**Supplementary files to**

Lázaro-Navarro J et al. *Blood Advances* 2021

The following supplementary files include:


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# Supplementary Methods

**Cell lines, patient derived xenografts and primary patient samples**

The human BCP-ALL cell lines NALM-6, SEM, REH, NALM-16, HAL-01 an 697 were purchased from the German Collection of Microorganisms and Cell cultures (DSMZ, Braunschweig, Germany). Cell lines were cultivated using RPMI 10% FCS and 5% penicillin-streptomycin at 37ºC, 5% $CO_2$. Cell lines were routinely tested for the expression of the corresponding surface markers and fusion genes by flow cytometry, quantitative real-time PCR and FISH.

Primary patient cells form bone marrow or peripheral blood were obtained at diagnosis of B cell precursor acute lymphoblastic leukemia and were transplanted into NSG or NOD/SCID (BH-3 profiling) mice and harvested once mice showed signs of progressing disease (Ebinger S et al. Cancer Cell 2016; Meyer L et al. Cancer Cell 2011). Patient derived xenograft (PDX) cells re-isolated from bone marrow and/or spleen were seeded onto 96well plates pre-coated with drugs, cultivated in RPMI medium with 20% FCS or used for BH-3 profiling (see below). Viability was measured by WST-1 assay after 24h. Written informed consent was obtained from all patients and from parents/ caregivers in the cases where patients were minors. The study was performed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. Animal trials were performed in accordance with the current ethical standards of the official committee on animal experimentation.

BCP-ALL primary samples were co-cultured in an established patient derived MSC model system[2]. Samples were selected according to availability of viable frozen or fresh cells. All patients were enrolled in the relapse trial *ALL-REZ BFM 2002* trial and *ALL-REZ BFM* registry, approved by the Institutional Review Board of the Charité-Universitätsmedizin Berlin, Berlin, Germany (ClinicalTrials.gov identifier: NCT00114348). Written informed consent was obtained from patients or guardians.

**Assessment of viability and apoptosis in "in vitro" models**

Viability and proliferation after treatment was assessed using the WST-1 Assay for Cell Proliferation and Viability (Roche Applied Science, Rotkreuz, Switzerland) according to manufacturer's instructions.

Apoptosis was assessed by staining cells with Annexin A5 and propidium iodide (PI) and flow cytometry analysis using BD LSRFortessa™X-20 cell analyzer (BD Biosciences, USA) and FlowJo CL Software v.10 (Treestar, Ashland, OR, USA). In the caspase inhibition assays, Q-VD was employed for this purpose and caspase 3/7 was assessed via FACS after staining with CellEvent™ Caspase-3/7 Green Detection Reagent (Thermo Scientific, Rockford, USA).

All inhibitors used in different treatment experiments were purchased from Selleckchem (TX, USA).

**MCL1 overexpression**

For MCL1 overexpression experiments, NALM-6 cells were transduced with an empty vector or with a lentiviral human Mcl-1 insert vector DNA pCMV6-Entry-hMcl-1 (Myc-DDK-Tagged; Origene, USA).

**GSK3 knock-out**

For GSK3 knock-out experiments, two guide RNAs targeting GSK3B exon2 were in-vitro synthesized (Synthego, Menlo Park, USA) in a chemically stabilized form and incubated with Cas9 protein (PNA bio, Newbury Park, USA) to form ribonucleoproteins which were introduced to NALM-6 cells via electroporation (Neon Transfection System, Thermo Scientific, Rockford, USA) following an established protocol (Gundry M et al. Cell reports 2016). The guide RNA sequences use were: CGGCAGCAAGGUGACAACAG and UAUACAGACACUAAAGUGAU

**Protein quantification**

Western blot analysis was performed in cell lysed with RIPA buffer and following the protocols described in the Trans-Blot® Turbo™ Transfer System (Bio-Rad Laboratories GmbH, München, Germany). For protein quantification in titration and MCL1 overexpression experiments, cells were lysed with M-PER™ Mammalian Protein Extraction Reagent (Thermo Scientific, Rockford, USA) and capillary western blot was performed using Simple Wes system (Protein Simple, San Jose, CA, USA). Antibodies used for western blot were purchased from Cell Signaling (Danvers, MA, USA): Anti-rabbit IgG HRP-linked Antibody (#7074), MCL1 (#5453), BCL2 (#4223) and phosphor-GKS3B(S9) (#5558), b-actin (#4967), alpha-tubulin (#2144) except for HSP60 (GTX110089, Genetex, USA).

MCL1 intracellular staining for FACS analysis was performed by fixating and permeabilization of cells using FIX & PERM Kit (Dianova, Hamburg, Germany) and staining with Mcl-1 (D2W9E) Rabbit mAb (PE Conjugate) from Cell Signaling (Danvers, MA, USA). MCL1-PE intensity was measured analyzing its Geometric Mean.

**BH3 profiling**

Baseline BH3 profiling of BCP-ALL patient-derived xenograft samples was carried out as previously described (Seyfried F et al. CDDis, 2019). For dynamic BH3 profiling (Montero J et al. Cell, 2015) BCP-ALL cell lines were exposed to venetoclax for 4 hours using their respective $EC_{10}$ concentrations (27 nM for 697 and 2 nM for HAL-01). After drug exposure, the cells were stained using the marker Zombie Violet (423113, Biolegend, Germany) for 15 minutes at room temperature to exclude dead cells. Thereafter, cells were permeabilized with 0.002% digitonin and exposed to the MS1 BH3 peptide (0.3 µM, 1 µM, 3 µM, 10 µM and 30 µM) for 60 minutes, 25 µM alamethicin (BML-A150-0005, Enzo, Germany) as positive control for cytochrome c release or DMSO negative control. After peptide exposure, cells were fixed in formaldehyde for 10 minutes and incubated in a neutralizing buffer for 10 minutes. Intracellular staining of cytochrome c was performed using an anti-Cytochrome c antibody (612308, Biolegend, Germany) overnight at 4°C. Samples were measured on an Attune NxT Flow Cytometer (Thermo Fisher, Germany) and analysis was performed using FlowJo 10.7.1 software (Becton Dickinson, USA). Delta priming to venetoclax was calculated as the difference of cytochrome c release (% priming) of venetoclax-treated to control-treated cells for the MS1 peptide.

**Transcriptome Sequencing**

NALM-6 cells were either treated with DMSO control, venetoclax (0.05µM), silmitasertib (5µM) or both drugs combined. After 3h and 12h RNA was isolated (AllPrep, Qiagen, Hilden, Germany) and used to prepare libraries for RNA-Seq (TruSeq RNA Library Prep Kit, Illumina, San Diego, USA). Libraries were sequenced 2x100 bp paired end, aiming for 30 Mio reads per sample. STAR (Dobin A et al. Bioinformatics, 2013) and HTSeq (Anders S et al. Bioinformatics, 2013 ) were used to align reads to the human reference and to obtain gene counts. DESeq (Anders S et al. Genome Biol, 2010) was used to analyze differential gene expression and variance stabilizing transformation was applied to obtain normalized gene expression values for visualization in heatmaps. Gene set enrichment analyses were performed using GSEA v4.1.0 (Submaranian A et al. PNAS, 2005) in pre-ranked mode.

**In vivo Zebrafish xenografts**

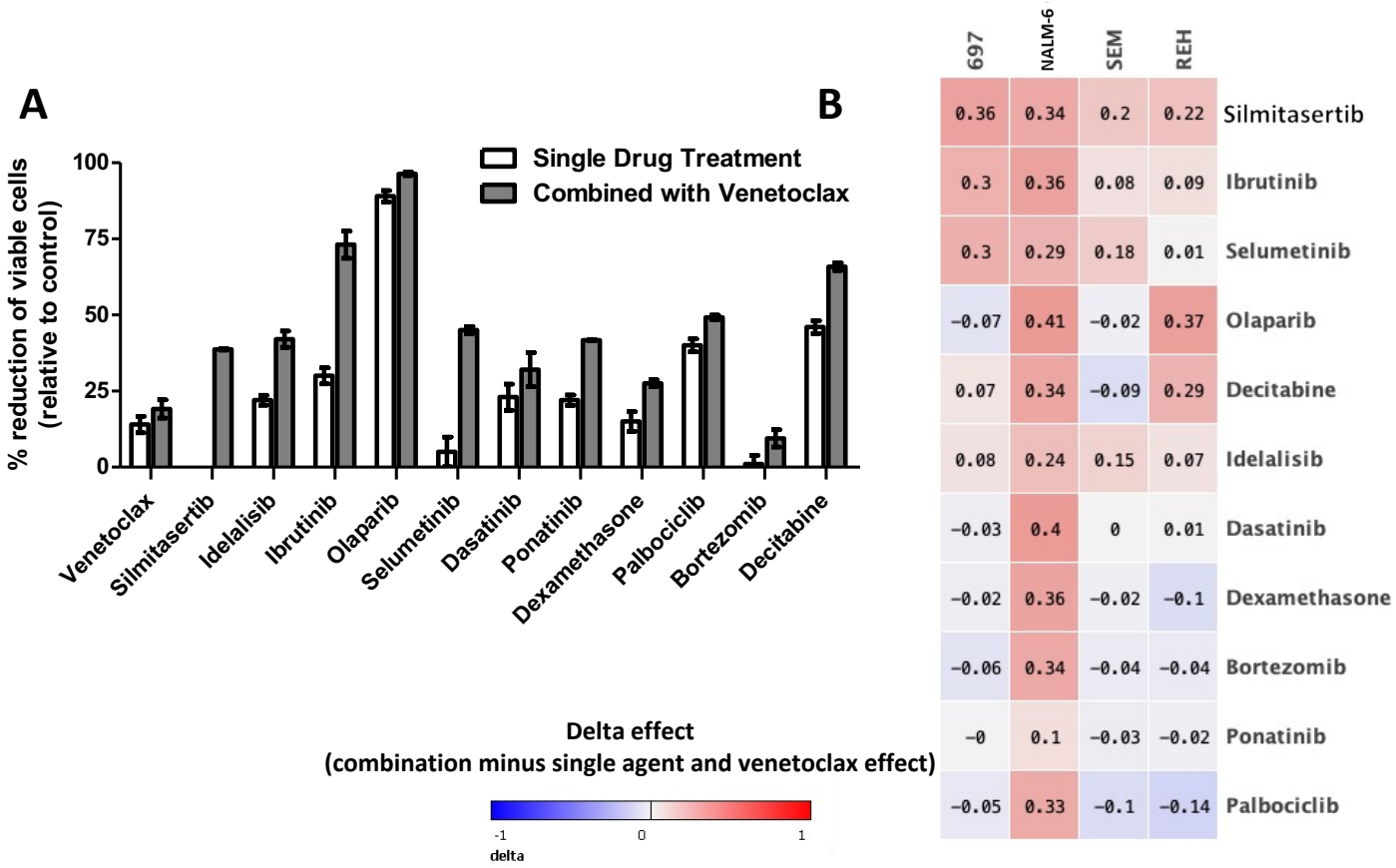
To create a transient 4-day immunosuppressed condition in zebrafish embryos, 50 µM each of morpholino antisense oligonucleotides directed against the ATG start site of spi1 and csf3r, both from Gene Tools, LLC, USA) were microinjected into 1–2 cell stage embryos in a total volume of 1 nL. Between 300–500 human CellTrace Violet (Thermo Scientific, Rockford, USA) stained SEM cells were injected into each embryo 48 h after fertilization. Embryos were allowed to recover in E3 medium (5 mM NaCl, 0.17 mM KCl, 0.33 mM CaCl, 0.33 mM MgSO4, pH 7.4) supplemented with 1% penicillin/streptomycin for 1 h at 28 °C before manually sorting for transplantation success on a M165 FC stereomicroscope (Leica Microsystems, Wetzlar, Germany). Treatments were performed by adding 1 µM venetoclax and 1 µM silmitasertib to the water bath (tolerated dose) together with 5 µM silmitasertib injected to the pericardium. Fish were kept in E3 medium at 35 °C for 72 h from 5

