JOURNAL CLUB

What's hot that the other lot got

Alice Davies

ADDITION OF DURVALUMAB TO FIRST-LINE CHEMOTHERAPY IN SMALL CELL LUNG CANCER

Prognosis and treatment options for small cell lung cancer (SCLC) remain poor and it is yet to see the benefits in prognosis conferred by immunotherapy in non-SCLC. CASPIAN was a randomised, open-label, phase III trial assessing the efficacy and safety of durvalumab (a monoclonal antibody that blocks PD-L1), with or without tremelimumab (a monoclonal antibody against CTLA-4) in combination with chemotherapy with platinum–etoposide, for the first-line treatment of patients with extensive stage SCLC (ES-SCLC). A total of 805 treatment-naive patients across 20 sites were randomly assigned into each cohort 1:1:1. Paz-Ares *et al* (*Lancet* 2019:doi10.1016/S0140-6736(19)32222-6) report the interim survival analysis of the durvalumab plus platinum–etoposide versus platinum–etoposide groups. The addition of durvalumab was associated with a significant improvement versus chemotherapy alone in clinical outcomes including overall survival, with a HR of 0.73 (95% CI 0.59 to 0.91; p=0·0047); median overall survival was also prolonged at 13.0 (95% CI 11.5 to 14.8) months versus 10.3 (95% CI 9.3 to 11.2) months. Similar adverse events profiles were reported in both groups. These results align with those reported in IMpower133 trial despite some notable differences in trial design. While these results are encouraging, longer follow-up is required as well as analyses of significance of biomarkers such as PD-L1 expression and tumour mutation burden.

PROLONGED LUNG CANCER SCREENING REDUCES 10-YEAR MORTALITY

The role of lung cancer screening remains controversial. Pastorino *et al* (*Ann Oncol* 2019;30:1162) report results of prolonged screening beyond 5 years from The Multicentric Italian Lung Detection (MILD) trial. The MILD study was a prospective randomised controlled lung cancer screening trial in which 4099 participants were randomised to a screening (n=2376) or usual care (n=1723). The screening arm was further randomised to annual or biennial low-dose CT (LDCT) screening. Lung cancer (LC) was diagnosed in 98 participants (431/100 000 person-years) in the screening arm and 60 participants (373/100 000 person-years) in the control arm. Patients undergoing screen had LC detected earlier and was more likely to be surgically resected (65% vs 27%, p<0.0001). At 10 years screening was associated with a reduced risk of all cause (HR 0.61, 95%CI 0.39 to 0.95) and LC specific (HR 0.80, 95%CI 0.62 to 1.03) mortality. The benefit of screening appeared greater after the fifth year. The resection rate of benign lesions was similar between groups. These longer-term follow-up data will add support to the case for nationwide LDCT screening.

COMBINATION IMMUNOTHERAPY IN ADVANCED NON-SCLC (NSCLC)

Immunotherapy with combination nivolumab (PD-1 blocker) plus ipilimumab (CTLA-4 inhibitor) in NSCLC has shown possible improved response rates; however, long-term survival follow-up data were lacking. Hellman *et al* (*New Engl J Med* 2019;doi:10.1056/NEJMoa1910231) report initial results from CheckMate227, a randomised, open-label, phase III trial. A total of 1739 adults with squamous or non-squamous stage IV or recurrent NSCLC, without driver mutations and an ECOG performance status score of 0 or 1 were stratified for PD-L1 expression (1% or more vs <1%). Patients with a PD-L1 <1% were randomised to receive nivolumab plus ipilimumab, nivolumab plus chemotherapy or chemotherapy; those with expression >1% received nivolumab monotherapy rather than combination with chemotherapy. There was a significantly improved survival in patients who received nivolumab plus ipilimumab compared with those who received chemotherapy (17.1 months, 95% CI 15.2 to 19.9 vs 13.9 months, 95% CI 12.2 to 15.1) regardless of PD-L1 expression. Importantly, there was no increase in grade 3 or 4 treatment-related adverse events (32.8% vs 36.0% respectively). Although not powered to compare nivolumab plus ipilimumab versus nivolumab monotherapy, the authors comment on better efficacy with the addition of ipilimumab. While further data are required, the study does provide evidence for the combination of immunotherapies in the future for the treatment of NSCLC.

USING DEEP LEARNING–BASED CLASSIFICATION OF MESOTHELIOMA TO PREDICT PATIENT OUTCOME

Despite overall poor outcomes in mesothelioma, there is significant variability related to tumour type and grade. Achieving a definitive histological diagnosis can be challenging and may impact on patient outcome. Courtiol *et al* (*Nat Med*;25:1519) report on using deep convolution neural networks, called MesoNet, to predict patient survival from whole-slide digitised images of standard clinical biopsies. MesoNet developed an algorithm to distinguish histological subtypes and markers located in the stroma and predict patient survival. The system was trained and tested using 2981 slides from the French MESOBANK/MESOPATH cohort, randomly divided into 2300 for training, 681 for testing. External validation was obtained from 56 images from The Cancer Genome Atlas (TCGA). TCGA samples were used as they came from different centres and employed a different slide colouration. MesoNet performance was then compared with other predictive models of increasing complexity: a pathologist-provided histology type (Histo), a histological type and tumour grade (Histo/Grade) and a naïve machine-learning approach (Meanpool). A *c* index was used to compare the predictive performance of each model. MesoNet performed better than Histo on the train, test and TCGA samples but less well compared with the Meanpool for train and test but better on the TCGA samples. MesoNet can identify both previously known predictive histological features as well as novel features which help with survival prediction. It remains to be seen if such systems will support clinical practice independently or aid pathologists in classifying mesothelioma types.

Correspondence to Dr Alice Davies, Lungs for Living Research Centre, UCL Respiratory, University College London, London WC1E 6JF, UK; alice.davies@ucl.ac.uk

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Davies A. *Thorax* 2020;**75**:192.

Published Online First 20 January 2020

Thorax 2020;**75**:192.
doi:10.1136/thoraxjnl-2019-214409