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Summary

Current algorithms in systemic management of advanced CRC

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Mechanisms & Personalised Medicine | Surgery | Digestive Oncology | Colorectal

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The speaker outlined treatment algorithms for advanced colorectal cancer that integrate tumour biology (microsatellite instability status, BRAF and RAS mutations, tumour location) with patient factors to guide sequencing of chemotherapy, biologics, targeted therapy, and immunotherapy across lines of treatment.

KEY POINTS

- The speaker stated that approximately 5% of metastatic colorectal cancers are mismatch repair deficient or microsatellite instability-high, and these are highly responsive to immunotherapy with either pembrolizumab alone or nivolumab plus ipilimumab, both superior to chemotherapy by a large margin with highly durable responses.
- For BRAF V600E-mutated tumours (6-10% of cases), the speaker reported that the combination of encorafenib, cetuximab, and chemotherapy proved superior to chemotherapy plus bevacizumab in a registrational trial, with median overall survival stated as over 30 months.
- In RAS wild-type left-sided tumours, the speaker stated that outcomes are superior with EGFR blockade (cetuximab or panitumumab) combined with chemotherapy compared to bevacizumab, whereas right-sided RAS wild-type tumours benefit more from bevacizumab based on meta-analysis data.
- The speaker recommended switching chemotherapy backbones in second line and continuing VEGF blockade regardless of prior use, and stated that third-line standard of care is trifluridine tipiracil plus bevacizumab, superior even after prior VEGF exposure.
- The speaker emphasised that tumour biology must be characterised very early with microsatellite instability, mismatch repair status, and BRAF mutational status as the main factors, along with RAS status and primary tumour location.

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