A pilot trial of the mTOR (mammalian target of rapamycin) inhibitor RAD001 in patients with advanced B-CLL.

Although B-cell chronic lymphocytic leukemia (CLL) is treatable, it remains an incurable disease and most patients inevitably suffer relapse. Many therapeutic options exist for those requiring therapy, including monoclonal antibodies and stem cell transplantation, but remissions tend to last shorter in the course of the disease. Targeting the cell cycle has recently been realized to be an attractive therapeutic approach in solid and hematological malignancies, and the proliferative nature of B-CLL is increasingly accepted. Here, we report data on a phase II pilot trial with the oral mammalian target of rapamycin (mTOR) inhibitor RAD001 5 mg/daily in patients with advanced B-CLL who had progressive disease after at least two lines of treatment. After treatment of seven patients, this trial was stopped because of toxicity concerns, although some degree of activity was observed (one partial remission, three patients with stable disease). Interestingly, cyclin E expression decreased in responding patients. Further strategies of mTOR inhibition by RAD001 in B-CLL should focus on different treatment schedules, adequate anti-infectious prophylaxis, or combinations with cytotoxic drugs.