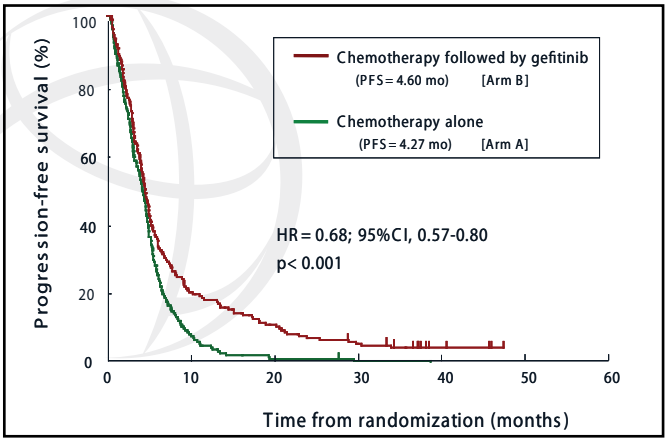
paclitaxel, vinorelbine, or gemcitabine. Most patients had adenocarcinoma (78% in the chemotherapy alone arm and 79% in the chemotherapy plus gefitinib arm), and most patients (82% overall) had stage IV disease.

Toyoaki Hida, MD, PhD, Aichi Cancer Center, Nagoya, Japan, presented the findings on behalf of the WJTOG investigators. Dr. Hida reported that there was no significant difference between the two arms with respect to the primary endpoint of overall survival (OS). The mean survival was 13.68 months for the chemotherapy plus gefitinib arm and 12.89 months for the chemotherapy alone arm (p=0.10). However, progression-free survival (PFS; a secondary endpoint) was significantly longer for patients who received gefitinib (Figure 1).

Figure 1. Sequential Therapy With Gefitinib After Platinum-Based Doublet Chemotherapy Led to a Significantly Longer PFS Than Chemotherapy Alone for Patients With Advanced NSCLC.



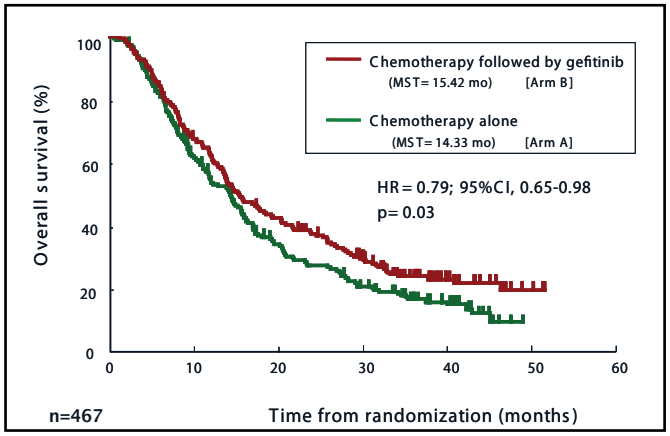
Dr. Hida added that a preplanned subset analysis showed that a platinum-based doublet followed by gefitinib was associated with a significantly superior OS for patients who had adenocarcinoma histology (Figure 2).

Chemotherapy followed by gefitinib was safe, with lower rates of adverse events than chemotherapy alone. Dr. Hida noted that the frequency of grade 3-4 anemia was significantly higher for the chemotherapy alone arm (21.8% vs 13.3%; p=0.006). All other toxicities were similar for the 2 arms. Among patients who received gefitinib, the 2 most common toxicities were elevated serum levels of liver enzymes (11.0%) and rash (4.1%).

Subgroup analysis showed that the hazard ratios (HRs) for death all favored sequential therapy with gefitinib except for non-adenocarcinoma histology (HR=1.24; 95% CI, 0.85-1.79) and stage IIIb disease (HR=0.99; 95% CI, 0.64-1.52).

Dr. Hida stated that in exploratory subgroup analyses, the mean survival was found to be longest for patients who had never smoked, with a slightly longer survival for patients in the chemotherapy alone arm (23.51 months vs 21.65 months; p=0.72). Among smokers, gefitinib led to significantly better survival (11.67 months vs 10.03 months; p=0.03); survival was further improved among smokers with adenocarcinoma histology (13.64 months vs 10.03 months; p=0.003).

Figure 2. Gefitinib was Associated With Significantly Better OS Only for Patients With Advanced NSCLC of Adenocarcinoma Histology.



A Randomized Phase 3 Trial of Intraperitoneal Cisplatin and Early Mitomycin C Plus Long-Term Doxifluridine Plus Cisplatin Versus Mitomycin C Plus Short-Term Doxifluridine

In patients with grossly serosa-positive advanced gastric cancer (AGC), postoperative adjuvant chemotherapy with intraperitoneal cisplatin and early mitomycin C (M) plus long-term doxifluridine plus cisplatin (iceMFP) improved recurrence-free and overall survival (OS). The comparator regimen in the phase 3 trial (AMC 0101) was M plus short-term doxifluridine (Mf), according to Yoon-Koo Kang, MD, Asan Medical Center, Seoul, Korea.

