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IN BRIEF

TARGETED THERAPIES

First MEK inhibition in *NRAS*-mutated melanoma

A new phase II clinical trial has demonstrated that treatment with MEK162, a small-molecule MEK inhibitor, resulted in a partial response in patients with advanced melanoma whose tumours harboured *NRAS* mutations. The study split patients according to their mutation status: those with *NRAS* mutations ($n=30$) versus those with Val600 *BRAF* mutations ($n=41$). Of the *NRAS*-mutated group, 20% had a partial response, which is promising as this is the first targeted therapy to demonstrate activity in this patient population. Adverse events led to 15 patients discontinuing treatment in both patient groups, most commonly because of peripheral oedema and skin-related toxicity. Other adverse events reported included diarrhoea, dehydration, malaise and small intestinal perforation.

Original article Ascierto, P. A. *et al.* MEK162 for patients with advanced melanoma harbouring *NRAS* for Val600 *BRAF* mutations: a non-randomised, open-label phase 2 study. *Lancet Oncol.* doi:10.1016/S1470-2045(13)70024-X

GENETICS

BRCA1 methylation predicts DFS after chemotherapy

The tumours of patients with triple-negative breast cancer often display *BRCA1* silencing via the methylation of the gene's promoter. A new study of 1,163 patients has found that in patients with triple-negative disease who received adjuvant chemotherapy ($n=167$), *BRCA1* methylation was associated with superior 10-year disease-free survival (DFS) compared with *BRCA1*-active tumours (78% versus 55%, $P=0.009$). *BRCA1* was also shown to be an independent variable of disease-specific survival (DSS) in this subgroup of patients. By contrast, *BRCA1*-methylation was an unfavourable predictor of DFS and DSS in non-triple-negative patients. Assessing the *BRCA1* methylation status in patients with breast cancer might help stratify patients likely to respond to adjuvant chemotherapy.

Original article Xu, L. *et al.* Promoter methylation of *BRCA1* in triple-negative breast cancer predicts sensitivity to adjuvant chemotherapy. *Ann. Oncol.* doi:10.1093/annonc/mdt011

HAEMATOLOGICAL CANCER

tAML risk is significant and must be considered

A study of nine population-based cancer registries comprising >400,000 patients has investigated changes in the therapy-related acute myeloid leukaemia (tAML) risk over time among patients who received chemotherapy as part of their initial cancer treatment. All patients aged 20–84 years with primary malignancies, except leukaemias, during the period 1975–2008 were included in the study. Overall, the risk of tAML was 4.70-fold higher than that of AML expected in the general population ($P<0.001$). The risk of tAML increased over time following therapy for non-Hodgkin lymphoma, but declined for ovarian cancer over the years 1975–2008. Similarly, since 2000, the risk of developing tAML has increased for patients initially treated for oesophageal, prostate and cervical cancers. Accordingly, these risks should be considered when treatment decisions are made.

Original article Morton, L. M. *et al.* Evolving risk of therapy-related acute myeloid leukaemia following cancer chemotherapy among adults in the United States, 1975–2008. *Blood* doi:10.1182/blood-2012-08-448068