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Editorial

Time for global efforts with clinical trials for advanced cervical cancer patients

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In Korea, the age specific rate (ASR) for cervical cancer has steadily decreased in the last 10 years (15 per 100,000 women in 1999-2002) and the overall five year survival rate for cervical cancer has improved to 81.1% in 2001-2005 from 77.5% in 1993-1995 according to a nationwide population-based cancer registry in Korea (http://www.cancer.go.kr/cms/statistics/stat). It is noticeable that cervical cancer was the 4th common malignancy in the young age group (age 15-34) and it was the 5th common one in the older age group (age 35-64). But cervix cancer is still a leading cause of cancer-related death in females' population worldwide. In Indonesia, cervical cancer was the most frequent cancer among female and was diagnosed with advanced stages at presentation (over 85% with stage II or higher).[1] Domingo and Dy Echo[2] from the Philippines reported that their ASR was 22.5 cases per 100,000 women and 75% were diagnosed at late stage of disease.

In this issue of *Journal of Gynecology Oncology*, there are 3 articles dealing with cervical cancer either with locally advanced tumor or with metastatic nodes at paraaortic region found at the time of operation.[3-5] Radiation has been the primary treatment modality for locally advanced cervical cancer (FIGO stage IB2-IVA). Weekly cisplatin is a standard one as a concurrent chemo-radiotherapy with improved local control and survival. In selected cases with far advanced and large tumor, physicians selected cisplatin and 5 FU together with radiation as seen in the article by Noh et al.[3] Once patients failed from primary treatment, it is very difficult to manage. Tewari and Monk[6] reviewed recent achievements and future developments in advanced and recurrent cervical cancer. It is essential to deliver the best treatment up front for better cure and improved quality of life.

Many patients with locally advanced disease are presented with abnormal renal function, thus interfering with cisplatin use. Due to these toxicities, alternative options for radiation sensitization for cervical cancer are on search. Phase I study with docetaxel as a radiation sensitizer has been reported.[7] Verma et al.[4] reported the results from observational study between weekly cisplatin and weekly gemcitabin during radiation therapy with equal disease control rate and tolerable toxicity profile. In his review, results from combined cisplatin and gemcitabin with radiation were thoroughly reviewed in discussion. But in patients with difficulty to receive cisplatin, his article added a possibility of gemcitabin alone as an alternative option for radiation sensitizer in advanced cervical cancer.

Effective treatment for recurrent or far advanced cervical cancer is limited. With more knowledge about altered molecular events, more clinical studies with target therapy are underway. Monoclonal antibodies targeting epidermal growth factor receptor or vascular endothelial growth factor signaling pathway are being evaluated.[8] They pointed out targeting a single target has generally proved inadequate and multiple molecular abnormalities within tumor cells for individualized treatment is necessary. COX-2 expression is known to relate with poor prognosis and the development of distant metastases in cervical cancer.[9-11] Recent phase I-II trial using celecoxib in patients with carcinoma of the cervix was published.[12] Yet there is no definite positive outcome with COX-2 inhibitor for cervix cancer patients and there was an increased late complications by review.[13] The article in this issue by Noh et al. is the first report showing the close relationship between radiation response and co-expression of COX-2 and EGFR. This result brought up the idea that initial molecular evaluation of primary tumor tissue could be helpful in selecting appropriate and individualized drugs for better tumor response to CCRT and with fewer complications possibly in advanced cervical cancer.

An article by Kim et al.[5] in this issue reports that concurrent extended field radiation and chemotherapy improved 5 year survival rate of 61% in patients with metastatic para-aortic nodes in early stage cervical cancer compared to postoperative radiation only. A recent report with concurrent paclitaxel and cisplatin during extended field radiation in patients with pos-

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itive paraaortic nodes and locally advanced stage cervical cancer showed promising results with improved survival rate of 56% at the time of report.[14] Previously Varia et al.[15] in 1998, treating patients with metastasis to para-aortic nodes with concurrent 5-fluorouracil (5-FU) and cisplatin with radiotherapy achieved 3 year overall survival rate of 39%. Results from these data suggest that paclitaxel and cisplatin even with extended field radiation could be tolerated (higher but manageable hematologic toxicities) with better outcome. Still more clinical study is warranted with larger number of patients for long-term benefit over cisplatin and 5-FU combinations.

High incidence and high percentage of advanced cervical cancer is a problem in majority of Asian countries. Well managed radiation therapy is essential for better local control and better survival with improved quality of life and fewer complications. Concurrent chemotherapy during radiation therapy is effective in improving the cure rate with acceptable toxicities in patients with high risk factors postoperatively or with locally advanced disease. Clinical studies with larger number of patients to define individualized radiation sensitizer or to prevent more effectively distant metastasis and/or local recurrences in advanced cases with combined chemotherapy or with target therapy will add significant benefits to women's lives.

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