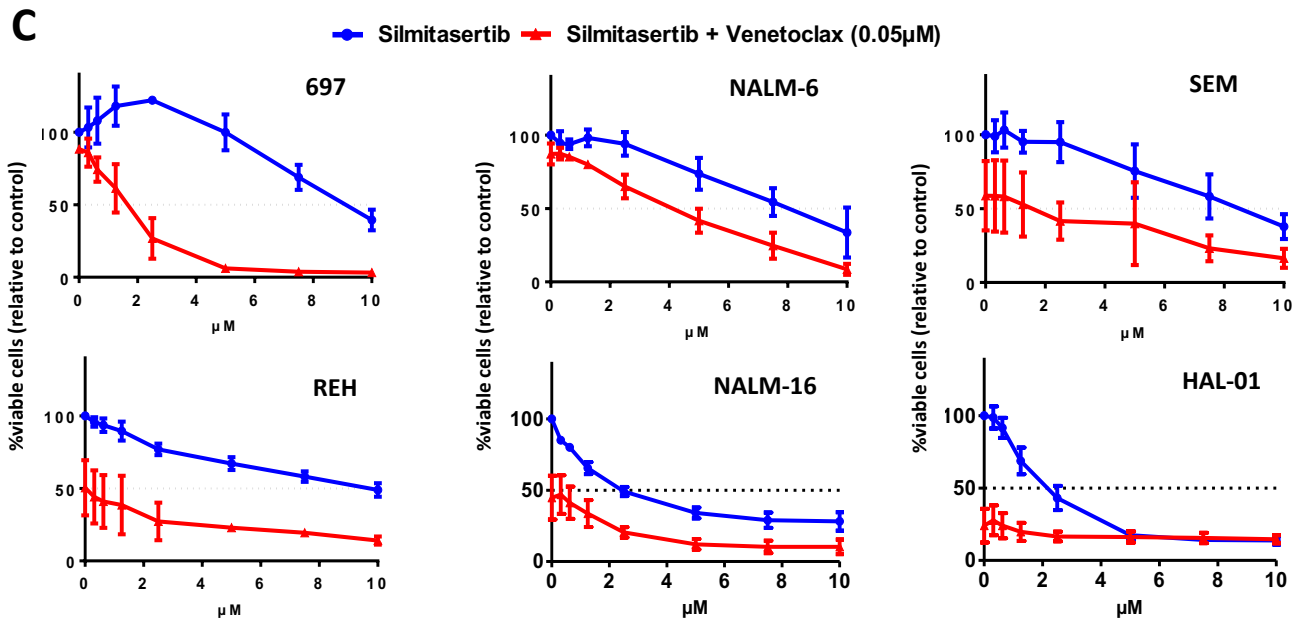
independent experiments assessed by flow cytometry (CD19+, ANXA5 - /7AAD -). Each experiment was measured as the mean of a pool of 10–20 embryos. Further details on this model are described in: Gauert A et al. Cancers (Basel), 2019.

**Combination effect and Statistical Analysis**

EC50 values were calculated using viability curves from WST-1 assays, using a linear regression model in Graphpad Software (v.7, San Diego, CA, USA). Statistical analysis was performed using Graphpad Software and analysis of synergy was carried out with Combenefit Software (University of Cambridge, Cambridge, UK).

## Supplementary Figure S1

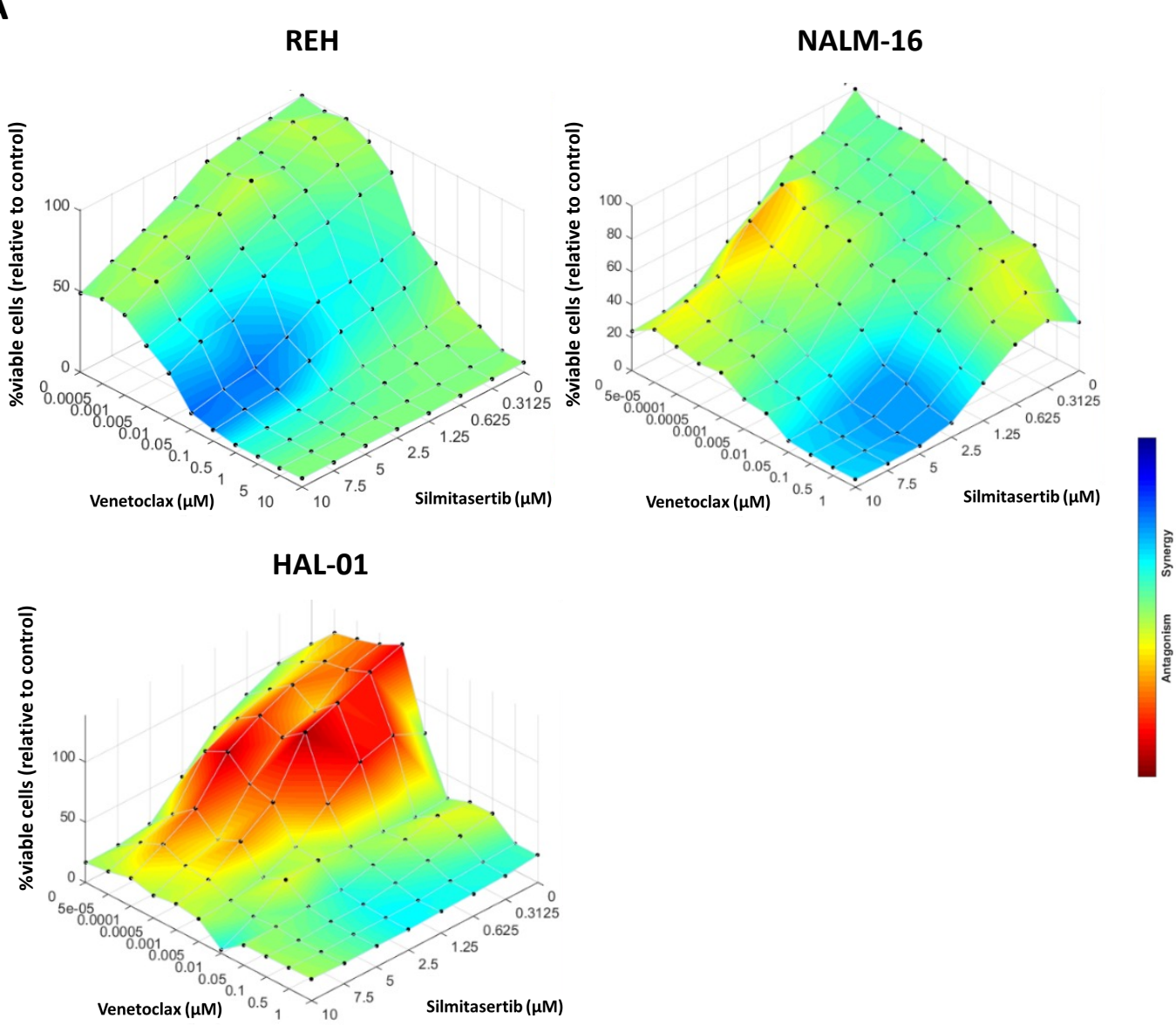


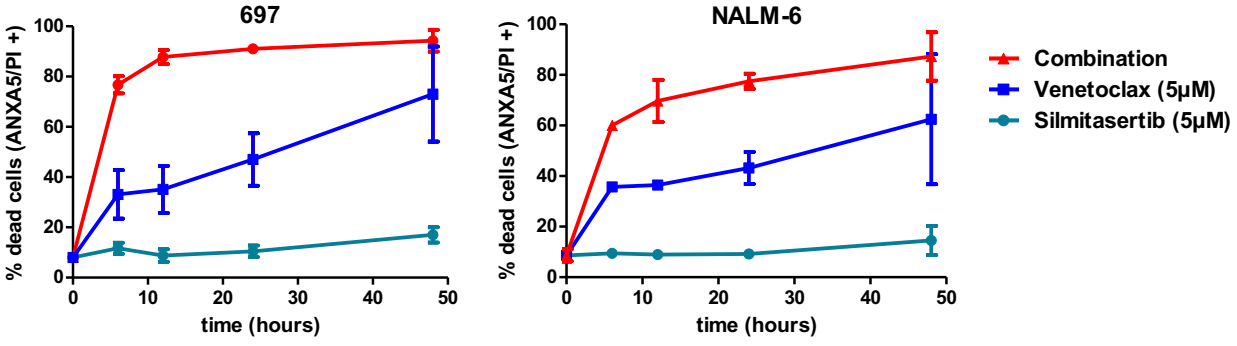
**Supplementary Figure S1. Silmitasertib is the most effective combination partner for venetoclax among the compounds tested, reducing viability and inducing apoptosis throughout numerous cell lines, dose ranges and time-points.**

(A) Cell viability of NALM-6 measured with WST-1 assay after 48h treatment with venetoclax 0.01µM or combined with the following compounds at minimal effect concentrations: silmitasertib 3 µM, palbocilib 0.1µM, dasatinib 1 µM, ponatinib 0.1 µM, dexamethasone 0.01 µM, ibrutinib 5 µM, idelalisib 10 µM, bortezomib 0.02 µM, decitabine 0.05 µM, selumetinib 10 µM and olaparib 7 µM. Figure shows mean and SD from triplicates. (B) Average additive reduction of viability of 11 compounds combined with venetoclax in 6 BCP-ALL cell lines measured with WST-1 after 48h of treatment (Delta = effect of the combination – single effects of both drugs). Figure shows mean values from triplicates. (C) Cell viability curves of 6 BCP-ALL cell lines measured with WST-1 assay after 48h treatment with serial dilutions of silmitasertib alone or combined with 0.05 µM venetoclax. Figure shows mean and SD from three independent experiments conducted in duplicates.

