**Supplementary Methods & Figure Legend**

**Methods**

**BCR stimulation and treatment of CLL B-cells with BTK inhibitors**

CLL B-cells from previously untreated CLL patients (n=5) were incubated with 10g/ml goat F(ab’)2 anti-human IgM antibody (MP Biomedicals) or left untreated, followed by exposing the cells to BTK inhibitors (ibrutinib or TP-4216) at increasing doses (0.25-0.75M) for 24 h. Cells were harvested and apoptosis induction was determined by flow cytometric analysis after staining with annexin V/PI.

**Figure Legend**

**Supplementary Fig. 1. BCR stimulation sensitizes CLL B-cells to BTK inhibitor induced apoptosis *in vitro***. CLL B-cells from previously untreated CLL patients (n=5) were treated with increasing doses of ibrutinib (**panel A**) or TP-4216 (**panel B**) as indicated in presence or absence of 10g/ml of goat anti-human IgM antibody. After 24 h, cells were harvested and apoptosis induction was determined by flow cytometry after staining the cells with annexin V-FITC/PI. Results are expressed as mean with standard deviation values at each dose of the inhibitors.