2016 ASCO Annual Meeting

Published Online
June 9, 2016
http://dx.doi.org/10.1016/S1470-2045(16)30225-X

The 52nd annual meeting of the American Society of Clinical Oncology was held in Chicago, IL, USA, on June 3–7, 2016

Trastuzumab biosimilar

The phase 3, randomised, double-blind, Heritage trial showed that women with HER2-positive metastatic breast cancer treated with trastuzumab or Myl-14010, a proposed trastuzumab biosimilar, had similar overall responses (the primary endpoint) and adverse events. 500 patients were randomly assigned 1:1 to either Myl-14010 or trastuzumab plus docetaxel or paclitaxel for at least eight cycles. At week 24, the proportion of patients with an overall response was 69·6% in those treated with Myl-14010 compared with 64% for those treated with trastuzumab, the ratio of overall response for the groups was 1·09, and the 95% CI (0·954–1·237) was within the predefined equivalence margin. Safety of the two drugs were also similar: serious adverse events occurred in 38% of patients in the Myl-14010 group and 36% in the trastuzumab group. There were four deaths in each treatment group, and no significant change in cardiac function from baseline to week 24 in either group. These data suggest Myl-14010 has similar activity and safety to trastuzumab.

Personalised chemotherapy

The PANTHER study, a phase 3 multicentre trial, randomly assigned 2017 patients with node-positive or high-risk node-negative breast cancer to either tailored and dose dense chemotherapy (tailored chemotherapy group) or standard chemotherapy (control group). The tailored group received dose-dense chemotherapy on the basis of their leukocyte cell counts with epirubicin doses from 38–120 mg/m^2 (starting at 90 mg/m^2) and cyclophosphamide 450–1200 mg/m^2 (starting at 600 mg/m^2) every 2 weeks, followed by a 3 week pause, and subsequently four cycles of docetaxel 75–100 mg/m^2, (starting at 75 mg/m^2) every 2 weeks. The control group received three cycles of standard fluorouracil (500 mg/m^2), epirubicin (100 mg/m^2) and cyclophosphamide (500 mg/m^2) every 3 weeks followed by 3 cycles of docetaxel (100 mg/m^2) every 3 weeks. The primary endpoint was breast cancer relapse-free survival, which was not significantly different between the two groups at 5 years: 88·7% for the tailored group and 85% for the control groups (HR 0·79 [95% CI 0·62–1·02]; p=0·064). However, 5-year event-free survival, a secondary endpoint, was significantly better in the dose-dense tailored chemotherapy group (86·7% in the tailored chemotherapy group *vs* 82·1% in the control group, HR 0·79 [0·63–0·99]; p=0·043). Toxicity was higher in the dose-dense group as expected, with more grade 3 or 4 events in the tailored group (93%) versus the control group (21%).

Utidelone for breast cancer

A study by Binghe Xu (Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China) and colleagues has shown that the combination of utiledone plus capecitabine might represent a new treatment option for patients with metastatic breast cancer. In the randomised phase 3 trial, 405 previously treated patients with metastatic breast cancer were randomly assigned to utidelone plus capecitabine or capecitabine alone, until disease progression or unacceptable adverse events occurred. The primary endpoint was progression-free survival, and this was significantly improved in the combination treatment group compared with capecitabine alone (HR 0·58 [95% CI 0·44–0·75]; p<0·0001). With the exception of neuropathy, which was higher in the combination group compared with the capecitabine alone group (14·2% *vs* 0%), the incidence of grade 3 or 4 adverse events was similar in the utiledone plus capeciatbine group versus the capecitabine alone group: hand-foot syndrome (10% *vs* 6·7%), nausea (1·5% *vs* 1·5%), hyperbilirubinaemia (0% *vs* 1·5%), diarrhoea (5% *vs* 0%), anaemia (3·1% *vs* 3%), leukopenia (4·2% *vs* 5·2%) and neutropenia (6·5% *vs* 5·2%).

Targeting small-cell lung cancer

Phase 1 study results from a first-in-human study of rovalpituzumab tesirine (SC16LD6.5), an antibody–drug conjugate consisting of an anti-DLL3 antibody linked to the cytotoxin pyrrolobenzodiazepine, for the treatment of small-cell lung cancer, were presented by Charles Rudin (Memorial Sloan Kettering Cancer Center, New York, NY, USA). 61 patients with treatment-refractory small-cell lung cancer who had been treated with 0·2–0·4 mg/kg of SC16LD6.5 every 3 or 6 weeks were evaluable. 15 (25%; [95% CI 15–37%]) of these 61 patients achieved a best response of complete or partial response and 44 (72%; [95% CI 59–83%]) achieved at least stable disease. When tissue specimens were available, patients were evaluated for DLL-3 expression, and a correlation between higher expression and better response was observed. The most common drug-related grade 3 or higher toxicities included serosal effusions (14%), thrombocytopenia (12%), and skin reactions (8%). These results are promising given the paucity of treatments available for treatment-refractory small-cell lung cancer.

