Harnessing the power of precision medicine for the treatment of colorectal cancer

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Module 1: Agenda

- Identifying patients for biomarker-targeted treatment in CRC
- Current CRC treatment landscape
- Clinical insights on anti-EGFR-rechallenge in the treatment of CRC

Identifying patients for biomarker-targeted treatment in CRC

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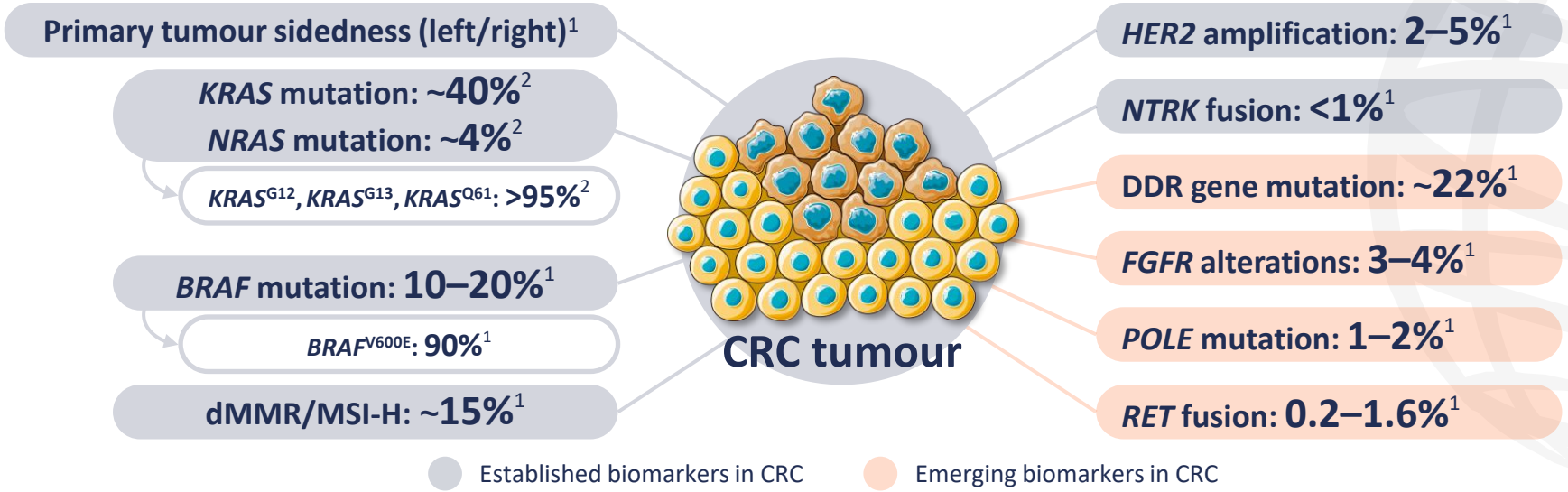
CRC biomarkers have sufficient actionable and clinical implications to warrant routine testing[1]

Prevalence of established and emerging biomarkers in patients with CRC



DDR, DNA damage repair; dMMR, deficient mismatch repair; FGFR, fibroblast-growth factor receptor; HER2, human epidermal growth factor receptor 2; MSI-H, microsatellite instability-high; NTRK, neurotrophic tyrosine receptor kinase; POLE, DNA polymerase epsilon.

