IN BRIEF

HAEMATOLOGICAL CANCER

Nivolumab effective in treatment-resistant HL

Outcomes of CheckMate 205, a phase II trial, confirm the efficacy of the anti-programmed cell death protein 1 (PD-1) antibody nivolumab in patients with Hodgkin lymphoma (HL) with treatment failure after autologous haematopoietic stem cell transplantation (auto-HSCT), regardless of prior treatment with brentuximab vedotin. A total of 243 patients were divided into three groups based on brentuximab vedotin treatment status: no previous treatment; treatment before auto-HSCT; or treatment after auto-HSCT. An objective response rate of 69% was observed across the entire study cohort, with response rates ≥63% observed in each group and a median progression-free survival duration of 14.7 months. Grade 3–4 adverse events were rare and included increased serum lipase levels (in 5% of patients) and neutropenia (3%). These findings demonstrate that nivolumab is safe and effective in this historically difficult to treat population, regardless of previous treatments received.

ORIGINAL ARTICLE Armand, P. et al. Nivolumab for relapsed/refractory classic Hodgkin lymphoma after failure of autologous hematopoietic cell transplantation: extended follow-up of the multicohort single-arm phase II CheckMate 205 trial. *J. Clin. Oncol.* https://doi.org/10.1200/JCO.2017.76.0793 (2018)

IMMUNOTHERAPY

Combination effective against brain metastases

The findings of a multicentre, open-label, randomized phase II study demonstrate the efficacy of combined inhibition of the programmed cell death protein 1 (PD-1) and cytotoxic T lymphocyte protein 4 (CTLA-4) immune checkpoints with nivolumab and ipilimumab, respectively, in patients with melanoma brain metastases. Of 36 patients who received combination immunotherapy, 16 (46%) had intracranial responses versus 5 (20%) of the patients who received nivolumab alone. Patients with neurological symptoms were assigned to a separate treatment group, of which only one patient (6%) had a response to nivolumab monotherapy. Patients receiving combination therapy had an increased risk of grade 3–4 adverse events (54%), versus 16% and 12% of patients receiving nivolumab alone.

ORIGINAL ARTICLE Long, G. V. et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicentre randomised phase 2 study. *Lancet Oncol.* https://doi.org/10.1016/S1470-2045(18)30139-6 (2018)

LUNG CANCER

Crizotinib active in patients of East Asian ethnicity

ROS1 rearrangements occur in 2–3% of East Asian patients with advanced-stage non-small-cell lung cancer (NSCLC). Now, data from a phase II study demonstrate the efficacy of targeting this alteration using the tyrosine-kinase inhibitor crizotinib in this patient population. In a single-arm trial, the efficacy of crizotinib was investigated in 127 patients with confirmed ROS1-positive NSCLC who received three or fewer prior lines of therapy. An overall response rate of 71.7% was observed with a median duration of 19.7 months, including 17 complete responses and 74 partial responses. Grade 3–4 adverse events occurred in 25.2% of patients, among which neutropenia (10.2%) and elevated serum transaminase levels (5.5%) were the most commonly observed. This study confirms the efficacy of crizotinib in patients of East Asian ethnicity, with response rates similar to those reported in trials involving European patients with advanced-stage ROS1-positive NSCLC.

ORIGINAL ARTICLE Wu, Y. L. et al. Phase II study of crizotinib in East Asian patients with ROS1-positive advanced non–small-cell lung cancer. *J. Clin. Oncol.* https://doi.org/10.1200/JCO.2017.75.5587 (2018)

LUNG CANCER

Pembrolizumab synergizes with chemotherapy

The outcomes of patients with chemotherapy-resistant advanced-stage and/or metastatic non-small-cell lung cancer (NSCLC) have improved considerably following the introduction of immune-checkpoint inhibitors, such as the anti-programmed cell death 1 (PD-1) antibody pembrolizumab; however, the value of these agents in the first-line setting remains unclear. Now, data from the phase III KEYNOTE-189 trial confirm that the addition of pembrolizumab to first-line chemotherapy improves the outcomes of patients with metastatic NSCLC.

"About 25–30% of patients have high programmed cell death 1 ligand 1 (PD-L1) expression [tumour proportion score ≥50%] and for them pembrolizumab is superior to chemotherapy, but for the majority, first-line platinum-based chemotherapy remains the standard of care (and a poor standard, with a survival benefit of a couple of months)," explains lead author Leena Gandhi. "Combining platinum–pemetrexed chemotherapy with pembrolizumab could provide immunogenic stimulation and thus broaden the potential for benefit from pembrolizumab to a larger group of patients," she adds.

Patients with treatment-naive metastatic NSCLC without sensitizing mutations in *EGFR* or *ALK* were randomly assigned in a 2:1 ratio to receive either pembrolizumab or placebo, plus cisplatin or carboplatin and pemetrexed. Both groups were matched in terms of clinical characteristics, including level of PD-L1 expression.

At a median follow-up duration of 10.5 months, patients in the pembrolizumab group had significantly improved median progression-free survival (8.8 months versus 4.9 months; $P < 0.001$)

IMMUNOTHERAPY

Only the best CAR T cells

Patients with chronic lymphocytic leukaemia (CLL) have variable responses to therapy with anti-CD19 chimeric antigen receptor (CAR) T cells (CTL019). New research reveals the association of a specific CTL019 cell population with favourable clinical outcomes.

"We hypothesized that the expansion and persistence of CAR T cells is the dominant driving feature of therapeutic success," explains Jos Melenhorst, lead investigator of this study. In a group of 41 patients with advanced-stage CLL who had received at least one dose of CTL019 cells, response to therapy was preceded by a robust in vivo expansion of CTL019 cells. This expansion was not correlated with patient or disease characteristics. Through transcriptional analyses of pre-manufacturing T cells and functional validation studies of pre-infusion CTL019 cells, IL-6–STAT3 signalling was identified as the pathway involved in the expansion of a $CD8^+$ population associated with a favourable response to therapy. Of note, in an in vivo stimulation assay, increased levels of STAT3 activation were detected in CTL019 cells from a patient with a complete response compared with those from a patient with no response to therapy.

Biomarker profiling revealed that $CD27^+PD\text{-}1^-CD8^+$ cells are the subpopulation that expands upon IL-6 stimulation and is associated with robust therapeutic responses.