AACR Annual Meeting 2019

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The AACR annual meeting was held on March 29–April 3, 2019, in Atlanta, GA, USA.

Breakthroughs for pancreatic cancer?

Three US studies have found potential advances in the treatment of pancreatic cancer. Phase 1 data presented by Kyle C Cuneo from the University of Michigan (Ann Arbor, MI, USA) testing a new Wee1 inhibitor (ADZ1775) in combination with gemcitabine and radiotherapy in 34 patients with locally advanced cancer showed an overall survival of 21·7 months (95% CI 16·7–24·7). Anorexia, nausea, and fatigue were the most common toxicities.

In comparison, Erkut H Borazanci (Virginia G. Piper Cancer Center, Scottsdale, AZ, USA) and colleagues investigated a five-drug regimen (nivolumab, nab-paclitaxel, paricalcitol [a vitamin D analogue], cisplatin, and gemcitabine) in a phase 2 trial involving patients with untreated metastatic pancreatic ductal adenocarcinoma (PDAC). Of the 25 patients enrolled thus far, overall survival has been recorded as 15·3 months, with an underlying overall response of 83%. Common adverse events were thrombocytopenia, anaemia, and colitis.

Finally, a multicentre study from across the USA by Mark H O'Hara (University of Pennsylvania, Philadelphia, PA, USA) and colleagues has looked at the use of a CD40 agonist (monoclonal antibody APX005M) to trigger a greater T-cell response in combination with nivolumab in patients with PDAC. Patients also received gemcitabine and nab-paclitaxel. Although follow-up was only 32 weeks, among the 30 patients enrolled, 14 had shown a partial response, and eight had stable disease. However, two patients died because of adverse events and two patients had dose-limiting toxicities. Despite this, the regimen will be tested in a randomised phase 2 trial.

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Mesothelioma advances

Final results from the phase 2 STELLAR trial of Tumor Treating Fields in patients with unresectable malignant mesothelioma have replicated the positive findings reported previously in patients with glioblastoma. Presenting data from 80 patients with unresectable, previously untreated mesothelioma, Giovanni L Ceresoli (Humanitas Gavazzeni, Bergamo, Italy) highlighted an overall survival of 18·2 months (95% CI 12·1–25·8). For epitheloid tumours, overall survival was 21·1 months (95% CI 13·2–25·8). Clinical benefit was achieved in 97% of patients, with dermatitis being the only side-effect of note.

Meanwhile, Prasad Adusumilli (Memorial Sloan Kettering Cancer Center, New York, NY, USA) and colleagues tested a mesothelin-targeted CAR-T therapy in a phase 1 trial including 19 patients with malignant pleural mesothelioma. The majority of patients (18 [90%] of 20) also received cyclophosphamide and an anti-PD1 checkpoint inhibitor. Two patients achieved a complete metabolic response, five had a partial response, and four achieved stable disease. No CAR T-cell-related toxicities higher than grade 2 were observed. The trial continues.

Triple negative breast cancer

A new triplet regimen shows promising antitumour activity in unresectable locally advanced or metastatic triple-negative breast cancer, according to results from an international phase 1b trial lead by Peter Schmid (Barts Cancer Institute, London, UK). Among 26 patients treated with ipatasertib (AKT inhibitor), atezolizumab (PD-L1 inhibitor), and nab-paclitaxel as first-line therapy, 19 (73%) achieved a confirmed overall response. 14 (54%) of 26 patients had grade 3 or worse adverse events, but all were manageable.

Metastatic melanoma

Patients with advanced melanoma progressing after previous PD-1-blocking antibodies respond well to a combination of entinostat and pembrolizumab. Ryan Sullivan (Massachusetts General Hospital, Boston, MA, USA) presented findings from an open-label study showing the doublet therapy had clinical benefit in 32% (95% CI 20–46) of 53 patients and a median progression-free survival of 4·2 months. Grade 3–4 treatment-related adverse events included neutropenia, fatigue, and hyponatraemia.

By contrast, a phase 1 trial of a novel PKC inhibitor (LXS196) for metastatic uveal melanoma yielded a clinical benefit of 77%. Reporting on behalf of a global team of colleagues, Ellen Kapiteijn (Leiden University Medical Centre, Leiden, Netherlands) highlighted that in this dose-finding study of 68 patients, the drug had tolerable toxicity and preliminary activity in line with preclinical predictions. Of 17 evaluable patients, two had confirmed partial responses and 12 had stable disease as their best response. The most common dose-limiting toxicity was hypotension, which was manageable with LXS196 interruption and dose reduction.

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