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

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Precision medicine has an increasingly important role in the treatment of solid tumours

Identification of genomic alterations known to drive tumour progression

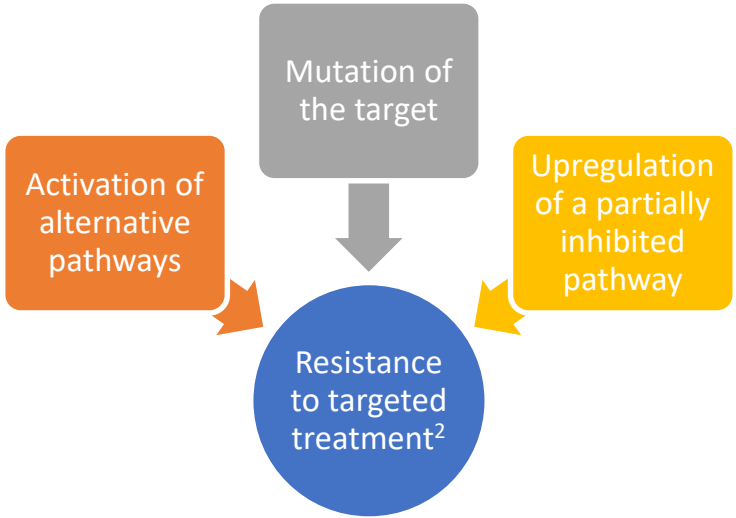
Patient mutation profiles used to predict the clinical response to targeted therapies

- However, not all patients with cancer derive clear benefit from matched targeted treatment
- Currently, precision medicine is mostly used with patients with late-stage disease, who are refractory to different therapies and with molecularly complex diseases

Remon J, Dienstmann R. ESMO Open 2018;**3**:e000446. doi:10.1136/ esmoopen-2018-000446.

Cancer treatment leads to emergence of resistant tumour cells

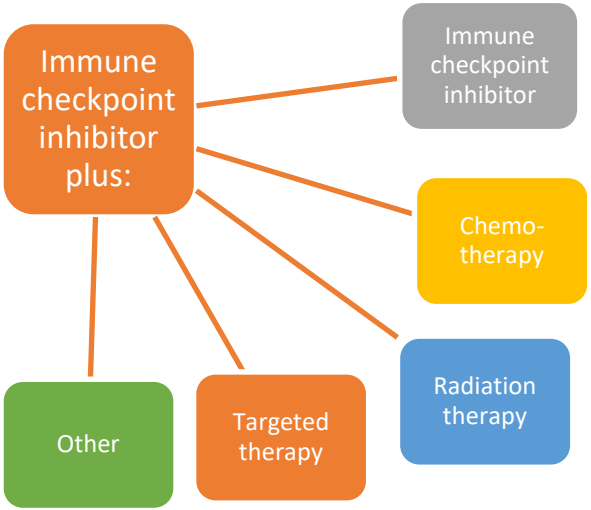
- There are complex and constantly evolving interactions between cancer cells and the immune system[1]
- Tumour evolution and presence of intra-tumour heterogeneity – between tumours in different sites, or from primary tumour and distant metastases adds to the complexity of cancer disease[2]



1. Oiseth S, et al. *J Cancer Metastasis Treat.* 2017;**3**:250-261; 2. Tannock I, et al. *N Engl J Med.* 2016;**375**:1289–1294.

New treatment combinations may help overcome resistance

- Combination strategies using multiple treatment modalities are emerging to overcome resistance to targeted treatment
- Combination treatment strategies with immune checkpoint inhibitors are being tested in clinical trials, with early data showing **high response rates**



MSI-H/dMMR, microsatellite instability-high/DNA mismatch repair deficient; mCRC, metasatic colorectal cancer.

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

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Combination treatment may increase susceptibility of tumour cells

- In a Phase II study (clinical update), the combination of nivolumab (PD-1) and low-dose ipilimumab (CTLA-4) immune checkpoint inhibitors in the primary setting in MSI-H/dMMR mCRC demonstrated clinical benefit and may represent a new treatment option for these patients

Study design

- Patients with MSIH/ dMMR mCRC and no prior treatment for metastatic disease received nivolumab 3 mg/kg every 2 weeks + low-dose ipilimumab 1 mg/kg every 6 weeks until disease progression or discontinuation

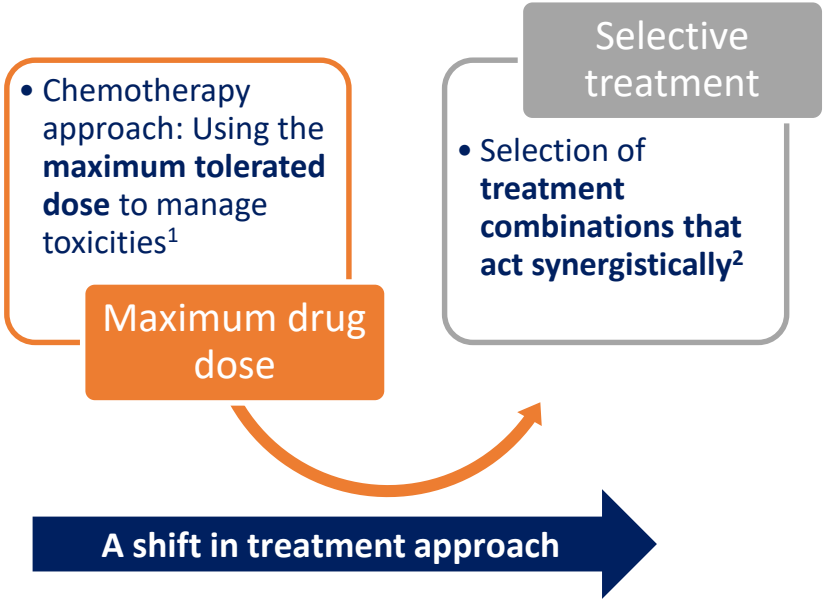
Results

- For all 45 patients (median follow-up was 13.8 months)
- **ORR was 60%** (95% CI 44.3–74.3)

MSI-H/dMMR, microsatellite instability-high/DNA mismatch repair deficient; mCRC, metastatic colorectal cancer.

1. Lenz H-J et al. *J Clin Oncol* 2019; 37(no. 15_suppl):3521–3521.

A tailored treatment approach to improve toxicity outcomes



- The intelligent selection of multiple molecular targeted agents to treat tumours (concurrently or sequentially) depending on the presence of side effects[2] – offers potential for lower dose

1. Sachs J, et al. *Clin Cancer Res.* 2016;**22**:1318–1324; 2. Tannock I, Hickman J. *N Engl J Med.* 2016;**375**:1289–1294.

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ESMO 2019

- New data on personalised, synergistic treatments based on an understanding of the patient's mutational status and tumour environment
- Advances in the understanding of the biology and immunology of solid tumours
- Cell-based treatment strategies

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