

COAD - Colon adenocarcinoma

Subtype	Proliferation	Prognosis	Therapy (Typical / Investigational)	Common Driver Alterations
CMS1 (MSI-Immune)	Low– Moderate	Good initial survival; poorer after relapse	Immune checkpoint inhibitors (anti-PD-1/PD-L1) for MSI-high; standard chemo otherwise	MSI-high (MLH1 methylation), CIMP-high; BRAF V600E (~40%); low APC/TP53
CMS2 (Canonical)	High (WNT/MYC activation)	Best overall	Surgery ± adjuvant 5-FU/oxaliplatin; EGFR-targeted antibodies in RAS-WT advanced cases	APC (~85%), TP53 (~60%), KRAS (~30%)
CMS3 (Metabolic)	Moderate	Intermediate	Standard chemo; metabolic pathway inhibitors (under study)	KRAS (~65%), PIK3CA (~30%); mixed CIMP status
CMS4 (Mesenchymal)	Moderate (stromal signature)	Worst	Chemo + anti-VEGF (bevacizumab); TGF-β pathway inhibitors; stroma-targeting agents	TGF-β activation/SMAD4 loss (~10–15%); TP53 (~60%); stromal/EMT gene upregulation