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Clinical Outcomes for Bevacizumab (BV)-treated Elderly Patients With Non-small Cell Lung Cancer (NSCLC) − Results From the ARIES Observational Cohort Study (OCS)

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Background: In the E4599 trial, addition of BV to 1st-line chemotherapy significantly improved overall survival (OS) in patients with advanced nonsquamous NSCLC, but a post hoc analysis found an OS benefit for BV-treated patients ⩾70 years that did not reach significance, coupled with an increased risk of toxicity. By contrast, analyses from SAiL and AVAiL showed similar efficacy and safety outcomes for BV-treated patients <65 years and those ⩾65 years. Here we report clinical outcomes by age group for NSCLC patients in the ARIES OCS, with a particular focus on elderly patients.
Methods: ARIES NSCLC enrolled patients with advanced NSCLC who received physician's choice of 1st-line BV-containing treatment. Kaplan–Meier estimates were used to calculate medians and 95% confidence intervals (CIs) for PFS and OS for patients ages <50, 50−59, 60−69, 70−79, and ⩾80 years. A Cox proportional hazards model was used to compare PFS and OS for older subgroups with those for patients <50 years while adjusting for baseline covariates.
Results: 1967 patients enrolled in ARIES NSCLC as of February 2011. Median PFS and OS values (Table) were similar for the age groups between 50 and 79 years relative to patients <50 years. Patients ⩾80 years had a lower median OS but a similar median PFS compared with patients <50 years. The incidence proportions of targeted adverse events were generally similar across all age groups.
Conclusions: In this real-world OCS, median PFS values and incidence proportions of targeted adverse events were similar across all patient age groups, and median OS values were similar for all patient age groups up to 79 years. These data support the effectiveness of BV in combination with chemotherapy in elderly patients with advanced nonsquamous NSCLC.

Age, years	N (%)	Median PFS, mo (95% CI)	HR (95% CI)	Median OS, mo (95% CI)	HR (95% CI)
<50	187 (10)	6.0 (5.6−6.8)	1 (ref)	13.3 (11.5−14.8)	1 (ref)
50−59	429 (22)	6.4 (6.0−7.1)	0.95 (0.80−1.14)	14.5 (12.1−15.7)	0.94 (0.77−1.14)
60−69	704 (36)	6.9 (6.3−7.3)	0.92 (0.78−1.09)	13.3 (12.1−15.0)	1.01 (0.84−1.21)
70−79	519 (26)	6.7 (6.2−7.0)	0.97 (0.82−1.16)	12.3 (10.8−13.5)	1.15 (0.96−1.39)
⩾80	128 (7)	5.9 (5.1−7.3)	1.08 (0.85−1.36)	10.9 (8.9−12.0)	1.39 (1.09−1.78)

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DNA Hypermethylation in Progressive Advanced Non Small Cell Lung Cancer

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Background: DNA hypermethylation of tumour-supressor genes results in decrease of their functions and tumour development. Epigenetic changes can play the role in cell cycle control, proliferation, differentiation, cell adhesion,invasion and metastasis, regulation of apoptosis, as well as DNA repair gene transcription and detoxification of DNA adducts, induced by cancer chemotherapy.
Methods and Patients: DNA hypermethylations were detected by Multiplex ligation-dependent probe amplification (MLPA) technique. We investigated 30 genes. Tissue samples from patients with advanced NSCLC, which progressed on chemotherapy and targeted therapy were xamined. Statistical analysis was performed using contingency tables, chi-square test, Wilcoxon test and Kruskal Wallis analysis.
Results: The study comprised 123 patients, 75 males, 48 females, the most frequent cancer types were adenocarcinomas (72), squamous cancers (32),anaplastic (9) and non specified NSCLC (10). KRAS mutations were found in 17, EGFR mutations in 10 and EGFR amplification in 12 patients. Second line therapy was given in 63, III.line therapy in 53 patients was performed. Hypermethylation of at least one gene was found in 11 patients (90.2%). Most frequently methylated genes were CDH 13 in 48%,WT 1 in 38.2%, APC in 30.1%, RASSF1A in 30.1%, ESR 1 in 23.6%, CDKN2B-22.8%, PAX5 19.5%, PAX6 13.8%, IGSF4 11.4% and GATA5 10.6%. Hypermethylations were found more frequently in adenocarcinomas. Most frequent combinations of methylated genes were: CDH 13 and WT1, APC and WT1, CDH 13 and PAX6 and APC and CDH13. All combinations were significantly increased in adenocarcinomas as well as in EGFR mutated tumours. We have found differences in methylation profile accordingly to sex, smoking status and clinical stage. In univariate analysis, methylations of genes WT 1 and BRCA 1, as well as EGFR amplification, female sex and stage of disease are related to survival. None of epigenetic changes is related to chemotherapy and targeted treatment effectiveness.
Conclusion: Epigenetic hypermethylations of tumour related genes in NSCLC are frequent and may be found in several different groups of genes simultaneously, particularly in adenocarcinomas and in EGFR mutated tumours. Epigenetic changes should be understood as evidence of diversity of lung cancer lesions and potentially serve as prognostic and/or predictive factors.
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ARIADNA Study – Evaluation of Symptoms on Daily Life and Health-related Quality of Life (HRQoL) of Patients With Advanced Non-small Cell Lung Cancer (NSCLC)

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Background: Health Related Quality of Life (HRQoL) in oncology patients is directly related to symptoms. The aim of the study was to assess the impact on daily life and HRQoL of the symptoms of advanced non-small cell lung cancer (NSCLC).
Material and Methods: The ARIADNA study is an observational prospective study, carried out in 32 Spanish institutions, which has included 257 patients. Patients had stage IIIB NSCLC with pleural or pericardial effusion or stage IV NSCLC and were about to initiate second-line treatment at the time for enrolment.
HRQoL and disease-related symptoms were assessed at baseline visit and at final visit (6−8 weeks later) with the lung-specific *Functional Assessment of Cancer Therapy* questionnaire (FACT-L) and the *Lung Cancer Symptom Scale* (LCSS), respectively. An *ad hoc* specific questionnaire correlating the impact of NSCLC symptoms on daily life was also evaluated.
Results: 257 patients with advanced NSCLC were enrolled, whose baseline characteristics were: 79.4% male; 97.3% Caucasian; 83.5% current/ever smokers; 56.4% had adenocarcinoma and 23.7% squamous-cell carcinoma; the median (SD) age was 65.0 (10.0) years. 78% of the patients were progression-free at the second scheduled visit (6−8 weeks) Second-line treatment did not deteriorate HRQoL or disease-related symptoms compared to baseline status: FACT-L score: 80.9 *vs.* 81.6; and LCSS score: 77.39 *vs.* 77.44. Impact of cough and pain on daily living was significantly decreased by the salvage treatment ($p = 0.040$ and $p = 0.020$. respectively). Patients who discontinued the therapy or experienced progressive disease showed a significant worsening of their symptoms. Impact of LC symptoms on daily life shows a high correlation with HRQoL assessed by the FACT-L questionnaire ($r = 0.82$).
Conclusions: Second-line treatment is associated with a reduction of the impact of disease-related symptoms (cough and pain) on the daily living of advanced NSCLC patients.