(500 mg/m^2 IV) or docetaxel (75 mg/m^2 IV) on Day 1 of a 21-day cycle (n=174). The primary endpoint was progression-free survival (PFS). The secondary endpoints included objective response rate (ORR), overall survival (OS), safety, and patient-reported outcomes. Median follow-up was 12.2 months for the crizotinib group and 12.1 months for the chemotherapy group. Baseline characteristics for the 2 treatment arms were similar.

Median PFS in the crizotinib group was 7.7 versus 3.0 months in the chemotherapy group (HR, 0.49; 95% CI, 0.37 to 0.64; p<0.0001). When stratified according to chemotherapy, median PFS was 4.2 months in the pemetrexed group (n=99; HR, 0.59; 95% CI, 0.43 to 0.80; p=0.0004) and 2.6 months in the docetaxel group (n=72; HR, 0.30; 95% CI, 0.21 to 0.43; p<0.0001).

ORR was 65.3% with crizotinib versus 19.5% with chemotherapy (pemetrexed, 29.3%; docetaxel, 6.9%; ORR ratio, 3.4; 95% CI, 2.5 to 4.7; p<0.0001). Interim analysis showed a median OS of 20.3 months with crizotinib (n=173) versus 22.8 months with chemotherapy (n=174 [111 patients who had disease progression were allowed to crossover to crizotinib]; HR, 1.02; 95% CI, 0.68 to 1.54; p=0.5394; HR adjusted for crossover, 0.83; 95% CI, 0.36 to 1.35).

Any-cause grade 3/4 adverse events (AEs) occurring in ≥3% of patients with crizotinib versus chemotherapy were elevated transaminases (16% vs 2%), pulmonary embolism (5% vs 2%), dyspnea (4% vs 3%), pneumonia (4% vs 2%), hypokalemia (4% vs 0%), electrocardiogram QTc prolongation (4% vs 0%), neutropenia (13% vs 19%), febrile neutropenia (1% vs 9%), anemia (2% vs 5%), decreased white blood cells (1% vs 5%), and fatigue (2% vs 4%). A total of 25 (15%) deaths occurred with crizotinib versus 7 (4%) with chemotherapy. There were 11 (6%) study treatment-related permanent discontinuations with crizotinib versus 17 (10%) with chemotherapy.

Patients reported greater improvement from baseline in lung cancer symptoms with crizotinib versus chemotherapy (p<0.0001). Patient-reported global quality of life (European Organization for Research and Treatment quality of life questionnaires QLQ-C30 and QLQ-LC13) was significantly better with crizotinib versus chemotherapy (estimated difference, 9.84; 95% CI, 5.39 to 14.28; p<0.0001).

PROFILE 1007 showed that crizotinib significantly prolonged PFS and improved ORR compared with single-agent chemotherapy in patients with advanced previously treated ALK+ NSCLC. No statistically significant difference in OS was observed, but the interim analysis was immature and may have been affected by crossover to crizotinib from the chemotherapy groups.

Crizotinib has a distinct AE profile compared with chemotherapy, but AEs generally were tolerable and manageable. Compared with single-agent chemotherapy, crizotinib was associated with significantly greater improvement from baseline in lung cancer symptoms and quality of life. According to Dr. Shaw, these results establish crizotinib as the standard of care for patients with advanced previously treated ALK+ NSCLC.

CORRECT Trial of Regorafenib in Metastatic Colorectal Cancer: Overall Survival Update

