Available from: http//www.healio.com/hematology-oncology/practice-management/news/pring/hematology-oncology.

[4] Goff BA, Matthews BJ, Larson EH, Andrilla CH, Wynn M, Lishner DM, et al. Predictors of comprehensive surgical treatment in patients with ovarian cancer. Cancer 2007;15(109(10)):2031–42.

[5] Thrall MM, Gray HJ, Symons RG, Weiss NS, Flum DR, Goff BA. Trends in treatment of advanced epithelial ovarian cancer in the Medicare population. Gynecol Oncol 2011;122(1):100–6.

[6] National Cancer Institute. Surveillance epidemiology and end results. Available from: http://seer.cancer.gov/csr/1975_2008/results_merged/topic_prevcounts.pdf.

[7] CancerCare Inc. Understanding the role of personalized medicine 2012. Available from: http://www.cancercare.org/publications/160understanding_the_role_of_personalized_medicine.

[8] Cree IA. Chemosensitivity and chemoresistance testing in ovarian cancer. Curr Opin Obstet Gynecol 2009;21(1):39–43.

Barbara A. Goff

Society of Gynecologic Oncology, Division of Gynecologic Oncology, University of Washington School of Medicine, Box 356460, Seattle, WA 98195-6460, USA

Corresponding author. Fax: +1 206 543 3669.

E-mail address: bgoff@u.washington.edu (B.A. Goff).

Calaneet Balas[1]

Cara Tenenbaum[1]

Ovarian Cancer National Alliance, 901 E Street, NW, Suite 405, Washington, DC 20004, USA

E-mail addresses: cbalas@ovariancancer.org (C. Balas), ctenenbaum@ovariancancer.org (C. Tenenbaum).

22 February 2013

[1] Fax: +1 202 331 2292.