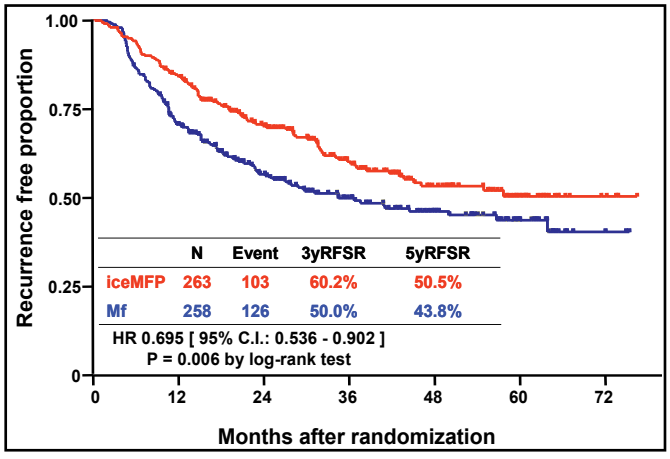
Dr. Kang noted that small but significant benefit for adjuvant chemotherapy in AGC has been demonstrated in meta-analyses and that a meta-analysis of M-based adjuvant chemotherapy studies from the 1960s-1980s in Japan (Nakajima et al. *Gan To Kagakis Ryoho* 1994)

also demonstrated efficacy. The clinical intent of the active therapy in trial AMC 0101 was to improve adjuvant chemotherapy with M and short-term oral fluoropyrimidine by adding cisplatin, prolonging the administration of low-dose fluoropyrimidine, starting chemotherapy early, and using an intraperitoneal administration route.

The trial tested whether these strategies would improve recurrence-free survival (RFS) and, secondarily, OS. It included curatively resected AGC performance status II-IV patients without metastases who were randomized at surgery to either of 2 arms: Mf or iceMFP. The Mf group received 20 mg/m2 of M injected 3-6 weeks after surgery and 4 weeks later, 460-600 mg/m2/day of doxifluridine administered orally for 3 months. For the iceMFP group, 100 mg of cisplatin in 1 L of saline was administered intraperitoneally for 2 hours during surgery, and 15 mg/m2 of M was injected 1 day after surgery. Doxifluridine was started 4 weeks after surgery and extended for a total of 12 months. Six shots of monthly 60 mg/m2 cisplatin were added.

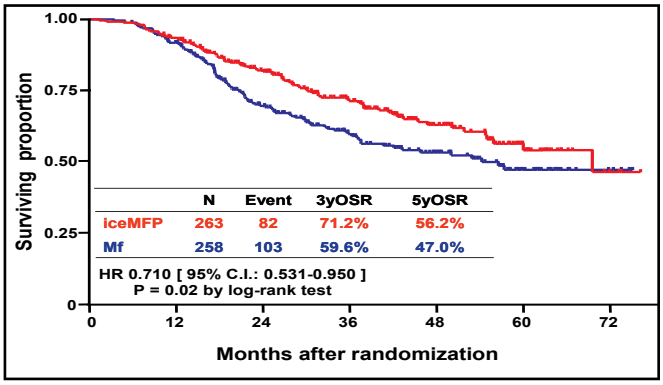
Among 521 patients who were analyzed (mean age~54.5 years, 67% male), after a median follow-up of 3.5 years, RFS favored the iceMFP arm significantly (HR 0.695; p=0.006; Figure 1). Five-year RFS was 50.5% in the iceMFP arm and 43.8% in the MF arm. OS also favored the iceMFP arm (HR 0.710; p=0.02; Figure 2), whereby the 5-year OS was 56.2% for iceMFP and 47.0% for Mf. Surgery-related complications were generally similar between groups.

Figure 1. RFS at 3.5 Years.



Dr. Kang also noted that recurrences were significantly less frequent in the iceMFP arm (94 vs 1184; p=0.02) and that the reduction of recurrences was observed not only in the peritoneum but also in other local or distant sites to a similar extent. Grade 3-4 neutropenia was more frequent in the iceMFP arm (34.2% vs 11.6%).

Figure 2. RFS at 5 Years.



Dr. Kang concluded, "Postoperative iceMFP chemotherapy was safe and significantly improved RFS and OS in patients with grossly serosa-positive AGC compared with Mf chemotherapy." He added, "Considering that adding cisplatin and prolonging oral doxifluridine provided no benefit in another trial, the AMC 0201 trial (Abstract #4531. ASCO 2008), early start of chemotherapy or intraperitoneal cisplatin seemed to be responsible for the improved efficacy in AMC 0101."