This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Mantle cell lymphoma (MCL)	Phosphoinositide 3-kinase (PI3K); cyclin dependent kinase 4 (CDK4); Bruton's tyrosine kinase (BTK)	<p>Human tissue and cell culture studies suggest CDK4 inhibitors could help treat Imbruvica ibrutinib-resistant MCL. In biopsies from patients with MCL who relapsed while on Imbruvica, genomic analysis identified a <i>BTK</i> cysteine 418 mutation—not found in patients with MCL who had primary or rapid resistance to Imbruvica—that induced CDK4 expression and PI3K signaling. In a chicken lymphoma cell line that expressed the mutant form of <i>BTK</i>, the CDK4 inhibitor palbociclib plus a PI3K inhibitor increased apoptosis compared with either agent alone. Ongoing work includes a Phase I trial of palbociclib and Imbruvica in patients with MCL, and planned work includes a Phase I trial of palbociclib and Zydelig idelalisib to treat MCL. Pharmacyclics Inc. and Johnson & Johnson market Imbruvica, an irreversible BTK inhibitor, to treat MCL and chronic lymphocytic leukemia (CLL), and they have the compound in Phase III testing to treat non-Hodgkin's lymphoma (NHL) and B cell lymphoma and in Phase II testing to treat multiple myeloma (MM) and lymphoma. Pfizer Inc. and Amgen Inc. have palbociclib (PD-0332991), an oral small molecule CDK4 and CDK6 inhibitor, in registration to treat breast cancer, Phase II testing to treat sarcoma and preclinical testing to treat melanoma. Gilead Sciences Inc. markets Zydelig idelalisib (GS-1101), a small molecule inhibitor of PI3Kδ, to treat CLL and NHL.</p> <p>SciBX 7(33); doi:10.1038/scibx.2014.982 Published online Aug. 28, 2014</p>	Patent and licensing status undisclosed	<p>Chiron, D. <i>et al. Cancer Discov.</i>; published online July 31, 2014; doi:10.1158/2159-8290.CD-14-0098 Contact: Selina Chen-Kiang, Weill Cornell Medical College, New York, N.Y. email: sckiang@med.cornell.edu</p>