Written by ***Phil Vinall***

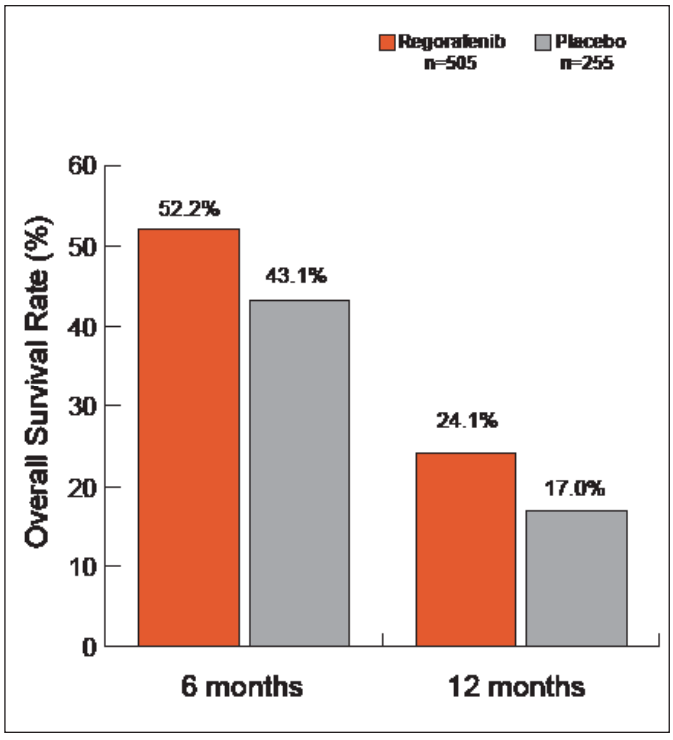
There is a significant unmet clinical need for treatment options for metastatic colorectal cancer (mCRC). Regorafenib (BAY 73-4506) is an oral multikinase inhibitor that targets multiple tumor pathways [Wilhelm SM et al. *Int J Cancer* 2011; Mross K et al. *Clin Cancer Res* 2012; Strumberg D et al. *Expert Opin Investig Drugs* 2012]. Eric Van Cutsem, MD, University Hospitals Gasthuisberg/Leuven, Leuven, Belgium, presented updated overall survival (OS) data from the Patients with Metastatic Colorectal Cancer Treated with Regorafenib or Placebo After Failure of Standard Therapy [CORRECT; NCT01103323] trial. The study demonstrated increased survival benefits following regorafenib treatment in patients with previously treated mCRC.

CORRECT was a multicenter, randomized, double-blind, placebo-controlled, Phase 3 trial conducted from May 2010 through March 2011 in 114 centers in 16 countries. Patients with mCRC treated with available standard therapies (chemotherapy and monoclonal antibodies) and progressing during or ≤3 months after last standard therapy were randomized to regorafenib (160 mg PO QD, 3 weeks on, 1 week off; no crossover at progression permitted) plus best supportive care (n=505) or placebo (QD, 3 weeks on, 1 week off) plus best supportive care (n=255), with treatment continued until disease progression, unacceptable toxicity, or patient or investigator stopped the treatment. The primary endpoint was OS. Secondary endpoints included disease control rate and safety. This trial met its primary endpoint at a preplanned interim analysis, the results of which have been presented previously [Van Cutsem E et al. *J Clin Oncol* 2012]. Updated OS data are reported here.

Subjects were mostly white (>77%) with a median age of 61 years (range 22 to 85). For regorafenib and placebo, they had an Eastern Cooperative Oncology Group Performance Status of 0 (52.5% vs 57.3%, respectively)

or 1 (47.5% vs 42.7%), and primary disease sites were the colon (64.0% vs 67.5%), rectum (29.9% vs 27.1%), or colon and rectum (5.9% vs 5.5%). The majority of patients in both groups had KRAS mutations, and most had received at least 4 prior lines of therapy. All were previously treated with bevacizumab. The median duration of treatment was 12.1±9.7 and 7.8±5.2 weeks for regorafenib and placebo, respectively. Median OS for this updated analysis (after 566 events) was 6.4 months for regorafenib and 5.0 months for placebo (HR, 0.79; 95% CI, 0.66 to 0.94; p=0.0038). The OS rates at 6 and 12 months were 52.2% and 24.1%, respectively, in the regorafenib arm versus 43.1% and 17.0% in the placebo arm (Figure 1). Disease control rates (partial response + stable disease ≥6 weeks after randomization) were 41.0% versus 14.9% (p<0.000001) in the regorafenib and placebo arms, respectively. With the exception of colon and rectum as the primary site of disease, analysis across all subgroups favored regorafenib.

Figure 1. OS Rates.



More drug-related treatment-emergent adverse events (in particular, hand-foot skin reaction, fatigue, hypertension, diarrhea, and rash and/or desquamation) occurred in the regorafenib arm than in the placebo arm. Subgroup analysis showed few differences in the rate of drug-related adverse events.

The benefits of regorafenib were sustained over time and across prespecified subgroups. Side effects were tolerable and manageable in this patient population.