Highlights in Ovarian Cancer

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ABSTRACT

The ovarian cancer presentations at the 2000 ASCO meeting did not yield any major paradigm shifts in the treatment of women with epithelial ovarian cancer. Emphasis at this year’s meeting focused on the potential incorporation of drugs such as topotecan, oxaliplatin, doxil, and gemcitabine into the initial treatment strategies of women with advanced ovarian cancer. These studies included the introduction of several active and tolerable regimens that are potentially worthy of direct comparison to the carboplatin and paclitaxel combination. In the woman with recurrent or persistent ovarian cancer there was a greater focus on phase III studies directly comparing various chemotherapy strategies in the treatment of women with recurrent disease. This included the comparisons of single-versus two-drug salvage regimens, alternate salvage schedules, and direct comparison of agents active in taxane- and platinum-resistant disease. Finally, several early studies of novel non-chemotherapeutic strategies were presented.

RANDOMIZED TRIALS EVALUATING INITIAL THERAPY FOR OVARIAN CANCER

Randomized Trial of Paclitaxel and Carboplatin versus a Control Arm of Carboplatin or CAP (Cyclophosphamide, Doxorubicin, and Cisplatin): The Third International Collaborative Ovarian Neoplasm Study (ICON 3). N Colombo, on behalf of the ICON Collaborators (ABSTRACT 1500).

Study Design and Results

This very large multinational European study was designed to better define the potential role of paclitaxel with carboplatin in the treatment of women with epithelial ovarian cancer. Specifically, patients were randomized approximately 2:1 to a control arm versus the treatment arm of paclitaxel 175 mg/m² over 3 h followed by carboplatin at a calculated area under the concentration time curve (AUC) of six. The choice of control was left to choice of the institution’s principal investigator, who could select either carboplatin AUC = 6 or alternatively, CAP (cyclophosphamide 500 mg/m², adriamycin 50 mg/m², and cisplatin 50 mg/m²). The allowance of two different control regimens is atypical, but was felt to be appropriate since the result of the ICON 2 study comparing single-agent carboplatin to CAP was not yet available for analysis at the initiation of ICON 3. (Fortunately, subsequent analysis has suggested equivalent survival for carboplatin compared to CAP [1]). Patients received assigned therapies every 21 days for six cycles. The primary endpoint of the trial was survival with the study stratified by the chosen control arm. The carboplatin versus paclitaxel and carboplatin subgroup contained 1,421 patients (943 treated with carboplatin and 478 with paclitaxel and carboplatin), and 636 were placed into the CAP versus paclitaxel and carboplatin subgroup (421 treated with CAP and 215 with paclitaxel and carboplatin).

Although not fully mature, the median follow-up is now 29 months, and the analysis of this trial currently supports the conclusions made during last year’s ASCO meeting,
namely that control therapy gives equivalent overall survival and progression-free survival (PFS) as carboplatin and paclitaxel. Table 1 demonstrates that women assigned to the control arm had a PFS of 16.2 months while those assigned to the paclitaxel arm had a PFS of 16.8 months. One-year survival rates were nearly identical. Two-year overall survival was 62% for those assigned to the control arm and 64% for those assigned to the paclitaxel arm (Table 2). Subgroup analysis of the individual control groups, stage, residual disease after primary debulking and age all failed to demonstrate a single subgroup that enjoyed statistically better survival with the paclitaxel-containing group. Early analysis suggested that pooling the centers with low patient accrual demonstrated a trend in these centers that favored the control therapy.

Commentary
The results from this very large multinational study continue to stand in direct contrast with the results of Gynecologic Oncology Group (GOG) 111 [2] and the Intergroup studies [3] that represent similar, albeit not identical, studies performed in the United States, Canada, and Europe, and it seems unlikely that further follow-up will change the conclusions of any of these trials. The reason for the discrepancies between ICON 3 and its well-known predecessor trials is unclear although the unusual method of assigning control arms, the inclusion of low- and high-stage patients, the potential for taxol contamination in the control arms, and the unexplained good median survival of 36 months in the control arm are all topics that give cause for caution in accepting these results. The question will require further observation as the trial matures over the next two years.

