Session VII: Novel Agents for Treatment of

Waldenström's Macroglobulinemia

Abstract 140

Presenter: I. Ghobrial

Regulation of the PI3K/mTOR pathway in Waldenström's Macroglublinemia (WM). Irene M. Ghobrial, Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA.

The PI3K/Akt and NF-kB pathways act as critical regulators of apoptosis, cell cycle, and tumor proliferation in lymphoproliferative disorders including Waldenström's Macroglobulinemia (WM). The Akt and NF-kB pathways are constitutively activated in WM cells. We demonstrated that the use of novel PI3K/Akt/mTOR inhibitors inhibit tumor proliferation in vitro and in vivo. The preclinical studies of novel therapeutic agents in WM will be presented as well as studies identifying mechanisms of resistance to therapy and methods to overcome it. In addition, we will present data on the clinical trials of the phase II study of the Akt inhibitor perifosine in relapsed WM as well as the phase II study of the mTOR inhibitor RAD001 in relapsed WM. Finally, we will present updates on the phase II clinical trial of weekly use of bortezomib in combination with rituximab in relapsed/refractory or upfront therapy in WM. These studies help advance the understanding of the biology and therapy of WM, and may be applicable to other hematological malignancies.