with afatinib plus paclitaxel, overall survival did not show any statistical difference between the 2 treatment arms (12.2 months in each arm; HR, 1.00; 95% CI, 0.70 to 1.43; $P = .994$), possibly attributed to differences in postprogression treatment between the arms. More patients in the ICC arm received 2 postprogression lines of therapy compared with the afatinib plus paclitaxel arm (36% vs 15%).

Despite prolonged exposure time to afatinib plus paclitaxel compared with ICC (133 vs 51 days), discontinuation due to treatment-related adverse events was low, and quality of life was comparable between arms (HR, 0.97; 95% CI, 0.6 to 1.5). The most common adverse events in afatinib plus paclitaxel vs ICC arms included diarrhea (53.8% vs 6.7%), alopecia (32.6% vs 15%), and asthenia (27.3% vs 28.3%).

Prof Schuler concluded that afatinib plus paclitaxel was superior to ICC and improved outcomes in patients who had an acquired resistance to erlotinib/gefitinib and had disease progression on afatinib monotherapy after an initial benefit. It should, however, be noted that this study did not include a mutational analysis. Future studies should include a mutational status analysis (including *EGFR* mutations) to evaluate how the efficacy of treatments differs based on mutational status.

Age-Stratified Subgroup Analysis of SQUIRE in Patients With Stage IV Squamous NSCLC

Written by Anita Misra-Press, PhD

The current treatment for advanced non–small cell lung cancer (NSCLC), the leading cause of cancer death, is a combination of a platinum agent with third-generation therapies [Socinski MA et al. *J Clin Oncol.* 2012]. However, with survival differences related to histology, the paucity of data for patients with squamous NSCLC underscores an unmet need for more effective treatment.

Nicholas Thatcher, PhD, The Christie NHS Foundation Trust, Manchester, United Kingdom, previously reported results from the SQUIRE trial [Thatcher N et al. *J Clin Oncol.* 2014], a multinational, randomized, open-label, phase 3 study demonstrating increased overall survival (OS), progression-free survival (PFS), and disease control rates by adding necitumumab (N) to gemcitabine/cisplatin (GC) as first-line treatment for stage IV squamous NSCLC.

Changing the prevalence of comorbidities (and associated toxicities) across the age spectrum may influence outcomes, particularly for the elderly squamous NSCLC population [Piccirillo JF et al. *Crit Rev Oncol Hematol.* 2008]. In the present poster, Prof Thatcher presented efficacy results from an age-stratified subgroup analysis of the SQUIRE trial (N + GC or GC alone) in elderly patients with stage IV squamous NSCLC [Thatcher N et al. *Ann Oncol.* 2015].

Prespecified subgroup analyses (< 70 years: N + GC [n = 437], GC [n = 451] vs ≥ 70 years: N + GC [n = 108], GC [n = 97]) for efficacy were based on the randomized intent-to-treat population. Baseline patient characteristics were comparable between the subgroups. Exposure to N and GC treatment cycles was slightly lower in the ≥ 70-year subgroup; N continuation monotherapy was initiated in 53% of the < 70-year subgroup and in 43% of the ≥ 70-year subgroup. Both subgroups showed predictable toxicities with similar grade ≥ 3 adverse events (AEs) in both arms; however, the higher incidence of serious AEs in the N plus GC arm in both age groups was likely responsible for the higher proportion of patients discontinuing treatment in that arm.

Kaplan–Meier curves for OS of the < 70-year subgroup demonstrated a significant increase from 9.9 months (GC) to 11.7 months (N + GC; HR, 0.81; 95% CI, 0.70 to 0.94; $P = .006$). However, OS in the ≥ 70-year subgroup showed no significant benefit from the addition of N (9.7 months GC vs 10 months N + GC; HR, 1.03; 95% CI, 0.75 to 1.42; $P = .858$).

PFS in the < 70-year subgroup increased slightly (5.5 months GC to 5.7 months N + GC; HR, 0.82; 95% CI, 0.70 to 0.95; $P = .007$). However, PFS in the ≥ 70-year subgroup demonstrated no change in the 2 treatment arms (5.5 months GC vs 5.6 months N + GC; HR, 1.07; 95% CI, 0.77 to 1.49; $P = .686$). This age-related decrease in survival response is consistent with previous studies in patients with advanced NSCLC [Pirker R et al. *Lancet.* 2009; Ramalingam SS et al. *J Clin Oncol.* 2008].

Prof Thatcher concluded that treatment benefit with N plus GC was observed for patients aged < 70 years; however, for the ≥ 70-year subgroup of elderly patients (representing 19% of the SQUIRE population), there was no significant difference in OS or PFS between the treatment arms.

