The American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium 2013

Highlights from the the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium 2013, 24-26 January, San Francisco CA, US

T. Feys

From the 24th till the 26th of January, San Francisco was the setting for the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium 2013. The meeting, cosponsored by ASCO, ASTRO and SSO, again focused on multidisciplinary approaches to the prevention, screening, evaluation, and management of gastrointestinal (GI) cancers.
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Adjuvant S-1 chemotherapy improves survival for Asian patients with pancreatic cancer

The phase III JASPAC-01 trial in stage I-III pancreatic cancer shows that postoperative (adjuvant) treatment with a chemotherapy drug called S-1 substantially increases overall survival (OS) rates compared to treatment with the standard postoperative drug gemcitabin. In the study at hand, 385 patients were randomly assigned to postoperative treatment with gemcitabin or S-1. An interim analysis of trial data found that patients who received S-1 had a 44% lower risk of death than patients who received gemcitabine. The two-year survival rates were 70% and 53% for S-1 and gemcitabine, respectively. Furthermore, relapse rates were also lower in the S-1 arm, with two-year relapse-free survival rates of 49% and 29% for S-1 and gemcitabine, respectively. Interestingly, S-1 was well tolerated, with over 70% of patients completing the therapy.

Due to metabolic differences between Asian and Caucasian ethnic groups, gastrointestinal side-effects of S-1 are more severe among Caucasians, requiring use of lower doses of the drug for Caucasian patients. The findings of this study are not immediately applicable to non-Asian populations, but similar studies of S-1 as adjuvant therapy for pancreatic cancer will soon be conducted in Europe and the United States among Caucasian patients, with adjustment of S-1 dose.[1]

Molecular subtypes of colorectal cancer

The availability of recent genomic classifiers, like Oncotype® or ColoPrint®, improves the identification of high-risk patients with stage II disease who have a higher risk for relapse and eventually could benefit from such additional treatment. However, clear recommendations for administration of postoperative chemotherapy in this stage are still lacking. Moreover, these tests are not useful in patients with later-stage disease who have already undergone treatment, nor can they help determine which therapy might be best for the individual patient.

In the presented study, a molecular subtype classi-

Author: T. Feys MSc MBA, Ariez International, c/o PO Box 271, 1520 AG Wormerveer, The Netherlands, tel: +32 (0)479 567890, e-mail address: t.feys@ariez.com.

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fication system was developed using gene expression data from 188 patients with colorectal cancer. The classification system was subsequently validated in tumour samples from 543 stage II and III patients and determined that 21.5% of samples belonged to subtype A, 62% to subtype B, and 16.5% to subtype C. These three subtypes differed in three biological hallmarks of the tumour – epithelial-to-mesenchymal transition, deficiency in mismatch repair genes, and the rate of cell proliferation. A 10-year patient follow-up revealed that patients with subtype C had the worst outcome and showed no benefit from adjuvant chemotherapy. Patients with subtypes A and B had better outcomes and did benefit from adjuvant chemotherapy. The study also found that, compared to subtype B, subtypes A and C had higher rates of alterations in many genes including those that play an important role in colorectal cancer development and growth, such as KRAS, BRAF, and PI3KCA.[2]

Phase III results for bevacizumab in meta- static colorectal cancer

In the phase III TRIBE trial, bevacizumab plus FOLFOXIRI was compared to bevacizumab plus FOLFIRI in patients with metastatic colorectal cancer (mCRC) who had not been previously treated with chemotherapy. A total of 508 patients was randomised one to one to either arm, which both included up to twelve cycles of 5 mg/kg bevacizumab followed by bevacizumab plus fluorouracil as a maintenance therapy. The study met its primary endpoint with a median progression-free survival (PFS) of 11.9 months in the FOLFOXIRI arm compared to 9.5 months in the FOLFIRI arm (p=0.001). Moreover, response rates were also higher for the FOLFOXIRI combination compared to the FOLFIRI group (64% versus 53%, p=0.015).

