2015 ASCO Annual Meeting

CheckMate 057
Luis Paz-Ares (Hospital Universitario Virgen Del Rocio, Sevilla, Spain) presented data from the phase 3 CheckMate 057 trial, showing that patients with non-squamous non-small-cell lung cancer treated with nivolumab had significantly increased overall survival compared with those treated with docetaxel. 582 patients with advanced non-squamous non-small-cell cancer who had progressive disease after treatment with platinum-based doublet chemotherapy and a tyrosine kinase inhibitor (if applicable) were randomly assigned (1:1) to nivolumab or docetaxel. Overall survival was significantly longer in the nivolumab group than in the placebo group (HR 0·73, 95% CI 0·59–0·89, p=0·00155). Progression-free survival (PFS) did not differ significantly between the two groups (HR 0·92, 95% CI 0·77–1·11, p=0·393). Nivolumab had a better safety profile than docetaxel; 10·5% of patients in the nivolumab group had grade 3–5 treatment-related toxicities compared with 53·7% in the placebo group.

INTEGRATE
Few treatment options are available after failure of first-line or second-line chemotherapy for patients with advanced oesophagogastric cancer. Nick Pavlakis (Royal North Shore Hospital, Sydney, NSW, Australia) presented results of the phase 2 INTEGRATE trial, in which 152 patients with refractory oesophagogastric cancer were randomly assigned (2:1) to regorafenib or placebo. Median PFS was 11·1 weeks (95% CI 7·7–13·3) for regorafenib versus 3·9 weeks (3·7–4·0) for placebo (HR 0·40; p<0·0001). In pre-specified analyses, patients were stratified by nationality (Korean vs Canadian or Australian) and greater benefit was seen for Korean patients than for Canadian or Australian patients (HR 0·12 vs 0·61; p=0·0009). No other differences were reported between subgroups.

RILOMET-1
David Cunningham (Royal Marsden Hospital, Sutton, UK) presented survival results from the phase 3 RILOMET-1 trial comparing the anti-hepatocyte growth factor antibody rilotumumab plus erlotinib, cisplatin, and capcitabine with placebo for treatment-naive patients with advanced, MET-positive gastric or gastroesophageal junction cancer. 609 patients were randomly assigned (1:1) to either treatment, but the study stopped early owing to an imbalance of deaths between the groups (128 in the combination group vs 107 in the placebo group). Overall survival, PFS, and the proportion of patients attaining an overall response were significantly worse in the rilotumumab group than in the control group. More patients had peripheral oedema, hypo-albuminemia, and deep vein thrombosis in the rilotumumab group than in the placebo group.

Cabozanitinib in NSCLC
Cabozanitinib either alone or in combination with erlotinib led to significantly better PFS for patients with EGFR wild-type non-small-cell lung cancer than did treatment with erlotinib alone. Joel Neal (Stanford Cancer Institute, Stanford, CA, USA) presented results of the phase 2 ECOG-ACRIN E1512 study, in which 125 patients were enrolled, and 115 eligible patients were assigned (1:1:1) to either agent alone or both agents in combination. Patients in the erlotinib alone group had a shorter median PFS of 1·9 months than either those treated with cabozanitinib (3·9 months [HR 0·33; p=0·0002]) or those treated with the combination (4·1 months [HR 0·31; p=0·0002]). However, the combination therapy and cabozanitinib groups experienced significantly more overall high-grade toxicities than did those treated with erlotinib alone.

Immediate ADT
Gillian Duchesne (Peter MacCallum Cancer Center, East Melbourne, VIC, Australia) presented results showing that immediate androgen deprivation therapy (ADT) significantly improved overall survival and time to clinical progression compared with delayed ADT in patients with prostate cancer. The phase 3 trial enrolled either men with prostate cancer who had increasing PSA after treatment with definitive therapy or asymptomatic men who were not suitable for curative therapy. 293 patients were randomly assigned (1:1) to either immediate or delayed ADT. Overall survival was significantly longer for men given ADT immediately than for those with delayed treatment (p=0·047); 6-year survival was 86% for immediate ADT and 79% for delayed ADT.

MARIANNE
Primary results from the phase 3 MARIANNE study suggested that trastuzumab emtansine with or without pertuzumab was non-inferior to trastuzumab plus a taxane as treatment for HER2-positive breast cancer. 1095 patients with centrally assessed HER2-positive progressive or recurrent locally advanced breast cancer or untreated metastatic HER2-positive breast cancer were randomly assigned (1:1:1) to each treatment group. The primary endpoint was PFS, with statistical testing done first for non-inferiority and only for superiority if non-inferiority was reached. Paul A Ellis (Guy’s Hospital and Sarah Cannon Research Institute, London, UK) presented data showing that the trastuzumab emtansine groups had non-inferior PFS to the trastuzumab plus taxane group, although they did not show superior PFS. Overall survival was similar between groups, but toxicity profiles differed.
Surgery for oral cancer

Both overall and disease-free survival are significantly better after elective neck dissection than after therapeutic neck dissection in patients with oral cancer. 596 patients with clinically node-negative, lateralis T1 or T2 squamous cell oral carcinoma were randomly assigned (1:1) to elective or therapeutic dissection. Anil D’Cruz (Tata Memorial Hospital, Mumbai, India) showed that patients given elective dissection had significantly longer overall survival than did those given therapeutic dissection (3-year overall survival 80·0% vs 67·5% [HR 0·63, 95% CI 0·44–0·89; p=0·01]), and better disease-free survival (69·5% vs 45·9% [HR 0·44, 95% CI 0·34–0·58; p<0·001]). He proposed that elective dissection should become the new standard of care in this population.

