Long term Update of US GI Intergroup RTOG 98 11 Phase III Trial for Anal Carcinoma. Concurrent Chemoradiation with 5FU_mitomycin Yields Better Disease free and Overall Survival than 5FU_cisplatin

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Purpose/Objective(s): On initial publication of GI Intergroup RTOG 98-11, concurrent chemo-radiation (CCRT) with 5-FU+mitomycin (MMC) decreased colostomy failure (CF) when compared with induction plus concurrent 5-FU+cisplatin (CDDP), but did not significantly impact disease-free or overall survival (DFS, OS). The intent of the updated analysis (27 February2011) is to determine the long-term impact of treatment on survival (DFS, OS, colostomy-free [CFS]), CF and relapse (local-regional [LRF], distant [DM]) in this patient group.

Materials/Methods: Stratification factors included gender, clinical node status and primary size. DFS/OS were estimated univariately by Kaplan-Meier method and treatment arms compared by log-rank test. Time to relapse and CF were estimated by cumulative incidence method and treatment arms compared by Gray's test. Multivariate analyses were done with Cox proportional hazard models to test for treatment differences, after adjusting for stratification factors.

Results: Of 682 patients accrued, 649 were analyzable for outcomes. Five year DFS and OS were statistically better for RT+5-FU/MMC vs. RT+5-FU/CDDP (67.8 vs. 57.8%; p = 0.006; 78.3 vs. 70.7%; p = 0.026). There was a trend toward statistical signifikance for CFS, LRF, and CF (71.9 vs. 65.0%, 20 vs. 26.4%, 11.9 vs. 17.3%; p = 0.05, 0.087, and 0.074). Multivariate analysis was statistically significant for treatment, gender, tumor diameter and clinical node status for both DFS and OS.

Conclusions: Concurrent chemoradiation with 5-FU-MMC has a statistically significant and clinically meaningful impact on DFS and OS vs. induction + concurrent 5-FU-CDDP and borderline significance for CFS, CF and LRF. Therefore, RT+5-FU/MMC remains the preferred standard of care. Potential strategies to improve outcomes include treatment intensification and individualized molecular-based treatment.