

The following slides are excerpted from a presentation for the Advocate Institute by Richard Schilsky, MD, University of Chicago. Full presentation is available through the Advocate Institute Focus on Research Course at www.researchadvocacy.org

What is “targeted therapy”?

- Pharmacological, immunological or genetic interference with specific molecular targets/pathways thought to be of fundamental importance in cancer pathogenesis, proliferation, survival or metastatic capability
- Goal is highly specific, potent, effective and non-toxic therapy

Requirements for targeted therapy

- Validated molecular target
- Reliable assay to measure target or pathway expression/activity
- Differential target expression in tumor cells
- Potent and specific inhibitor with good pharmaceutical properties
- Demonstrable target inhibition in human tumors

Target Validation

- Is the target expressed, overexpressed or mutated in tumor tissue?
- Is the target important in cell proliferation, cell death, metastatic ability?
- Does inhibition of the target result in inhibition of tumor growth or spread?

Agent Generic/Brand	Method of delivery	Target	Goal	Cancer
Bevacizumab/ Avastin	Monoclonal antibody	Vascular endothelial growth factor (VEGF)	Stop angiogenesis in tumor	Metastatic CRC
Trastuzumab/ Herceptin	Monoclonal antibody	<u>HER2 receptor</u> One of the epidermal growth factor receptors (ERFR)	Slow or stop tumor growth or proliferation	Breast
Rituximab/ Rituxan	Monoclonal antibody	<u>CD 20</u> An antigen that promotes the growth of B-lymphocytes	Attach to CD 20 to recruit natural defenses to kill marked B-cells	Non-Hodgkin's lymphoma (NHL)
Ibritumomab tiuxetan/ Zevalin	Monoclonal antibody and radio- immunotherapy	<u>CD20</u>	Attach to CD 20 to recruit natural defenses to kill marked B-cells and radiation to lymphoma cells	NHL
Tositumomab and iodine-131 tositumomab/ Bexxar	Monoclonal antibody and radio- immunotherapy	<u>CD 20</u>	Attach to tumor cell and recruit T- lymphocytes to kill and deliver radiation to tumor cells	NHL
Cetuximab/ Erbix	Monoclonal antibody	EGFR	Slow or stop proliferation	Colon
Imatinib mesylate/ Gleevec	Tyrosine Kinase Inhibitor (TKI)	Abnormal enzyme in tumor cells	Turn off signal of protein know to cause cancer	CML GIST
Gefitinib/ Iressa	TKI			Metastatic NSCLC
Erlotinib HCL/ Tarceva	TKI	HER1 signaling pathway	Stop cell growth signal	Metastatic NSCLC
Bortezomib/ Velcade		Proteasome (26S) Enzyme complexes that degrade intracellular proteins. Cancer cells depend on proteins regulated by the proteasome for proliferation, metastasis and survival	Inhibition of 26S proteasome and degradation of proteins leads to disruption of signaling cascades and tumor cell death	multiple myeloma