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**Title:** Prevalence and effectiveness of third-line therapy for advanced non-small cell lung cancer (A-NSCLC)

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**Body:** Background: Systemic chemotherapy is the main option for A-NSCLC. Few patients receive third-line therapy and in this setting little is known about outcomes. Objectives: Evaluate demographics, histology, performance status (PS), sites of metastases, response, toxicity, progression-free survival (PFS) and overall survival (OS) in patients with A-NSCLC treated with third-line therapy. Methods: We reviewed 5 years of clinical practice (Jan. 2006 - Dec. 2010): 676 patients with A-NSCLC were diagnosed and 330 received systemic chemotherapy. Of these, 44 completed 3 lines. Results: 73% male, mean age 61.8Y ( $\pm$  9.4). Smoking status: 36% non-smokers, 36% former-smokers and 28% active smokers. Histology: 66% adenocarcinomas, 27% squamous cell carcinomas, 5% large cell carcinomas and 2% NSCLC-NOS. Initially all patients had PS 0-1. Main sites of metastases: lung (80%) and bone (43%), with 34% of patients with  $\geq$  2 metastatic foci. First-line platinum-based duplet: 50% achieved an objective response, 30% had stable disease, PFS 6.4M. Second-line setting (docetaxel/ pemetrexed/ erlotinib): partial response (PR) 30%, stable disease (SD) 52%, PFS 5.4M. Third-line (erlotinib/ pemetrexed): PR 14%, SD 36%, PFS 4.2M. Hematological toxicity: 18% in 1st-line, 16% in 2nd-line and 7% in 3rd-line. Non-hematological toxicity: 16% in 1st-line, 20% in 2nd-line and 14% in 3rd-line. OS was 24.05M. Conclusions: Third-line therapy was used in 6.5% of the patients. 1st-line platin-based chemotherapy with new-generation agents like pemetrexed and erlotinib in the subsequent lines had good efficacy with less toxicity and strongly contributed to the 24 months in overall survival in our patients.