Supplemental Figure Legends

Supplemental Figure S1. ABT-199 has higher potency than ABT-737 in sensitive AML cell lines (A) and sensitive primary AML samples (B). A non-parametric two-tailed paired t-test was used to calculate the p values (A: n = 6; B: n = 19).

Supplemental Figure S2. Knockdown of MCL-1 significantly sensitized OCI-AML3 cells to ABT-737. OCI-AML3 cell lines were treated with indicated concentrations of ABT-199 or ABT-737 for 48 h. Live cell number was determined by flow cytometry using counting beads. The absolute cell number was normalized to that of untreated control.

Supplemental Figure S3. Resistant MOLM-13 cells have relatively low expression of BCL-2 protein.

A). Representative histograms of BCL-2 protein expression in MOLM-13 parental and resistant cells. B). Median Fluorescence Intensity (MFI) of MOLM-13 parental and resistant cells, as determined by intracellular Flow cytometry for BCL-2 protein.

Supplemental Figure S4. Incubation of AML cell lines and AML primary cells with FBS does not influence apoptotic priming.

The AML cell line MOLM-13 and AML primary cells (AML 31) were incubated in the presence or absence of FBS for 8 h. Intracellular BH3 profiling was performed and the % Cytochrome c was measured.

Supplemental Figure S5. Clinical characteristics of AML patients do not correlate with ABT-199 sensitivity.

A. Patients from Figure 4B were classified by their FAB status (French-American-British classification). There was no significant difference between the IC50 values between various cohorts (note, M1 was not

included in the analysis because there were not enough samples to perform the analysis). B. Patient samples used in Figure 4B were stratified by their nucleophosmin 1 status (an NPM1 mutation is a good prognostic factor). There was no difference in IC50 values between patients who had an NPM1 mutation and those who were WT. C. Patient samples used in Figure 4B were stratified by their FLT3 status (a FLT mutation is a poor prognostic factor). There was no difference in IC50 values between patients who had an FLT3 mutation and those who were WT. D. Patient samples used in Figure 4B were stratified into newly diagnosed patients who achieved a complete response (CR), newly diagnosed patients who did not achieve a CR and relapsed patients. There is no difference in ABT-199 IC50 values between the three groups. A Mann-Whitney t test was used for these comparisons.

Supplemental Figure S6. No correlation was observed between ABT-199 EC50 values and relative MCL-1 protein levels in primary AML samples.

Non-parametric one-tailed Spearman test was used to determine the correlation coefficient (r = -0.1399, p = 0.344).

Supplemental Figure S7. Expression of *BCL2L1*, *MCL1*, and *BCL2L11* across cytogenetic and molecular genetic subgroups.

Boxplots represent the quartiles and range of log2 values of mRNA expression for BCL2L1 (gene encoding BCL-X) (A), MCL1 (B) and BCL2L11 (gene encoding BIM) (C) genes in different subgroups.

Supplemental Figure 8. Sensitivity of Bulk and LSC AML myeloblasts to ABT-737. Patient AML samples treated with 100 nM ABT-737 for 24 hours were subjected to FACS analysis of specific apoptosis based on Annexin V staining in the bulk AML myeloblast and CD34+/CD38-/CD123+ LSC-containing population. p value determined via paired t-test. of AML and normal bone marrows. The median is indicated by the black line in each box. Numbers on top indicate number of patients in each specified subgroup. Differences in gene expression with P values ≤ 0.005 were considered statistically significant, as denoted by *.

Supplemental Figure 8. Sensitivity of Bulk and LSC AML myeloblasts to ABT-737.

Patient AML samples treated with 100 nM ABT-737 for 24 hours were subjected to FACS analysis of specific apoptosis based on Annexin V staining in the bulk AML myleoblast and CD34+/CD38-/CD123+ LSC-containing population. p value determined via paired t-test.

Supplemental Figure 9. The mitochondrial response to ABT-263 correlates with the mitochondrial response to the BAD BH3.

AML myeloblast mitochondria were exposed to either BAD BH3 (80uM) or ABT-263 (1uM) and the release of cytochrome c was measured. Correlations were tested using a one-tailed Spearman r correlation using GraphPad Prism software.