tolerance of treatment, predictive markers, and presence of circulating tumor cells were secondary endpoints.

In the LAP07 study, CRT was demonstrated not to be superior to chemotherapy in the treatment of LAPC. In the chemotherapy arm, OS was 16.4 months, compared with 15.2 months in the CRT arm (HR, 1.03; 95% CI, 0.79 to 1.34; p=0.8295). Following the first randomization, there was a trend for decreased OS in the gemcitabine plus erlotinib arm at 11.9 months compared with the gemcitabine arm at 13.6 months (HR, 1.19; 95% CI, 0.97 to 1.45; p=0.093); however, this result was not statistically significant.

Following the first randomization, a greater number of patients experienced adverse events such as decreased hemoglobin, febrile neutropenia, diarrhea, and acneiform rash in the gemcitabine plus erlotinib arm, compared with the gemcitabine arm. Following the second randomization, both treatment regimens were well tolerated with a similar frequency of adverse events except for an increase in the number of patients that experienced nausea in the CRT arm (0 vs 6 patients; p=0.009).

Dr. Hammel stated that, in his opinion, the data from the LAP07 trial suggest that the standard of care for the treatment of LAPC should be chemotherapy, with CRT reserved for use as an option if the disease is controlled by chemotherapy. Although CRT or erlotinib provided no additional advantage to patients in the present study, there may be a subset of patients that could benefit, which is currently under investigation.

Targeting Telomerase With GV1001 Vaccine Does Not Prolong OS in Advanced Pancreatic Cancer

Written by Emma Hitt, PhD

Sequential or concurrent treatment with the vaccine GV100 with chemotherapy does not result in a survival advantage in patients with advanced pancreatic cancer. Gary W. Middleton, MD, University of Birmingham, Birmingham, United Kingdom, presented data from the fourth interim analysis of the Gemcitabine and Capecitabine With or Without Vaccine Therapy in Treating Patients With Locally Advanced or Metastatic Pancreatic Cancer study [TeloVac; NCT00425360; Middleton GW et al. *J Clin Oncol* 2013 (suppl; abstr LBA4004)].

Reactivation of the telomerase enzyme is a common mechanism by which cancer cells prevent their senescence and ~80% of pancreatic cancers overexpress telomerase. The GV1001 vaccine targets the hTERT subunit of telomerase that is expressed on the surface of pancreatic cancer cells. In addition, gemcitabine (GEM) has been demonstrated to have immune priming effects that are dependent on the dosing schedule [Nowak AK et al. *Cancer Res* 2003]. The hypothesis of the TeloVac study was that the addition of GV1001 to the current standard of care for advanced pancreatic cancer would provide an overall survival (OS) advantage.

In the multicenter, Phase 3 TeloVac trial, 1062 patients with advanced pancreatic cancer and an ECOG PS of 0 to 2 were randomized 1:1:1 to receive GEM plus capecitabine (CAP); GEM plus CAP followed by GV1001 followed by additional chemotherapy if disease had not progressed by Week 8; and concurrent administration of GEM, CAP, and GV1001.

The median follow-up was 6.11 months and 72.7% of patients died during the study. The primary endpoint was OS. Overall response rate (ORR), time to progression (TTP), and adverse events were secondary endpoints. Prof. Middleton commented that the TeloVac trial was closed following the fourth interim analysis due to declaration of futility.

Administration of GV1001 did not provide a significant benefit when given concurrently or sequentially following GEM and CAP therapy. OS in the sequential GV1001 arm was statistically nonsignificantly inferior at 6.94 months with a 12-month survival rate of 25.3% (HR, 1.19; 95% CI, 0.97 to 1.48; p=0.0466), compared with 7.89 months and 33.7% in the GEM plus CAP arm and 8.36 months and 32.3% in the concurrent arm (HR, 1.05; 95% CI, 0.85 to 1.29; p=0.6378). The ORR was 17.6% in the GEM plus CAP arm (referent), 8.6% in the GEM plus CAP with sequential GV1001 arm (p=0.001), and 15.5% in the concurrent GEM, CAP, and GV1001 arm (p=0.536).

Sequential GV1001 therapy also resulted in a significant inferiority in TTP compared with the other two arms (HR, 1.50; 95% CI, 1.26 to 1.78; p<0.001). The frequency of hematologic and nonhematologic adverse events was similar among each of the treatment arms.

Although GV1001 was well tolerated, it did not appear to provide a benefit in regard to OS, TTP, or ORR. Prof. Middleton pointed out that in the GV1001 sequential arm, progression rates began to increase as soon as patients discontinued chemotherapy for GV1001 treatment, although this did not translate into a significant difference. Immunological analyses, including for predictive biomarkers, are currently ongoing.

Treatment Based on BRCA1 and RAP80 Does Not Extend PFS

Written by Emma Hitt, PhD

Patients that received customized lung cancer treatment based on their levels of BRCA1 and RAP80 did not experience an improvement in progression-free survival

(PFS) or overall survival (OS), compared with standard cisplatin (CIS) plus docetaxel (DOC). Rafael Rosell, MD, USP Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Barcelona, Spain, presented data from the Multicenter, Predictive, Prospective, Phase 3, Open, Randomized Pharmacogenomic Study in Patients With Advanced Lung Carcinoma study [BREC; NCT00617656; Moran T et al. *J Clin Oncol* 2013 (suppl; abstr LBA8002)].

