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Management of colorectal cancer liver metastases from clinical practice to molecular understanding

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Colorectal cancer (CRC) is one of the most common malignances worldwide. Hepatic metastatic disease from CRC is a significant clinical problem. The liver is the dominant metastatic site for patients with CRC, and a main cause to the death of CRC. For patients with isolated liver metastases, regional treatment approaches may be considered as an alternative to or in combination with systemic chemotherapy. For patients with initially respectable liver metastases, a common sequence (particularly for patients with a synchronous presentation of metastatic disease) is initial systemic chemotherapy to allow early aggressive disease progression to become manifest, followed by reevaluation for surgery. The remarkable improvement in recent years in both drug development and multidisciplinary team approach in the management of CRC liver metastasis has greatly improved the cure opportunity of patients. Also, recent studies have provided a robust and unified classification, defining four different subtypes: CMS1 (MSI Immune), hypermutated, microsatellite unstable, with strong immune activation; CMS2 (Canonical), epithelial, chromosomally unstable, with marked WNT and MYC signalling activation; CMS3 (Metabolic), epithelial, with evident metabolic dysregulation; and CMS4 (Mesenchymal), prominent TGF- β activation, stromal invasion and angiogenesis. This effort provides the most robust and reproducible classification system currently available for CRC and may form the basis for future clinical trials.

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