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IN BRIEF

GENETICS

BRCA-mutant breast/ovarian cancer revealed

The findings of a large prospective cohort study involving 9,856 women with *BRCA1* or *BRCA2* mutations indicate a 72% cumulative lifetime risk of breast cancer in those harbouring a *BRCA1* mutation and a 69% risk for those harbouring a *BRCA2* mutation. Futhermore, the cumulative lifetime risk of ovarian cancer was found to be 44% and 17% in those with *BRCA1* or *BRCA2* mutations, respectively. The risk of breast cancer increased further in line with the number of first-degree, or second-degree relatives already diagnosed with either *BRCA1*-mutant or *BRCA2*-mutant breast cancer. These findings provide further evidence that will guide the counselling and treatment of women harbouring these mutations.

ORIGINAL ARTICLE Kuchenbaecker, K. B. *et al.* Risks of breast, ovarian, and contralateral breast cancer for *BRCA1* and *BRCA2* mutation carriers. *JAMA* **317**, 2402–2416 (2017)

TARGETED THERAPY

ctDNA identified in patients with CUP

A next-generation sequencing analysis of circulating tumour DNA (ctDNA) from 442 patients with cancer of unknown primary (CUP) has revealed the presence of at least one detectable alteration in 79.9% of patients, of which 89.6% of alterations were potentially targetable through off-label use of FDA-approved agents. Furthermore, investigators were able to monitor dynamic changes in the presence of specific mutations over time in ctDNA from blood samples taken at various time points in the treatment of two selected patients. These findings demonstrate the potential of liquid biopsy approaches in the delivery of targeted therapies to patients with CUP.

ORIGINAL ARTICLE Kato, S. *et al.* Utility of genomic analysis in circulating tumor DNA from patients with carcinoma of unknown primary. *Cancer Res.* http://dx.doi.org/10.1158/0008-5472.CAN-17-0628 (2017)

MELANOMA

Neadjuvant BRAF inhibition enables resection

Data from a consecutive series of 13 patients with stage III malignant melanoma indicate that patients with $BRAF^{V600E}$-mutant marginally resectable or irresectable melanoma are able to derive clinical benefit from neoadjuvant BRAF inhibition. This approach enabled all patients to undergo surgical resection, which was macroscopically successful in all cases. A total of four patients had a complete pathological response with no viable tumour cells detected in resection specimens, and 10 patients remain free of disease after a median follow-up duration of 20 months.

ORIGINAL ARTICLE Zippel, D. *et al.* Perioperative BRAF inhibitors in locally advanced stage III melanoma. *J. Surg. Oncol.* http://dx.doi.org/10.1002/jso.24744 (2017)

HAEMATOLOGICAL CANCER

Low-dose CAR T cells are safe and effective

The findings of a single-arm cohort study involving 42 patients with refractory and/or relapsed B-cell lymphoblastic leukaemia (B-ALL) indicate that low-dose (1×10^5/kg) chimeric antigen receptor (CAR) T cells are safe and effective in this setting. 90% of patients entered complete remission, or complete remission with an incomplete count recovery, with only mild, or mild-to-moderate cytokine-release syndrome reported in most patients. These findings indicate a need for comparative studies designed to explore the efficacy of this approach.

ORIGINAL ARTICLE Pan, J. *et al.* High efficacy and safety of low-dose CD19-directed CAR-T cell therapy in 51 refractory or relapsed B acute lymphoblastic leukemia patients. *Leukemia* http://dx.doi.org/10.1038/leu.2017.145 (2017)