22LBA LATE BREAKING ABSTRACT

Overall survival analyses from the SATURN phase III placebo-controlled study of erlotinib as first-line maintenance therapy in advanced non-small-cell lung cancer (NSCLC)

F. Cappuzzo[1], B. Coudert[2], R. Wierzbicki[3], K. Park[4], F. Custers[5], G.A. Curbera[6], G. Giaccone[7], W. Hilbe[8], G. Klingelschmitt[9], T.E. Ciuleanu[10]. [1]*Istituto Clinico Humanitas, Oncology, Rozzano Milano, Italy;* [2]*Centre George-François Leclerc, Medical oncology, Dijon, France;* [3]*RS McLaughlin Durham Regional Cancer Centre, Oncology, Oshawa, Canada;* [4]*Samsung Medical Centre, Oncology, Seoul, South Korea;* [5]*Atrium Medisch Centrum, Oncology, Heerlen, The Netherlands;* [6]*Medical Oncology Service Hospital Juan Canalejo, Oncology, La Coruña, Spain;* [7]*National Institutes of Health, Oncology, Bethesda, USA;* [8]*University Hospital, Oncology, Innsbruck, Austria;* [9]*F. Hoffmann-La Roche Ltd, Statistics, Basel, Switzerland;* [10]*Institute of Oncology Ion Chiricuta, Oncology, Cluj-Napoca, Romania*

Background: Erlotinib is an established option for 2nd-line treatment of patients (pts) with advanced NSCLC. A substantial proportion of pts do not, however, receive 2nd-line therapy, possibly because of worsening overall condition. In the phase III, randomised, placebo-controlled SATURN study (BO18192; Roche), erlotinib was evaluated as 1st-line maintenance therapy in pts whose disease had not progressed after 1st-line chemotherapy.
Materials and Methods: Pts without progressive disease or residual toxicity following 4 cycles of 1st-line platinum-doublet chemotherapy were randomised to erlotinib 150 mg/day or placebo until progression or unacceptable toxicity. Co-primary endpoints were PFS in all pts and in pts with EGFR IHC+ tumours. OS was a secondary endpoint, and was measured from the time of randomisation. Tumour sampling was mandatory, with pre-planned biomarker analyses performed.
Results: 889 pts were randomised to maintenance therapy (erlotinib n = 438; placebo n = 451). Baseline characteristics were well balanced between arms. A diverse range of post-study therapies was received by 71% pts in the erlotinib group and 72% in the placebo group; the use of specific therapies was similar between arms, except for subsequent EGFR TKIs (11% and 21% pts in the erlotinib and placebo groups, respectively). The co-primary endpoints were met: HR for PFS: 0.71 in all pts, 0.69 in EGFR IHC+ (both $p < 0.0001$). Erlotinib produced a significant OS benefit (HR 0.81; $p = 0.0088$) in the ITT population, with a larger benefit obtained in the adenocarcinoma subgroup (HR 0.77). As observed for PFS, an OS benefit was obtained in both *EGFR* wild-type and *EGFR* mutation+ groups (see table); median OS has not been reached in the mutation+ group, and there was a high-degree of cross-over to 2nd-line EGFR TKI in the placebo arm of this group.
Conclusions: Erlotinib significantly prolongs both PFS and OS in the overall population when used as 1st-line maintenance therapy. The OS benefit was obtained against a background of high use of diverse subsequent therapies, and was particularly large in patients with adenocarcinoma histology. Furthermore, the OS benefit was not driven by the *EGFR* mutation-positive subgroup, with a significant improvement in OS observed in the *EFGR* wild-type group.

Group	n	HR for OS
All patients	889	0.81
Adenocarcinoma	403	0.77
Squamous-cell carcinoma	360	0.86
EGFR mutation+	49	0.83
EGFR wild-type	388	0.77

Melanoma and skin cancer
Wednesday 22 September 2009, 14:45–17:00

23LBA LATE BREAKING ABSTRACT

BEAM: A randomized phase II study evaluating the activity of BEvacizumab in combination with carboplatin plus paclitaxel in patients with previously untreated Advanced Melanoma

