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IN BRIEF

IMMUNOTHERAPY

CAR T cells drive remission after alloHSCT, without GvHD as a passenger

After allogeneic haematopoietic stem-cell transplantation (alloHSCT), many patients with progressive B-cell malignancies receive unmanipulated donor lymphocyte infusions; however, responses are often poor and graft-versus-host disease (GvHD) is common. Infusion of genetically engineered T cells that express a chimeric antigen receptor (CAR) targeting the B-cell antigen CD19 might be a more-effective post-alloHSCT therapy, but GvHD remains a concern. In a new study, eight of 20 patients who received anti-CD19 CAR T cells achieved remission, including six complete remissions. In particular, four of five patients with acute lymphoblastic leukaemia achieved complete remission, and a patient with chronic lymphoblastic leukaemia had an ongoing complete response of >30 months. Importantly, none of the patients had acute GvHD. These results support a key role for CAR T cells in the future of alloHSCT.

ORIGINAL ARTICLE Brudno, J. N. *et al.* Allogeneic T cells that express an anti-CD19 chimeric antigen receptor induce remissions of B-cell malignancies that progress after allogeneic hematopoietic stem-cell transplantation without causing graft-versus-host disease. *J. Clin. Oncol.* http://dx.doi.org/10.1200/JCO.2015.64.5929 (2016)

LUNG CANCER

Metabolic heterogeneity and paradoxical glucose usage in NSCLC

Genetic and microenvironmental factors are known to influence tumour metabolism, and these factors vary considerably among patients with non-small-cell lung cancers (NSCLCs). Investigators have now examined the uptake of ^{13}C-glucose intraoperatively in nine patients with NSCLC, revealing that tumour tissues have increase glycolysis and glucose oxidation compared with adjacent benign lung tissues; however, they observed considerable heterogeneity in the metabolic pathways used, both within and between tumours. Multiple alternatives to glucose (such as lactate) were oxidized in all tumours and, unexpectedly, the use of alternative nutrients was common in highly perfused regions of the tumours — where presumably glucose is abundant. These results highlight gaps in our understanding of tumour metabolism.

ORIGINAL ARTICLE Hensley, C. T. *et al.* Metabolic heterogeneity in human lung tumors. *Cell* http://dx.doi.org/10.1016/j.cell.2015.12.034 (2016)

HAEMATOLOGICAL CANCER

Digging deep to reveal how the mutational dynamics of CLL might inform patient management

Ultra-deep next-generation DNA sequencing of genes commonly mutated in patients with chronic lymphocytic leukaemia (CLL) has been used to investigate the clonal and subclonal dynamics of the disease. Subclonal mutations were found to be common, with or without clonal mutations. Importantly, clonal *SF3B1* mutations, and clonal or subclonal mutations in *ATM* and *NOTCH1* predicted shorter time to first treatment, independent of *IGHV* mutational status. Moreover, clonal and subclonal mutations in *TP53*, and clonal mutations in *NOTCH1* were associated with shorter overall survival. Clonal evolution occurred over time, particularly after treatment, but was also observed in untreated patients. These results suggest that longitudinal evaluation of the clonal architecture of CLL could guide patient management.

ORIGINAL ARTICLE Nadeu, F. *et al.* Clinical impact of clonal and subclonal *TP53*, *SF3B1*, *BIRC3*, *NOTCH1* and *ATM* mutations in chronic lymphocytic leukemia. *Blood* http://dx.doi.org/10.1182/blood-2015-07-659144 (2016)