**A**


REH
NALM-16
HAL-01
%viable cells (relative to control)
Venetoclax (μM)
Silmitasertib (μM)
Synergy
Antagonism

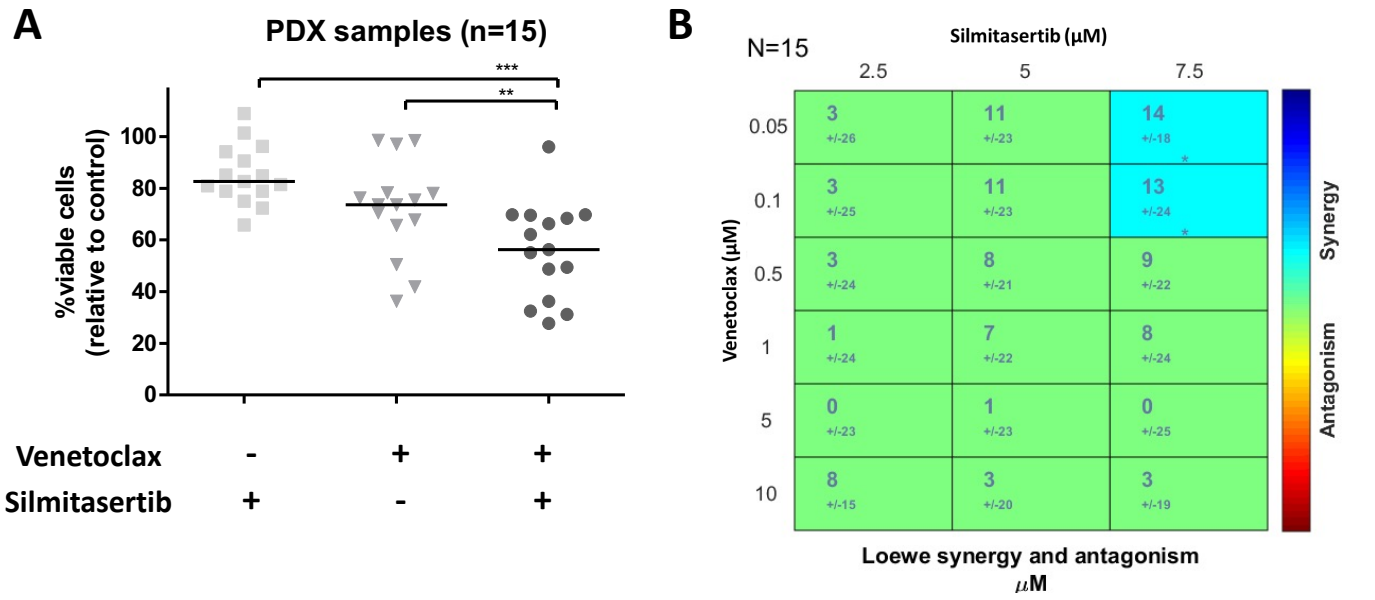
**B**


697
NALM-6
% dead cells (ANXA5/PI +)
time (hours)
Combination
Venetoclax (5μM)
Silmitasertib (5μM)

**Supplementary Figure S2. Venetoclax and silmitasertib show a more limited synergistic effect through different dose ranges in BCP-ALL cell lines with higher basal sensitivity to venetoclax.**

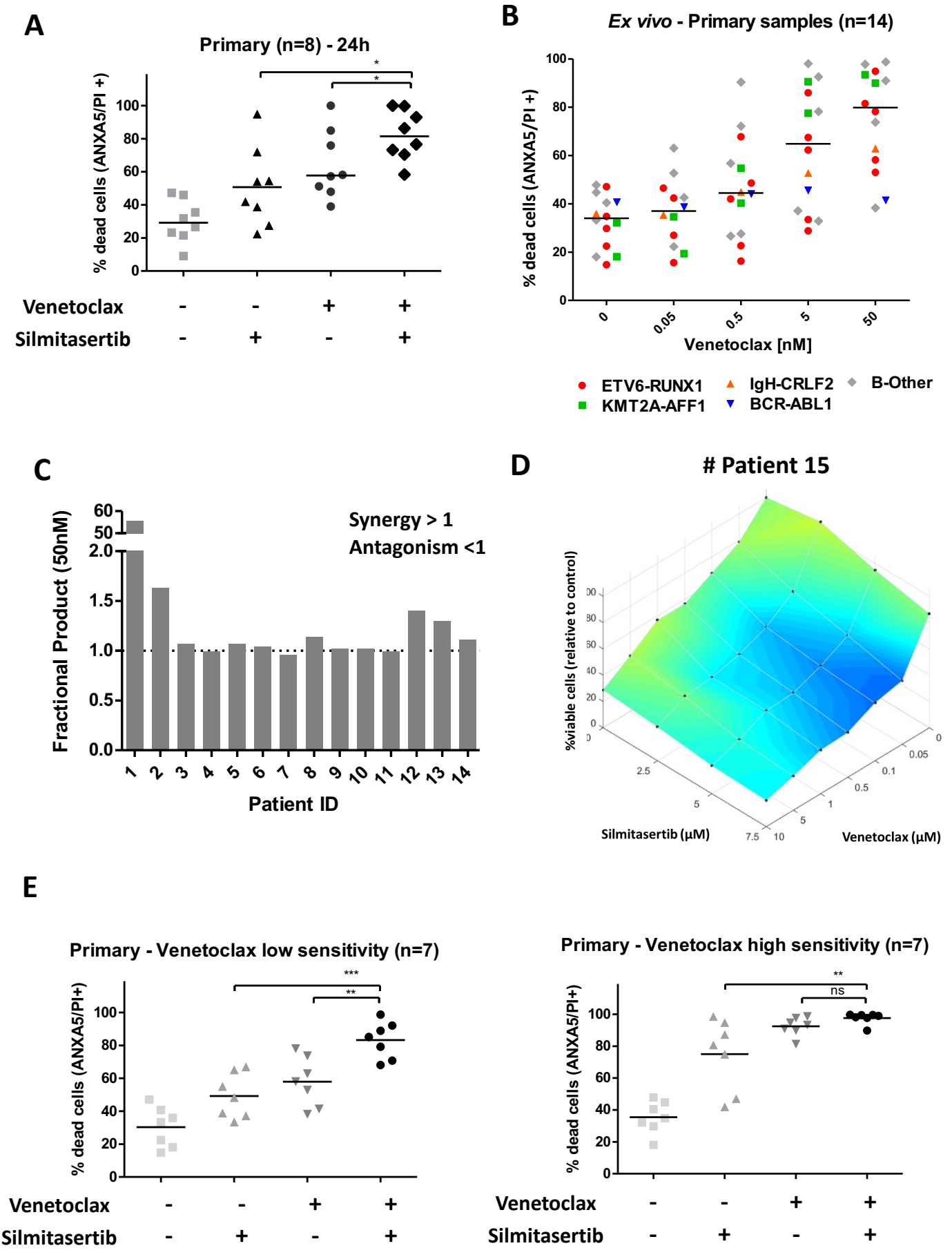
(A) Combination effects of venetoclax and silmitasertib in BCP-ALL cell lines REH, NALM-16 and HAL-01 were analyzed using WST-1 assay after 48h of treatments with serial dilutions of single and combined compounds. Combenefit software was used to calculate combination effects applying a LOEWE synergy model. Each datapoint represents one drug / drug combination treatment. Model integrates three independent experiments. (B) Proportion of dead cells (apoptotic/necrotic) in 697 and NALM-6 cells stained with ANXA5 and/or PI after 6/12/24/48h treatment with 5 µM venetoclax and/or 5 µM silmitasertib and analyzed by flow cytometry. Data represent mean ± SD of three independent experiments.

## Supplementary Figure S3



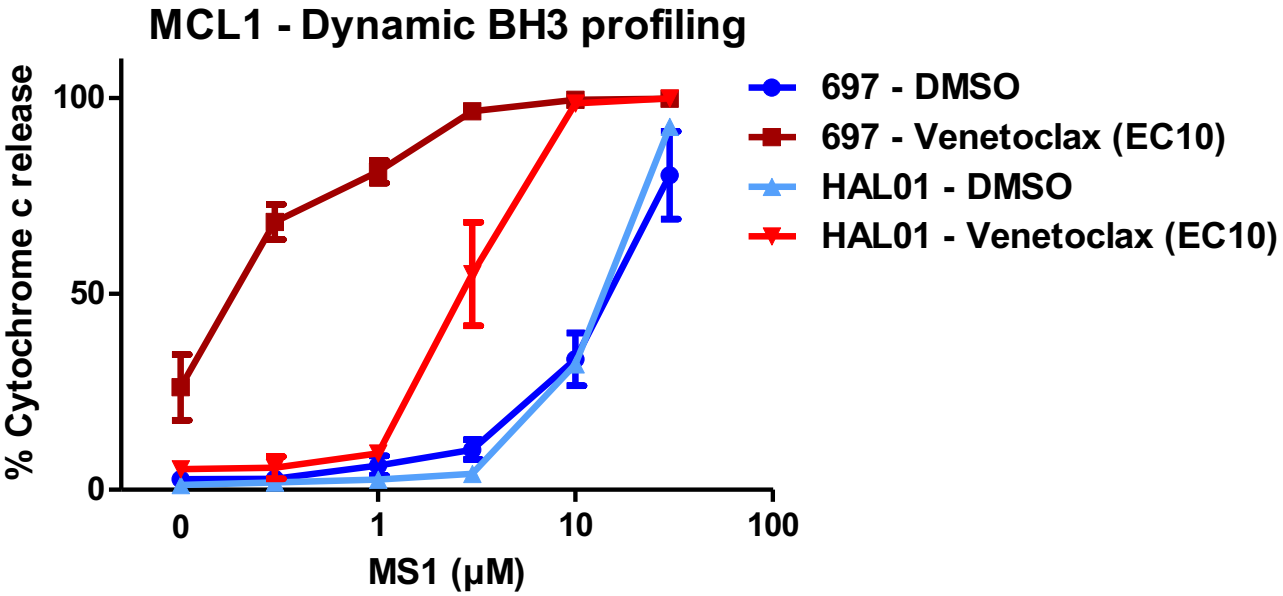

**Supplementary Figure S3. Ex vivo effect of venetoclax and/or silmitasertib in patient derived mouse xenografts (PDX) across different dose ranges.**

(A) Cell viability of PDX cells after 24h of treatments with silmitasertib (7.5 µM) and/or venetoclax (0.1 µM) as measured by WST-1 assay. Each dot represents one PDX sample, measured in triplicate, and lines indicate medians of the corresponding treatments. Mann-Whitney U test used for calculation of P values. (B) Combination effect analysis of venetoclax and silmitasertib in n=15 PDX samples were analyzed using WST-1 assay after 24h of treatment with serial dilutions of single and combined compounds, including data from Main Figure 1D and Supplementary Figure S3A. Combenefit software was used to calculate combination effects applying a LOEWE synergy model. Each datapoint represents one drug combination treatment. The model integrates n=15 samples, measured in triplicates.*P value < 0.05, **P value < 0.01, ***P value < 0.001.


