Predicting response to neo-adjuvant chemotherapy in muscle invasive bladder cancer

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Introduction & objectives

Neo-adjuvant chemotherapy (NAC) is considered to be the gold standard in patients having radical surgery for muscle invasive bladder cancer offering a ~5% 5-year survival benefit.

Not all patients respond to NAC. Predicting a response is challenging as no reliable radiological or molecular markers exist.

The objectives of this study were to:

1. Assess factors associated with response to NAC.
2. Assess the use and response rate to NAC.
3. Assess the overall survival benefit of NAC.

Materials & methods

A retrospective observational study was conducted across 2 centres on patients undergoing radical cystectomy for cT2-4N0 disease. Data was obtained on pre-operative clinical, radiological and pathological staging and overall survival.

Results

49.5% (54/109) patients received NAC. Renal impairment and poor performance status were the most common reasons for omission. 55.5% (30/54) patients responded to NAC, 35.2% histological complete (T0N0, 19/54) and 20.4% showed a partial (TCIS-T1, 11/54) response. 44.5% (24/54) did not respond: 7.4% (4/54) T2N0, 14.8% (8/54) T3-4N0 and 22.2% (12/54) with nodal positive disease. In the no NAC cohort, 21.8% (12/55) had positive pathological nodal disease.

There were no differences in the pre-operative stage between the NAC responders and non-responders. The mortality rate was 3.3% (1/30, median follow up=27 months [6-77]) in the NAC responders and 50.0% (12/24, median survival=22.1 months, median follow up=21 months [9-49]) in the NAC non-responder. In patients with nodal positive disease the median survival was 19.9 versus 19.3 months, in the NAC and no NAC cohorts, respectively.

The presence of lympho-vascular invasion (LVI) was associated with poor response to NAC, present in 0% (0/30) of NAC responders and 54.2% (13/24) of NAC non-responders final cystectomy pathological specimens. In patient with LVI, 7.7% (1/13) had pT2N0, 30.8% (4/13) had pT3-4N0 and 61.5% (8/13) had pathological nodal positive disease. 5/13 of cases of LVI were present on initial TURBT. Smoking status had weak correlation with response to NAC, with 46.7% of responders versus 33.3% non-responders smoking (p=0.63). The presence of carcinoma in situ, micro-papillary variant, squamous differentiation, perineural invasion, hydronephrosis or tumour location had no correlation with NAC response.

Conclusion

Patients that respond to NAC have an excellent outcome. Those that do not, in particular those with nodal positive disease, do very poorly. The presence of LVI is strongly correlated with poor response to NAC and these patients may be considered for upfront cystectomy.

Response to NAC is not predictable by other histological features or preoperative stage. Future developments in radiological imaging such as PET-CT and molecular markers are essential to identify those patients that will benefit from NAC.