# Immunotherapy is beneficial in gastric and oesophageal cancers, studies show

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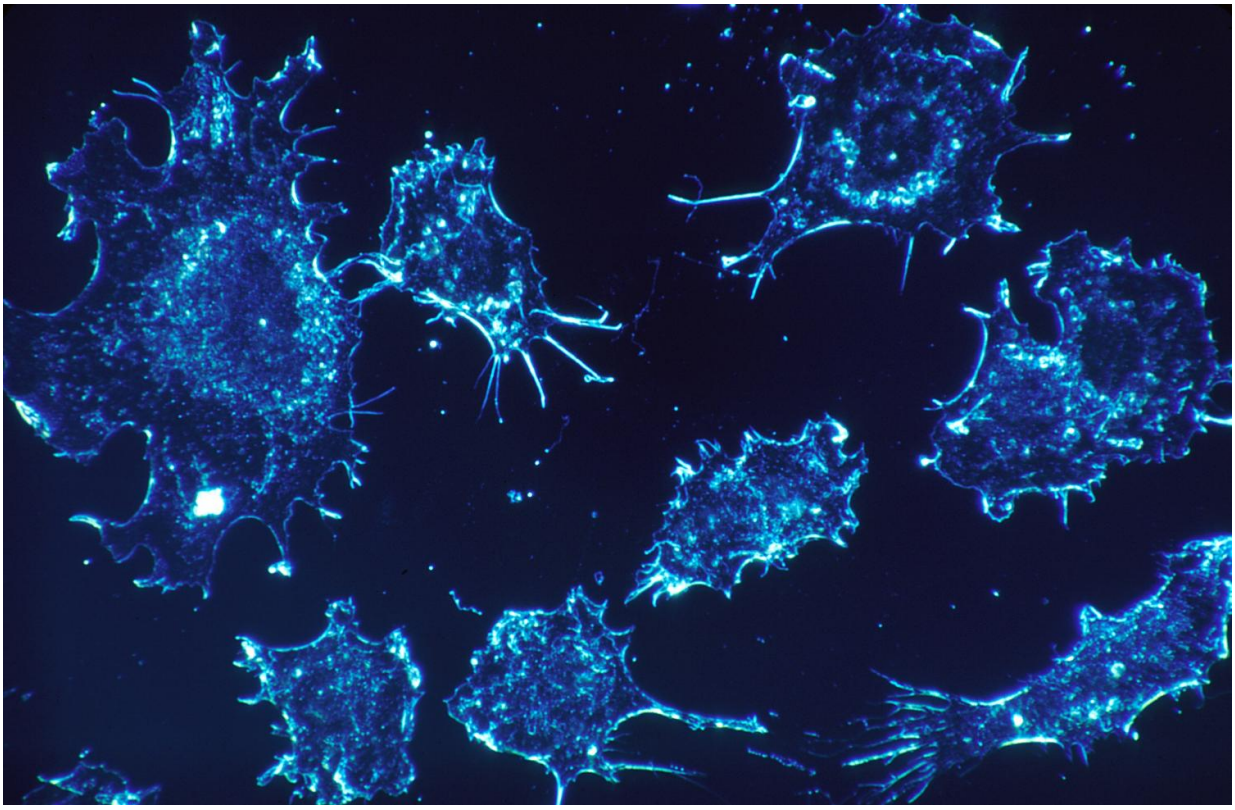

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New data presented at ESMO 2020 have shown that immunotherapy is beneficial for patients with gastric and oesophageal cancers who currently have poor survival.

Immune therapy would be a big change in treatment, since immune checkpoint inhibitors are not yet approved for early therapy in Western countries. Three studies provide evidence, based on different patient populations and different immune checkpoint inhibitors used as first-line therapy.

## CheckMate 649

The CheckMate 649 trial evaluated nivolumab plus chemotherapy versus chemotherapy alone as first-line treatment in patients with non-HER-2-positive advanced gastric cancer, gastro-oesophageal junction cancer, or oesophageal cancer—all with adenocarcinoma histology. The results show that nivolumab and chemotherapy improved overall survival and progression-free survival in patients with PD-L1 combined positive score (CPS) greater than or equal to 5 tumors. Improvements were also observed in patients with PD-L1 CPS greater than or equal to 1 tumors and in the overall patient population.

Additional analysis of subgroups and biomarkers (e.g. MSI-High) are planned to better characterize the efficacy benefit in patients across all CPS cutoffs.

Commenting on the new data, Prof Salah-Eddin Al-Batran, Director, Institute of Clinical Cancer Research and Director of GI Oncology, Krankenhaus Nordwest-University Cancer Centre, Frankfurt, Germany, ESMO 2020 upper GI track chair, said, "The results are clinically very relevant. Based on this trial, for patients with HER2-negative gastric adenocarcinoma, oesophageal adenocarcinoma, or gastro-oesophageal junctional adenocarcinoma with PD-L1 CPS greater than or equal to 5 tumors, the addition of nivolumab to chemotherapy will become the standard of care for first-line treatment. The open question is the effect in patients who have a PD-L1 CPS smaller than 5."

## Attraction 4

The ATTRACTION 4 trial was similar to CheckMate 649 except for two important differences: it was performed only in Asian patients and the primary endpoints were designed for all-comers, rather than a specific CPS value. First-line treatment with nivolumab plus chemotherapy improved the co-primary progression-free survival endpoint, but not overall survival.

"The improvement in progression-free survival was clinically relevant and the trial strongly supports the results of CheckMate 649," said Al-Batran. "Overall survival was not improved, possibly because all-comers were treated or because patients in Asia receive more subsequent therapies than Western populations."

## Keynote 590

The KEYNOTE 590 trial examined first-line chemotherapy, with or without pembrolizumab, in patients with squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus, or Siewert type 1 gastro-oesophageal junction adenocarcinoma. It demonstrated that pembrolizumab plus chemotherapy improved overall survival in patients with squamous cell carcinoma of the esophagus with PD-L1 CPS greater than or equal to 10 tumors, all squamous cell carcinomas, all patients with CPS greater than or equal to 10, and the study population as a whole. Progression-free survival was also improved.

Most oesophageal cancer patients in the trial had squamous cell carcinoma (73%) and those with adenocarcinoma were a small subgroup. The results in the subgroup of patients with adenocarcinoma were an experimental analysis, but in the adenocarcinoma subgroup, median overall survival (OS) was 11.6 months and 9.9 months (hazard ratio

[HR]=0.74), and median progression-free survival (PFS) was 6.3 months and 5.7 months (HR=0.63) in the Pembro+Chemo and Chemo group, respectively. The OS- and PFS-benefit observed in the adenocarcinoma subgroup was consistent with the benefit observed in the overall patient population.

Commenting on the findings, Al-Batran said: "I expect that KEYNOTE-590 will change practice for patients with metastatic squamous cell carcinoma or adenocarcinoma of the esophagus who have PD-L1 CPS greater than or equal to 10 tumors, for whom pembrolizumab added to chemotherapy will become the standard of care in the first-line."

Al-Batran concluded: "The results of these trials offer oncologists new treatment options. In the first-line setting, there is a clear change of our standard of care, in which patients with high PD-L1 expression will be candidates for immune checkpoint inhibitors plus chemotherapy. However, more data are needed on the subgroups who benefit from the treatment (e.g. PD-L1 CPS groups and MSI)."

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