A
Primary (n=8) - 24h
% dead cells (ANXA5/PI +)
Venetoclax - - + +
Silmitasertib - + - +
B
Ex vivo - Primary samples (n=14)
% dead cells (ANXA5/PI +)
Venetoclax [nM]
ETV6-RUNX1
KMT2A-AFF1
IgH-CRLF2
BCR-ABL1
B-Other
C
Fractional Product (50nM)
Synergy > 1
Antagonism <1
Patient ID
D
# Patient 15
%viable cells (relative to control)
Silmitasertib (µM)
Venetoclax (µM)
E
Primary - Venetoclax low sensitivity (n=7)
% dead cells (ANXA5/PI+)
Venetoclax - - + +
Silmitasertib - + - +
Primary - Venetoclax high sensitivity (n=7)
% dead cells (ANXA5/PI+)
ns
Venetoclax - - + +
Silmitasertib - + - +

**Supplementary Figure S4. Silmitasertib in patient derived primary samples across different dose ranges and time points.**

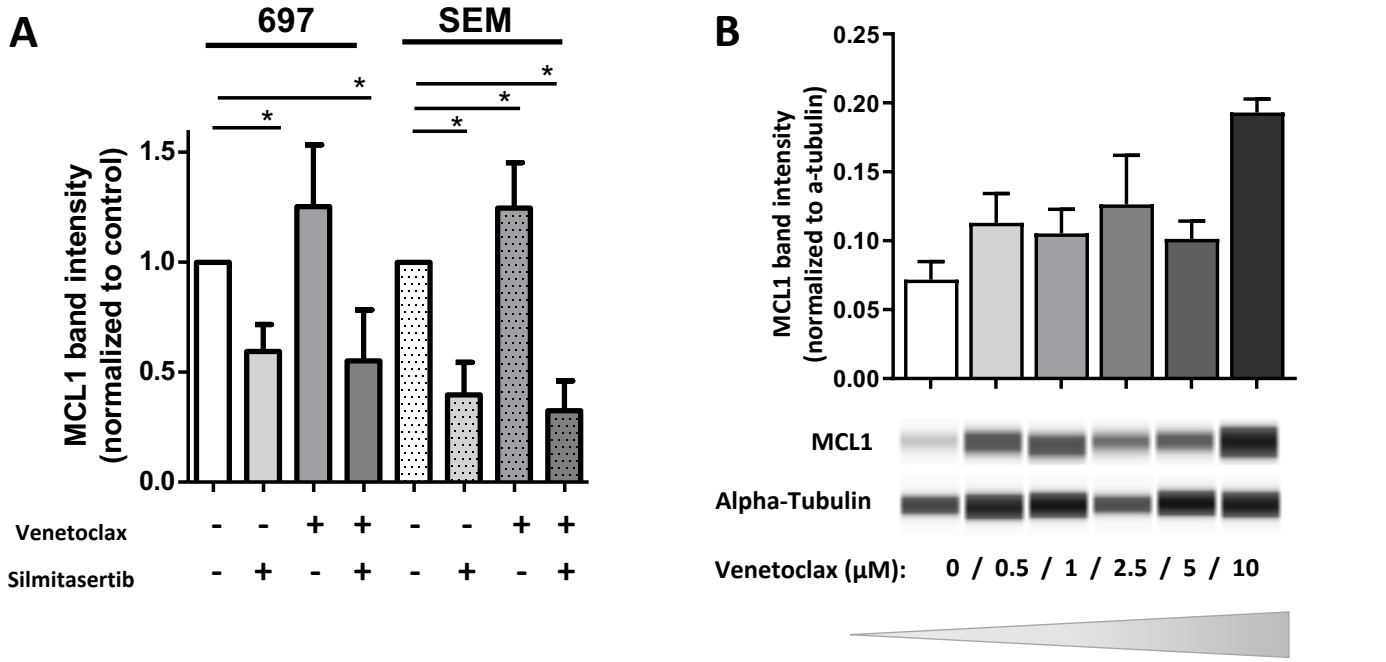
(A) Proportion of dead cells from BCP-ALL primary samples co-cultured on mesenchymal stem cells was analyzed by flow cytometry after 24h treatment with silmitasertib 5 µM and/or 50 nM venetoclax and staining with ANXA5 and PI. (B) Proportion of dead cells from BCP-ALL primary samples co-cultured on mesenchymal stem cells was analyzed by flow cytometry after 48h treatment with increasing concentrations of venetoclax. Each data point represents one sample with colours indicating molecular ALL subgroups. (C) Combination effect analysis of treatments in primary samples depicted in Main Figure 1E was performed via calculation of Webb's fractional product. (Fractional product = effect of drug combination / ((effect of drug A + effect of drug B)-(effect of drug A*effect of drug B); Webb JL. Effect of more than one inhibitor. Enzymes and metabolic inhibitors. New York: Academic Press; 1963. p. 66–79 & 487–512.). Values <1 indicate antagonism, values around 1 indicate additivity and values >1 indicate synergism. (D) Combination effect analysis in one primary sample 15 (Supplementary Table S3) were analyzed with WST-1 assay after treatment with serial dilutions of single and combined compounds (6 concentrations of venetoclax and 3 of silmitasertib). Freshly isolated sample was treated in monoculture for 24h in 20%RPMI medium. Combination effects were determined by a LOEWE synergy model (Combenefit software) integrating means of duplicate measurements. Each data point represents one drug or combination. (E) Primary samples from analysis in Main Figure 1E were grouped as "venetoclax high sensitivity" (EC50 < median) or (F) "venetoclax low sensitivity" (EC50 > median) to evaluate differences in the magnitude of the synergistic effect. Mann-Whitney U test was used for calculation of P values. *P value < 0.05, **P value < 0.01, ***P value < 0.001.

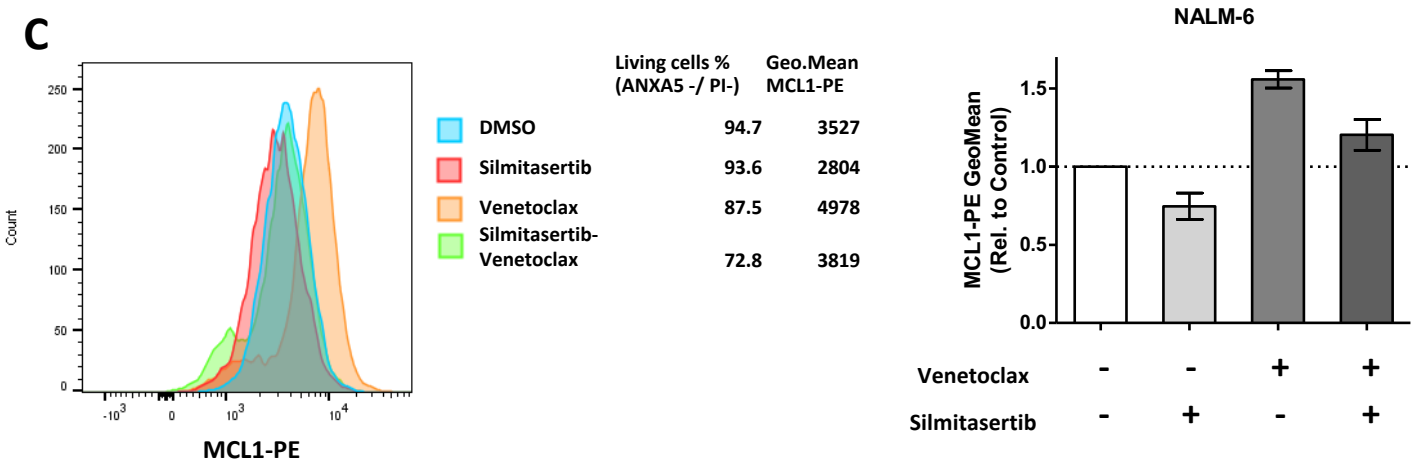


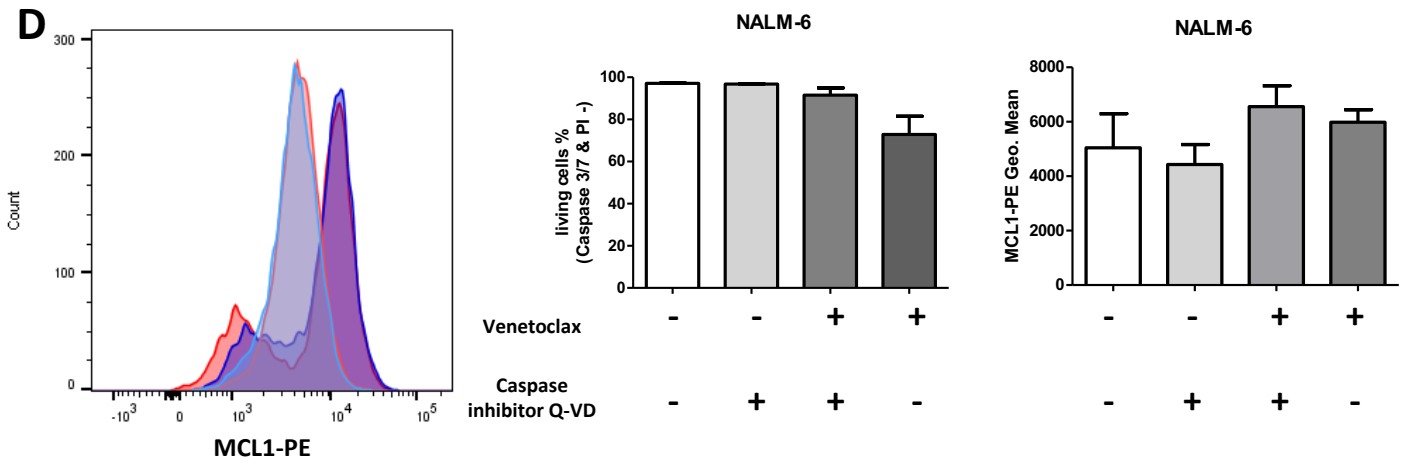

**Supplementary Figure S5. MCL-1-dependence of venetoclax sensitivity in BCP-ALL cell lines.**

(A) Venetoclax low-sensitive and high sensitive cells were treated at their corresponding EC10 concentrations (697: 27 nM venetoclax / HAL-01: 2 nM venetoclax) for 4 hours followed by 1h exposure to increasing concentrations of the MCL1 specific inhibitor peptide MS1 (dynamic BH-3 profiling) or vehicle control (DMSO) before cytochrome C release was measured by FACS. Main Figure 2A depicts the same experiments focused on selected MS1 concentrations and with MS1 treatments normalize to vehicle control (delta priming).

## Supplementary Figure S6



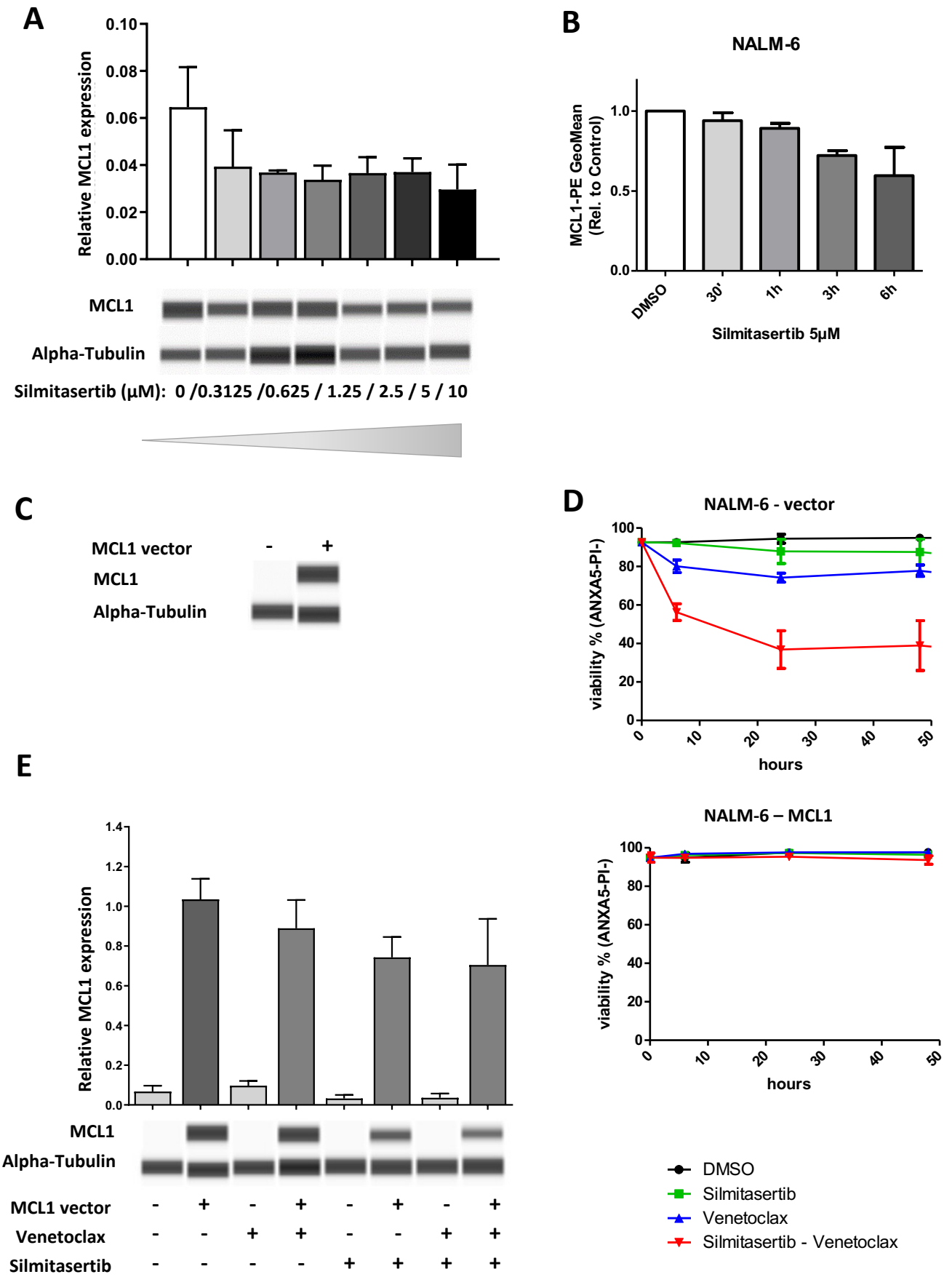




| | Geo.Mean MCL1-PE |
|---|---|
| DMSO | 4221 |
| Q-VD | 3923 |
| Venetoclax + Q-VD | 6799 |
| Venetoclax | 5598 |