Wee1 inhibitor in ovarian cancer

The first-in-class Wee1 inhibitor AZD1775 in combination with paclitaxel and carboplatin significantly improved PFS in women with ovarian cancer compared with paclitaxel and carboplatin alone. Amit Oza (Princess Margaret Cancer Centre, Toronto, Canada) presented results from the phase 2 trial, in which 121 women with ovarian cancer were randomly assigned (1:1) to each combination. PFS, as assessed by independent central review, was significantly longer in the AZD1775 group than in the paclitaxel and carboplatin group (median PFS 42·86 vs 34·86 weeks [HR 0·55, 95% CI 0·32–0·95; p=0·030]). 78% of patients in the AZD1775 group had grade 3 or worse treatment-related adverse events compared with 65% in the paclitaxel and carboplatin group alone.

Avelumab in ovarian cancer

Mary Disis (University of Washington School of Medicine, Seattle, WA, USA) presented results of a phase 1b expansion trial showing that the anti-PD-L1 antibody avelumab had acceptable safety and clinical activity in patients with previously treated, recurrent, or refractory ovarian cancer. Of the 23 patients who had been followed for 2 months, 14 (60·9%) achieved a best overall partial response, 11 (47·8%) had stable disease, and two (8·6%) patients had 30% tumour shrinkage after progression was reported. All-grade treatment-related adverse events were reported in 18 (78%) of 23 patients, the most common being fatigue, nausea, and diarrhoea; two (9%) of 23 patients had grade 3 or worse adverse events, but no serious adverse events were reported. Median PFS was 11·9 weeks (95% CI 5·9 to not reached) and the 24-week PFS was 33·3% (11·5–57·2). 75 women were enrolled in the expansion cohort.

GADOLIN

Laurie Helen Sehn (British Columbia Cancer Agency, Vancouver, BC, Canada) presented the primary results of a phase 3 study comparing obinutuzumab plus bendamustine with bendamustine alone in patients with rituximab-refractory indolent non-Hodgkin lymphoma. 396 patients were randomly assigned (1:1) to each treatment; after the protocol-specified interim analysis, the international data monitoring committee recommended unblinding of the study because the primary endpoint for PFS had been reached. Median PFS, as assessed by independent radiology facility review, was 14·9 months in the bendamustine alone group and was not reached for the obinutuzumab group (HR 0·55 [95% CI 0·4–0·7; p=0·00011]). Fewer grade 3 or worse adverse events were reported in the bendamustine alone group (62·1% of patients) than in the obinutuzumab group (68·0% of patients).

ENDEAVOR

Efficacy data from the phase 3 ENDEAVOR study were reported by Meletios Dimopoulos (National and Kapodistrian University of Athens, Athens, Greece). ENDEAVOR compared the efficacy of carfilzomib and dexamethasone with that of bortezomib and dexamethasone in patients with relapsed multiple myeloma. 929 patients who had received one to three previous treatments were randomly assigned (1:1) to either treatment combination. At the preplanned interim analysis, patients treated with carfilzomib and dexamethasone had significantly longer PFS than those treated with bortezomib and dexamethasone (18·7 months vs 9·4 months [HR 0·53; p=0·0001]). Common adverse events of interest were hypertension (8·9% in the carfilzomib group vs 2·6% in the bortezomib group), dyspnoea (5·6% vs 2·2%), cardiac failure (4·8% vs 1·8%), and acute renal failure (4·1% vs 2·6%). Follow-up continues for overall survival data.

PET-NECK

Patients with locally advanced head and neck cancer with nodal metastases given PET-CT guided active surveillance have similar overall survival outcomes to those with planned neck dissection. The phase 3 PET-NECK trial enrolled patients with oro-pharynx, hypopharynx, larynx, oral, or occult squamous cell cancer receiving primary radical chemoradiotherapy who were judged fit for neck dissection. 564 patients were randomly assigned (1:1) to either active surveillance or planned neck dissection. 54 neck dissections were done in the surveillance group, with 22 surgical complications, compared with 221 dissections in the dissection group, with 85 complications. Hisham Mehanna (University of Birmingham, Birmingham, UK) showed that overall survival did not differ between the two groups (HR 0·92 [95% CI 0·65–1·32]), suggesting non-inferiority between the two strategies.

Cassandra Coburn