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Results of the SPARE Feasibility Study – Selective Bladder Preservation Against Radical Excision in Muscle Invasive T2/T3 Transitional Cell Carcinoma of the Bladder (CRUK/07/011)

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Purpose/Objective(s): SPARE investigated the feasibility of recruitment to a multi-centre randomized trial comparing cystectomy (CYS) with a policy of selective bladder preservation (SBP) in patients (pts) receiving neo-adjuvant gemcitabine-cisplatin chemotherapy (NAC) for muscle invasive transitional cell bladder cancer (MIBC).

Materials/Methods: MIBC pts staged T2-3, N0, and M0, fit for both treatments and receiving 3 cycles of NAC were randomized (1:1) to CYS or SBP. Pts had a cystoscopy after cycle 3 of NAC to assess response. Treatment policy was for responders (\leq T1 residual tumor) to receive a fourth cycle of NAC followed by radical radiation therapy (RT) in SBP group and CYS in CYS group; non-responders in both groups proceeded immediately to CYS. The primary endpoint was accrual rate; secondary endpoints included adherence to randomized treatment policy, toxicity, disease-free survival (DFS) and overall survival (OS).

Results: Forty-five pts were randomized (25 CYS; 20 SBP). The target accrual of 110 pts was not met over 30 months of recruitment and the trial closed in February 2010. Median age was 65.3 years (IQR 62, 71); 42/44 (95%) tumors were pT2, 39 (89%) pts were male (1 SBP pt with all data missing was excluded). Twenty-two pts received CYS and 22 received RT as definitive treatment. Thirty-three of 42 (79%) pts responded to NAC (response data missing for 2 pts). In those allocated CYS, 17/22 (77%) responders received CYS as per protocol policy and 5 (23%) received RT. In the SBP group, 10/11 responders (91%) received RT as per SBP policy and 1 received CYS. Across both randomized groups 3 non-responders received CYS as per protocol policy, 6 received RT. Two pts with unknown response status were allocated CYS; 1 received CYS and 1 received RT. Due to high levels of non-adherence to protocol treatment policies, subsequent analyses were conducted by treatment received. With a median follow-up of 31 months, 14 (64%) CYS and 8 (36%) RT pts experienced grade 3/4 CTC toxicity post treatment ($p = 0.07$); salvage cystectomy rate was 18% (4/22) in pts receiving RT. In responders, 12 month DFS was 89% (95% CI: 61%-97%) in those receiving CYS and 65% (36%-84%) in those receiving RT (HR = 0.3 (0.07-1.07), $p = 0.06$). No statistically significant differences in OS were seen.

Conclusions: Response to neo-adjuvant NAC was high. Recruitment to a trial randomizing between CYS and SBP for MIBC was problematic and non-adherence to allocated treatment policy was frequent. A large phase III trial with this design would not be feasible within the UK health system. The sample size was too small to make robust statements on the relative merits of treatments. As anticipated there was a trend to a higher rate of DFS with CYS at the cost of increased toxicity but no evidence of survival differences.

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