**Supplementary Figure S6. MCL1 upregulation after venetoclax treatments**

(A) Western Blot band intensities of MCL1 protein levels depicted in Main Figure 2C were quantified using ImageJ 1.48v software (Rasband, W.S., ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA, https://imagej.nih.gov/ij/, 1997-2018.). Bands where normalized to the DMSO control. Data shows mean and standard deviation from n=4 (697) and n=3 (SEM) independent experiments. Mann-Whitney U test used for calculation of P values. *P value < 0.05. (B) MCL1 protein quantification after venetoclax serial dilution treatments in NALM-6. Protein lysates were extracted from cells after 48h treatment and analyzed by capillary western blot using the Simple Wes System. Blots show staining for MCL1 and house-keeping gene alpha-tubulin. MCL1 levels were normalized to the housekeeping-gene, with mean ± SD from four independent experiments. (C) MCL1 intracellular staining and quantification via FACS analysis of NALM-6 cells treated for 24h with 0.5 µM venetoclax or 5 µM silmitasertib or combination of both. Viability was established by staining with ANAX5A/PI. Histograms show MCL1-PE staining (n=1; left) and bar graphs show the mean and SD of the intensity in three independent experiments (geometric mean of MCL1-PE). (D) MCL1 intracellular staining and quantification via FACS of NALM-6 cells treated for 6h with 5 µM venetoclax or 10 µM of caspase inhibitor Q-VD or combination of both. Viability was established by staining with Caspase 3/7 and PI. Histograms show MCL1-PE staining (n=1; left) and bar graphs show the mean and SD of the viability (middle) and intensity (right; geometric mean MCL1-PE) in three independent experiments.

## Supplementary Figure S7

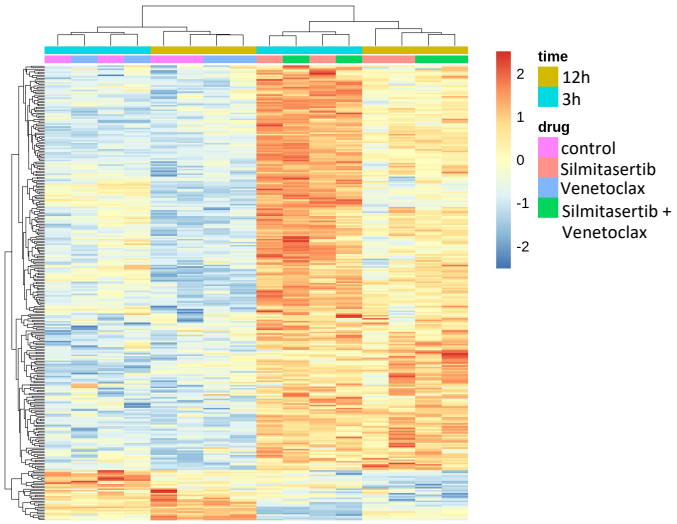


**Supplementary Figure S7. MCL1 downregulation after silmitasertib treatment and inhibition of the synergistic treatment effect in an MCL1 overexpression model.**

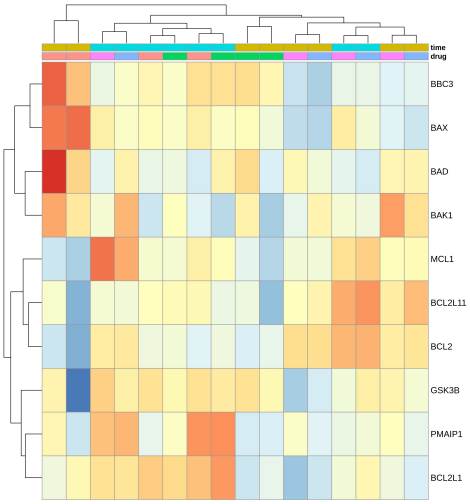
(A) MCL1 protein quantification after treatment with serial dilutions of silmitasertib in NALM-6. Protein lysates were extracted from cells after 48h treatment and analyzed by capillary western blot using the Simple Wes System. Blots show staining for MCL1 and house-keeping gene alpha-tubulin. MCL1 levels were normalized to the housekeeping-gene, with mean ± SD from two independent experiments. (B) MCL1 intracellular staining and quantification via FACS of NALM-6 cells treated for a time series (30', 1/3/6h) with 5 µM silmitasertib. Bar graphs show the mean and SD of MCL1-PE intensity (geometric mean, relative to DMSO control) in three independent experiments. (C) MCL1 protein expression of NALM-6 eGFP cells transduced with an empty vector or with a lentiviral human Mcl-1 insert vector DNA pCMV6-Entry-hMcl-1, for MCL1 overexpression. Protein lysates were analyzed by capillary western blot using the Simple Wes System. Blots show staining for MCL1 and house-keeping gene alpha-Tubulin. (D) Proportion of living NALM-6 cells transduced with an empty vector or with a lentiviral human Mcl-1 insert vector, stained with ANXA5 after 6/12/24/48h treatment with 0.5µM venetoclax and/or 5µM silmitasertib and analyzed by flow cytometry. Data represent mean ± SD of five independent experiments. (E) MCL1 protein expression of NALM-6 eGFP cells transduced with an empty vector or with a lentiviral human Mcl-1 insert vector DNA pCMV6-Entry-hMcl-1, for MCL1 overexpression and subsequent treatment with silmitasertib and/or venetoclax. Cells were treated with 0.5 µM venetoclax and/or 5 µM silmitasertib or DMSO (vector). Cells were harvested 48h treatment and proteins lysates were analyzed by capillary western blot using the Simple Wes System. Blots show staining for MCL1 and house-keeping gene alpha-Tubulin.

# Supplementary Figure S8

**A**




**B**

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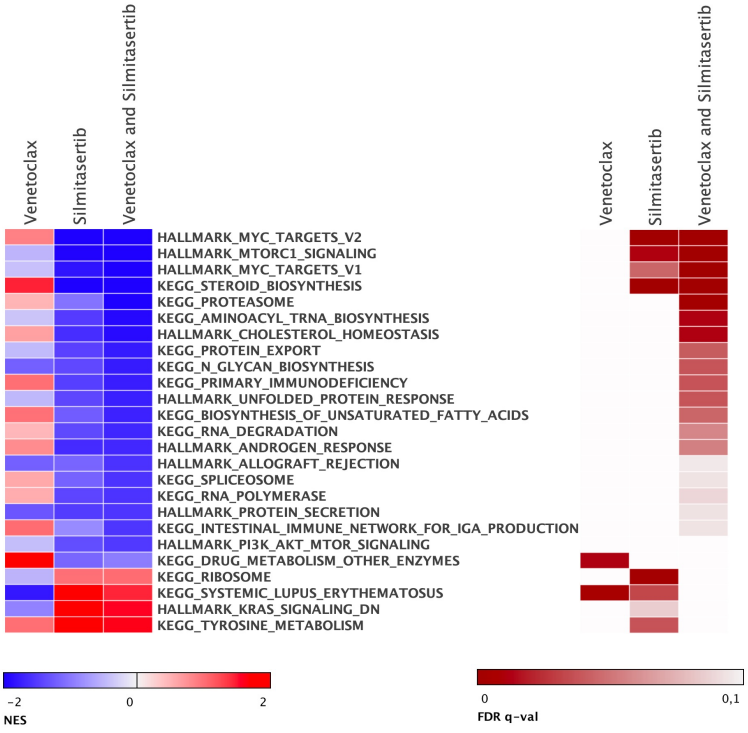


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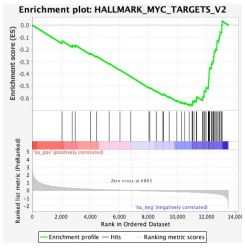
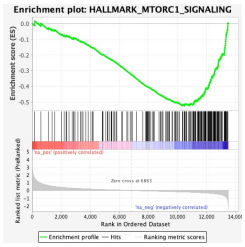
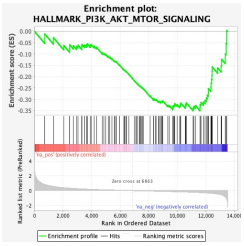