1. Puccini A, et al. *Cancers (Basel)*. 2022;14:4828; 2. Patelli G, et al. *ESMO Open.* 2021;6:100156.

Current CRC treatment landscape

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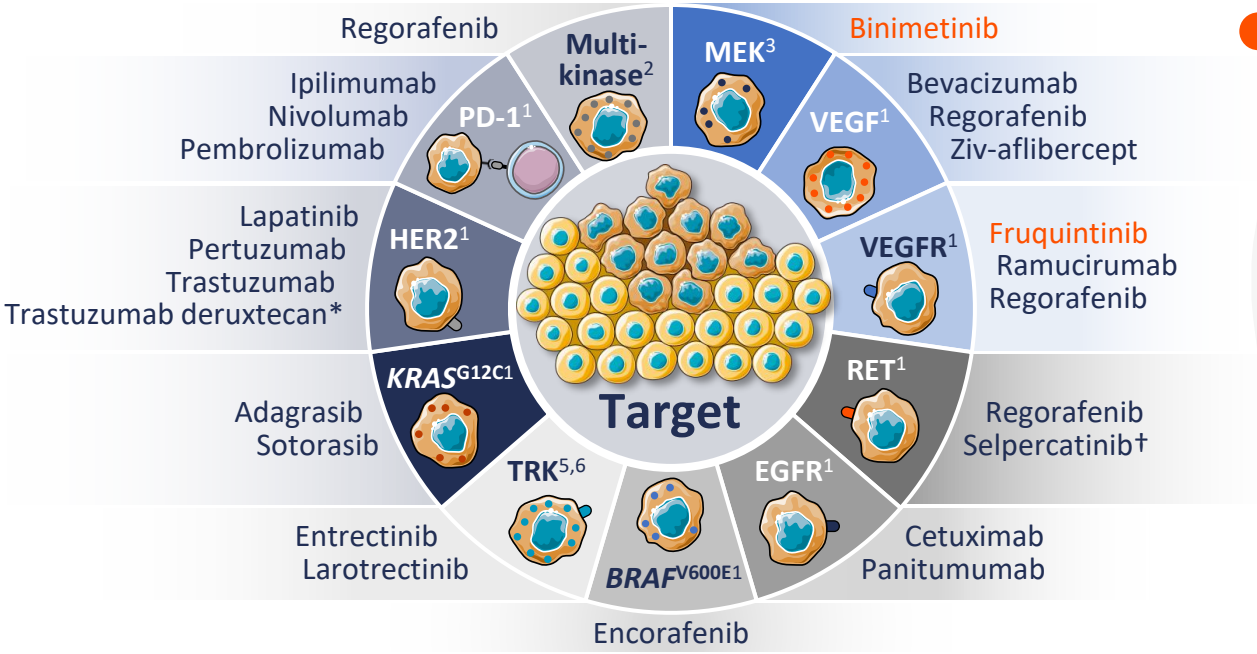
A range of biomarker-targeted therapies are available for the treatment of patients with CRC



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*HER2 amplification; †*RET* fusion. CRC, colorectal cancer; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; PD-1, programmed cell death protein 1; VEGF, vascular endothelial growth factor; VEGFR, vascular endothelial growth factor receptor.

1. Alese OB, et al. *Am Soc Clin Oncol Educ Book.* 2023;43:e389574; 2. Cervantes A, et al. *Ann Oncol.* 2023;34:10–32;
3. Kopetz S, et al. *N Engl J Med.* 2019;381:1632–43; 4. Yoshino T, et al. *ESMO Open.* 2023;8:101558; 5. Entrectinib SmPC. Updated July 2023. Available at: https://bit.ly/3IMW5m8 (accessed 21 March 2024); 6. Larotrectinib SmPC. Updated September 2023. Available at: https://bit.ly/492kYEV (accessed 21 March 2023).