While the ICON 3 trial does not support the inclusion of paclitaxel into the upfront treatment of epithelial ovarian cancer, on balance, the total body of clinical trial evidence still supports paclitaxel with carboplatin as the standard first-line regimen in women with ovarian cancer who require systemic therapy. Nevertheless, it is probably reasonable to consider that paclitaxel and carboplatin may not be vastly superior to treatment with carboplatin followed subsequently by paclitaxel. Indeed, similar conclusions have been suggested by GOG 132 [4] that suggested cisplatin followed by paclitaxel was equivalent to cisplatin and paclitaxel. Indeed, ICON 3, GOG 132, and several of the second-line studies discussed below suggest that doublet and triplet therapy may not be superior to sequential single-agent therapy.


Study Design and Results
Oxaliplatin is a platinum analog with activity in ovarian cancer. Work done both prior to and after the initiation of this trial demonstrates that this compound crosslinks a bulkier side chain to the DNA helix, potentially explaining its activity in cisplatin and carboplatin-resistant cell lines in vitro. In addition, it has activity in cisplatin-resistant cells with documented mismatch repair defects [5-7]. This study evaluates the safety and toxicity profile of oxaliplatin at 130 mg/m² with cyclophosphamide compared to cisplatin at 100 mg/m² with the same dose of cyclophosphamide. Both doublets are repeated on a 21-day schedule. Since cyclophosphamide doses are equivalent in both arms, this serves as a direct comparison of the oxaliplatin with cisplatin. Although not powered to definitely answer an efficacy endpoint, response rate, PFS and overall survival were examined as secondary endpoints.

The trial enrolled 177 women between 1992 and early 1996 with stage II, III, and IV ovarian cancer, with 85 evaluable patients in the oxaliplatin arm and 92 patients in the cisplatin arm. Compared to the cisplatin arm, the oxaliplatin arm had fewer dose delays, less hematologic toxicity and

### Table 1. Results ICON 3

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Taxol/Carboplatin</th>
</tr>
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<tbody>
<tr>
<td>N*</td>
<td>1,364</td>
<td>693</td>
</tr>
<tr>
<td>PFS**</td>
<td>16.2 mo</td>
<td>16.8 mo</td>
</tr>
<tr>
<td>1-year PFS</td>
<td>60%</td>
<td>61%</td>
</tr>
<tr>
<td>OS**</td>
<td>36 mo</td>
<td>38.7 mo</td>
</tr>
<tr>
<td>2-year OS</td>
<td>62%</td>
<td>64%</td>
</tr>
</tbody>
</table>

*Median follow-up 29 months, 80% of patients completed assigned therapy.  
**Expressed as medians.  
PFS = progression-free survival; OS = overall survival.

### Table 2. Grade III/IV toxicity and efficacy of oxaliplatin and cyclophosphamide versus cyclophosphamide and cisplatin

<table>
<thead>
<tr>
<th></th>
<th>Cisplatin (n = 92)</th>
<th>Oxaliplatin (n = 85)</th>
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<tbody>
<tr>
<td>Anemia</td>
<td>34%*</td>
<td>6%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>55%*</td>
<td>24%</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>55%**</td>
<td>38%</td>
</tr>
<tr>
<td>PFS</td>
<td>13.3 mo***</td>
<td>13 mo</td>
</tr>
<tr>
<td>OS</td>
<td>25 mo***</td>
<td>36 mo</td>
</tr>
</tbody>
</table>

*p < 0.001; **p < .05; ***Not significant.
fewer withdrawals from the treatment plan. Specifically 18% of the woman assigned to cisplatin were withdrawn from treatment for toxicity concerns compared to only 2% of patients on the oxaliplatin arm. Table 3 reviews the incidence of various grade III/IV toxicities, all of which favored oxaliplatin. Moderate grade I/II neuropathy was more common with oxaliplatin compared to cisplatin, but was reversible within one year.

Although not sufficiently large to generate meaningful survival comparisons, oxaliplatin was clearly active with a median overall survival of 36 months for the oxaliplatin arm compared to 25 months for the cisplatin arm (not significant); both treatments had an identical PFS of 13 months.