NES -2.57
FDR <0.001




NES -2.48
FDR <0.001

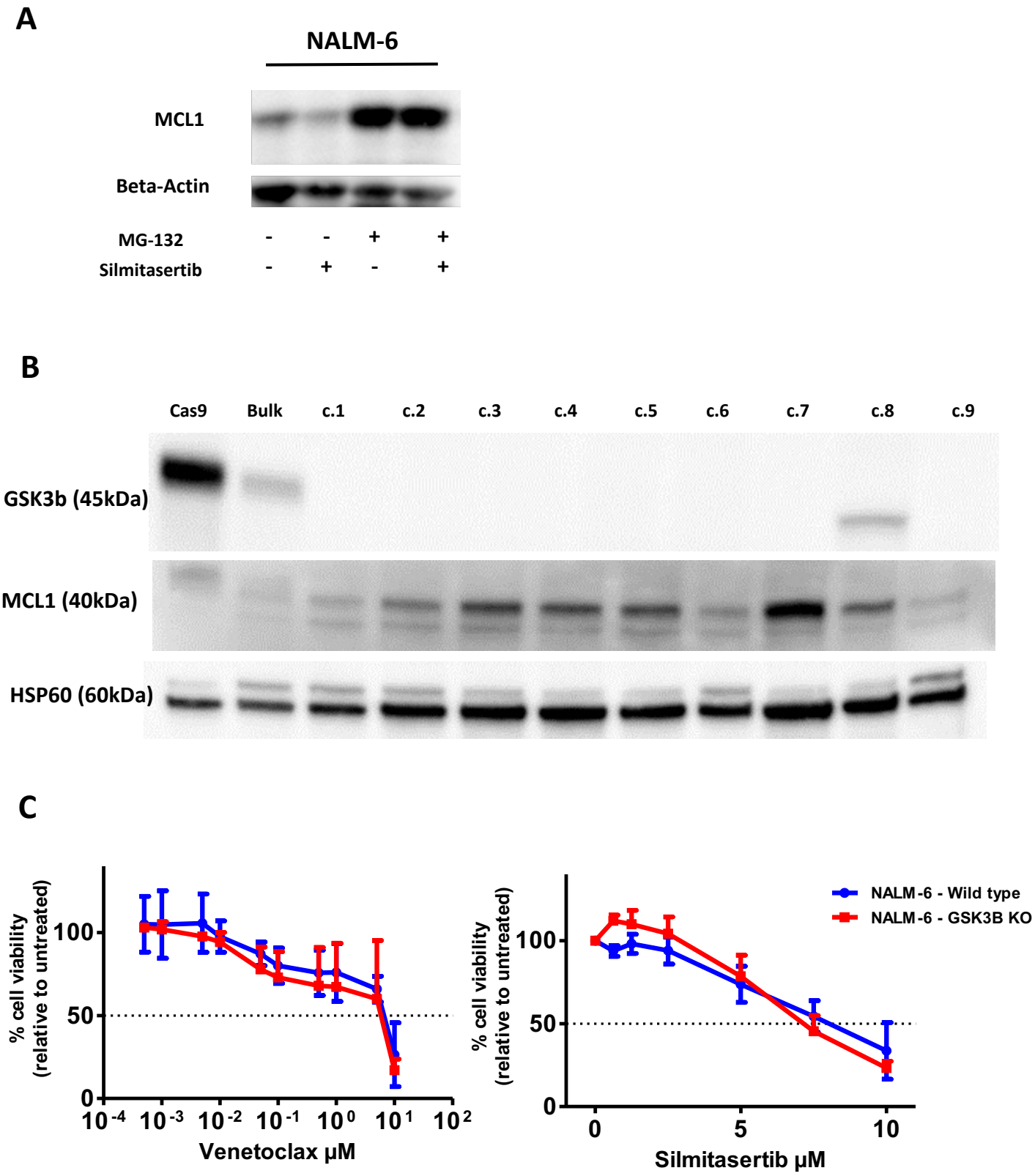



NES -1.52
FDR 0.103

**Supplementary Figure S8. Gene expression analysis of venetoclax / silimitasertib treatments.**

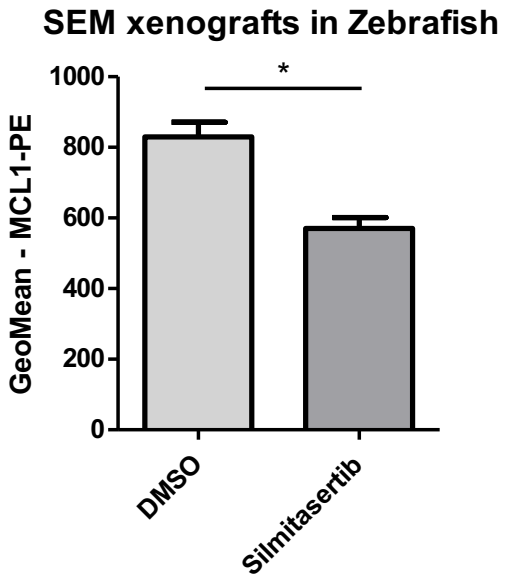
(A) NALM-6 cells were treated with venetoclax (0.05 µM) or silmitasertib (5 µM) or combination of both. After 3h and 12h of drug exposure, RNA was isolated transcriptome sequencing was performed as described in Supplementary Methods. Biological duplicates were obtained for all treatment and time points. For statistical analyses both time points were considered together. Gene lists of differentially expressed genes are included in Supplementary Tables. Heatmap depicts unsupervised clustering of top differentially expressed genes (FDR <0.05) after combined venetoclax / silmitasertib treatment compared to vehicle control. Differentially expressed genes after combined treatments show a largely similar expression pattern after silmitasertib single treatment, indicating that the synergistic treatment effect occurs most likely on the post-transcriptional level. (B) Heatmap depicts unsupervised clustering of gene expression of selected genes related to regulation of mitochondrial apoptosis obtained after single and combined treatments as in (A). (C) Gene set enrichment analysis was performed using GSEA v.4.1.0. in pre-ranked mode. Fold changes in gene expression after single and combined treatments was analyzed in relation to vehicle treated control and compared to MSigDB HALLMARK and KEGG-PATHWAY gene sets. Pathways with significant enrichment in at least one treatment condition (FDR ≤0.01) were included in heatmap showing normalized enrichment score together with corresponding FDR value. (D) GESA plots for selected signaling pathways are shown.

**Supplementary Figure S9**



**Supplementary Figure S9. Proteasomal degradation of MCL1 after silmitasertib and establishment of GSK3B knock-out clones.**

(A) Western blot analysis performed with the indicated antibodies using lysates of NALM-6 cells treated 6h with vehicle (DMSO), 5 µM silmitasertib or 1 µM of the proteasome inhibitor, MG132, or the combination of both. Beta-actin was used as loading control. (B) Western blot analysis performed with the indicated antibodies using protein lysates from NALM-6 GSK3B Knock-Out clones described in Main Figure 2C. HSP60 was used as loading control. (D) Cell viability curves in NALM-6 -Wild type and NALM-6 GSK3B knock-out clones measured with WST-1 after 48h treatment with serial dilutions of venetoclax or silmitasertib. Figure shows mean and SD from three independent experiments conducted in duplicates (NALM-6) or n=4 GSK3B KO clones.




**Supplementary Figure S10. MCL1 is downregulated in vivo in SEM Zebrafish xenografts.**

SEM cells were engrafted into the pericardium in 2d immunosuppressed zebrafish embryos, which were bathed in 1µM silmitasertib (tolerated dose), with 5µM silmitasertib injected to the pericardium. After 24h, cells were stained with CD19, LIVE/DEAD stain and MCL1-PE for FACS analysis. Each experiment (n=3) was measured as the mean of a pool of 12 PDX embryos. Bars represent means of the MCL1-PE signal (Geometric Mean) from each experiment with SD. One- tail Mann-Whitney U test. *P value < 0.05, **P value < 0.01, ***P value < 0.001.

**Supplementary Table S1. Summary of drug synergies in BCP-ALL cell lines**

| Cell line | Genetic background | Venetoclax EC50 (μM)* | Combination EC50 (μM)* | Dose reduction (%) | Number of synergistic combinations** | Maximum synergy score** | Sum of synergy scores** |
|---|---|---|---|---|---|---|---|
| 697 | TCF3-PBX1 | 3.9 | 0.003 | 99.9 | 37 | 72.5 | 141.1 |
| Nalm6 | DUX4 rearranged | 6.58 | 0.096 | 98.5 | 31 | 52.1 | 96.4 |
| SEM | KMT2A-AFF1 | 3.07 | 0.062 | 98 | 20 | 26.1 | 36.7 |
| REH | ETV6-RUX1 | 2.18 | 0.014 | 99.3 | 13 | 27.8 | 48.1 |
| Nalm16 | Near Haploid | 0.39 | 0.107 | 72.9 | 12 | 17.9 | 28.7 |
| HAL01 | TCF3-HLF | 0.37 | 0.101 | 72.3 | 0 | 6.5 | 5.6 |

*EC50 values calculated from WST-1 viability assays performed after 48h treatment with a minimal effective silmitasertib dose (5/1.25μM), using a linear regression model with GraphPad Software. Main Figure 1A depicts the experiments where this analysis was performed.
**Data analyzed using Combenefit software. Main Figure 1B and Supplementary Figure S2A represents the experiments where this analysis was carried out.

**Supplementary Table S2. Summary of drug synergies in mouse PDX samples.**

| Sample | Genetic Background | Number of synergistic combinations* | Maximum synergy score* | Sum of synergy scores* |
|---|---|---|---|---|
| PDX 1 | P2RY8-CRLF2 | 3 | 19.4 | 6.2 |
| PDX 2 | High Hyperdiploidy | 1 | 28.2 | 5.7 |
| PDX 3 | MLL_E9-AF4_E6 | 7 | 19.5 | 10.0 |
| PDX 4 | DUX4 | 4 | 18.2 | 11.5 |
| PDX 5 | Unassigned | 1 | 15.7 | 8.0 |
| PDX 6 | KMT2A-MLLT3 | 8 | 25.7 | 8.5 |
| PDX 7 | Unassigned | 5 | 45.2 | 13.4 |
| PDX 8 | DUX4 | 17 | 18.3 | 3.2 |
| PDX 9 | TCF3_HLF | 4 | 17.2 | 9.9 |
| PDX 10 | MLL_E9-AF4_E6 | 2 | 17.5 | 7.0 |
| PDX 11 | B-Other (homozygous TP53 mutation) | 14 | 23.1 | 5.8 |
| PDX 12 | Unassigned | 5 | 14.3 | 4.1 |
| PDX 13 | Unassigned | 3 | 13.3 | 4.4 |
| PDX 14 | Unassigned | 10 | 27.1 | 6.5 |
| PDX 15 | MLL_E9-AF4_E6 | 6 | 17.7 | 9.5 |
| Median | | 5 | 18.3 | 7.0 |

*Data obtained from WST-1 viability assays performed after 24h treatment with silmitasertib-venetoclax combinations (6 venetoclax and 3 silmitasertib concentrations combined per sample), analyzed using Combenefit software.

**Supplementary Table S3. Clinical characteristics of patient samples**

| Patient* | Disease state | Genetic Background | Response to induction treatment (MRD) |
|---|---|---|---|
| 1 | 1st relapse | B-other | Good ($<10^{-3}$) |
| 2 | 1st relapse | ETV6-RUNX1 fusion gene | Good ($<10^{-3}$) |
| 3 | 1st relapse | B-other | Good ($<10^{-3}$) |
| 4 | 1st relapse | KMT2A-AFF1 fusion gene, TP53mutation | Poor ($\geq 10^{-2}$) |
| 5 | Initial diagnosis | KMT2A-AFF1 fusion gene | Morphological poor response |
| 6 | 1st relapse | B-other | Poor ($\geq 10^{-2}$) |
| 7 | 1st relapse | ETV6-RUNX1 fusion gene | Good ($<10^{-3}$) |
| 8 | 1st relapse | ETV6-RUNX1 fusion gene | Good ($<10^{-3}$) |
| 9 | 2nd relapse | B-other | Unknown |
| 10 | 1st relapse | ETV6-RUNX1 fusion gene | Good ($<10^{-3}$) |
| 11 | 1st relapse | ETV6-RUNX1 fusion gene | Good ($<10^{-3}$) |
| 12 | 1st relapse | IgH-CRLF2 fusion gene | Poor ($\geq 10^{-2}$) |
| 13 | 1st relapse | BCR-ABL1 fusion gene | Poor ($\geq 10^{-2}$) |
| 14 | 2nd relapse | B-other | Poor ($\geq 10^{-2}$) |
| 15 | 1st relapse | TCF3-ZNF348 fusion gene | Poor ($\geq 10^{-2}$) |

