This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Chronic lymphocytic leukemia (CLL)	Bruton's tyrosine kinase (BTK); phospholipase C _{γ2} (phosphatidylinositol-specific) (PLCG2)	<p>Studies in human samples identified mutations responsible for resistance to the irreversible BTK inhibitor Imbruvica ibrutinib in patients with CLL that could guide the development of new therapies. Whole-exome sequencing of peripheral blood samples from patients with CLL before and after ibrutinib treatment identified a resistance-associated C481S mutation in BTK that prevented irreversible binding of the drug in five of six patients. In two of six patients, gain-of-function resistance mutations in PLCG2 were identified that induced B cell receptor signaling independent of BTK. Next steps could include designing compounds that could overcome the identified resistance mechanisms.</p> <p>Pharmacyclics Inc. and Johnson & Johnson market Imbruvica to treat CLL and mantle cell lymphoma (MCL). The compound is in Phase III testing to treat B cell lymphoma and non-Hodgkin's lymphoma (NHL) and Phase II testing to treat multiple myeloma (MM) and lymphoma.</p> <p>SciBX 7(26); doi:10.1038/scibx.2014.762 Published online July 10, 2014</p>	Patent and licensing status unavailable	<p>Woyach, J.A. <i>et al. N. Engl. J. Med.</i>; published online May 28, 2014; doi:10.1056/NEJMoa1400029</p> <p>Contact: John C. Byrd, The Ohio State University, Columbus, Ohio e-mail: john.byrd@osumc.edu</p>