IN BRIEF

MELANOMA

Interferon enhances immune-checkpoint inhibition

Type I interferon (IFN) signalling is involved in the antitumour immune response in patients with melanoma. The combination of pegylated (PEG)-IFNα2b with the anti-PD-1 antibody pembrolizumab was tested in a phase Ib/II trial involving 43 patients with stage IV melanoma. At a median follow-up duration of 25 months, the objective response rate was 60.5% and 46.5% of patients had ongoing responses. The median progression-free survival duration was 11.0 months in the whole cohort and not reached in patients with a response. The median overall survival duration was not reached. Grade 3–4 treatment-related adverse events (AEs) occurred in 48.8% of patients and immune-related AEs of any grade in 34.9% of patients. No treatment-related deaths were observed. Results from large-cohort randomized trials are needed to further determine the potential clinical benefit of adding IFNα to immune-checkpoint inhibitors.

ORIGINAL ARTICLE Davar, D. et al. Phase Ib/II study of pembrolizumab and pegylated-interferon alfa-2b in advanced melanoma. *J. Clin. Oncol.* https://doi.org/10.1200/JCO.18.00632 (2018)

PAEDIATRIC CANCER

Outcomes depend on tumour histology

In a phase III trial, children with newly diagnosed supratentorial primitive neuroectodermal tumour of the central nervous system (CNS-PNET) or pineoblastoma were randomly assigned to receive additional carboplatin during standard chemoradiotherapy after surgery, and subsequently to receive maintenance chemotherapy with or without adjuvant isotretinoin. Of 60 patients, 31 had tumours with a nonpineal location, 18 of which were high-grade gliomas (HGGs), not intended for trial inclusion. At 5 years, event-free survival was 62.8% for patients with CNS-PNETs or pineoblastoma and 5.6% for those with HGG, and overall survival was 78.5% and 12.0%, respectively. Survival outcomes were not significantly affected by therapy, which indicates that an accurate histological diagnosis is needed to spare children with HGG from receiving unnecessary treatments.

ORIGINAL ARTICLE Hwang, E. I. et al. Extensive molecular and clinical heterogeneity in patients with histologically diagnosed CNS-PNET treated as a single entity: a report from the children's oncology group randomized ACNS0332 trial. *J. Clin. Oncol.* https://doi.org/10.1200/JCO.2017.76.4720 (2018)

HAEMATOLOGICAL CANCER

Benefit with VR-CAP in mantle cell lymphoma

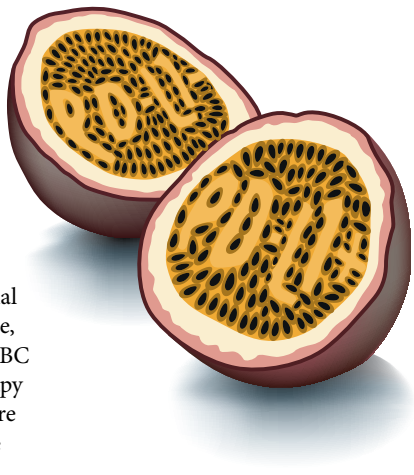
In the phase III LYM-3002 trial, patients with untreated stage II–IV mantle cell lymphoma were randomly assigned to receive either rituximab, cyclophosphamide, doxorubicin, bortezomib, and prednisone (VR-CAP) or rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). In an 82-month follow-up analysis of 140 patients in the VR-CAP group and 128 patients in the R-CHOP group, median overall survival was significantly longer in the VR-CAP group (90.7 months versus 55.7 months; $P = 0.001$). The toxicity profile of both regimens was considered manageable: discontinuation owing to treatment-related adverse events (AEs) occurred in 8% of patients in the VR-CAP group and 6% of the R-CHOP group; 4% of patients in each group died owing to treatment-related AEs.

ORIGINAL ARTICLE Robak, T. et al. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. *Lancet Oncol.* https://doi.org/10.1016/S1470-2045(18)30685-5 (2018)

IMMUNOTHERAPY

Benefit in patients with PD-L1-positive TNBC

Patients with metastatic triple-negative breast cancer (TNBC) typically have overall survival (OS) durations of ≤18 months after diagnosis. Two newly published studies reveal that a subgroup of patients with TNBC can derive an OS benefit from immune-checkpoint inhibitors.



Credit: Simon Bradbrook/Springer Nature Limited

The phase III IMpassion130 trial involved patients with unresectable, locally advanced or metastatic TNBC who had received prior radiotherapy and/or chemotherapy. Patients were randomly assigned (1:1) to receive nab-paclitaxel plus either the anti-PD-L1 antibody atezolizumab or placebo. The percentage of patients with expression of PD-L1 on ≥1% of tumour-infiltrating immune cells was 41% in both arms.

At a median follow-up duration of 12.9 months, median progression-free survival (PFS) was longer with atezolizumab than with placebo, both in the intention-to-treat (ITT) population (7.2 months versus 5.5 months; $P = 0.002$) and in those with PD-L1$^+$ disease (7.5 months versus 5.0 months; $P < 0.001$). The first interim OS analysis revealed favourable outcomes with atezolizumab versus placebo: 21.3 months versus 17.6 months in the ITT population ($P = 0.08$), and 25.0 months versus 15.5 months in the PD-L1$^+$ subgroup.

"This is the first phase III trial with positive survival results in TNBC, with a nearly 10-month OS benefit observed in a subgroup of patients," summarizes Peter Schmid, co-lead investigator of the trial. "Importantly, PD-L1 proved to be a biomarker of benefit from therapy. Our next task is to improve the outcomes of patients who are negative for the expression of this biomarker," he adds.

IMpassion130 was preceded by GP28328, a phase Ib study also involving patients with unresectable stage III–IV TNBC. In this trial, 33 patients received nab-paclitaxel plus atezolizumab. At 24.4 months, median PFS was numerically longer in patients previously untreated disease than in those who had received prior chemotherapy (8.6 months versus 5.1 months), and in patients with PD-L1$^+$ tumours versus those with PD-L1$^-$ tumours (6.9 months versus 5.1 months). Consistent OS data were observed: 24.2 months versus 12.4 months, and 21.9 months versus 11.9 months, respectively.

"Both trials allowed the omission of nab-paclitaxel if a good response to immunotherapy was detected. This approach can greatly improve the quality of life (QOL) of patients," highlights Sylvia Adams, who was involved in both trials. "QOL data will be available next year; at the moment, the toxicity profile seems favourable," clarifies Schmid.

"Patients with TNBC do not have many treatment options beyond chemotherapy. We can learn a lot from these studies about how to develop additional immunotherapy strategies for these patients, and how to implement them in the clinic," summarizes Leisha Emens, co-lead investigator of IMpassion130.

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ORIGINAL ARTICLES Schmid, P. et al. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1809615 (2018) | Adams, S. et al. Atezolizumab plus nab-paclitaxel in the treatment of metastatic triple-negative breast cancer with 2-year survival follow-up: a phase 1b clinical trial. *JAMA Oncol.* https://doi.org/10.1001/jamaoncol.2018.5152 (2018)