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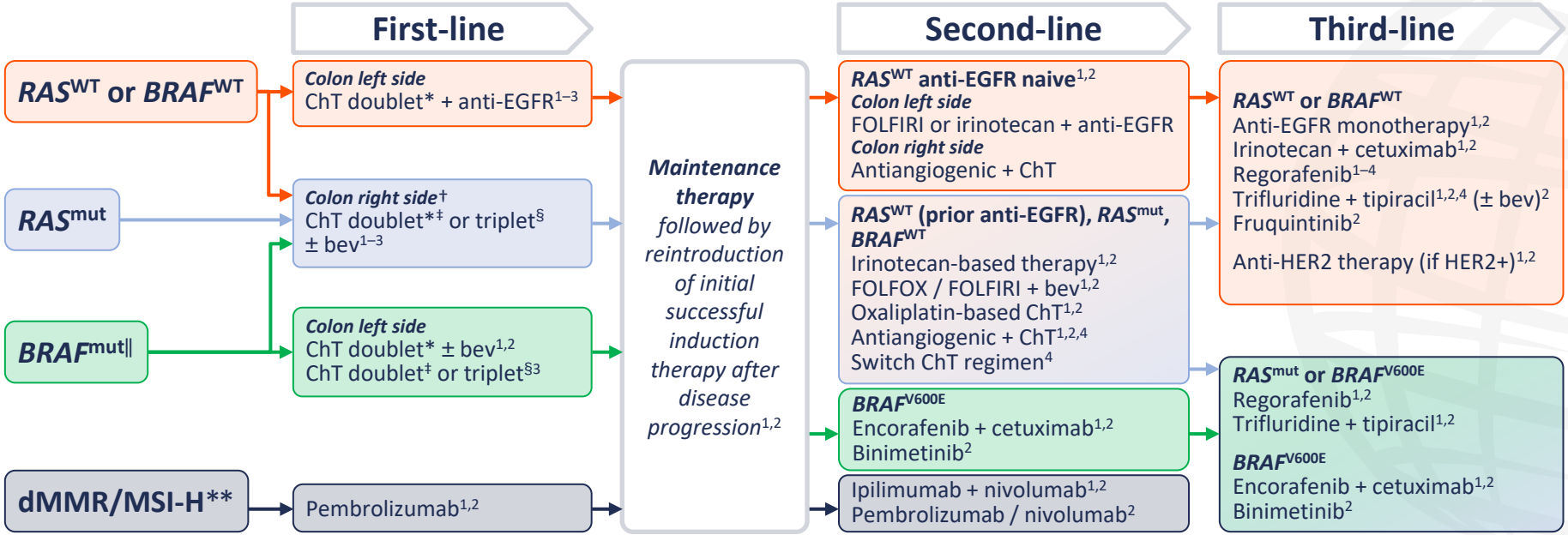
EU, Pan-Asian and Latin American recommendations for the management of unresectable mCRC generally align[1–3]



*FOLFOX or FOLFIRI or CAPOX in the majority of patients (EU and Asia); FOLFIRI or mFOLFOX6 (Latin America). †ChT doublet + anti-EGFR may be considered if tumour shrinkage is the aim (EU and Asia).[1,2]
‡FOLFOX or FOLFIRI (Latin America).[3] §FOLFOXIRI;[1–3] ChT triplet alone recommended in Latin America.[3] ‖Pan-Asia guidelines recommend ChT doublet or triplet ± bev regardless of side.[2]
**No specific guidance for third-line treatment for patients with dMMR/MSI-H tumours.[1–3]
Bev, bevacizumab; ChT chemotherapy; dMMR, deficient mismatch repair; EGFR, epidermal growth factor receptor; FOLFIRI, leucovorine–5-fluorouracil–irinotecan; FOLFOX, leucovorine–5-fluorouracil–oxaliplatin; FOLFOXIRI, leucovorin–5-fluorouracil–oxaliplatin–irinotecan; MSI-H, microsatellite instability-high; mut, mutant; WT, wild type.

1. Cervantes A, et al. *Ann Oncol.* 2023;34:10–32; 2. Yoshino T, et al. *ESMO Open.* 2023;8:101558;
3. Stefanon LR, et al. *J Pain Manage.* 2019;12:315–24; 4. López RI, et al. *ESMO Open.* 2018;3:e000315.

