BLADDER CANCER ACCELERATING MVAC

To address concerns relating to delayed cystectomy and toxicity with neoadjuvant methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) therapy, Plimack *et al.* and Choueiri *et al.* have evaluated an accelerated, dose-dense regimen (AMVAC), in which the cycle time was halved, doubling the dose intensity of doxorubicin and cisplatin. Growth factor support was also used to avoid neutropenia-related toxicity.

In each study, approximately 40 patients with cT2–T4N0–N1 muscle-invasive bladder cancer completed 3–4 treatment cycles, around 50% of whom were downstaged to non-muscle-invasive disease ($\leq$ T1M0N0) at surgery. Only 12 patients across both studies experienced grade 3–4 adverse events, and the median time to surgery was shorter than previously reported for standard MVAC. “These studies show that AMVAC can achieve pathological responses similar to 12-week regimens, but in a shorter timeframe,” states Plimack. “Shortening the time required to administer chemotherapy is important as patients are able to take less time off work, and in patients who do not respond to chemotherapy, definitive surgery is not excessively delayed,” she explains.

“We also found that a good pathological or radiological response after completion of chemotherapy were good surrogates for disease-free survival (DFS),” says Choueiri. “This approach of correlating DFS and response is innovative in a prospective trial in bladder cancer,” he continues.

To identify biomarkers of response to AMVAC, Plimack *et al.* also sequenced DNA from the patients’ pretreatment tumour samples. “Our findings will be reported at the 2014 ASCO annual meeting, and preliminarily show that alterations in any one of three DNA-repair genes predicted response to neoadjuvant AMVAC,” claims Plimack. “The genetic test is commercially available, and the three-gene signature has high sensitivity and specificity,” she adds.

Plimack *et al.* have also investigated an alternative accelerated regimen: dose-dense gemcitabine and cisplatin. “Our results, also to be presented at the 2014 ASCO meeting, show that, unfortunately, this study had to close early due to a high rate of vascular events.” Thus, “AMVAC should be the neoadjuvant treatment of choice due to the favourable toxicity profile and efficiency of administration that allows for cystectomy within 10 weeks,” Plimack concludes.

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Original articles Choueiri, T. K. *et al.* *J. Clin. Oncol.* doi:10.1200/JCO.2013.52.4785 | Plimack, E. R. *et al.* *J. Clin. Oncol.* doi:10.1200/JCO.2013.53.2465