Editorial-II

Chemotherapy for Cervical Cancer

Between 1999 and 2002 results of 6 large prospective randomized trials were published. These studies compared concurrent chemo radiation in one arm using cisplatin with radiation (RT) (5FU also in 3 of the studies) versus either RT alone or RT and hydroxyurea. 5 of these studies (GOG85, RTOG9001, GOG120, GOG123 & SWOG8797) showed a significant improvement in the progression free survival (PFS) and overall survival (OS) in the chemo radiation arm. In the 6th study (NCIC) the difference was not significant. This was confirmed by 2 meta-analyses of these trials and the long term results also till date do not show any significant long term adverse effects due to chemo-radiation. Though the dose and scheduling of cisplatin was slightly different in all the trials, the most commonly used schedule was weekly cis platinum. As a result external beam RT with weekly cisplatin has become the standard for locally advanced cervical cancer (IB2 and above) against which all future regimens have to be compared.

A lot of other agents have been tried instead of cisplatin. Mitomycin alone and in combination with 5-flourouracil (5FU) resulted in increased GI toxicity. A randomized study comparing 5FU + RT over RT alone showed no benefit except in stage IB or IIB disease with unilateral parametrial involvement. The GOG165 study which compared 5FU with cisplatin along with RT was closed prematurely as interim results indicated a higher treatment failure rate in the 5FU arm. Carboplatin with a weekly low dose AUC 2 has been found to be safe and effective in combination with RT in phase I & II studies. It has less GI and renal toxicity when compared to cisplatin. However, there are no phase III studies as yet. Nedaplatin is less nephrotoxic but the dose limiting toxicity is hematological. Initial phase I&II studies yielded good results. Paclitaxel, gemcitabine, topotecan and vinorelbine have all been used with modest activity as single agents in patients with advanced and recurrent cervix cancer. Initial phase I and phase II studies have shown that doses of gemcitabine upto 300mg/m2 (even upto 600) weekly can be given safely with RT and that it can be given safely in patients with renal dysfunction due to ureteral obstruction by tumour. In this issue of the journal, Kundu et al describe a randomized study comparing cisplatin with gemcitabine along with RT in Indian patients. Gemcitabine was well tolerated, but neither less toxic nor more effective than cisplatin[3]. Factors such as anemia, malnutrition, hypoalbuminemia may make the tolerance of patients to chemo radiation even poor resulting in undue treatment breaks especially in the non-trial situations. The cost of support and the chemotherapy may further encourage drop-outs in this group of patients, majority of who come from the poorer strata of society. Also the benefits of chemo-RT for patients with positive para-aortic nodes have not been tested in randomized trials.

Most of research efforts are now focused on combination of agents such as cisplatin & gemcitabine and carboplatin & Paclitaxel along with RT in a bid to get even better outcomes. Also in the pipeline are newer approaches using chemotherapy with biologic agents like bevacizumab, cetuximab, celecoxib and sorafenib.

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