

## BLADDER CANCER

**Neoadjuvant MVAC chemotherapy best for ‘mixed’ tumors?**

New research indicates that patients with locally advanced urothelial carcinomas of mixed histology respond better to pre-cystectomy chemotherapy with methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) than their counterparts with ‘pure’ urothelial tumors. “Mixed histology cancers responded significantly better to neoadjuvant MVAC in terms of both downstaging to stage pT0 (complete pathological response) and overall survival than pure urothelial cancers,” elaborates author Edward Messing.

Bladder tumors with a mixed histological profile (that is, a nonurothelial component) are common. Moreover, presence of mixed bladder tumors has been associated with more aggressive

“...presence of mixed histology tumors may be an indication for neoadjuvant chemotherapy before cystectomy”

disease. It was previously believed that patients with these tumors would have a poor outcome and respond less well to neoadjuvant MVAC.

For their secondary analysis of the 2003 S8710 trial, Messing and colleagues classified patients with urothelial carcinoma as having either pure (80%) or mixed (20%; including squamous and/or glandular differentiation) histology. Among patients with mixed tumors, 34% in the MVAC plus cystectomy group were downstaged to pT0 versus 4% in the cystectomy only group. The effect of neoadjuvant chemotherapy was not as marked in the pure tumors cohort (29% downstaged in the MVAC plus cystectomy group versus 14% in the cystectomy only group). Furthermore, a marked survival benefit of neoadjuvant MVAC was observed in the mixed tumors group (hazard ratio 0.46; 95% CI 0.25–0.87;  $P=0.02$ ) with marginal evidence that this benefit was greater than it was for patients harboring pure tumors.

“The excellent response by mixed histology tumors accounted for almost all of the overall survival benefit seen for neoadjuvant MVAC in the entire study,” notes Messing. The study authors now plan to analyze data collected during larger trials to verify their findings, which, if confirmed, could support the hypothesis that presence of mixed tumors is an indication for chemotherapy prior to radical cystectomy. Additionally, Messing hopes that new molecular markers that predict response to chemotherapy (neoadjuvant, adjuvant or salvage) will explain “why mixed histology cancers responded so well”.

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**Original article** Scosyrev, E. *et al.* Do mixed histological features affect survival benefit from neoadjuvant platinum-based combination chemotherapy in patients with locally advanced bladder cancer? A secondary analysis of Southwest Oncology Group-Directed Intergroup Study (S8710). *BJU Int*. doi: 10.1111/j.1464-410X.2010.09900.x.