

**Title:** Impact of adherence to NCCN-recommended first-line therapy on treatment duration for patients with advanced non-squamous non-small cell lung cancer

**Background:** Identification of molecular alterations can provide essential information to guide personalized treatment selection for advanced non-small cell lung cancer (aNSCLC) patients. However, in routine oncology practice, not all eligible patients receive biomarker testing and receive treatment according to the testing results following the National Comprehensive Cancer Network (NCCN) guideline. We aim to examine the impact of adherence to guideline-recommended therapy on the duration of treatment in a real-world setting.

**Methods:** Patients diagnosed with non-squamous aNSCLC (stage IIIB and above) and received the first-line of therapy (FLOT) between 2011 and 2019 from the nationwide Flatiron Health electronic health record-derived de-identified database were included in this analysis. Adherence was defined as using any NCCN guideline-recommended FLOT consistent with a patient's biomarker testing results (EGFR, ALK, ROS1, BRAF and PD-L1) assessed up to 90 days before and/or 14 days after the FLOT start date. Non-adherence was defined as not receiving guideline-recommended FLOT based on the above-mentioned biomarker results, or patients treated without evidence of biomarker testing. Median time to treatment discontinuation (TTD) of FLOT was calculated using Kaplan-Meier analysis. Unadjusted and adjusted Cox proportional hazards regression models were used to evaluate the association between guideline adherence and TTD.

**Results:** A total of 17,137 eligible patients were included (67.5% adherent, 32.5% non-adherent). Mean age at diagnosis was 67 years (SD: 10 years). The majority of patients (92%) received care at a community clinic, and 73% reported having insurance plans. Overall, 87.2% had discontinuation of FLOT, including 84.9% in the adherent group and 92.0% in the non-adherent group. The median TTD was 155 days (95% CI 153-159) in the adherent group and 128 days (95% CI 125-132) in the non-adherent group. Adherent patients had a lower risk of FLOT discontinuation in the unadjusted analysis (hazard ratio [HR] 0.78, 95% CI 0.76-0.81), which remained significant after adjusting for potential confounders including age at FLOT start, sex, history of smoking, and stage at initial diagnosis (HR 0.76, 95% CI 0.74-0.79).

**Conclusions:** Among non-squamous aNSCLC patients, the majority of patients were adherent to NCCN guidelines. Adherence was associated with lower risk of discontinuation and longer duration of FLOT.

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**Word count:** 2,216 characters excluding spaces (limit 2,300)

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