Previous studies have demonstrated that levels of BRCA1 and a component of the BRCA1 complex, called RAP80, can influence patient outcomes when treated with CIS plus gemcitabine (GEM), CIS plus DOC, or DOC alone [Rosell R et al. *PLoS ONE* 2009]. Overexpression of BRCA1 can confer resistance to agents such as CIS, yet high sensitivity to agents such as paclitaxel, DOC, and vinorelbine [Quinn JE et al. *Cancer Res* 2003]. The hypothesis of the BREC trial was that customizing lung cancer treatment based on BRCA1 and RAP80 levels would improve patient outcomes compared with noncustomized CIS plus DOC.

In the multicenter, prospective Phase 3 BREC trial, 382 patients with advanced lung cancer and wild-type EGFR were randomized 1:1 to receive treatment based on BRCA1 or RAP80 levels or standard treatment with CIS and DOC. Patients with low levels of RAP80 received CIS and GEM, regardless of BRCA1 levels; patients with intermediate to high levels of RAP80 and low to intermediate levels of BRCA1 received CIS and DOC; and patients with intermediate to high levels of RAP80 and high BRCA1 levels received DOC only.

The histology of the tumors was 50.9% adenocarcinoma, 35.5% squamous-cell carcinoma, 8.2% large-cell carcinoma, and 5.4% undifferentiated carcinoma. The primary endpoint of the BREC study was PFS. OS and tumor response rate, as measured by RECIST, were the secondary endpoints of the trial. The planned interim analysis occurred when disease progression occurred in 50% of the patients. The interim analysis analyzed data from 287 patients.

The primary endpoint was not reached. PFS was significantly longer in the control arm, with a PFS of 5.49 months, compared with 4.38 months in the experimental arm (p=0.07), resulting in an HR of 1.35 (95% CI, 1.02 to 1.78; p=0.03). Interestingly, the PFS was similar among the patients that received DOC plus CIS (control arm; 5.49 months), GEM plus CIS (5.43 months), and DOC plus CIS (5.49 months). However, patients that received only DOC had a median PFS of 2.50 months (p=0.003) associated with an HR of 2.65 (p=0.0001). In addition, the rate of OS was 12.66 months in the control arm, compared with 8.52 months in the experimental arm (p=0.006). Patients that received GEM plus CIS, DOC plus CIS, and DOC alone had an OS of 7.70 months (p=0.02), 11.25 months (p=0.28), and 7.24 months (p=0.001), respectively.

A multivariate analysis of the experimental arm, BRCA1, RAP80, tumor histology, smoking status, and metastatic site was performed. An increased risk of progression was associated only with extrathoracic metastases (HR, 1.78; p=0.02).

Due to the increased risk of PFS in the experimental group, the BREC trial was closed prematurely. Prof. Rosell concluded by suggesting that the negative outcome of the study may have been, in part, due to the poor predictive capacity of RAP80 for treatment customization. In addition, he pointed out that DOC plus CIS may not be an optimal choice for the control arm.

PRONOUNCE Study Results

Written by Mary Beth Nierengarten

In patients with advanced nonsquamous non-small cell lung cancer (NSCLC), first-line treatment with pemetrexed plus carboplatin (PemC) followed by maintenance Pem is not associated with superior progression-free survival without Grade 4 toxicities (G4PFS) compared with treatment with paclitaxel/carboplatin/bevacizumab (PCB) followed by maintenance bevacizumab (BEV).

Ralph Zinner, MD, University of Texas MD Anderson Cancer Center, Houston, Texas, USA, presented the results of the Study of Patients With Advanced Non-Small Cell Lung Cancer [PRONOUNCE; NCT0948675; Zinner R et al. *J Clin Oncol* 2013 (suppl; abstr LBA8003)], a randomized, open-label, Phase 3 study that assessed the superiority of 2-drug regimen PemC compared with 3-drug regimen PCB in patients with advanced NSCLC.

A total of 361 patients were enrolled in the study, all of who met the eligibility criteria: age ≥18 years, stage IV NSCLC, an ECOG PS of 0 to 1, chemotherapy-naïve status, and stable treated central nervous system metastases. Patients with uncontrolled effusions were excluded from the study.

Of the 361 patients, 182 were randomized to PemC and 179 to PCB. Patients in both arms received 4 cycles of induction therapy followed by maintenance therapy in the absence of progressive disease or discontinuation of therapy. The PemC group received 4 cycles of induction Pem (500 mg/m^2) and CBP (area under the curve [AUC]=6) followed by Pem maintenance therapy, and the PCB group received induction paclitaxel (200 mg/m^2), CBP (AUC=6), and BEV (15 mg/kg) followed by BEV maintenance therapy.

Baseline characteristics were similar between the two treatment groups, with a median age of 66 years, 42% female, the majority Caucasian, 47% ECOG PS 0, and 70% disease stage M1b.

The primary endpoint of the study was a composite endpoint of G4PFS. Secondary endpoints included PFS, overall survival (OS), response rates (RR), disease-control rates (DCR), and safety/tolerability.