FIRST-LINE BEVACIZUMAB PLUS CHEMOTHERAPY IN CHINESE PATIENTS WITH ADVANCED OR RECURRENT NONSQUAMOUS NSCLC: SUBANALYSIS OF SAiL (MO19390)

Yi-Long Wu[1], Caicun Zhou[2], Guoliang Jiang[3], Mengzhao Wang[4], Zhongzhen Guan[5], Chun-Ming Tsai[6], Affiliation Group[7]

[1]Guangdong General Hospital (GGH), Chinese Society of Lung Cancer, Guangdong General Hospital, China, [2]Shanghai Pulmonary Hospital, China, [3]Fudan University Cancer Hospital, China, [4]Peking Union Medical College Hospital, China, [5]Sun Yat-Sen University of Medical Science, China, [6]Taipei Veterans General Hospital, Taiwan, [7]on behalf of the SAiL investigators

Introduction: Two pivotal phase III trials demonstrated that addition of bevacizumab to first-line chemotherapy improves outcomes in patients with advanced or recurrent NSCLC (E4599 and AVAiL). The international, multicentre, single-arm SAiL study was aimed at further assessing the safety profile of bevacizumab-based therapy in first-line advanced NSCLC in a real-life clinical population (n=2,166). We present a subanalysis of SAiL performed in Chinese patients (August 2009 final cut-off).

Methods: Chemonaive patients with inoperable stage IIIB or IV or recurrent nonsquamous NSCLC were enrolled if they had ECOG PS 0-1, life expectancy ≥3 months and adequate bone marrow, hepatic and renal function. Patients were excluded for having evidence of CNS metastases, even if previously treated, major blood vessel invasion, haemoptysis, history of coagulation disorders, uncontrolled hypertension, clinically significant cardiovascular disease or history of abdominal fistula, gastrointestinal perforation or intra-abdominal abscess within 6 months of enrolment. Eligible patients received bevacizumab (15mg/kg every 3 weeks) plus carboplatin (AUC 6.0, every 3 weeks) paclitaxel (175mg/m^2 every 3 weeks) for up to 6 cycles (to ensure homogeneity and comparability with the E4599 trial), followed by bevacizumab monotherapy until progression. Primary endpoint was safety; secondary endpoints included TTP and OS.

Results: The ITT population (received ≥1 dose of study drug) consisted of 198 patients from nine centres (China mainland only): 55% were male, mean age was 55 years, 46% were past or active smokers, 70% had stage IV disease. At the clinical cut-off (21 August 2009), median number of bevacizumab cycles was 10, with 71.2% of patients receiving ≥7 cycles. 74.2% of patients had an AE of special interest of any grade. The most common AEs of special interest were grade 1-2 proteinuria (41.9%) and epistaxis (39.4%). Grade ≥3 AEs of special interest included: proteinuria (8.6%), hypertension (3%), epistaxis (1.5%) and haemoptysis (0.5%). No CNS bleeding was reported, including in patients who developed CNS metastases during therapy. No grade

TABLE. AEs in Chinese patients in SAiL

AE	SAiL China subpopulation (n=198), %
Serious AE	11.6
AE leading to death	1.0
AE of Special Interest	74.2
Grade≥ 3	13.6
Bleeding	2.5
Epistaxis	1.5
Haemoptysis	0.5
Hypertension	3.0
Thromboembolic events	0.5
Congestive heart failure	0.0
Gastrointestinal perforations	0.5
Proteinuria	8.6
Wound healing complication	0.0%

≥3 wound-healing complications or congestive heart failure events were reported. Seven serious AEs occurred that were deemed by the investigator to be related to bevacizumab: 2 haemoptysis, 1 epistaxis, 1 angle closure glaucoma, 1 pyrexia, 1 neutropenia and 1 headache. Bevacizumab was temporarily interrupted due to AEs in 25.3% of patients, most frequently because of haematological AEs. One death was related to a haemoptysis AE. Overall, the safety profile of bevacizumab used in combination with chemotherapy in this Chinese population is consistent with that reported for the global SAiL population and for the E4599 and AVAiL trials. Among Chinese patients in the SAiL study, median TTP was 8.8 months (95% CI 6.0-12.5) and median OS was 18.5 months (95% CI 10.8-NR; conservative estimate owing to high censoring: 49.5% of patients were still alive at final analysis). Overall response and disease control rates were: 68.7% and 96.4%, respectively.

Conclusions: This study shows that addition of bevacizumab to carboplatin-paclitaxel is well tolerated and effective in Chinese patients with advanced/recurrent nonsquamous NSCLC. Importantly, no unexpected toxicity or new safety signals were identified in this analysis of Chinese patients. Furthermore, the efficacy of bevacizumab in this population appears consistent with that reported in E4599 and AVAiL.