Nature Reviews Clinical Oncology | Published online 27 Sep 2016

IN BRIEF

SKIN CANCER

Avelumab effective against Merkel-cell carcinoma

Data from a phase II trial indicate that avelumab, an anti PD-L1 monoclonal antibody, is safe and effective in patients with advanced-stage Merkel-cell carcinoma. In a cohort of 88 patients, who were not selected for PD-L1 expression, 28 (31.8%) had an objective response to treatment, including eight complete responses and 20 partial responses, of which 23 patients had an ongoing response at a median of 10.4 months of follow-up monitoring. Grade 3 treatment-related adverse events ocurred in four patients, these events included lymphopenia, and increases in serum creatinine phosphokinase levels, aminotransferase levels and cholesterol levels. No grade 4 treatment-related adverse events ocurred. On the basis of these data, avelumab provides a new treatment option for patients with advanced-stage Merkel-cell carcinoma.

ORIGINAL ARTICLE Kaufman, H. L. *et al.* Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial. *Lancet Oncol.* http://dx.doi.org/10.1016/S1470-2045(16)30364-3 (2016)

GASTROINTESTINAL CANCER

Mutational signatures reveal distinct subgroups

Data from a whole-genome sequencing analysis of 129 patients with oesophageal adenocarcinoma reveal the existence of three distinct molecular subtypes of this heterogeneous cancer: tumours enriched with *BRCA* mutations, with defective homologous recombination; those dominated by T>G mutations, with a high mutational load and neoantigen burden; and those with a C>A/T pattern of mutations, with evidence of an ageing imprint. These findings were confirmed using an independent validation cohort of 87 patients. Researchers tested the clinical relevance of these mutations in cell lines reflecting the characteristics of these three signature groups, and found that the *BRCA* mutation signature conferred greater sensitivity to poly [ADP-ribose] polymerase inhibition in combination with topotecan, while the T>G mutational signature conferred greater sensitivity to WEE1/CHK1 inhibition. These subtypes provide a basis for the selection of patient-specific treatment strategies.

ORIGINAL ARTICLE Secrier, M. *et al.* Mutational signatures in esophageal adenocarcinoma define etiologically distinct subgroups with therapeutic relevance. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3659 (2016)

THYROID CANCER

BRAF and/or *TERT* mutations increase mortality

Results of a clinical correlation study indicate that patients with papillary thyroid cancer harbouring mutations in established oncogenes have inferior survival outcomes compared with patients harbouring wild-type forms of these genes. The genotypes of 1,051 patients with papillary thyroid cancer were investigated for the presence of mutations in the *TERT* promoter region and $BRAF^{V600E}$ mutations. A total of 292 patients had $BRAF^{V600E}$ mutations, 64 had *TERT* promoter mutations and 66 had both *TERT* promoter and $BRAF^{V600E}$ mutations; these groups of patients had 3.08, 6.62, and 29.86 cancer-specific deaths per 1,000 person years, respectively, compared with 0.8 in patients without either type of mutation. Further investigations of these risks of cancer-specific mortality confirmed this increased risk after adjustment for other clinicopathological variables.

ORIGINAL ARTICLE Liu, R. *et al.* Mortality risk stratification by combining BRAF V600E and TERT promoter mutations in papillary thyroid cancer: genetic duet of BRAF and TERT promoter mutations in thyroid cancer mortality. *JAMA Oncol.* http://dx.doi.org/10.1001/jamaoncol.2016.3288 (2016)