## Supplementary Table S4. Differentially expressed transcripts after silmitasertib treatment

| GeneID | log2FoldChange | pvalue | padj | | GeneID | log2FoldChange | pvalue | padj |
|---|---|---|---|---|---|---|---|---|
| KLHL35 | 5,323361165 | 4,01E-06 | 9,04E-05 | | INTS6-AS1 | 1,804336836 | 3,66E-05 | 0,000543738 |
| CYS1 | 4,241697509 | 0,00039969 | 0,003718524 | | CLDN4 | 1,796154605 | 0,003061394 | 0,018555994 |
| FOXE3 | 3,67724247 | 4,55E-05 | 0,000648053 | | ZNF382 | 1,786246448 | 1,26E-05 | 0,000230231 |
| LOC102724488 | 3,553309479 | 5,08E-05 | 0,000708285 | | PSD2 | 1,781881554 | 1,07E-05 | 0,000200788 |
| SMIM38 | 3,431150559 | 0,003101962 | 0,018684509 | | DRP2 | 1,772319584 | 1,60E-12 | 3,86E-10 |
| GUCY1B2 | 3,238637182 | 0,005997738 | 0,030827915 | | IL11 | 1,766608225 | 0,000508993 | 0,004526686 |
| ADAP2 | 3,167001166 | 0,002315051 | 0,014987961 | | DPCD | 1,764630728 | 0,007292304 | 0,035651851 |
| HCAR3 | 3,143794697 | 0,003873006 | 0,022165661 | | TAS2R5 | 1,763855366 | 0,000224014 | 0,00234382 |
| KIZ-AS1 | 3,099462913 | 0,002818336 | 0,017444264 | | SSBP3-AS1 | 1,761045729 | 0,000358826 | 0,003411116 |
| KLKB1 | 2,954605461 | 0,000531549 | 0,004678044 | | OVGP1 | 1,749358076 | 4,22E-11 | 6,48E-09 |
| POLL | 2,912433812 | 4,52E-13 | 1,36E-10 | | BBC3 | 1,74928382 | 3,52E-09 | 2,53E-07 |
| FGFR4 | 2,853864449 | 3,64E-21 | 1,23E-17 | | OPRL1 | 1,724976894 | 4,66E-10 | 4,56E-08 |
| ZNF560 | 2,811829018 | 0,002959876 | 0,018120342 | | CLDN5 | 1,716921867 | 1,27E-05 | 0,00023066 |
| LRRC4B | 2,666881887 | 0,00156194 | 0,010957087 | | LOC100130691 | 1,710425741 | 0,00036532 | 0,003465544 |
| EFCAB12 | 2,662851954 | 1,46E-09 | 1,21E-07 | | ADAM11 | 1,703842011 | 4,12E-10 | 4,14E-08 |
| FBXO39 | 2,660194897 | 0,000753013 | 0,00619929 | | AQP6 | 1,700076373 | 0,000159689 | 0,001767962 |
| CD44 | 2,613394777 | 1,23E-05 | 0,000225363 | | SYT12 | 1,699450467 | 2,48E-10 | 2,73E-08 |
| TMEM216 | 2,561630514 | 1,97E-13 | 6,35E-11 | | KIAA1324 | 1,67543865 | 0,001809745 | 0,012343152 |
| LGI4 | 2,516412806 | 1,66E-06 | 4,34E-05 | | ZNF844 | 1,669689699 | 3,84E-06 | 8,71E-05 |
| MATN1-AS1 | 2,507554562 | 0,004741367 | 0,025889952 | | TCTE1 | 1,637119085 | 1,87E-05 | 0,000312474 |
| GTF2H4 | 2,47952975 | 0,000215021 | 0,002266199 | | OPALIN | 1,634016925 | 6,97E-09 | 4,58E-07 |
| KIAA1324L | 2,433533701 | 0,007487822 | 0,036410208 | | LOC101929439 | 1,630716657 | 0,00991696 | 0,044865285 |
| TLL2 | 2,428201352 | 1,49E-08 | 8,48E-07 | | CATSPER3 | 1,625954739 | 0,000199568 | 0,002127902 |
| LINC00515 | 2,4231062 | 0,006908967 | 0,034286129 | | LBX2 | 1,617841262 | 6,70E-05 | 0,000885594 |
| CPO | 2,42191623 | 0,005283336 | 0,027920306 | | ARTN | 1,61164442 | 2,69E-05 | 0,000423802 |
| TTLL10 | 2,415295968 | 4,07E-05 | 0,00059067 | | PLXDC1 | 1,609628903 | 0,008358946 | 0,039633892 |
| SULT1A2 | 2,398210764 | 7,77E-06 | 0,000155369 | | GNMT | 1,604643618 | 1,08E-11 | 2,00E-09 |
| SGK2 | 2,375605405 | 6,39E-05 | 0,000852898 | | C1S | 1,598137943 | 3,55E-09 | 2,53E-07 |
| TBC1D30 | 2,346719708 | 5,58E-08 | 2,62E-06 | | INSL3 | 1,59357922 | 0,001088028 | 0,008327476 |
| TREML1 | 2,325853504 | 0,001050763 | 0,008125984 | | LINC01749 | 1,591076101 | 1,23E-06 | 3,38E-05 |
| TUNAR | 2,289012178 | 0,00606319 | 0,031061729 | | COLQ | 1,590142436 | 3,38E-10 | 3,54E-08 |
| MFSD4A | 2,28407589 | 0,000500938 | 0,004484555 | | C1RL | 1,581308963 | 7,89E-05 | 0,001009613 |
| EPHA8 | 2,260726014 | 0,009855231 | 0,044716631 | | MYO1E | 1,572522892 | 1,42E-05 | 0,00025166 |
| OR2H2 | 2,22179066 | 0,011109353 | 0,048869585 | | GLIS2 | 1,569921226 | 4,32E-09 | 3,04E-07 |
| LINC01354 | 2,206573324 | 8,43E-05 | 0,001066587 | | NOSTRIN | 1,569075749 | 3,50E-09 | 2,53E-07 |
| ETV7 | 2,154828074 | 0,010068121 | 0,045457871 | | ANKRD34A | 1,565275316 | 4,82E-06 | 0,000105696 |
| LBX2-AS1 | 2,151059711 | 1,31E-07 | 5,29E-06 | | YPEL3 | 1,558018266 | 2,13E-15 | 1,31E-12 |
| DMGDH | 2,149068473 | 1,23E-12 | 3,07E-10 | | INKA2 | 1,552287598 | 0,009782276 | 0,044526414 |
| FAM209B | 2,147767837 | 0,000109361 | 0,001302507 | | NPIPB6 | 1,551942089 | 1,49E-06 | 3,98E-05 |
| TF | 2,131207146 | 0,000121443 | 0,0014189 | | ITGB5 | 1,54638871 | 0,003556093 | 0,020710877 |
| CRABP2 | 2,129189187 | 2,23E-10 | 2,57E-08 | | SLFN5 | 1,542459668 | 8,21E-14 | 3,00E-11 |
| EPS8L1 | 2,128976523 | 1,39E-10 | 1,72E-08 | | RDH5 | 1,54176585 | 6,55E-07 | 2,06E-05 |
| RAB9B | 2,128945762 | 6,93E-05 | 0,000908682 | | SMO | 1,538028496 | 0,000190185 | 0,002043652 |
| LINC01762 | 2,12641653 | 7,54E-05 | 0,000974383 | | TUBA8 | 1,536091846 | 0,000140204 | 0,001603456 |
| JCAD | 2,110140816 | 0,009126801 | 0,042441036 | | SCART1 | 1,535627398 | 3,15E-12 | 7,10E-10 |
| FAM169A | 2,099657562 | 1,92E-05 | 0,000319727 | | TSPAN18 | 1,530439205 | 0,007038058 | 0,034748161 |
| HHIPL1 | 2,094501586 | 0,000136084 | 0,001562943 | | TSPOAP1 | 1,528807539 | 1,13E-07 | 4,74E-06 |
| EPB41L4A | 2,081001143 | 0,001503926 | 0,010649593 | | HMOX1 | 1,512570223 | 0,007442684 | 0,036255927 |
| RSPH4A | 2,075686451 | 1,20E-06 | 3,33E-05 | | ADRB3 | 1,511899721 | 0,000393601 | 0,00367198 |
| FGF18 | 2,064848722 | 0,000130522 | 0,001509322 | | PRSS27 | 1,510843113 | 0,00020916 | 0,002214118 |
| RRH | 2,05972265 | 0,010094176 | 0,045529887 | | TCP11L2 | 1,510531035 | 0,002174771 | 0,014314799 |
| ASPDH | 2,045836309 | 3,40E-07 | 1,19E-05 | | FLACC1 | -1,556041656 | 0,010418569 | 0,046635172 |
| TLCD3B | 2,04421504 | 9,89E-17 | 9,55E-14 | | MIR3176 | -1,560073508 | 0,000424622 | 0,003912775 |
| NSG2 | 2,003367785 | 0,000124477 | 0,001448086 | | DGCR5 | -1,637347312 | 0,002196565 | 0,014406079 |
| FAM209A | 2,002801364 | 0,00105785 | 0,008171437 | | AGPAT4-IT1 | -1,695500434 | 0,006809165 | 0,033877913 |
| SUSD5 | 2,002347885 | 0,000388982 | 0,003641451 | | SNORD12B | -2,038085671 | 0,004177372 | 0,023402286 |
| LINC02356 | 1,999889938 | 0,007714883 | 0,037179961 | | UPB1 | -2,383931238 | 0,000609227 | 0,005218969 |
| TJP3 | 1,995307559 | 0,001071169 | 0,008224531 | | | | | |
| MCMDC2 | 1,993428686 | 5,23E-06 | 0,000112329 | | | | | |
| RGS1 | 1,990752088 | 0,000284521 | 0,002849007 | | | | | |
| RSAD2 | 1,976470734 | 1,28E-05 | 0,000232797 | | | | | |
| F3 | 1,976355861 | 0,000722309 | 0,00599029 | | | | | |
| TAS2R4 | 1,973132169 | 0,000187892 | 0,002022231 | | | | | |
| LMOD1 | 1,950632722 | 0,000838511 | 0,00676312 | | | | | |
| FAM182A | 1,95007528 | 0,00450303 | 0,024845699 | | | | | |
| GUCA1B | 1,948133954 | 1,06E-15 | 7,54E-13 | | | | | |
| CASS4 | 1,946571983 | 0,000931402 | 0,007350082 | | | | | |
| CPB2-AS1 | 1,926042855 | 2,10E-06 | 5,25E-05 | | | | | |
| ERBB3 | 1,920524939 | 0,00034337 | 0,003291971 | | | | | |
| OLFM2 | 1,900573095 | 0,011086916 | 0,048834451 | | | | | |
| TNXB | 1,899132061 | 4,11E-10 | 4,14E-08 | | | | | |
| HDHD2 | 1,873487971 | 0,000482605 | 0,004346343 | | | | | |
| SMTNL1 | 1,869196918 | 0,000112033 | 0,001324988 | | | | | |
| CCR7 | 1,831199552 | 0,003414166 | 0,0200926 | | | | | |
| MCF2 | 1,829806773 | 2,61E-06 | 6,31E-05 | | | | | |
| TMEM269 | 1,824522842 | 2,24E-05 | 0,000362493 | | | | | |
| CMTM1 | 1,815843205 | 4,02E-05 | 0,000586886 | | | | | |
| OTUD7B | 1,806984694 | 1,02E-05 | 0,000194291 | | | | | |

*For details on the experimental procedures and analyses performed please, refer to Supplementary Methods and Supplementary Figure S8. No differentially expressed genes were observed after venetoclax single treatments.*