**Commentary**

This study demonstrates that oxaliplatin can be delivered with cyclophosphamide with acceptable toxicity and indeed it appears to be less toxic than cisplatin (at a dose of 100 mg/m²). Available response and survival data suggest this will be a very active doublet in ovarian cancer. The trial was started prior to the conclusion of GOG 111 [2] and the general availability of paclitaxel; hence the comparison of the oxaliplatin to cisplatin-cyclophosphamide is less relevant today than it was in 1992. Also, the dose of cisplatin (100 mg/m²) is higher than necessary. At the current time there are several relevant questions. How does oxaliplatin-paclitaxel compare to carboplatin-paclitaxel? Will the increased neurotoxicity of oxaliplatin be problematic when combined with paclitaxel? While alternating or combining carboplatin with cisplatin has not provided increased therapeutic efficacy, the different mechanism of resistance to oxaliplatin compared to cisplatin and carboplatin makes it possible that alternating oxaliplatin doublets with carboplatin doublets may be efficacious. Evaluating these possibilities will require further toxicity studies and eventually further randomized studies.

**ADDITIONAL STUDIES AND REVIEW**


A Phase II Study of Docetaxel and Carboplatin in the Treatment of Suboptimally Debulked Stage III and Stage IV Ovarian Carcinoma. JA Ruiz, I Smith, A Wertheim, A Troxel, P Rosenman, KH Antman, A Tiersten (ABSTRACT 1593).


The ASCO 2000 had numerous posters exploring the efficacy and toxicity of novel doublets such as gemcitabine with cisplatin, docetaxel with cisplatin, and topotecan with carboplatin, as well as novel triplets incorporating either topotecan or doxil into the taxol and platinum backbone. All of these regimens demonstrate efficacy and acceptable toxicity if dosed appropriately. Further definition of the activity of these doublets and triplet regimens will require randomized trials comparing the novel regimen to carboplatin with paclitaxel.

**SECOND-LINE THERAPIES IN THE TREATMENT OF RECURRENT/PERSISTENT OVARIAN CANCER**

This year’s ASCO presentations included three relatively large randomized studies evaluating treatment strategies for recurrent disease. Trials evaluating three different and important questions were asked. First, is there superiority for one salvage regimen over another (e.g., doxil versus topotecan) in terms of survival, response, or toxicity? Second, is there superiority of schedules of the same drug (e.g., paclitaxel)? Third, is there superiority of doublet salvage therapy compared to treatment with a single drug (e.g., epirubicin/paclitaxel versus paclitaxel alone)? All three of these trials are...
important in beginning to address central issues in the management of women receiving palliative care for their recurrent disease.

**Interim Analysis of a Phase II Randomized Trial of Doxil/Caelyx versus Topotecan in the Treatment of Patients with Relapsed Ovarian Cancer.** A Gordon, J Fleagle, D Guthrie, D Parkin, M Gore, A Lacave, D Mutch (ABSTRACT 1504).

**Study Design and Results**

Both topotecan and doxil have activity in ovarian cancer including disease that is considered paclitaxel- and platinum-resistant. This study was performed to evaluate the toxicity and response to these two agents in a randomized trial. Near equal numbers of woman with potentially platinum-sensitive and platinum-resistant recurrent ovarian cancer were included. Women randomized to topotecan received 1.5 mg/m² per day for five consecutive days repeated on a 21-day cycle while those randomized to doxil received 50 mg/m² on a 28-day schedule. A total of 104 sites have enrolled 481 patients, although this interim analysis includes only the first 237 patients.

Review of the patient population reveals good balance between the known prognostic factors. Response rates, time to progression as well as overall survival are equivalent in the two groups (Table 4). Not surprisingly, both drugs demonstrated significantly better activity in the subgroup with potentially platinum-sensitive disease. Curiously, survival of the platinum-sensitive group with doxil was 86 weeks compared to 63 weeks for the topotecan arm ($p = 0.012$). Toxicity data demonstrated that topotecan had a much higher rate of grade III/IV neutropenia, thrombocytopenia, anemia, need for G-CSF, erythropoietin, and blood transfusion, while doxil had a higher rate of grade III/IV palmar-plantar erythrodysethesia and stomatitis (Table 5).

