

Genomic Complexity and Survival Differences Between Ewing Sarcoma and Desmoplastic Small Round Cell Tumor

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Abstract:

Introduction: Ewing sarcoma and desmoplastic small round cell tumor (DSRCT) are aggressive round cell sarcomas driven by distinct oncogenic fusions, yet differences in their broader genomic architecture and clinical behavior remain incompletely characterized. We investigated whether DSRCT and Ewing sarcoma differ in chromosomal genomic complexity and whether genomic alteration burden is associated with survival.

Methods: We performed a secondary analysis of the MSK 2023 cBioPortal cohort comprising 290 tumor samples from 277 patients. To avoid non-independence from repeated sampling, one tumor sample per patient was retained. One discordant Ewing sarcoma of soft tissue case was excluded, yielding 276 patients: 172 with Ewing sarcoma and 104 with DSRCT. Fraction genome altered (FGA) was compared between diagnoses using the Mann–Whitney U test. Overall survival (OS) and progression-free survival (PFS) were evaluated using Kaplan–Meier analysis and log-rank testing. Cox proportional-hazards models assessed FGA as a continuous predictor of survival.

Results: DSRCT showed significantly greater chromosomal alteration burden than Ewing sarcoma, with median FGA of 0.129 versus 0.066, respectively ($p < 0.001$). Survival was markedly inferior in

DSRCT: 60-month OS was 16.1% versus 54.4% in Ewing sarcoma, and 60-month PFS was 12.8% versus 36.3% (both log-rank $p < 0.001$). Across the cohort, each 0.10 increase in FGA was associated with worse OS (HR 1.28, 95% CI 1.16–1.42; $p < 0.001$) and PFS (HR 1.19, 95% CI 1.09–1.30; $p < 0.001$).

Conclusions: DSRCT demonstrates substantially greater chromosomal genomic complexity and poorer survival than Ewing sarcoma. Higher FGA was independently associated with adverse outcomes, supporting chromosomal alteration burden as a potentially informative marker of aggressive sarcoma biology.

Keywords: *Ewing Sarcoma; Desmoplastic Small Round Cell Tumor; Fraction Genome Altered; Genomic Complexity; Overall Survival; Progression-Free Survival*