**Supplemental figures**

**Figure S1**

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**Figure S2**

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**Figure S3**

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**Figure S4**

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**Figure S5**

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**Figure S6**

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**Figure S7**

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**Figure S8**



**Supplemental figure legends**

**Figure S1**

**TBZ-induced cell death is increased in BL cells compared to normal blood cells (PBMCs)**. Cells were treated with the indicated concentrations of BV6 and TRAIL (BL-30: 5 ng/ml, BL-2: 15 ng/ml) in the presence of zVAD.fmk (20 µM) for 24 h (BL-30) and 48 h (BL-2). Cell death was determined by analysis of PI/Hoechst staining and ImageXpress Micro XLS system. Mean and SEM of three independent experiments are shown; \*\*p<0.01; \*\*\*p<0.001.

**Figure S2**

**FASL/BV6/zVAD.fmk treatment induces necroptotic cell death.** Cells were treated with BV6 (BL-2: 4 µM, BL-30: 6 µM, Seraphine: 7 µM, RAMOS: 18 µM), FASL (Seraphine and RAMOS: 10 ng/ml and BL-2, BL-30: 200 ng/ml) and zVAD.fmk (20 µM) in the presence or absence of Dabrafenib (BL-30: 5 µM, BL-2, RAMOS: 10 µM) or GSK’872 (10 µM), Nec-1s (20 µM) and NSA (1,5 µM) for 24 h (RAMOS, Seraphine, BL-30) and 48 h (BL-2). Cell death was determined by analysis of PI/Hoechst staining and ImageXpress Micro XLS system. Mean and SEM of three independent experiments are shown; \*\*p<0.01; \*\*\*p<0.001. (B) Protein levels of FASR were assessed by Western blotting, GAPDH served as a loading control.

**Figure S3**

**TNF/BV6/zVAD.fmk treatment induces necroptotic cell death.** (A) Cells were treated with BV6 (BL-2: 4 µM, BL-30: 6 µM, Seraphine: 7 µM, RAMOS: 18 µM), TNF (RAMOS: 30 ng/ml and BL-2, Seraphine, BL-30: 100 ng/ml) and zVAD.fmk (20 µM) in the presence or absence of Dabrafenib (BL-30: 5 µM, BL-2, RAMOS: 10 µM) or GSK’872 (10 µM), Nec-1s (20 µM) and NSA (1,5 µM) for 24 h (RAMOS, Seraphine, BL-30) and 48 h (BL-2). Cell death was determined by analysis of PI/Hoechst staining and ImageXpress Micro XLS system. Mean and SEM of three independent experiments are shown; \*\*\*p<0.001. (B) Protein levels of TNFR1 were assessed by Western blotting, GAPDH served as a loading control.

**Figure S4**

**BL cell lines express TRAIL-R1 and TRAIL-R2.** Protein levels of TRAIL-R1 and TRAIL-R2 were analyzed by Western blotting, GAPDH served as loading control.

**Figure S5**

**Doxycycline induces expression of RIPK3 in DOX-inducible RIPK3 overexpressing cells.** Cells were treated with 100 ng/ml doxycycline for the indicated time points. Protein levels of RIPK3 were analyzed by Western blotting, GAPDH served as loading control.

**Figure S6**

**Knockdown of MLKL in MLKL/RIPK3-overexpressing cells rescues TRAIL/BV6/zVAD.fmk-induced cell death**. MLKL/RIPK3-overexpressing RAJI and DAUDI cells were transfected twice with 200 nM non-silencing control siRNA (siCtrl) or siRNAs against MLKL. Protein levels of MLKL were assessed by Western blotting, GAPDH served as loading control. Cells were then treated with BV6 (DAUDI: 5 µM, RAJI: 8 µM), TRAIL (15 ng/ml), zVAD.fmk (20 µM) and DOX (100 ng/ml) for 8 h. Cell death was determined by analysis of PI/Hoechst staining and ImageXpress Micro XLS system. Mean and SEM of three independent experiments are shown; \*p<0.05; \*\*\*p<0.001.

**Figure S7**

**DNA sequence of the promoter region of MLKL**. Non-methylated cytosines of isolated DNA were converted into uracils by bisulfite conversion. PCR (recognizing uracil as thymine) of the promoter region of MLKL was performed followed by Sanger sequencing.

**Figure S8**

**SGI-110/TBZ treatment leads to upregulation and phosphorylation of MLKL.**

(A) Cells were pre-treated with 1,5 µM SGI-110 for 24 h (Salina) and 72 h (RAJI RIPK3 OE, DAUDI RIPK3 OE). BV6 (DAUDI: 5 µM, Salina: 6 µM, RAJI: 8 µM), TRAIL (15 ng/ml) and zVAD.fmk (20 µM) were applied for 8 h. Protein levels of RIPK3, MLKL and p-MLKL were assessed by Western blotting, GAPDH served as loading control. (B) Cells were pre-treated with 1,5 µM SGI-110 for 24 h (Salina) and 72 h (RAJI RIPK3 OE, DAUDI RIPK3 OE). BV6 (DAUDI: 2 µM, RAJI, Salina: 4 µM), TRAIL (15 ng/ml) and zVAD.fmk (20 µM) were applied for 24 h. Cell death was determined by analysis of PI/Hoechst staining and ImageXpress Micro XLS system. Mean and SEM of three independent experiments are shown; \*p<0.05; \*\*p<0.01.