The AVEX trial compares bevacizumab in combination with capecitabine to capecitabine alone in previously untreated patients of 70 years or older. The results show the combination may be a better treatment improving elderly patient outcomes and validating the use of bevacizumab with capecitabine, a fluoropyrimidine, in elderly patients.[4]
The open-label trial administered bevacizumab to one half of the patients at a 7.5 mg/kg dose every three weeks. A total of 280 patients (median age of 76) in ten countries were part of the trial, which showed the combination prolonged PFS compared to chemotherapy alone. PFS was 9.1 months for patients taking the combination compared to 5.1 months in the chemotherapy alone arm (p<0.001). The OS was also improved, but the difference between the two arms was not statistically significant (20.7 versus 16.8 months, p=0.182). Grade 3 and higher adverse events were more frequently observed in the combination arm, but in general the regimen was well tolerated.[4]

Surgery after imatinib therapy improves survival for metastatic or recurrent GIST

A new retrospective study reports that patients who underwent surgery to remove residual tumours after imatinib therapy had significantly improved OS and PFS compared to those receiving imatinib therapy alone.
The presented study included patients with metastatic or recurrent GIST that were treated with imatinib alone (N=92) or imatinib plus surgery to remove residual tumour laesions (N=42). The PFS in the imatinib and surgery plus imatinib groups was 42.8 months and 87.7 months, respectively. The OS was also significantly better among patients who received surgery with patients in the imatinib plus surgery group having a 5.5 fold lower risk of death.[5]

Nab-paclitaxel plus gemcitabine new standard of care for first-line metastatic pancreatic cancer

The addition of nab-paclitaxel to gemcitabine in patients with metastatic pancreatic cancer yielded statistically significant and clinically meaningful improvements in all endpoints across all subgroups compared to gemcitabine alone. In the phase III MPACT trial a total of 861 patients with previously untreated metastatic adenocarcinoma of the pancreas were randomly assigned to receive nab-paclitaxel plus gemcitabine or gemcitabine alone.[6]
The median OS was 8.5 months with nab-paclitaxel plus gemcitabine versus 6.7 months with gemcitabine alone (p=0.000015). At twelve months, the survival rate was 35% with the combination versus 22% with gemcitabine alone, translating into a 59% increase in survival (p=0.00020). Moreover, survival at two years doubled with the addition of nab-

paclitaxel to gemcitabine, increasing from 4% to 9% (p=0.02123). In addition to OS, the nab-paclitaxel combination surpassed gemcitabine alone for median PFS (5.5 versus 3.7 months; HR: 0.69; p=0.000024) and the overall response rate (ORR) by independent review (23% versus 7%; p=1.1 x 10-10).[6]

Ramucirumab, a potential new second-line treatment option for metastatic gastric or GEJ adenocarcinoma

Findings from the REGARD trial, the largest phase III trial of second-line therapy for advanced gastric or gastro-oesophageal junction (GEJ) adenocarcinoma, demonstrate that ramucirumab significantly improves OS and PFS following progression on first-line chemotherapy.[7]

This global, randomised, double-blind, placebo-controlled trial of 355 patients with disease progression on first-line platinum- or fluoropyrimidine-containing combination therapy showed that the addition of ramucirumab to best supportive care significantly prolonged median OS from 3.8 to 5.2 months (p=0.0473). This translated into a 22% reduction in the risk of death with ramucirumab. Moreover, ramucirumab also significantly prolonged median PFS from 1.3 months to 2.1 months when added to best supportive care (p<0.0001) and more than doubled the disease control rate (48.7% versus 23.1%; p<0.0001). The most common events of grade 3 or higher included hypertension (7.6% versus 2.6% with placebo), anaemia (6.4% versus 7.8% with placebo), fatigue (6.4% versus 9.6% with placebo), abdominal pain (5.9% versus 2.6% with placebo), and ascites (4.2% versus 4.3% with placebo).[7]

Second-line docetaxel improves both survival and quality of life in oesophagogastric cancer

The phase III COUGAR-02 trial included 168 adult patients with EGC who progressed within six months of receiving first-line treatment with platinum/ fluoropyrimidine combination therapy.

Second-line treatment with docetaxel plus ASC significantly prolonged the median OS in comparison to ASC alone (5.2 versus 3.6 months; p=0.01) translating into a 33% reduction in the risk of death with docetaxel. This survival benefit remained consistent after adjustment for several prognostic factors. However, select subgroups of patients demonstrated greater survival benefits than others, including patients with a longer disease-free interval, patients with an ECOG performance status of 0 and patients with oesophageal junction tumours. Importantly, treatment with docetaxel not only helped patients live longer, but it also resulted in significantly better symptom scores in the chemotherapy arm, particularly for pain (p=0.0008). Of note, only 23% of patients assigned to the docetaxel arm completed all eighteen weeks of treatment. The most notable grade 3/4 adverse events experienced by patients receiving docetaxel were related to bone marrow suppression and included neutropaenia (18%) and febrile neutropaenia (7%).[8]

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