Oncogene addiction refers to dependence of malignancy on a single molecular aberration that drives proliferation and aggressive behavior of tumor cells. In the past decade, deeper understanding of driving molecular aberrations in lung adenocarcinoma led to clinical development of targeted therapies with substantial survival prolongation in respective cohorts of patients. Moreover, it is now apparent that these groups of patients have particular biological and clinical characteristics. Mutations in EGFR, HER2, RAS, BRAF as well as rearrangements in ALK, ROS1, RET and gene amplification of MET serve as validated examples of clinically relevant targets in non-small-cell lung cancer in 2014. For these targets, we have several effective agents and we also understand molecular and clinical characteristics of the most common resistance mechanisms with possibility to block these mechanisms with another set of effective therapies, as exemplified by novel generation of EGFR inhibitors. The challenge for the future is how to characterize new relevant molecular targets in dominant oncogenes but also in tumor suppressor oncogenes and how to effectively document the clinical benefit of their blockade. Integration of targeted therapies with cytotoxic agents and immune checkpoint inhibitors is hoped to further increase therapeutic potential of single-agent inhibitor strategies.

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