# **RESEARCH HIGHLIGHTS**

Nature Reviews Clinical Oncology | Published online 24 May 2016

# **IN BRIEF**

## SKIN CANCER

### DT01 DNA-repair inhibitor shows promise

A number of therapies have been approved for patients with metastatic melanoma, but responses are often limited and mortality remains high; therefore, new therapeutic options are needed. In a phase I trial, a novel DNA-repair inhibitor, DT01, was evaluated in 23 patients with melanoma skin metastases. DT01 is an injectable oligonucleotide mimic of DNA lesions that sequesters the DNA-repair machinery from lesions in genomic DNA. Thus, DT01 was used in combination with radiotherapy to induce genomic lesions. Dose escalation revealed no dose-limiting toxicities after intratumoural and peritumoural injection of DT01, and a maximum tolerated dose was not reached; grade 1–2 injection-site reactions were the most common adverse events. Evaluation of efficacy at 76 lesions in 21 patients revealed promising objective and complete response rates of 59% and 30%, respectively.

ORIGINAL ARTICLE Le Tourneau, C. *et al.* First-in-human phase I study of the DNA-repair inhibitor DT01 in combination with radiotherapy in patients with skin metastases from melanoma. *Br. J. Cancer* <u>http://dx.doi.org/10.1038/bjc.2016.120</u> (2016)

#### HAEMATOLOGICAL CANCER

#### Study provides clearer genetic landscape of APL

The PML-RARA fusion is pathognomic in acute promyelocytic leukaemia (APL); however, other mutations have also been implicated in APL pathogenesis. Whole-genome sequencing of 12 primary diagnosis samples and eight matched relapse samples revealed 109 genes harbouring nonsilent mutations. Subsequently, targeted sequencing was performed on these 109 genes, as well as another 289 genes implicated in APL, in 153 primary and 69 relapse samples. Apart from the PML-RARA fusion, the most frequent recurrent alterations in primary AML samples were in FLT3, WT1, NRAS, and KRAS, as well as previously unidentified mutations in the ARID1A and ARID1B genes that both encode components of the SWI–SNF complex. Of note, ARID1B was mutated at a higher frequency at relapse than in primary samples, as were PML, RARA, and RUNX1. These genes are thus implicated in treatment resistance. Results of in vitro experiments suggested that loss of ARID1B impairs treatment-induced cell differentiation.

ORIGINAL ARTICLE Madan, V. et al. Comprehensive mutational analysis of primary and relapse acute promyelocytic leukemia. *Leukemia* <u>http://dx.doi.org/10.1038/leu.2016.69</u> (2016)

#### GASTROINTESTINAL CANCER

#### Dietary marine ω-3 fatty acids and CRC risk

Immunomodulatory dietary marine  $\omega$ -3 polyunsaturated fatty acids (PUFAs) are hypothesized to protect against the development of cancer, particularly colorectal cancer (CRC). Now, a large prospective cohort study has been conducted to test this hypothesis in 173,229 white individuals. After a follow-up duration of 2,895,704 person-years, 2,504 CRCs were reported, 614 of which were analysed for FOXP3+ regulatory T ( $T_{reg}$ -cell infiltation. A daily marine  $\omega$ -3 PUFA intake of  $\geq$ 0.35 g versus <0.15 g was associated with a reduced risk of  $T_{reg}$ -cell-high CRC (multivariable HR 0.57;  $P_{trend}$  <0.001), but not  $T_{reg}$ -cell-low tumours (HR 1.14;  $P_{trend}$  =0.77;):  $P_{heterogeneity}$  =0.01. The suppressive role of  $T_{reg}$  cells on effector T cells was reduced by around twofold after treatment with a  $\omega$ -3 PUFA in vitro. These findings support the immunopreventive role of dietary marine  $\omega$ -3 PUFAs in CRC via modulation of  $T_{reg}$  cells.

**ORIGINAL ARTICLE** Song, M. *et al.* Marine ω-3 polyunsaturated fatty acid intake and risk of colorectal cancer characterized by tumour-infiltrating T cells. JAMA Oncol. http://dx.doi.org/10.1001/jamaoncol.2016.0605 (2016)