Kiran Summan

Novel therapy for gastric cancer

Salah-Eddin Al-Batran (Institute of Clinical Cancer Research, Frankfurt, Germany) presented results of the FAST trial, a randomised phase 2 trial of 161 patients with advanced gastric or gastroesophageal junction adenocarcinoma whose tumours expressed high levels of CLDN18.2 and who were treated with combination chemotherapy (epirubicin, oxaliplatin, and capecitabine) with or without IMAB362, a first-in class anti-CLDN18.2 antibody. The primary endpoint was median progression-free survival, and with a power of 70%, was significantly higher in patients treated with anti-CLDN18.2 (5·7 months) compared with patients treated with the chemotherapy alone (7·9 months; HR 0·5 [95% CI 0·35–0·78]; p=0·001). The occurrence of grade 3 or 4 adverse events was similar in both groups, and the most common adverse events in the IMAB362 group were grade 1–2 vomiting, neutropenia, and anaemia.

Inhibiting PI3K in HNSCC

Buparlisib, a novel pan-PI3K inhibitor, was studied in a 1:1 randomised phase 2 study of 158 patients with HNSCC who had recurred after treatment with platinum-based chemotherapy. Patients were randomly assigned to buparlisib and paclitaxel or placebo and paclitacel (control group). The primary endpoint was progression-free survival, which was improved in the buparlisib group compared with the control group (median progression-free survival 4·6 *vs* 3·5 months, HR 0·65 [95% 0·45–0·95]). The occurrence of grade 3 or 4 adverse events was similar between the buparlisib and the control group and included hyperglycaemia (22% *vs* 3%), anaemia (18% *vs* 12%), neutropenia (17% *vs* 5%), and fatigue (8% *vs* 10%).

Ixazomib in multiple myeloma

Two trials have studied ixazomib, an oral proteasome inhibitor, in novel combinations for the treatment of multiple myeloma. Martha Lacy (Mayo Clinic, Rochester, MN, USA) and colleagues investigated the substitution of ixazomib for bortezomib, in the combination of bortezomib, cyclophosphamide, and dexamethasome for treatment of newly diagnosed multiple myeloma in a phase 1/2 trial. 51 patients were enrolled, ten for the phase 1 part, and 41 for the phase 2 part of the trial, and treated on a 28-day cycle with 4 mg ixazomib on days 1, 8, and 15, 40 mg dexamethasone on days 1, 8, 15, and 22, and cyclophosphamide doses of 300 mg/m^2 or 400 mg/m^2 on days 1, 8, 15, and 22. The recommended phase 2 dose of cyclophosphamide was found to be 400 mg/m^2 weekly. The best confirmed response of a partial response or better occurred in 78% of patients; two patients had a complete response. Grade 3 or worse adverse events that were considered possibly related to the combination were reported in 73% of patients; the most common adverse events included cytopenia, fatigue, and gastrointestinal effects. Preliminary results were also reported for a related phase 1 dose escalation study (using a 3+3 design) that treated patients with relapsed or refractory multiple myeloma with the combination of ixazomib, pomalidomide, and dexamethasone. 21 patients were treated, 20 of whom were assessable for toxic effects, with 4 mg pomalidomide on days 1–21, 40 mg dexamethasone on days 1, 8, 15, and 22, and either 3 mg or 4 mg ixazomib on days 1, 8, and 15. One patient had a dose-limiting toxicity on the 3 mg ixazomib dose, so the study proceeded to the higher dose, for which no further dose limiting toxicities have been reported. Other adverse events considered related to pomalidomide were noted, including grade 3 anaemia (two patients), neutropenia (six patients), and thrombocytopenia (three patients). Both studies are promising and suggest that a completely oral regimen, which is more convenient, might be feasible for patients in this setting.

Liposomal drugs in AML

A phase 3 trial has shown that liposomal formulations of cytarabine and daunorubicin significantly improved overall survival in high-risk patients with AML. 309 patients with high-risk secondary AML who were aged 60–75 years were randomly assigned to either the liposomal formulation of cytarabine and daunorubicin (n=153) or standard cytarabine and daunorubicin (n=156; control group). The primary endpoint was overall survival, which was significantly improved in the liposomal forumulation group (median 9·56 months) compared with the control group (median 5·95 months; HR 0·69; p=0·005) after a minimum follow-up of 13·7 months. Frequency of adverse events of grade 3–5 were almost identical (92% *vs* 91%) in the two treatment groups, suggesting that this new treatment is promising in this high-risk setting.

CASTOR trial

The CASTOR study, a phase 3, randomised controlled trial, compared bortezomib and dexamethasone with or without daratumumab, an anti-CD38 antibody, in 498 patients with relapsed or refractory multiple myeloma. The primary endpoint was progression-free survival, which was not reached in the daratumumab group and 7·16 months in the control group (HR 0·39 [95% CI 0·28–0·53]; p<0·0001). Adverse events were similar in both groups and the most common included thrombocytopenia (59% in the daratumumab group *vs* 44% in the control group), peripheral sensory neuropathy (47% *vs* 38%), diarrhoea (32% *vs* 22%), and anaemia (26% *vs* 31%).

Isabel Lokody