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IN BRIEF

HAEMATOLOGICAL CANCER

Clarithromycin salvages relapsed or refractory lymphoma

Findings of a phase II study in patients with relapsed or refractory extranodal marginal zone lymphoma (rrEMZL) reveal that treatment with high doses of the macrolide antibiotic clarithromycin is safe and effective. In a study cohort of 23 patients with rrEMZL and at least one detectable lesion, six had a complete remission and a further six had a partial response following four 2-week courses (given every 21 days) of oral clarithromycin treatment. At a median follow-up of 2 years, only two patients who were responsive to clarithromycin treatment relapsed, and all patients were alive. Nausea, reported by two patients, was the only major adverse event associated with this treatment; these data support further testing of this agent in phase III clinical trials.

Original article Ferreri, A. J. *et al.* High-dose clarithromycin is an active monotherapy for patients with relapsed/refractory extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT): the HD-K phase II trial. *Ann. Oncol.* doi:10.1093/annonc/mdv214

LUNG CANCER

Diverse *EGFR* mutations explain AZD9291 resistance

Patients with advanced-stage non-small-cell lung cancer (NSCLC) who harbour the *EGFR* T790M mutation often develop resistance to EGFR tyrosine-kinase inhibitors (TKIs), such as AZD9291. Now, an association study in patients who developed resistance to AZD9291 has identified three distinct mutations that all underlie resistance to this agent in patients with advanced-stage NSCLC and EGFR T790M mutations before commencing treatment. Analysis of plasma cell-free DNA samples from 15 patients with advanced-stage NSCLC who were resistant to AZD9291 revealed that six patients retained the T790M mutation and gained a further EGFR mutation (C797S), five patients retained the T790M mutation and a further four lost the T790M mutation but remained resistant to AZD9291. These findings indicate that the mutational landscape of patients with advanced-stage NSCLC is more complex than previously thought.

Original article Thress, K. S. *et al.* Acquired EGFR C797S mutation mediates resistance to AZD9291 in non-small cell lung cancer harboring EGFR T790M. *Nat. Med.* doi:10.1038/nm.3854

COLORECTAL CANCER

NTHL1 mutations predispose to adenomatous polyposis

Newly published research using whole-exome sequencing has identified a new form of familial adenomatous polyposis that occurs in individuals who are homozygous for loss-of-function mutations in the base-excision repair gene *NTHL1*. This loss of function arises from a range of mutations, including c.268C>T and c.391C>T. In total, 51 individuals from three families with a family history of adenomatous polyposis, were selected for this study. Seven individuals from the three families had various cancers, including colorectal cancer. All patients with cancer were homozygous for *NTHL1* loss-of-function mutations, unaffected family members were either heterozygous or did not carry mutant *NTHL1*. These findings suggest that *NTHL1* is a susceptibility gene for recessive adenomatous polyposis and possibly other types of cancer.

Original article Weren, R. D. *et al.* A germline homozygous mutation in the base-excision repair gene *NTHL1* causes adenomatous polyposis and colorectal cancer. *Nat. Genet.* doi:10.1038/ng.3287