

## IN BRIEF

 CELL SIGNALLING**Paradox breakers — promising novel RAF inhibitors**

Treatment with RAF inhibitors confers a survival benefit to patients with mutant-BRAF-driven melanoma. Paradoxically, in tumours that also contain oncogenic mutations in RAS or its upstream signalling receptors, RAF inhibitors can stimulate tumour growth by further activating MAPK signalling. Now, new research shows that the next-generation RAF inhibitors PLX7904 and PLX8394 can inhibit downstream MAPK signalling in cultured cells with BRAF mutations. Importantly, these compounds did not activate MAPK signalling in those cell lines with additional mutations that cause basal activation of this pathway.

**ORIGINAL ARTICLE** Zhang, C. *et al.* RAF inhibitors that evade paradoxical MAPK pathway activation. *Nature* 526, 583–586 (2015)

 CNS CANCER**TERT alterations define high-risk neuroblastoma**

Only a few genes are recurrently mutated in patients with neuroblastoma. In a new study, whole-genome sequencing was used to analyse tumour samples from 39 patients with high-risk neuroblastoma and 17 patients with low-risk neuroblastoma. Rearrangements affecting the telomerase reverse transcriptase (*TERT*) gene were found in 31% of patients with high-risk neuroblastoma, but not in patients with low-risk disease. These results were confirmed in an additional cohort ( $n = 75$  high-risk;  $n = 86$  low-risk).

**ORIGINAL ARTICLE** Peifer, M. *et al.* Telomerase activation by genomic rearrangements in high-risk neuroblastoma. *Nature* 526, 700–704 (2015)

 RADIO THERAPY**Partial breast irradiation is a valid option**

Whole-breast irradiation is the standard radiotherapy technique used after breast-conserving surgery. In the accelerated partial breast irradiation (APBI) protocols, only the lumpectomy bed plus a 1–2 cm margin are irradiated. The utility of APBI as sole adjuvant radiation therapy for early invasive and *in situ* breast cancer was investigated in a phase III randomized trial performed in 16 European hospitals. In patients who received APBI, disease-free survival and overall survival were similar to patients who received conventional whole-breast irradiation, validating APBI as an adjuvant radiation therapy option for breast cancer.

**ORIGINAL ARTICLE** Strnad, V. *et al.* 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and *in-situ* carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet* doi:10.1016/S0140-6736(15)00471-7

 BREAST CANCER**Mastectomy — not always required**

Patients with nonmetastatic invasive breast tumours >5 cm are usually not eligible for lumpectomy and radiation as a treatment option; instead, mastectomy is considered as a safer therapeutic choice for these patients. Now a study has evaluated data from 5,685 patients with breast tumours >5 cm who underwent breast surgery between 1992 and 2009. Only 15.6% of these patients underwent breast-conserving surgery. The adjusted overall and breast-cancer-specific survival rates were equivalent regardless of whether the patients underwent mastectomy or breast-conserving surgery.

**ORIGINAL ARTICLE** Bleicher, R. J. *et al.* Breast conservation versus mastectomy for patients with T3 primary tumors (>5 cm) a review of 5685 medicare patients. *Cancer* doi:10.1002/cncr.29726