**Commentary**

At the time of final analysis, this will be the largest randomized trial of patients with relapsed ovarian cancer. The results confirm that both agents are active in recurrent ovarian cancer including platinum-resistant ovarian cancer. Topotecan, a myelotoxic drug, frequently requires growth-factor support, while doxil is toxic to both skin and oral mucosa. Doxil’s simple administration schedule and potentially superior safety profile make it a strong candidate for second-line therapy in the treatment of women with recurrent disease. Several additional pieces of information are needed before making firm conclusions, including the review of the quality-of-life data collected in this trial, final analysis of the entire patient data set for response and toxicity, and further data on the potential survival advantage of doxil in platinum-sensitive patients. Finally, two further points must be considered, but unfortunately will not be answered by this study. First, the dose of both doxil and topotecan used in clinical practice is now typically delivered at about 80% of the dose intensity delivered in this study and hence, the toxicities reported for both drugs in this trial are higher than those seen in typical practice. Also if one assumes that many patients with recurrent ovarian cancer will receive both doxil and topotecan as part of their salvage therapies, it may be logical to give the most myelotoxic regimen, (i.e., topotecan) first followed by doxil.

Finally, response rates of 7% to 12% in platinum-resistant disease are far from satisfactory and highlight the need for new agents in this difficult patient population.

**An Updated Analysis of a Randomized Study of Single Agent Paclitaxel Given Weekly versus Every Three Weeks to Patients with Ovarian Cancer Treated with Prior Platinum Therapy.** H Andersson, K Bowman, M Ridderheim, P Rosenberg, B Sorbe, U Puistola, G Horvath (ABSTRACT 1505).

**Study Design and Results**

Since the late 1980s, it has been apparent that paclitaxel has activity in recurrent ovarian cancer [8]. Now, nearly 15 years later, debate still persists about the best dose and

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**Table 4. Grade III/IV toxicities of doxil versus topotecan**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Doxil (n = 103)</th>
<th>Topotecan (n = 103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>12*</td>
<td>77</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Anemia</td>
<td>1</td>
<td>34</td>
</tr>
<tr>
<td>Palmar-Plantar erythrodysethesia</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

*All results expressed in percentage.

**Table 5. Efficacy and toxicity of weekly versus every three-week paclitaxel**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Weekly (n = 105)</th>
<th>Three-week (n = 103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>11</td>
<td>29</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Alopecia</td>
<td>46</td>
<td>79</td>
</tr>
<tr>
<td>Nail Toxicity</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Response Rate</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>TTP</td>
<td>6.3 mo</td>
<td>8.2 mo</td>
</tr>
</tbody>
</table>

*Numbers presented as percentages.
schedule of this drug. In particular, frequent low-dose administration of the drug may have enhanced endothelial toxicity that provides antiangiogenesis activity with this schedule compared to the more traditional once every three-week schedule. Swedish investigators performed a phase III comparative study of these two schedules to better understand the activity and toxicity of these two paclitaxel schedules.

To minimize the potential effect of dose intensity, patients on the weekly schedule started on 67 mg/m²/week while patients on the q three-week schedule were treated with 200 mg/m²/3 week, which calculates to identical dose intensity. Depending on toxicity, patients could be either dose escalated or dose escalated. The primary endpoint was overall response rate, and patients were allowed only one prior platinum-containing regimen. Patients had not received paclitaxel prior to study entry. Two hundred and six eligible patients were evaluated with approximately 50% of patients defined as platinum-resistant. Patients treated on the weekly schedule achieved a dose intensity of 77 mg/m²/week of paclitaxel, while those on every three-week paclitaxel had a median-dose intensity of 72 mg/m²/week. The three-week paclitaxel schedule had significantly more leukopenia, neutropenia, and alopecia while there was more nail toxicity with weekly taxol. Response rates were essentially identical at 37% with a very similar time to progression.

**Commentary**

This study confirms that both weekly and every three-week paclitaxel have significant activity in ovarian cancer. There appears to be no major therapeutic advantage to weekly paclitaxel when compared to approximately 210 mg/m²/week of paclitaxel. It is not clear how this weekly schedule would compare to the more typical dose of 175 mg/m² every three weeks although the differences, if any, would presumably be modest. While the every three-week schedule offers advantages of convenience, the weekly schedule is a viable alternative when concerns about myelosuppression or hair loss are important. In addition, milder myelosuppression with equal efficacy may allow the weekly schedule of paclitaxel to be more easily combined with other active, but myelotoxic drugs, such as gemcitabine and topotecan.

