What's on the horizon for the treatment of GI tumours in 2019?

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GI, gastrointestinal

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Novel treatment strategies for GI tumours

- During the past 10–15 years, **novel tumour immunotherapeutic approaches** have revolutionised GI cancer treatment

Immune checkpoint inhibitors

- Such as PD-1/PD-L1 or CTLA-4, have demonstrated innovative progression in mCRC and gastric cancers[1,2]

PARP inhibitors

- Have shown potential benefit in patients with pancreatic cancer and BRCA1/2 mutation[3]
- When used in combination, may enhance the effect of other therapies[4]

- The use of a **biomarker-based strategy** will help select patients for an individualised therapy approach[2]

CTLA-4, T lymphocyte antigen 4; GI, gastrointestinal; mCRC, metastatic colorectal cancer; PARP, poly(adenosine diphosphate-ribose) polymerase; PD-1/PD-L1; programmed cell death protein 1/programmed cell death ligand 1.

1. Sanz-Garcia E, et al. *Ann Oncol.* 2017;**28**:2648–2657; 2. Seliger B. *Front Immunol.* 2019;**10**:999. Published online 2019 May 22. doi: 10.3389/fimmu.2019.00999; 3. Golan T, et al. *N Engl J Med.* 2019;**381**:317–327; 4. Guo X, et al. *Cancer Manag Res.* 2018;**10**: 2553–2562.

Treatment choice based on individual patient and disease characteristics

- Knowledge of the patient's genomic, biological, and immunological condition will contribute to selecting the most curative treatment

For example:

Responses to BRAF monotherapy treatment are limited in patients with mCRC and the *BRAF* mutation (V600E)

Gene expression profiling establishes mCRC molecular classification to help inform treatment

Doublet and triplet combinations offer a potential strategy to overcome resistance in BRAF-mt CRC[1]

Doublet and triplet combinations of BRAF inhibitors with antibodies targeting EGFR, MEK and/or PI3K inhibitors have been tested in BRAF-mt CRC with encouraging results

- However, the low prevalence of the BRAF mutation means more large collaborative studies are needed to improve survival in these patients[1]

EGFR, epidermal growth factor receptor; mCRC, metastatic colorectal cancer.

1. Sanz-Garcia E, et al. *Ann Oncol.* 2017;**28**:2648–2657.

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The sequencing of therapies is challenging

- Improvements in **biomarker-based patient selection,** the number of lines of therapy administered and sequencing are factors that have improved treatment outcomes for patients with mCRC
- **Uncertainty remains** as to which is the best combination to use for patients stratified according to the molecular profile of their disease
- In a rapidly evolving field, as more treatment options become available, sequencing will become even more important and challenging

ESMO guidelines provide evidence-based guidance on first and subsequent lines of treatment

mCRC, metasatic colorectal cancer.

1. Van Cutsem E, et al. *Ann Oncol.* 2016;**27**:1386–1422.

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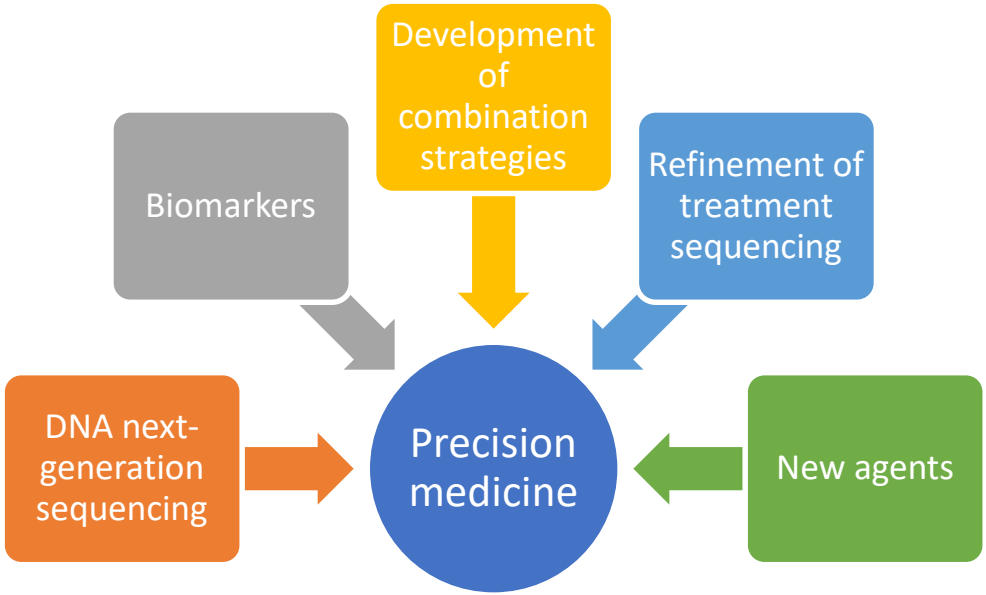
Advances in precision oncology

Aim to improve treatment options and patient outcomes



1. Fares C et al. *ASCO Educational Book* 2019;**39**:147–164.

Latest updates from ESMO 2019

- New data in GI cancer including:

Selective combination therapy for patients with $BRAF^{V600E}$ mCRC

Data for first line treatment with checkpoint inhibitors in gastric cancer

PARP inhibitors in pancreatic cancer

IDH inhibition in metastatic biliary tract cancer

GI, gastrointestinal; IDH, isocitrate dehydrogenase; mCRC, metastatic colorectal cancer; PARP, poly(adenosine diphosphate-ribose) polymerase.
https://www.esmo.org/Conferences/ESMO-Congress-2019/Programme

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