## Supplementary Table S5. Differentially expressed transcripts after combined treatment with silmitasterib and ventoclax

| GeneID | log2FoldChange | pvalue | padj | | GeneID | log2FoldChange | pvalue | padj |
|---|---|---|---|---|---|---|---|---|
| KLHL35 | 4,944759617 | 1,97E-05 | 0,000345291 | | SUSD5 | 1,862137869 | 0,000985203 | 0,008130635 |
| CYS1 | 4,025606341 | 0,000793618 | 0,006882721 | | ZNF382 | 1,849289805 | 5,29E-06 | 0,000114699 |
| SMIM38 | 3,959729923 | 0,000536147 | 0,005057664 | | UCN2 | 1,846571611 | 0,003542214 | 0,021657011 |
| KIZ-AS1 | 3,519644426 | 0,000592859 | 0,005463035 | | CPB2-AS1 | 1,835626659 | 6,06E-06 | 0,000128695 |
| CLDN11 | 3,2566544 | 0,001852683 | 0,013258111 | | SCART1 | 1,815452307 | 1,14E-16 | 1,10E-13 |
| POLL | 3,177122771 | 1,71E-15 | 1,10E-12 | | MCF2 | 1,790646465 | 4,07E-06 | 9,21E-05 |
| FOXE3 | 3,042080146 | 0,00086397 | 0,007345378 | | DRP2 | 1,774029518 | 1,35E-12 | 3,37E-10 |
| LOC102724488 | 3,007523241 | 0,000684823 | 0,006119623 | | TSPOAP1 | 1,770507998 | 7,97E-10 | 7,64E-08 |
| ADAP2 | 2,967963038 | 0,004431694 | 0,025788909 | | SPATC1 | 1,768004859 | 0,004377117 | 0,025504252 |
| NPR3 | 2,953999081 | 0,005441111 | 0,030132299 | | TAC4 | 1,754006236 | 0,004776476 | 0,027249464 |
| HCAR3 | 2,891369893 | 0,008176149 | 0,040980789 | | PLXDC1 | 1,742321441 | 0,003887498 | 0,023293969 |
| FGFR4 | 2,859195677 | 2,47E-21 | 1,12E-17 | | ZNF844 | 1,739340618 | 1,23E-06 | 3,38E-05 |
| TUNAR | 2,839172859 | 0,000484042 | 0,00467389 | | LOC101929439 | 1,73923705 | 0,00542599 | 0,030060874 |
| KLKB1 | 2,828196269 | 0,000925859 | 0,007749698 | | CATSPER3 | 1,738807787 | 5,87E-05 | 0,000850159 |
| EFCAB12 | 2,691308716 | 9,55E-10 | 8,90E-08 | | CAPN13 | 1,732679473 | 2,21E-12 | 5,24E-10 |
| LGI4 | 2,688711522 | 2,56E-07 | 9,36E-06 | | OPRL1 | 1,723898499 | 4,01E-10 | 4,27E-08 |
| EPHA8 | 2,662294572 | 0,002004165 | 0,014066613 | | CASS4 | 1,715899283 | 0,003621812 | 0,022024136 |
| SLC26A4 | 2,54074541 | 0,009850026 | 0,047368429 | | EPB41L4A | 1,715706582 | 0,009710249 | 0,046846235 |
| HHIPL1 | 2,536557924 | 2,34E-06 | 5,79E-05 | | MYO1E | 1,71282324 | 1,86E-06 | 4,84E-05 |
| TLL2 | 2,531939313 | 2,85E-09 | 2,26E-07 | | TMEM269 | 1,707949364 | 7,26E-05 | 0,001017899 |
| CPO | 2,525623616 | 0,003391307 | 0,020941124 | | CFAP53 | 1,703213209 | 0,000393354 | 0,003953429 |
| SOX30 | 2,504066949 | 0,004085622 | 0,024117657 | | GLIS2 | 1,700839104 | 1,65E-10 | 1,97E-08 |
| MFSD4A | 2,497160189 | 0,000120674 | 0,001550639 | | LOC100130691 | 1,697281583 | 0,000385695 | 0,003902565 |
| FGF18 | 2,495477888 | 2,46E-06 | 6,08E-05 | | RDH5 | 1,695212048 | 3,59E-08 | 1,78E-06 |
| CD44 | 2,46249743 | 3,88E-05 | 0,000600219 | | TECTA | 1,689166878 | 0,001939672 | 0,013728 |
| RSAD2 | 2,403384428 | 6,09E-08 | 2,76E-06 | | GOLGA8H | 1,68316935 | 0,007953596 | 0,040065815 |
| TTLL10 | 2,390474634 | 4,80E-05 | 0,000717177 | | CXCL16 | 1,682999901 | 0,007752005 | 0,03936574 |
| ARHGAP8 | 2,37786283 | 0,00144923 | 0,010981327 | | CSPG5 | 1,68267647 | 0,00014359 | 0,001784055 |
| RSPO4 | 2,352269992 | 0,001830106 | 0,013124339 | | FRMD5 | 1,682395417 | 9,07E-05 | 0,001233773 |
| RSPH4A | 2,340130927 | 3,06E-08 | 1,56E-06 | | PRSS27 | 1,67219204 | 3,37E-05 | 0,000536138 |
| FAM209A | 2,325469765 | 0,000119359 | 0,001538133 | | AZIN2 | 1,671025046 | 0,003312172 | 0,020652184 |
| MAP3K20-AS1 | 2,310525547 | 0,005594877 | 0,030707082 | | OVGP1 | 1,662732365 | 3,52E-10 | 3,81E-08 |
| TMEM216 | 2,310074346 | 4,33E-11 | 6,57E-09 | | TMEM220-AS1 | 1,656186282 | 0,010475273 | 0,049598857 |
| LINC01762 | 2,304529674 | 1,51E-05 | 0,00027863 | | NSG2 | 1,655012556 | 0,001733189 | 0,012637137 |
| TBC1D30 | 2,293575197 | 1,06E-07 | 4,37E-06 | | CLDN4 | 1,643459013 | 0,006906045 | 0,036016942 |
| LINC01354 | 2,258263897 | 5,23E-05 | 0,000769964 | | ARTN | 1,626501023 | 2,14E-05 | 0,000370388 |
| RAB9B | 2,233778713 | 2,63E-05 | 0,000435352 | | SYT12 | 1,617878156 | 1,63E-09 | 1,40E-07 |
| LBX2-AS1 | 2,219099259 | 4,39E-08 | 2,11E-06 | | HYPK | 1,599548748 | 5,07E-05 | 0,000752481 |
| EPS8L1 | 2,213434977 | 1,84E-11 | 3,02E-09 | | OPALIN | 1,596829647 | 1,43E-08 | 8,39E-07 |
| DMGDH | 2,203622006 | 2,39E-13 | 7,17E-11 | | SLFN5 | 1,589765479 | 9,93E-15 | 4,63E-12 |
| FAM169A | 2,167834902 | 9,00E-06 | 0,00018024 | | TCTE1 | 1,582761394 | 3,38E-05 | 0,000537067 |
| TLCD3B | 2,163824576 | 7,79E-19 | 1,17E-15 | | PLA2G4C | 1,582102097 | 0,000555417 | 0,005188756 |
| LBX2 | 2,150191922 | 6,67E-08 | 2,96E-06 | | KIAA1324 | 1,570183747 | 0,003460431 | 0,021276437 |
| SULT1A2 | 2,148562614 | 6,78E-05 | 0,000959018 | | CFP | 1,565268775 | 0,000137812 | 0,001734663 |
| ASPDH | 2,140152267 | 7,56E-08 | 3,31E-06 | | SNX32 | 1,564755007 | 6,02E-12 | 1,18E-09 |
| TAS2R5 | 2,136287509 | 5,32E-06 | 0,000115047 | | NPIPB2 | 1,564658069 | 0,000651552 | 0,005903267 |
| ADAM11 | 2,130357868 | 2,89E-15 | 1,77E-12 | | NOSTRIN | 1,56072656 | 3,76E-09 | 2,86E-07 |
| AQP6 | 2,113792932 | 1,60E-06 | 4,26E-05 | | TMEM169 | 1,543393496 | 0,008601887 | 0,042718704 |
| GPC1 | 2,095333149 | 0,002763186 | 0,018097264 | | RAB6B | 1,534439917 | 9,79E-09 | 6,27E-07 |
| SMTNL1 | 2,091759562 | 1,20E-05 | 0,000231039 | | C20orf204 | 1,531689151 | 1,45E-06 | 3,91E-05 |
| SSBP3-AS1 | 2,082513376 | 1,64E-05 | 0,000298484 | | CCDC114 | 1,513809656 | 2,22E-08 | 1,20E-06 |
| TF | 2,078920787 | 0,000173365 | 0,002085002 | | SLC45A2 | 1,513601052 | 0,004174039 | 0,024489872 |
| TNXB | 2,0534172 | 1,13E-11 | 2,06E-09 | | FBLL1 | 1,513307078 | 0,002570475 | 0,017133967 |
| INTS4P2 | 2,036240543 | 0,007951315 | 0,040065815 | | COLQ | 1,500304394 | 3,10E-09 | 2,45E-07 |
| TJP3 | 2,014959183 | 0,000900756 | 0,007591281 | | DEGS2 | 1,500218523 | 0,001543454 | 0,011552831 |
| F3 | 2,011568377 | 0,000541825 | 0,005082848 | | WDR72 | -1,562572624 | 9,10E-07 | 2,70E-05 |
| SGK2 | 2,005741009 | 0,00084349 | 0,00720752 | | LINC00471 | -1,567933924 | 0,002058187 | 0,014371163 |
| FAM209B | 2,004225215 | 0,000312238 | 0,003302338 | | CCR5 | -1,593654995 | 0,004154139 | 0,02443592 |
| ZNF687-AS1 | 2,003005099 | 0,004960611 | 0,028104584 | | JMJD7 | -2,056433752 | 0,001836668 | 0,01316441 |
| CRABP2 | 1,996992026 | 2,76E-09 | 2,21E-07 | | RASGRP1 | -2,165761468 | 0,007161556 | 0,037106137 |
| SLIT1 | 1,995936525 | 0,00016229 | 0,001976423 | | | | | |
| HDHD2 | 1,984983332 | 0,000199391 | 0,002325593 | | | | | |
| MCMDC2 | 1,966651281 | 6,57E-06 | 0,000137741 | | | | | |
| CLDN5 | 1,9630633 | 4,73E-07 | 1,55E-05 | | | | | |
| GTF2H4 | 1,935463187 | 0,004494985 | 0,026089829 | | | | | |
| KCNH3 | 1,921856087 | 0,000755067 | 0,006619324 | | | | | |
| FAM182A | 1,917028195 | 0,005106027 | 0,028723794 | | | | | |
| LMOD1 | 1,897845265 | 0,001135534 | 0,009061481 | | | | | |
| PSD2 | 1,895215289 | 2,28E-06 | 5,70E-05 | | | | | |
| NUTM1 | 1,892934964 | 0,007685525 | 0,039129808 | | | | | |
| ERBB3 | 1,88856451 | 0,00041623 | 0,004149403 | | | | | |
| GUCA1B | 1,880151445 | 9,18E-15 | 4,43E-12 | | | | | |
| CMTM1 | 1,870227078 | 2,19E-05 | 0,000375816 | | | | | |
| LINC01749 | 1,865841582 | 7,83E-09 | 5,22E-07 | | | | | |

*For details on the experimental procedures and analyses performed please refer to Supplementary Methods and Supplementary Figure S8. No differentially expressed genes were observed after venetoclax single treatments.*