Novel Compound Beneficial as Adjunct to Antibody-Based Therapy for Stage IV NSCLC Patients

Written by Anita Misra-Press, PhD

Recent reports show that PGG beta-glucan, a novel immune cell modulator, increased objective response rates in patients with stage IV non–small cell lung cancer (NSCLC) when added to the first-line regimen of carboplatin/paclitaxel (C/P) chemotherapy and cetuximab, an EGFR-targeted antibody [Schneller F. *J Thorac Oncol.* 2014]. Bevacizumab is a vascular endothelial growth factor

targeted antibody, approved in both the United States and Europe, for first-line treatment of unresectable, locally advanced, recurrent, or metastatic NSCLC when administered in combination with C/P chemotherapy.

Ada Braun, MD, PhD, Biothera, Eagan, Minnesota, USA, and colleagues presented results from a multicenter, open-label, randomized phase 2 trial [Braun A et al. *Ann Oncol*. 2015] investigating the efficacy of PGG beta-glucan when added to bevacizumab and C/P combination therapy for previously untreated stage IV nonsquamous NSCLC. The primary end point for this study was an objective response rate, whereas the secondary end points included duration of response, progression-free survival, time to progression, overall survival, and safety.

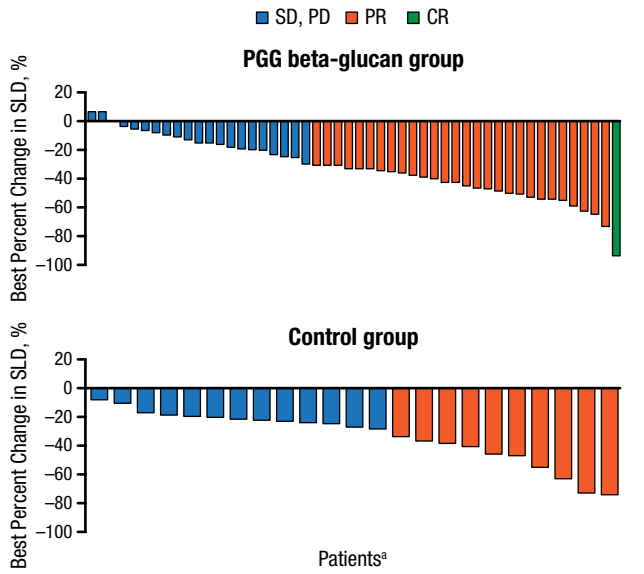
The investigators enrolled 92 patients between 2009 and 2013 from 12 centers across Germany and the United States, with histologically or cytologically confirmed, previously untreated, stage IV nonsquamous NSCLC. Eligibility required adequate organ function (hematologic, hepatic, renal, coagulation) and an ECOG performance status (PS) of 0 or 1. Patients were randomized 2:1 to bevacizumab plus PGG (n = 61; PGG 4 mg/kg intravenously; day 1, 8, 15 of each cycle; PGG beta-glucan group) or bevacizumab alone (n = 31; control group) in combination with C/P for 4 to 6 cycles until documented progression or unacceptable toxicity. All patients had either progressed or had completed at least 18 treatment cycles.

Baseline patient characteristics including age, sex, race, time from diagnosis to randomization, and prior treatments (surgery, radiation therapy) were balanced between the PGG beta-glucan and control treatment groups. A higher proportion of patients in the control group than in the PGG beta-glucan group had a good ECOG PS of 0 at baseline (66.7% vs 52.5%). Thus, a better clinical prognosis and clinical outcomes would have been expected in the patients in the control group, because ECOG PS 0 is a major prognostic factor, according to Prof Braun.

An objective response was achieved in 29 of 48 (60.4%; 95% CI, 45.3 to 74.2) patients in the PGG beta-glucan group and in 10 of 23 (43.5%; 95% CI, 23.2 to 65.5) patients in the control group ($P = .2096$; Figure 1). The investigators reported that the tumor size continued to regress post chemotherapy in the PGG beta-glucan maintenance group.

In the PGG beta-glucan and control groups, respectively, the median duration of response was 10.3 months and 5.6 months ($P = .9040$); the time to disease progression was 11.6 months and 9.6 months (HR, 1.31; 95% CI, 0.54 to 3.65; $P = .5639$); and progression-free survival was 11.9 months and 10.2 months (HR, 0.86; 95% CI, 0.49 to 1.54; $P = .5901$).

Figure 1. Best Overall Response (Change in Tumor Size) in PGG Beta-Glucan vs Control Group



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SLD, sum of the longest diameters.

[a]Each bar shows the results for a single patient.

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The overall survival was a median 11.6 months in the control group and 16.1 months in the PGG beta-glucan group (HR, 0.66; 95% CI, 0.38 to 1.16; $P = .1345$); the study was not powered to detect a statistical difference in survival between the study groups.

The incidence of adverse events (AEs) was similar between the treatment arms; however, 37.3% of the PGG beta-glucan cohort and 43.3% of the control cohort discontinued the study due to AEs. PGG beta-glucan-related AEs included chills (13.6%); dyspnea and fatigue (10.2% each); and nausea, pyrexia, and infusion-related reactions (8.5% each). The investigators concluded that PGG beta-glucan showed promise as an adjunct to antibody-based therapies for improving clinical outcomes in patients with NSCLC.