**Randomized Trial Comparing Paclitaxel + Epirubicin Versus Paclitaxel as Second-Line Therapy for Advanced Ovarian Cancer Patients in Early Progression after Platinum-Based Therapy. V Torri, I Florianì, A Tinazzi, PF Conte, A Ravaïoli, MG Cantù, R Rossi, L Grassì, G Parma, N Colombo, M Negri (Abstract 1506).**

**Study Design and Results**

There is very little known regarding the value of single-agent therapy versus doublet or triplet drug therapy in the treatment of recurrent epithelial ovarian cancer. To begin to address this issue, several institutions in Italy compared the efficacy and toxicity of single-agent paclitaxel with the combination of epirubicin and paclitaxel in a group of women all defined to have platinum-resistant epithelial ovarian cancer.

This was a large study with 227 women who were enrolled a mean of three months from the completion of primary platinum-based therapy. While approximately 50% of the patients had received only single-agent carboplatin, about 25% of woman had had a previous anthracycline with their initial therapy. All women were paclitaxel-naïve. Paclitaxel was delivered at 175 mg/m² every three weeks in both arms, while the women assigned to the doublet arm also received epirubicin at 80 mg/m².

The women received four cycles of therapy. Those demonstrating stable or responding disease then received two additional cycles, assuming toxicity was acceptable. Paclitaxel single-agent therapy was completed in 70% of patients, although 11% of patients required dose reduction or dose delay. Only 59% of patients completed the doublet regimen as scheduled. Grade 3 or 4 neutropenia was much higher in doublet arm (41%) than in the single-agent arm (18%). Response rates were statistically identical in the two arms with no difference in progression-free or overall survival. As suggested in earlier studies, patients with platinum-resistant ovarian cancer carry a poor prognosis with median survival of only 12 months from study entry.

**Commentary**

This study demonstrates that paclitaxel has activity in platinum-resistant ovarian cancer and that the combination of epirubicin with paclitaxel is more toxic and no more efficacious than paclitaxel alone. To date there are no studies that demonstrate that two agents are superior to single-agent or sequential single agents in the treatment of recurrent ovarian cancer. Since some preclinical models suggest synergy of certain doublets, this concept requires further study in the setting of clinical trials, although current data would suggest that single-agent therapy is appropriate in the care of women not participating in a clinical study.

**Additional Studies and Review**

**Mitoxantrone Plus Paclitaxel: A Highly Active Salvage Regimen for Heavily Pretreated Ovarian Cancer.**
Study Design and Results

The relatively recent availability of docetaxel, gemcitabine, topotecan [9], irinotecan, doxil, as well as further exploration into the efficacy of etoposide [10], epirubicin, and mitoxantrone provide fertile ground for evaluating novel doublets and schedules for delivering these agents in combination. Once again this year ASCO had a large number of presentations evaluating the potential efficacy and toxicity of these doublets. Several investigators have successfully defined deliverable doses and schedules of these doublets in women with recurrent ovarian cancer. None of the reported doublets appeared to be clearly superior to single-drug therapy, with the possible exception of mitoxantrone and paclitaxel.

The mitoxantrone and paclitaxel study explored two different schedules of mitoxantrone and paclitaxel in 33 heavily treated patients of whom 28 were regarded to be platinum-refractory. The regimen was myelotoxic and approximately half of the patients required G-CSF support. An overall response rate was 69% with 12 complete remissions. PFS was 9.5 months with an encouraging overall survival of 20.5 months. This response is more than double those seen with many other salvage regimens using similar drugs such as doxorubicin with paclitaxel or epirubicin and paclitaxel. The reasons for the superior response are not clear and the trial will require confirmation in other clinical centers.

**Novel Therapies**

**Phase II Study of Irofulven (MGI-114) in Platinum- and Paclitaxel-Resistant Epithelial Ovarian Cancer.**

SJ Vukelja, AN Gordon, JJ Muscato, KC Hancock, G Weems, SL Smith, JR MacDonald, L Herdrich (Abstract 1578).

