

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Lung cancer	Anaplastic lymphoma kinase (ALK); insulin-like growth factor-1 receptor (IGF1R; CD221)	<p>Studies in patient-derived cell lines and mice, based on a patient case study, suggest combined inhibition of ALK and IGF1R could be useful for treating ALK⁺ lung cancers resistant to Xalkori crizotinib. A patient with ALK⁺ stage 4 lung cancer responded to Tarceva erlotinib plus an IGF1R-specific mAb, whereas patients with ALK⁺ lung cancers generally do not respond to Tarceva. In a mouse xenograft model of ALK⁺ lung cancer, the ALK inhibitor Xalkori plus an IGF1R-specific mAb delayed tumor growth and increased apoptosis compared with either agent alone. ALK⁺ human lung cancer cell lines resistant to Xalkori showed greater activation of the IGF1R pathway than the Xalkori-sensitive parental cell line. Next steps could include planning a clinical trial to evaluate a combination of ALK and IGF1R inhibitors in a cohort of patients with ALK⁺ non-small cell lung cancer (NSCLC). Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd. and the Genentech Inc. unit of Roche market the small molecule epidermal growth factor receptor (EGFR) inhibitor Tarceva to treat various cancers including NSCLC and pancreatic cancer. Pfizer Inc. markets the c-Met receptor tyrosine kinase and ALK inhibitor Xalkori to treat ALK fusion-positive NSCLC. Astellas Pharma has the IGF1R inhibitor linsitinib in Phase III testing to treat adenocarcinomas. The compound also is in Phase II or earlier testing to treat various other cancers, including lung cancer. Amgen Inc. and Takeda Pharmaceutical Co. Ltd. have ganitumab, a human mAb antagonist of IGF1R, in Phase III trials to treat pancreatic cancer. The mAb also is in Phase II or earlier testing to treat various other cancers. At least 11 other companies have IGF1R-targeted compounds in Phase II or earlier trials to treat various cancers.</p> <p>SciBX 7(38); doi:10.1038/scibx.2014.1121 Published online Oct. 2, 2014</p>	Patent and licensing status unavailable	<p>Lovly, C.M. <i>et al. Nat. Med.</i>; published online Aug. 31, 2014; doi:10.1038/nm.3667 Contact: Christine M. Lovly, Vanderbilt University, Nashville, Tenn. e-mail: christine.lovly@vanderbilt.edu</p>