Concurrent Chemoradiation With 5FU-Mitomycin vs 5FU-Cisplatin Improves Disease-Free and Overall Survival

**Background**

- Initial analysis of U.S. GI Intergroup RTOG 98-11 found that concurrent chemoradiation (CCRT) with 5FU + mitomycin (MMC) had a decrease in colostomy failure (10% vs 19%, p=0.02) when compared with induction plus concurrent 5FU+cisplatin (CDDP).
- The intent of the current analysis is to determine the long-term impact of treatment on survival (disease-free [DFS], overall survival [OS], colostomy-free [CFS]), disease-free [DFS], overall survival [OS], and colostomy failure (CF).

**Methods**

- Stratification factors included gender, primary tumor size, and clinical node status.
- DFS and OS were estimated using the Kaplan-Meier method, and treatment arms were compared by the log-rank test.
- Time to relapse and colostomy failure were estimated using the cumulative incidence method and treatment arms were compared using Gray's test.
- Multivariant analyses were done with Cox proportional hazard models to test for treatment differences, after adjusting for stratification factors.

**Results**

1. **Table 1: Impact of Treatment Arm on Survival**
   - Treatment arm
   - DFS
   - OS
   - CFS
   - RT+5FU/MMC
   - 325
   - 117
   - 80
   - 78.2
   - (67.2, 76.7), p=0.0044
   - RT+5FU/CDDP
   - 324
   - 156
   - 108
   - 66.4 (57.6, 76.0), p=0.092
   - Impact of RT+5FU/MMC vs RT+5FU/CDDP on (A) DFS (p=0.0044) and (B) OS (p=0.021)

2. **Table 2: Impact of Treatment Arm on Relapse and Colostomy Failure**
   - Treatment arm
   - LRF
   - DM
   - CF
   - RT+5FU/MMC
   - 325
   - 67
   - 45
   - 21.6 (13.6, 22.1), p=0.075
   - RT+5FU/CDDP
   - 324
   - 86
   - 55
   - 13.1 (8.3, 15.4), p=0.0043
   - Impact of RT+5FU/MMC vs RT+5FU/CDDP on (A) LRF (p=0.092) and (B) DM (p=0.12)

3. **Table 3: Multivariate Analysis for DFS**
   - Variable
   - Comparison
   - Adjusted HR (95% CI)
   - Gender
   - Female vs Male
   - 1.67 (1.08, 2.57)
   - Age
   - >70 vs ≤70
   - 1.98 (1.04, 3.82)
   - Race
   - White vs Black
   - 1.33 (0.86, 2.03)
   - Clinical node status
   - Positive vs Negative
   - 1.86 (1.04, 3.35)
   - Multivariate analysis: Revealed similar results (Tables 3-4).

4. **Table 4: Multivariate Analysis for OS**
   - Variable
   - Comparison
   - Adjusted HR (95% CI)
   - Gender
   - Female vs Male
   - 1.29 (1.13, 1.47)
   - Age
   - >70 vs ≤70
   - 1.30 (1.05, 1.59)
   - Race
   - White vs Black
   - 1.27 (0.85, 1.90)
   - Clinical node status
   - Positive vs Negative
   - 2.15 (1.23, 3.74)

**Conclusions**

- CCRT with 5FU/MMC has a significant impact on DFS and OS (p=0.0044 and 0.021).
- RT+5FU/MMC has borderline statistical significance for DFS, LRF, and CF (p=0.092, 0.075, and 0.075).
- Male gender, >5 cm tumor diameter and clinical N+ are independent poor prognostic factors for DFS and OS.
- RT+5FU/MMC remains the standard of care for patients with anal canal carcinoma.
- Potential strategies to improve outcomes include: Treatment intensification and individualized, molecular-based treatment approaches.