**Study Design and Results**

This phase II study done by the Texas Oncology Group evaluates Irofulven (MGI-114), a novel agent related to a mushroom-derived illudin toxin that has demonstrated broad activity in vitro and in vivo against several tumor types including epithelial ovarian cancer. This study evaluated the activity and toxicity of Irofulven at 11 mg/m² given daily for five sequential days and repeated on 28-day cycles. The study is limited to 16 women with platinum-resistant ovarian cancer. At least one partial remission (PR) has been reported with a second awaiting confirmation. Toxicity of the five-day schedule is considerable and included nausea/vomiting, fatigue, and mental status problems (psychosis).

**Commentary**

Dr. Eddie Reed and colleagues at the United States National Cancer Institute have also evaluated Irofulven [11]. In the American Association of Cancer Research 2000 meeting in San Francisco, Dr. Reed reported a phase II study of Irofulven in women with heavily pretreated (but not necessarily formally platinum-resistant) ovarian cancer. In that study, shortening the schedule to four days of Irofulven led to considerably less toxicity and preserved activity with an approximate 35% response rate with activity in women with platinum-sensitive as well as platinum-resistant tumors. These studies suggest that this drug merits further investigation to optimize drug schedule, dose, and efficacy.

**A Phase I Trial of AD p53 for Ovarian Cancer Patients: Correlation with p53 and Anti-Adenovirus AB Status.**


**Phase I Trial of Intraperitoneal ONYX-015 Adenovirus in Patients with Recurrent Ovarian Cancer.**


**Study Design and Results**

These two studies were designed to evaluate the feasibility and toxicity of delivering intraperitoneal adenovirus to women with recurrent ovarian cancer. The study by Wolf and colleagues evaluated an adenovirus carrying the human p53 gene with the hypothesis that insertion of the p53 gene into p53-deficient ovarian carcinoma cells would reestablish an important cell checkpoint. Insertion of a wild-type p53 is postulated to reinstate apoptotic pathways and potentially reestablish sensitivity to more conventional chemotherapy agents. Alternatively, the second study evaluated Onyx-015 virus which is a modified adenovirus that is missing the E1b gene. E1b loss impairs viral replication in wild-type cells but not in p53 mutant or null cells. In theory viral replication in tumor cells should cause cellular destruction while sparing normal tissues.

Both studies evaluated the toxicities associated with intraperitoneal delivery of adenovirus over five sequential days. Dose-limiting toxicities in both studies included fatigue, fever, and abdominal pain (particularly with the Onyx-015 virus). Many patients on the Onyx-015 trial had symptoms consistent with a viral syndrome suggesting viral replication. One PR was seen in the p53 adenovirus trial. A second patient had stable disease and is continuing on her fourteenth cycle of therapy. No responses were seen in the 16 patients treated with Onyx-015, although two patients...
defined as having platinum-resistant ovarian cancer at the time of trial enrollment responded to subsequent carboplatin after Onyx-015 administration. The appropriate daily dose of the replication incompetent p53 adenovirus is unclear but may be $3 \times 10^{12}$ pfu, while the dose-limiting toxicity for the replication impaired Onyx-015 virus was between $1 \times 10^{10}$ pfu and $1 \times 10^{11}$ pfu daily dose.

Commentary

The therapeutic role of viral-based intraperitoneal treatment strategies in ovarian cancer requires more investigation. These two studies demonstrate that the approach is feasible and reasonably well tolerated. The p53 adenovirus trial demonstrated that patients do develop very elevated antibody titers to adenovirus during repeat administrations, and that attempts to isolate adenovirus in tumor or peritoneal fluid in the Onyx-015 trial were difficult. Taken together these findings suggest that immune clearance of adenovirus-based approaches may limit efficacy; further modification of the adenovirus or the use of alternative vectors may be necessary.

OVERALL CONCLUSIONS

ASCO 2000 serves to further explore the uses of drugs such as topotecan, oxaliplatin, gemcitabine, doxil, and paclitaxel. Unfortunately, there was little to suggest that these drugs will dramatically improve survival of women with ovarian cancer over and above current standards, thus emphasizing the need to continue to incorporate new cytotoxics and novel biologic agents into the treatment scheme for these women. Fortunately, a very large number of new agents are now in phase I clinical trial and have or will enter phase II clinical trials in ovarian cancer within the next two years. Hopefully ASCO 2001 will provide important information on how these compounds may be used to positively impact the lives of women with ovarian cancer.

REFERENCES


