WSU-WM-SCID mouse xenograft model: utility in developing new therapeutic strategies in Waldenstrom's Macroglobulinemia (WM). Al-Katib AM, Aboukameel A, Mohammad RM. Wayne State University (WSU) School of Medicine, Detroit, MI, USA

The WSU-WM, a permanent EBV-negative cell line established in 1993 and propagated in mice with severe combined immune deficiency (SCID), is the only pre-clinical xenograft model available for human WM. This cell line was established from malignant pleural effusion of a 60-year-old man with a pre-terminal IgMκ WM. In addition to *in vitro* growth in liquid culture, WSU-WM also forms subcutaneous (sc) tumors in SCID mice. This xenograft model was used to investigate the activity of a variety of therapeutic agents including standard and experimental cytotoxic agents, biological agents (bryostatin 1) and monoclonal antibodies (rituximab), as single agents or in combination. Some of the agents demonstrated activity but none led to the cure of animals. The $\log_{10}$Kill for active agents was: L-phenylalanine mustard (L-PAM) = 3.96, Vincristine 2.8, 2-Chlorodeoxyadenosine (2-CdA) 1.3, rituximab 1.9. The only cure of all animals (8/8) bearing WSU-WM was noticed with a combination of rituximab (150 mg/kg intravenously daily for 5 days) and 2-CdA (30 mg/kg sc daily for 5 days). One mechanism of synergism between these two agents is the enhancement of the 2-CdA phosphorylating enzyme, deoxycytidine kinase (dCK) by rituximab. There was a progressive increase in dCK activity in WM tumor cells in SCID mice following 1, 3 and 5 injections of rituximab (170, 210 and 258% increase, respectively) compared with control. We conclude that a combination of rituximab with 2-CdA is very effective against this WM xenograft model and warrants clinical investigation in patients with WM.