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Targeting the PI3K/AKT/MTOR pathway in KSHV-associated cancers

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Kaposi's sarcoma-associated herpesvirus (KSHV) is linked to three different human cancers: Kaposi's sarcoma (KS), primary effusion lymphoma (PEL) and multicentric Castleman's disease (MCD). We have previously reported that the PI3K/Akt/mTOR pathway is critical for the survival of KSHV-infected endothelial cells and B cells, and have demonstrated that Rapamycin/Sirolimus, an inhibitor of mTOR, can induce PEL cell death *in vitro* and *in vivo* (Sin et al., Blood. 2007. 109(5):2165–73). We have now extended these findings and demonstrate that therapeutic targeting of other members of the PI3K/Akt/mTOR signal transduction pathway can also induce cell death in PEL *in vitro* and inhibit tumor growth in murine xenograft models. Importantly, some of these novel drug candidates have passed clinical trials for other indications and can therefore be tested for efficacy against KS and AIDS-associated lymphomas.