9006 ORAL

Safety of bevacizumab (BV) combined with chemotherapy (CTX) in patients (pts) with non-small cell lung cancer (NSCLC): interim results from the ARIES Lung observational cohort study (OCS)

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Background: The clinical benefit of BV, an anti-VEGF monoclonal antibody, in pts with NSCLC has been shown in 2 randomized controlled trials (RCTs) in which BV was combined with carboplatin/paclitaxel (C/P) or cisplatin/gemcitabine (C/G). However, many pts are underrepresented in RCTs and receive CTX other than C/P or C/G. The ARIES Lung OCS (NCT00388206) evaluates clinical outcomes for NSCLC pts receiving 1st-line BV-containing regimens, in a real-world setting. Preliminary information on safety is presented in this report based on CTX utilized, and for underrepresented pt subpopulations in RCTs, such as pts with ECOG PS $\geqslant$ 2, with brain metastases, pts on anticoagulants (AC), or the elderly.
Material and Methods: ARIES Lung will enroll ~2000 pts with locally advanced or metastatic NSCLC. CTX choice, BV dose and schedule are by investigator decision. Data is collected electronically at baseline (BL) and quarterly, including BL characteristics, all treatments, and targeted BV-associated adverse events (AEs) and serious AEs (SAEs). BV-associated AEs for the overall NSCLC cohort and by BL CTX are summarized descriptively.
Results: As of 2/9/09, there are 1758 BV-treated NSCLC pts in ARIES. Median follow-up time is 8.36 mos; 90.6% of pts have $\geqslant$1 quarterly update. BL characteristics: age $\geqslant$70 yrs, 33.2% (n = 584); ECOG PS $\geqslant$ 2, 9.6%; therapeutic AC, 4.8%; known brain metastases, 7.2%. BL CTX selections among subgroups were generally similar to the overall cohort, except for a slight increase in use of nonplatinum single agents among pts $\geqslant$80 yrs. Observed rates of BV-targeted events such as bleeding and arterial thromboembolism (ATE), in pts on C/P, and on CTX containing G or pemetrexed (Pm), are shown below. Rates of hypertension and gastrointestinal perforation were <10% and $\leqslant$1%, respectively, across common CTX regimens.
Conclusions: ARIES is a large, ongoing, community-based OCS that will describe safety of BV combined with different CTX regimens not included in pivotal RCTs, and among underrepresented subgroups. Summaries of BV-associated AEs across CTX regimens will be presented at the meeting.

AEs/SAEs	All BV treated Pts (n = 1758)	Pts on BV + C/P* (n = 1083)	Pts on BV + G-containing regimen* (n = 242)	Pts on BV + Pm-containing regimen* (n = 112)
Gr 3–5 Bleeding events, n (%)	57 (3.2)	32 (3.0)	15 (6.2)	1 (0.9)
Severe pulmonary hemorrhage	12 (0.7)	8 (0.7)	2 (0.8)	1 (0.9)
CNS hemorrhage	2 (0.1)	1 (0.1)	1 (0.4)	0
ATE, n (%)	29 (1.6)	16 (1.5)	6 (2.5)	2 (1.8)

*CTX categories are overlapping.

Oral presentations (Tue, 22 Sep, 09:00–11:00)
Lung cancer II

9007 ORAL

Randomized, double-blind phase II/III study of first-line paclitaxel (P) plus carboplatin (C) in combination with vorinostat or placebo in patients with advanced non-small-cell lung cancer (NSCLC)

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Background: Preclinical and phase I clinical data suggest that vorinostat (Zolinza®), a potent histone deacetylase inhibitor, may potentiate antitumor activity of P and C. This study assessed whether vorinostat added to P and C provides clinical benefit in first-line treatment of patients with advanced NSCLC.
Material and Methods: Patients $\geqslant$18 years with Stage IIIB (wet)/Stage IV NSCLC, ECOG performance status $\leqslant$1, and no prior systemic chemotherapy (except adjuvant therapy for NSCLC) were randomized to receive P 200 mg/m^2 and C AUC 6 on Day 1 and either vorinostat 400 mg or a placebo control on Days −4−10 of Cycle 1 (25-day cycle) and Days 1−14 of each subsequent 21-day cycle for $\leqslant$6 cycles. Primary endpoints were overall survival (OS) and safety. Secondary endpoints were progression-free survival (PFS) and objective response rate (ORR), as assessed by independent radiological review. P values were one-sided and interpreted to favor placebo if p>0.5.
Results: 253 patients were randomized. Patients' characteristics were balanced between the arms except for age and sex, both favoring the control arm. Median OS favored patients in the control arm vs. the vorinostat arm (14.0 vs. 11.0 months, respectively, HR 1.78, 95% CI 1.11 to 2.84, p = 0.99). Median PFS was. 5.5 vs. 4.3 months in the control arm vs. the vorinostat arm (HR 1.18, 95% CI 0.86 to 1.63, p = 0.86). ORR was also higher in the control arm vs. the vorinostat arm (29.3% vs. 22.4%; p = 0.899). In 248 patients evaluable for safety, relevant grade 3−5 adverse experiences (vorinostat vs. control) included febrile neutropenia (9% vs. 5%), thrombocytopenia (19% vs. 9%), diarrhea (4% vs. 2%), asthenia (6% vs. 2%), and fatigue (6% vs. 5%). Median exposure to P and C was 4 cycles in the vorinostat arm and 6 cycles in the control arm. Study discontinuation during cycles 1 and 2 was 35% vs. 23% (vorinostat vs. control).
Conclusions: Based on recommendations of an independent data safety monitoring board at the second interim analysis, this study was terminated as the pre-specified proof-of-concept criterion (p < 0.10 for the test of treatment effect on PFS based on the first 100 PFS events) to go to phase III was not met. The addition of vorinostat on this dose and schedule, despite the baseline demographic imbalance, does not improve clinical efficacy obtained with P and C in patients with previously untreated NSCLC. Ongoing studies of vorinostat with chemotherapy in NSCLC patients may provide more information.