LUNG CANCER

Doublet therapy effective in elderly patients

Pemetrexed plus platinum-based chemotherapy has emerged as an effective combination in patients with nonsquamous non-small-cell lung cancer (NSCLC). However, the efficacy of this combination in elderly patients (≥75 years of age) with advanced-stage disease remains unknown. Now, data from a phase III trial demonstrate the efficacy of pemetrexed plus cisplatin in this setting.

A total of 433 elderly patients with chemotherapy-naive advanced-stage non-squamous NSCLC (stage IV disease, or stage III and not amenable to radiotherapy) were randomly assigned (1:1) to receive carboplatin plus pemetrexed followed by maintenance pemetrexed versus docetaxel monotherapy. Overall survival (OS) was the primary end point of this study.

At a median follow-up duration of 17.1 months, patients in the carboplatin plus pemetrexed group had a median OS of 18.7 months versus 15.5 months (stratified HR 0.85, 95% CI 0.68–1.06; $P_{noninferiority} = 0.003$). Progression-free survival (PFS) outcomes also favoured carboplatin plus pemetrexed: median 6.4 months versus 4.3 months (unstratified HR 0.74, 95% CI 0.61–0.9; $P < 0.001$).

More patients in the docetaxel group discontinued therapy owing to tolerability (13.6% versus 9.8%), although type of events varied: patients receiving docetaxel were more likely to have grade 3–4 neutropenia (86.0% versus 46.3%), white blood cell count (68.7% versus 28.0%) and febrile neutropenia (17.8% versus 4.2%), while those receiving carboplatin plus pemetrexed were more likely to have grade 3–4 anaemia (29.4% versus 1.9%) and reductions in platelet count (25.7% versus 1.4%).

These data demonstrate the noninferiority of carboplatin plus pemetrexed in elderly patients with nonsquamous NSCLC. No significant improvement in OS was observed, although secondary end points support the use of carboplatin plus pemetrexed.

Peter Sidaway

ORIGINAL ARTICLE Okamoto, I. et al. Comparison of carboplatin plus pemetrexed followed by maintenance pemetrexed with docetaxel monotherapy in elderly patients with advanced nonsquamous non–small cell lung cancer. *JAMA Oncol.* https://doi.org/10.1001/jamaoncol.2019.6828 (2020)

GASTROINTESTINAL CANCER

Benefit from pemigatinib in cholangiocarcinoma

Virtually no effective therapies are available for the substantial proportion of patients with cholangiocarcinoma with disease progression after surgery and standard-of-care chemotherapy with gemcitabine plus cisplatin. Now, results of the single-arm phase II FIGHT-202 trial provide evidence of clinical benefit with the FGFR1–3 inhibitor pemigatinib in this setting.

FIGHT-202 involved patients with locally advanced or metastatic cholangiocarcinoma harbouring *FGFR2* fusions or rearrangements ($n = 107$), other alterations in *FGF* or *FGFR* ($n = 20$) or no alterations in these genes ($n = 18$), with disease progression after at least one line of systemic therapy. At a median of 17.8 months, 38 patients with *FGFR2* fusions or rearrangements (35.5%; 95% CI 26.5–45.4) had an objective response, including three complete responses. No responses were observed in the other two subgroups. The median progression-free survival durations were 6.9 months, 2.1 months and 1.7 months in patients with *FGFR2* fusions or rearrangements, other *FGF* or *FGFR* alterations and no alterations, respectively. Although data were not mature at the time of reporting, the median overall survival durations were 21.1 months, 6.7 months and 4.0 months, respectively. The incidence of grade ≥3 and serious AEs was 64% and 45%, respectively; 6 patients had fatal AEs that were not deemed to be treatment-related.

The results of FIGHT-202 suggest that the 10–16% of patients with cholangiocarcinoma harbouring *FGFR2* fusions might derive considerable benefit from pemigatinib. These results warrant further studies including an active comparator arm to further establish the clinical benefit from premigatinib in this population.

Diana Romero

ORIGINAL ARTICLE Abou-Alfa, G. K. et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. *Lancet Oncol.* https://doi.org/10.1016/S1470-2045(20)30109-1 (2020)

PROSTATE CANCER

PSMA PET–CT improves staging

The limited performance of conventional CT and bone scanning in detecting non-localized prostate cancer during primary staging can lead to suboptimal treatment. Now, evidence from the phase III proPSMA trial indicates that prostate-specific membrane antigen (PSMA) PET–CT is a superior staging modality.

In proPSMA, 302 men with biopsy-proven high-risk localized prostate cancer were randomly assigned (1:1) to first-line imaging with either gallium-68 PSMA-11 PET–CT or conventional single-photon emission CT plus technetium-99m bone scanning. The primary outcome of the trial was the accuracy of first-line imaging for identifying pelvic nodal or distant metastatic disease, as defined by the receiver-operating curve using a predefined reference standard comprising histopathology, imaging and biochemical analyses after a follow-up duration of 6 months.

PSMA PET–CT had greater accuracy than conventional imaging (area under the curve (AUC) 92% versus 65%; $P < 0.0001$), reflecting the higher sensitivity and specificity of the former modality (85% versus 38% and 98% versus 91%, respectively). Subgroup analyses revealed that PSMA PET–CT was superior in the detection of both pelvic nodal metastases (AUC 91% versus 59%) and distant metastases (AUC 95% versus 74%), and yielded similar absolute improvements in accuracy independent of Gleason grade group or serum prostate-specific antigen concentration.

Accordingly, PSMA PET–CT findings more often prompted a change in treatment intent, modality or technique than did conventional imaging (28% versus 15%; $P = 0.008$) and resulted in fewer equivocal findings (7% versus 23%; $P < 0.001$). Moreover, patients were exposed to less radiation with PSMA PET–CT (8.4 mSv versus 19.2 mSv; $P < 0.001$), and inter-reader agreement was high ($\kappa = 0.87–0.88$).

The proPSMA trial fills a knowledge gap left by previous case series evaluating PSMA PET–CT, which lacked comparisons with a reference standard. The results of this trial indicate a suitable replacement for conventional imaging in prostate cancer staging. Health-economic analyses are required, however, to support widespread reimbursement and uptake.

David Killock

ORIGINAL ARTICLE Hofman, M. S. et al. *Lancet* https://doi.org/10.1016/S0140-6736(20)30314-7 (2020)