This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Melanoma	MAP kinase 1 (MAPK1; ERK-2); MAPK3 (ERK-1)	<p>Studies in human tissue and cell culture suggest inhibiting ERK-1 and 2 could be useful for treating melanoma resistant to a combination of BRAF and MEK inhibitors. Whole-exome sequencing of recurring tumors in patients treated with BRAF inhibitors identified a number of mutations and gene duplications in the MAPK pathway in tumors after the onset of resistance that were absent prior to treatment. In a subset of patients with acquired resistance to a combination of BRAF and MEK inhibitors, sequencing identified activating mutations in MAP kinase kinase 2 (MAP2K2; MEK2). In cell culture, a small molecule ERK-1 and 2 inhibitor decreased growth of the MEK2-mutant cells compared with vehicle. Next steps could include testing a triple combination of BRAF, MEK and ERK-1 and 2 inhibitors in mouse models of melanoma.</p> <p>Tafinlar dabrafenib (GSK2118436) from GlaxoSmithKline plc and Zelboraf vemurafenib from Roche and Daiichi Sankyo Co. Ltd. are BRAF inhibitors marketed to treat BRAF-mutant melanoma.</p> <p>GSK also markets Mekinist trametinib (GSK1120212), a small molecule MEK inhibitor, to treat BRAF-mutant melanoma.</p> <p>At least 14 other companies have MEK inhibitors in Phase III or earlier testing to treat various cancers.</p> <p>Aeterna Zentaris Inc. has the phosphoinositide 3-kinase (PI3K) and ERK-1 and 2 inhibitor AEZS-136 in preclinical development for cancer.</p> <p>SciBX 7(1); doi:10.1038/scibx.2014.12 Published online Jan. 9, 2014</p>	Patent and licensing status undisclosed	<p>Wagle, N. <i>et al. Cancer Discov.</i>; published online Nov. 21, 2013; doi:10.1158/2159-8290.CD-13-0631 Contact: Jennifer A. Wargo, Harvard Medical School, Boston, Mass. e-mail: jwargo@mdanderson.org Contact: Levi A. Garraway, Dana-Farber Cancer Institute, Boston, Mass. e-mail: levi_garraway@dfci.harvard.edu</p> <p>Van Allen, E.M. <i>et al. Cancer Discov.</i>; published online Nov. 21, 2013; doi:10.1158/2159-8290.CD-13-0617 Contact: Dirk Schadendorf, University Hospital Essen, Essen, Germany e-mail: dirk.schadendorf@uk-essen.de Contact: Levi A. Garraway, Dana-Farber Cancer Institute, Boston, Mass. e-mail: levi_garraway@dfci.harvard.edu</p>