Weekly oxaliplatin and preoperative radiotherapy as a new neoadjuvant therapy for locally-advanced rectal cancer

We read with interest Aschele’s paper entitled ‘A phase I–II study of weekly oxaliplatin, 5-fluorouracil continuous infusion and pre-operative radiotherapy in locally advanced rectal cancer’ in a recent issue of *Annals of Oncology* [1]. They addressed the efficacy of weekly Oxaliplatin (OXA), combined with infusional 5-fluorouracil (FUra) and radiotherapy (RT) as a new regimen of neoadjuvant therapy for locally advanced rectal cancer. They developed and tested in the phase I–II study a novel chemoradiation regimen that incorporates OXA, administered weekly, into a standard regimen of infusional Fura and RT. They set the recommended doses (RDs) of OXA and Fura, administered as a 2-h infusion weekly for 6 weeks and as a 6-week continuous infusion, respectively, concurrent to pre-operative pelvic RT (50.4 Gy). In the escalation phase, dose-limiting toxicities only occurred in one patient at the fourth level and one of six patients treated at the last planned dose level. Therefore, they stated that OXA 60 mg/m² and Fura 225 mg/m²/day are the RDs for the regimen in the treatment of locally advanced rectal cancer and concluded that weekly OXA can be combined with full dose, infused Fura and radiotherapy. However, in order to draw this conclusion, there is a major issue to be discussed in their study.

In Aschele’s study, among 25 patients treated at these doses, the incidence of grade III diarrhea was 16% with no grade IV toxicity and neurotoxicity did not exceed grade II (12%). However, as is well known, post-operative complication related to neoadjuvant chemoradiotherapy is a major problem in the surgical treatment of rectal cancer. Previous study of pre-operative chemoradiotherapy for rectal cancer has demonstrated that post-operative complication occurred in 36% [2]. We have also demonstrated that postoperative complication occurred in 50–56% of patients with advanced rectal cancer who underwent pre-operative radiotherapy [3]. However, Aschele et al. did not provide any specific data concerning total morbidity rate. Furthermore, in Aschele’s study, although no post-operative deaths were encountered, re-operation was required in four patients (anastomotic dehiscence in two; pelvic abscess in one; emoperitoneum in one). This means more than 10% of patients actually needed re-operation due to post-operative complication. This rate is quite high compared with previous studies. Aschele et al. used weekly administration of OX. However, in most previous regimens with OXA, such as FOLFOX or FLOX, OXA is used biweekly and not weekly [4]. Only in FUFOX is OXA administered weekly but Fura is not administered continuously in this regimen [5].

Considering a comparatively high rate of adverse effects caused by OXA, the high re-operation rate in Aschele’s study might be due to weekly administration of OXA. Although Aschele et al. stated that other surgical complications will be detailed in a separate report, not only re-operation rate but also total morbidity rate needs to be demonstrated.

Although Aschele’s paper discusses an important issue, we need additional details, especially if we want to draw conclusions concerning the safety of their new regimen with weekly administration of OXA.


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