S.J. O'Day[1], K.B. Kim[2], J.A. Sosman[3], A.C. Peterson[4], S. Feng[5], D.R. Minor[6], J.P. Fruehauf[7], G.P. Linette[8], S.N. Markovic[9], W.E. Carson[10]. [1]*The Angeles Clinic and Research Institute, Medicine, Santa Monica, USA;* [2]*The University of Texas M.D. Anderson Cancer Center, Medicine, Houston, USA;* [3]*Vanderbilt-Ingram Cancer Center, Medicine, Nashville, USA;* [4]*Genentech, BioOncology, S. San Francisco, USA;* [5]*Genentech, BioStatistics, S. San Francisco, USA;* [6]*California Pacific Medical Center, Medicine, San Francisco, USA;* [7]*Chao Family Comprehensive Cancer Center, Medicine, Irvine, USA;* [8]*Washington University, Medicine, St. Louis, USA;* [9]*Mayo Clinic, Medicine, Rochester, USA;* [10]*The Ohio State University Comprehensive Cancer Center, Surgery, Columbus, USA*

Background: Malignant melanoma (MM) is a highly vascular tumor and expression of VEGF has been associated with a worse overall prognosis. Bevacizumab (B) prevents the interaction of VEGF with its receptors and neutralizes its biological activity. The combination of carboplatin (C) and paclitaxel (P) has demonstrated activity in MM. As in other cancers, B may enhance the efficacy of this chemotherapy in MM.
Materials and Methods: AVF4096g is a phase II randomized, placebo-controlled Genentech sponsored study designed to estimate the clinical benefit and characterize the safety of B when added to CP in subjects with stage IV, treatment naïve MM. Randomization was 2:1 (CPB:CP) and stratified on ECOG PS (0,1) and disease stage (M1a/b, M1c). C (AUC = 5, maximum of 10 cycles), P (175 mg/m^2) and B (15 mg/kg) were administered IV on Day 1 every 3 weeks. Evaluations for RECIST response were performed every 2 cycles. Progression free survival (PFS) was the primary endpoint, secondary endpoints included overall survival (OS), response rates (RR) and safety.
Results: 214 subjects were randomized from 2/07–8/08. Baseline characteristics were well balanced between treatment groups, 73% of subjects had M1c disease, 54% of M1c subjects had abnormal LDH levels. Median follow up at the time of analysis was approximately 13mos for each arm. There was a trending benefit in PFS with the addition of B (median 5.6 vs 4.2 mos, HR 0.78 with 95% CI 0.56–1.09, $p = 0.14$). A statistically significant improvement in OS was observed with CPB vs CP, with median of 12.3 vs 8.6 months, HR 0.67 (95% CI 0.46, 0.98), and $p = 0.04$. RR were also higher in the CBP arm (25.5% vs 16.4%, $p = 0.16$). Grade 3–5 AEs occurring with 2% or more increase incidence over CP included febrile neutropenia, neutropenia, peripheral neuropathy, pulmonary embolism, hypertension, anorexia and musculoskeletal pain.
Conclusions: This is the first randomized placebo controlled trial in metastatic melanoma to demonstrate a statistically significant and clinically meaningful improvement in OS. Similar trending benefits were seen in PFS and RR. The majority of subjects had M1c disease. The combination of CPB was well tolerated; no new safety events were observed and B-related safety events were in line with observations from other disease-based clinical studies using similar chemotherapy.

24LBA LATE BREAKING ABSTRACT

Temozolomide combined with bevacizumab in metastatic melanoma. A multicenter phase II trial (SAKK 50/07)

R. Von Moos[1], B. Seifert[2], A. Ochsenbein[3], R. Cathomas[1], M. Schläppi[4], S. Gillessen[4], J.C. Schuller[5], O. Michielin[6], S. Goldinger[7], R. Dummer[7]. [1]*Kantonsspital Graubuenden, Medical Oncology, Chur, Switzerland;* [2]*University Hospital Basel, Medical Oncology, Basel, Switzerland;* [3]*University Hospital Bern, Medical Oncology, Bern, Switzerland;* [4]*Kantonsspital St. Gallen, Medical Oncology/Hematology, St. Gallen, Switzerland;* [5]*Swiss Group for clinical cancer research (SAKK), Headquarter, Bern, Switzerland;* [6]*Centre Hospitalier Universitaire Vaudois (CHUV), Medical Oncology, Lausanne, Switzerland;* [7]*University Hospital Zürich, Department of Dermatology, Zürich, Switzerland*

Background: Single agent DTIC is the standard therapy for metastatic melanoma (MM) with response rates of 5–20%. Temozolomide (Tem) as an oral drug has shown equal efficacy in phase III trials. Preclinical models have shown an inhibitory effect for bevacizumab (Bev) on the proliferation of melanoma cells as well as on sprouting endothelial cells. Therefore, a therapeutic approach that combines angiogenesis inhibitors with cytotoxic agents may provide clinical benefit in MM.