READ - Rectum adenocarcinoma

Subtype (CMS)	Biology & Expression	Genomic Alterations	Clinical Features
CMS1: MSI Immune	• Strong immune and inflammatory signatures (high PD-L1, cytotoxic T-cell markers) • CpG island methylator phenotype (CIMP-high)	• BRAF^V600E^ mutations • MLH1 promoter methylation leading to MSI-H • Low SCNA burden	• Often right-sided tumors • Better overall survival but poor after relapse • Candidate for immunotherapy
CMS2: Canonical	• Epithelial differentiation with upregulated WNT and MYC targets • High epithelial marker expression	• APC and TP53 mutations • Chromosomal instability (high SCNA)	• Generally left-sided tumors • Best overall prognosis • Sensitive to standard chemo-targeted regimens
CMS3: Metabolic	• Metabolic dysregulation (lipid, glucose, glutamine pathways) • Mixed epithelial signatures	• KRAS mutations enriched • Intermediate SCNA burden	• Variable location • Intermediate prognosis • Potential for metabolic-targeted therapies
CMS4: Mesenchymal	• Strong TGF-β activation and EMT programs • High stromal and angiogenesis signatures	• Frequent TP53 and SMAD4 alterations • High SCNA and stromal infiltration	• Worst relapse-free and overall survival • Resistant to standard therapies • May benefit from stroma-targeted approaches