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Assessing recurrence risk following intraperitoneal chemotherapy for ovarian cancer: A day late and a dollar short?

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Dear Editor,

We read with great interest the recent publication from Grette and colleagues from the University of South Alabama describing their prospective evaluation of the collection of cytology from intraperitoneal (IP) ports at their surgical removal following completion of traditional intravenous and intraperitoneal chemotherapy (Grette et al., 2019). The authors demonstrated in this prospective cohort that women with evidence of malignant cytology at the time of port removal, following at least one cycle of IP chemotherapy, had both a higher likelihood of recurrence, HR 3.2 (95% CI 0.4–28.9) and more importantly death, HR 6.5 (95% CI 0.7–58.8). Notably, the current study started in 2007, likely corresponding to the excitement generated from the improved overall survival (OS) of approximately 16 months for patients receiving at least some IP chemotherapy on GOG trial 172 (Armstrong et al., 2006). In spite of this substantial improvement in OS for IP chemotherapy, from 2009 to 2013, physicians administered IP therapy in less than 15% of eligible women, while dose dense or weekly chemotherapy use increased (Wright et al., 2016a). These findings prompted Secord and Havrilesky in an editorial to question if IP chemotherapy was “dead” in the care of women with ovarian cancer (Secord and Havrilesky, 2016)?

While IP chemotherapy use was declining, neoadjuvant chemotherapy (NAC) use was increasingly, especially following the publication of the EORTC experience from Vergote and colleagues (Vergote et al., 2010). Subsequent uptake of and additional clinical trial experience with NAC ultimately resulted in both the development and publication of a consensus statement from the Society of Gynecologic Oncology (SGO) and the American Society of Clinical Oncology (ASCO) with concurrent publication in each Society's journal (Wright et al., 2016b; Wright et al., 2016c).

With the increase use of NAC, it is not surprising that there remain unanswered questions about the role of IP chemotherapy in this group of patients. Fortunately, both the Gynecologic Cancer Intergroup (GCIG) as well as the Netherlands Cancer Institute published trials evaluating approaches for IP chemotherapy following NAC (Provencher et al., 2018; van Driel et al., 2018). While these trials were vastly different in both design and administration, there may yet still be a role for IP therapy in women with ovarian cancer. In OVHIPEC-1, the Dutch evaluated the administration of hyperthermic intraperitoneal chemotherapy (HIPEC) as a single intraoperative dose of cisplatin 100 mg/m^2, following completion of 3 cycles of NAC paclitaxel and carboplatin for stage III epithelial ovarian cancer (van Driel et al., 2018). In a group of 245 women, of the 122 women receiving HIPEC the HR for recurrence or death was 0.66 (95% CI 0.50–0.87) with a median OS of 45.7 months. While provocative, HIPEC results were obtained through a very regimented and time intensive protocol that requires both special equipment and adds 120 min of operative time. Perhaps more applicable to general practice are the results from the GCIG OV21/PETROC trial (Provencher et al., 2018). This two-stage Phase 2 trial evaluated 2 distinct IP regimens: (1) IP cisplatin in addition to IV/IP paclitaxel and (2) IP carboplatin in addition to IV/IP paclitaxel as compared to standard IV chemotherapy with carboplatin and paclitaxel after NAC. Importantly the chemotherapy used in this study was room temperature IP therapy (RTIP) rather than HIPEC from the Dutch experience. As designed, the study sought to determine the most active of the two evaluated RTIP arms. Secondary to a higher rate of progressive disease at 9 months of 45.1%, the RTIP cisplatin arm was discarded and thus the final comparison was between RTIP carboplatin with IV/IP paclitaxel and IV carboplatin and paclitaxel. As reported, progressive disease at 9 months was less in the IP arm 24.5% (95% CI 16.2–32.9%) vs. 38.6% (95% CI 29.1%–48.1%) ($p = .065$). Due to poor accrual and a modification of the study design, it is difficult to know the true impact of these data; however, in the absence of a significant increase in toxicity and an apparent lack of worsening quality of life metrics, the RTIP regimen remains one that could be considered in clinical practice, although additional clinical trials are preferred. Perhaps results from the completed iPocc Trial (NCT0150856), evaluating the role of RTIP carboplatin in combination with IV paclitaxel will rekindle interest in IP therapy overall.

Thus, with some renewed interest in IP chemotherapy administration, be it through a HIPEC or RTIP approach, how are we to take the results from Grette and colleagues? If in fact we do begin to administer more RTIP, these results could be important in helping to determine which women might benefit from additional therapy, or perhaps more frequent assessments based on their reported higher risk of recurrence. However, if HIPEC becomes the only IP therapy to be utilized and RTIP is completely discarded, while provocative, the results from Grette and colleagues may unfortunately be a day late and a dollar short.

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Declaration of Competing Interest

The authors affirm they have no conflicts of interest for the current manuscript.

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