Clinical insights on anti-EGFR-rechallenge in the treatment of CRC

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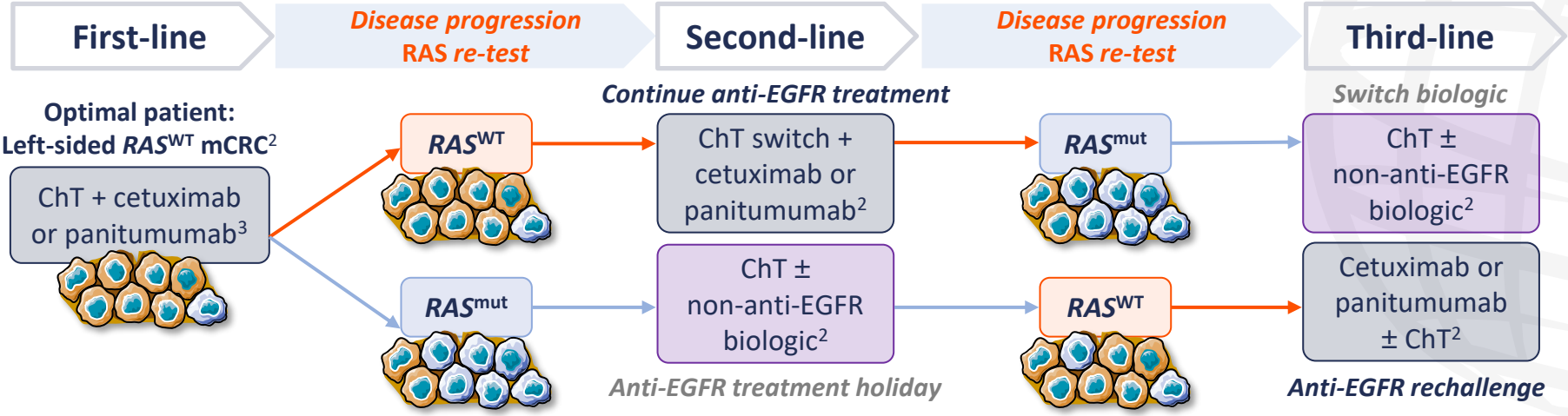
Anti-EGFR rechallenge has emerged as an active and well-tolerated therapeutic strategy[1,2]

Continuous anti-EGFR therapy can favour the proliferation of pre-existing, or insurgence of, new treatment-resistant mutant subclones of *RAS*^{WT} mCRC. These clones may decay with anti-EGFR treatment withdrawal, meaning the patient may become a candidate for anti-EGFR rechallenge[1]



Anti-EGFR rechallenge can offer tumour regression and disease stabilization for patients in the later-line setting[1]

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ChT, chemotherapy; EGFR, epidermal growth factor receptor; mCRC, metastatic colorectal cancer; mut, mutant; WT, wild type.

1. Ciardello D, et al. *Cancer Treat Rev*. 2024;124:102683; 2. Goldberg RM, et al. *ESMO Open.* 2018;3:e000353; 3. Cervantes A, et al. *Ann Oncol.* 2023;34:10–32.

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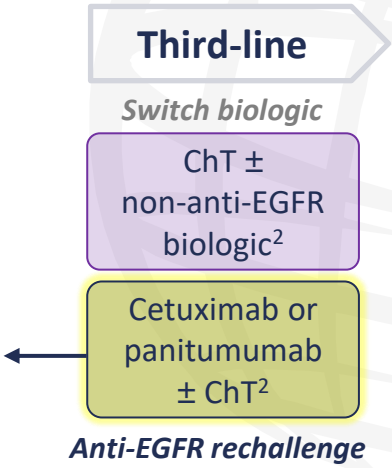
Various anti-EGFR rechallenge regimens have been investigated:[1]

- Cetuximab monotherapy
- Panitumumab monotherapy
- Cetuximab + irinotecan-based ChT
- Panitumumab + irinotecan-based ChT
- Panitumumab + trifluridine–tipiracil
- Cetuximab + avelumab

However, despite a small difference in the safety profile depending on the anti-EGFR mAb therapeutic partner, optimal regimens are yet to be identified[1]



Anti-EGFR rechallenge can offer tumour regression and disease stabilization for patients in the later-line setting[1]

ChT, chemotherapy; EGFR, epidermal growth factor receptor; mAb, monoclonal antibody; mCRC, metastatic colorectal cancer; WT, wild type.

1. Ciardello D, et al. *Cancer Treat Rev*. 2024;124:102683; 2. Goldberg RM, et al. *ESMO Open.* 2018;3:e000353; 3. Cervantes A, et al. *Ann Oncol.* 2023;34:10–32.

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