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Are we finally moving toward personalized therapy in colorectal cancer?

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Colorectal cancer (CRC) will represent 12% of all new cancer cases and 12% of all cancer deaths in 2019, with more than 26,300 Canadians being diagnosed and 9500 Canadians dying of CRC this year[1]. This disease is the 2nd leading cause of death from cancer in men and the 3rd leading cause of death from cancer in women. Despite the significant burden of CRC, therapeutic advances since 2009 can be recognized as having translated into better survival outcomes for patients. Still, much remains to be done. In this special supplement to *Current Oncology*, we review the changing multimodality landscape of CRC management, with its increasing focus on the importance of multidisciplinary care and a tailored strategy.

In this issue, Drs. Fournier and Brown ask the surgical question "Can less be more?"[2]. A paradigm shift is occurring in the surgical management of rectal cancer: from a standard of resection with total mesorectal excision for all, to options of local excision and organ-preserving strategies for carefully selected patients with favourable histopathology. The organ-sparing approach acknowledge the significant morbidity and quality of life implications of rectal cancer surgery, and the importance of multidisciplinary care and review.

For patients with early-stage resected CRC, the question of who is most likely to benefit from adjuvant chemotherapy remains an important clinical challenge. Dr. Bender and colleagues[3] review the current evidence supporting adjuvant chemotherapy and its optimal duration, and the approach to risk-stratification in the adjuvant setting. From clinicopathologic criteria to the exciting opportunity that lies in the assessment of minimal residual disease by circulating tumour DNA, those authors emphasize how personalizing decision-making about adjuvant therapy helps the patients most likely to benefit from adjuvant chemotherapy while sparing patients with low-risk disease from unnecessary toxicity.

Despite best efforts, an estimated 35% of patients with early-stage disease will relapse and another 20%–25% will present with synchronous metastatic disease. The systemic therapy options for patients with unresectable metastatic CRC have improved, with consequent improvements in median survival now approaching 30 months in contemporary clinical trials[4]. However, with the recent recognition of the molecular heterogeneity of CRC, one-size therapy no longer fits all. Drs. Jin and Hubbard[5] review the considerations that currently define optimal sequencing of biologic therapy in the first-line setting, highlighting the importance of primary tumour location and *RAS* mutation status in identifying patients most likely to benefit from upfront therapy targeting the epidermal growth factor receptor. Drs. Lee and Loree[6] extend that discussion in their comprehensive review of the state of the art in molecular stratification of CRC, particularly as it relates to the prognostic and predictive utility of critical biomarkers such as mismatch repair and *RAS* and *BRAF* in the management of advanced CRC.

In the post-progression setting, the number of patients who have exhausted standard chemotherapy options and yet are still well enough to pursue further therapies is increasing. In their review, Dr. Parmar and colleagues[7] provide an evidence-based perspective of that clinically challenging setting. In recent years, new therapeutic options have emerged for chemorefractory disease, including the oral multikinase inhibitor regorafenib and the oral cytotoxic agent trifluridine/tipiracil. Although associated with modest survival benefits, those agents do have a recognized clinically meaningful benefit in an area of considerable unmet need[8]. However, significant challenges remain and better, more precise therapies are needed.

Finally, although treatment advances in CRC have been largely and appropriately driven by randomized controlled trials, appreciation is growing for the utility of real-world evidence to improve the generalizability of new therapies to the entire population and to inform the optimal use of therapies in diverse patient populations. In their insightful review, Drs. Batra and Cheung provide an overview of the strengths and limitations of real-world evidence and the knowledge gaps that such evidence has addressed, translating the best of that evidence into clinical practice in CRC.

As evidenced in this supplement, considerable progress has been made in the management of CRC, which is good news for our patients. A more personalized approach is emerging in CRC, including, but not limited to, consideration for tumour molecular heterogeneity, clinicopathologic features, and patient preferences. I thank and congratulate all the authors for their excellent contributions, and I hope that this special issue of *Current Oncology* will prove to be a valuable educational resource for our oncology community of care providers and patients.

CONFLICT OF INTEREST DISCLOSURES

I have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and I declare the following related interests: I have received speaker fees or advisory board honoraria from Amgen, Taiho, Roche, and Bayer.

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