This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Acute myelogenous leukemia (AML)	Chemokine (C-X-C motif) receptor 4 (CXCR4); chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) (CXCL12; SDF-1 α)	<p>Studies in mice suggest that CXCR4 antagonists may sensitize leukemic cells to kinase inhibitors. In a murine leukemia xenograft model, combination therapy with the CXCR4 inhibitor AMD3456 plus the fms-related tyrosine kinase 3 (FLT3) inhibitor Nexavar sorafenib and colony stimulating factor 3 (granulocyte) (CSF3; GCSF) significantly increased median survival compared with that seen in mice that received vehicle, Nexavar or AMD3456 and GCSF alone ($p < 0.001$). Imaging studies showed that AMD3456 mobilized bone marrow-resident AML cells into circulation, thus making them vulnerable to kinase inhibitors. Two clinical trials with CXCR4 inhibitors in combination with chemotherapy and FLT3 inhibitors will soon begin at M.D. Anderson Cancer Center.</p> <p>Nexavar sorafenib, a multi-kinase inhibitor from Onyx Pharmaceuticals Inc. and Bayer AG, is marketed to treat renal and liver cancers.</p> <p>Mozobil plerixafor, a synthetic CXCR4 receptor antagonist and analog of AMD3456 from Genzyme Corp., is under regulatory review to enhance mobilization of hematopoietic stem cells for collection and subsequent autologous transplantation in patients with lymphoma or multiple myeloma (MM).</p> <p>At least six other companies have CXCR4 antagonists in Phase I/II testing or earlier to treat cancer.</p>	Genzyme holds the patent for use of CXCR4 inhibitors for stem cell mobilization	<p>Zeng, Z. <i>et al. Blood</i>; published online Oct. 27, 2008; doi:10.1182/blood-2008-05-158311</p> <p>Contact: Marina Konopleva, University of Texas M.D. Anderson Cancer Center, Houston, Texas e-mail: mkonople@mdanderson.org</p>
		<p>SciBX 1(41); doi:10.1038/scibx.2008.992 Published online Nov. 13, 2008</p>		