



Weekly paclitaxel in ovarian cancer— the latest success story

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Weekly paclitaxel, ovarian cancer, adjuvant chemotherapy, intraperitoneal chemotherapy

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Taxane and platinum combination chemotherapy forms the cornerstone for the management of epithelial ovarian cancer. Recently, altering the schedule of every-3-weeks paclitaxel to weekly paclitaxel has shown benefits in platinum-resistant epithelial ovarian cancer, and it is one of the treatment options for this subgroup of patients¹.

The recent data from the Japanese Gynecologic Oncology Group on first-line weekly paclitaxel in ovarian cancer is a new horizon of success in the management of epithelial ovarian cancer². That phase III open-label trial compared dose-dense weekly paclitaxel with every-3-weeks paclitaxel in combination with carboplatin in advanced ovarian cancer. Of the 637 enrolled patients, 631 were eligible for treatment and were included in the intention-to-treat population (dose-dense regimen: $n = 312$; conventional regimen: $n = 319$). Table 1 describes the results.

Women assigned to dose-dense paclitaxel and carboplatin had a 29% lower risk of disease progression and a 25% lower risk of death than did patients assigned to the conventional regimen. This is the first study to show benefits for dose density over dose intensity in the first-line setting in epithelial ovarian cancer. The main concerns arising from the trial are its significant dropout rate because of hematologic toxicity, which exceeds that of the Eastern Cooperative Oncology Group 1199 trial of weekly paclitaxel in breast cancer³.

A study published by Rose *et al.*⁴ showed benefits with weekly paclitaxel 60 mg/m², also pointed out by Bookman *et al.*⁵ For future clinical trials,

60 mg/m² can therefore be used as an optimal dosing schedule.

What are the implications of the Japanese trial in clinical practice?

First, after decade of research, this trial is the first to have shown survival benefit with a taxane-platinum regimen using a conventional intravenous route of delivery. The trials of triplet regimens have failed to show benefit over doublet regimens.

After the results about the role of intraperitoneal cisplatin-based chemotherapy in optimally cytoreduced epithelial ovarian cancer were published in 2006 by Armstrong *et al.*⁶, the National Cancer Institute issued a clinical announcement that all patients should be given the option of intraperitoneal chemotherapy. The problems of intraperitoneal chemotherapy are catheter-related complications, fatigue, pain, and hematologic, gastrointestinal, metabolic, and neurologic toxicity. The median progression-free survival was 23.8 months in the intraperitoneal group as compared with 18.3 months in the intravenous group.

As pointed out by Rao *et al.*⁷, the intraperitoneal chemotherapy trials have these weaknesses: None of the trials tested purely the benefits of intraperitoneal chemotherapy, and in all the trials, the control arm was not the standard paclitaxel-carboplatin combination. The standard reference regimen for subsequent trials with an intraperitoneal chemotherapy arm has been day 1 intravenous paclitaxel and day 8 intraperitoneal paclitaxel⁶. Therefore, whether the intraperitoneal route was the reason for benefit or whether the dose-dense paclitaxel was beneficial is poorly understood.

A cross-comparison of the Katsumata *et al.* and Armstrong *et al.* trials shows that progression-free survival in the weekly paclitaxel trial is as good as that with intraperitoneal chemotherapy, with fewer toxicities. Hogberg⁸ recently undertook careful observation of these trials and concluded that weekly paclitaxel appears more promising than intraperitoneal chemotherapy because the weekly paclitaxel trial is a trial of “real world” circumstances, with a more representative epithelial ovarian cancer population

TABLE 1 Results of the trial by Katsumata *et al.*²

Parameter	Paclitaxel trial arm	
	Dose-dense weekly, with every-3-weeks carboplatin	Every-3-weeks, in combination with carboplatin
Response rate (%)	56	53
Median PFS (months) ^a	28.0 (95% CI: 22.3 to 35.4)	17.2 (95% CI: 0.58 to 0.88)
Overall survival ^b	72.1	65
Patients discontinuing treatment (<i>n</i>)	165	117
Neutropenia (%)	92	88
Grade III or IV anemia (%)	69	44

^a Hazard ratio 0.71 and $p = 0.0015$ in favour of dose-dense regimen.

^b Hazard ratio 0.75 and $p = 0.03$ in favour of dose-dense regimen.

PFS = progression-free survival; CI = confidence interval.

than the optimally cytoreduced population of the intraperitoneal chemotherapy trials.

The role of weekly paclitaxel in epithelial ovarian cancer is therefore evolving, but it must be kept in mind that multiple visits are required and that, surprisingly, more neurotoxicity is seen in breast cancer trials than in epithelial ovarian cancer trials.

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CONFLICT OF INTEREST DISCLOSURES

The authors declare that no financial conflict of interest exists.

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