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Treatment pathways, genotype and outcomes of colorectal cancer patients with peritoneal metastases

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Traditionally patients with colorectal peritoneal metastases (CRPM) have been offered palliative chemotherapy and best supportive care. With the recognition that cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can be offered with curative intent in selected patients, nationally approved centers have been established in the UK. In our centre we introduced a prospective register of referrals recording demographics, prior treatments and specialist multidisciplinary team (MDT) decisions. Patients undergoing CRS+HIPEC have peritoneal cancer index (PCI) recorded intra-operatively and complete cytoreduction was deemed when a CC0/1 score was achieved. Between 2004 and 2017, despite increasing numbers of referrals annually, the proportion of patients selected for CRS+HIPEC decreased from 64.5% to 37.1% ($p<0.017$). Reasoning of the MDT decision not to treat included extent of peritoneal disease unlikely to achieve CC0/1 (40.5%), active systemic disease (28.6%) progressive disease on chemotherapy (11.3%) and unfit for surgery (9.5%). Seven patients (4.2%) refused CRS+HIPEC when offered 195 CRPM patients underwent CRS+HIPEC: median age 57.8y, median PCI 7; CC0/1 was achieved in 86.3%. NCI CTCAE grade 3/4 complication rates were 11%; 30-day mortality was 0.85%. Median follow-up was 19.8m (1.7-143.9m), median OS was 31.1m with an estimated 5-year survival of 30.9% (SE 4.8). A sub-analysis of 170 patients not offered surgery had a median OS of 13.2m which parallels meta-analysis results of patients in drug trials of 16.3m (Franko et al. 2016). KRAS wild-type (wt) tumors had higher OS of 35.9m compared to mutant tumors at 29.8m. Multivariate analysis confirmed KRAS as a negative prognostic indicator for OS (HR: 2.362, 95% CI 1.233-4.525, $p=0.010$), in addition to right-sided primary cancer, higher PCI and CC scores. This series demonstrates the importance of MDT selection allowing CRS+HIPEC to be undertaken with low morbidity and mortality. Patients with right sided tumors and KRAS mutations have a decreased OS. In future opportunities to exploit KRASwt targeted treatment can be explored.

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