LETTER TO THE EDITOR

Combination therapy of a PSEN1-selective γ-secretase inhibitor with dexamethasone and an XPO1 inhibitor to target T-cell acute lymphoblastic leukemia

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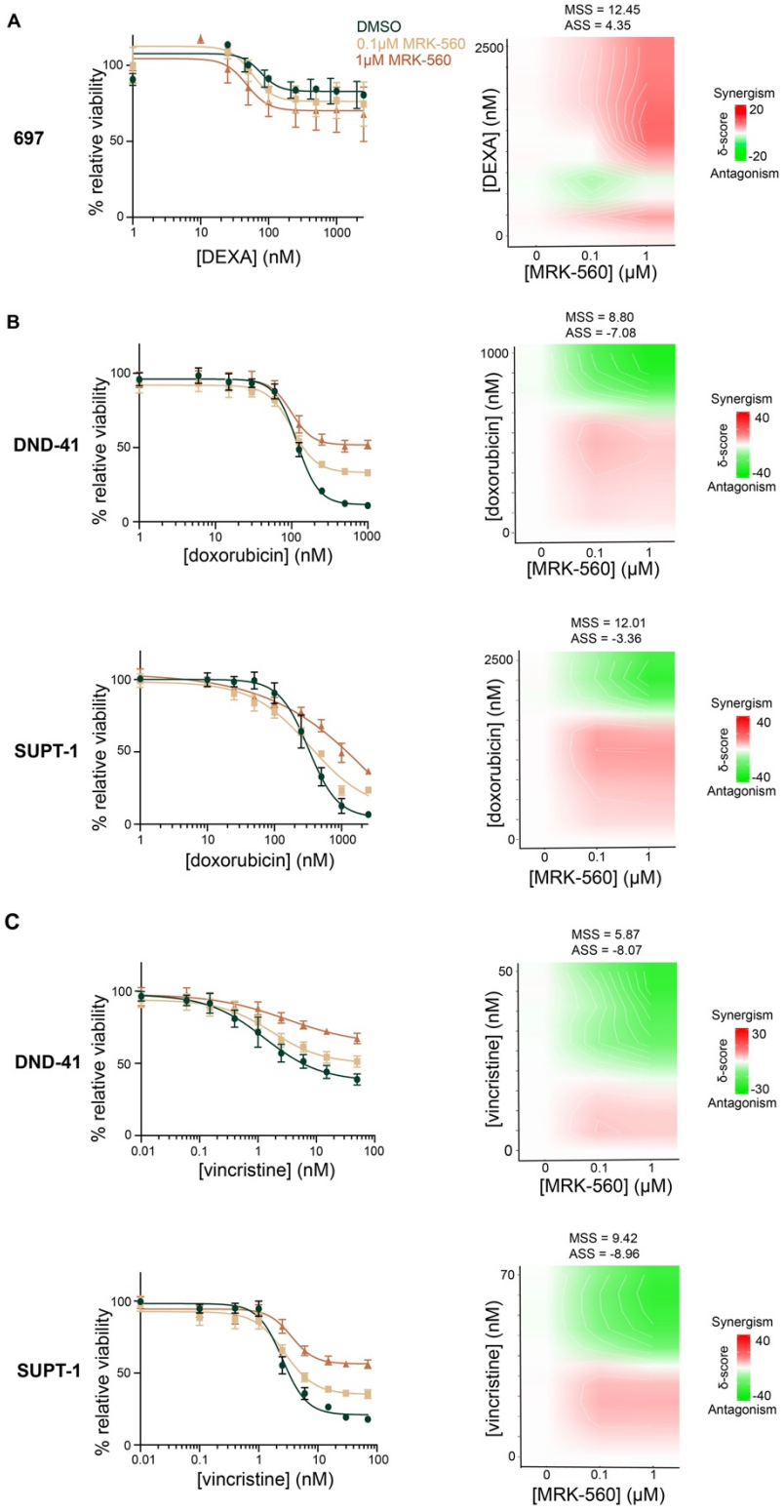
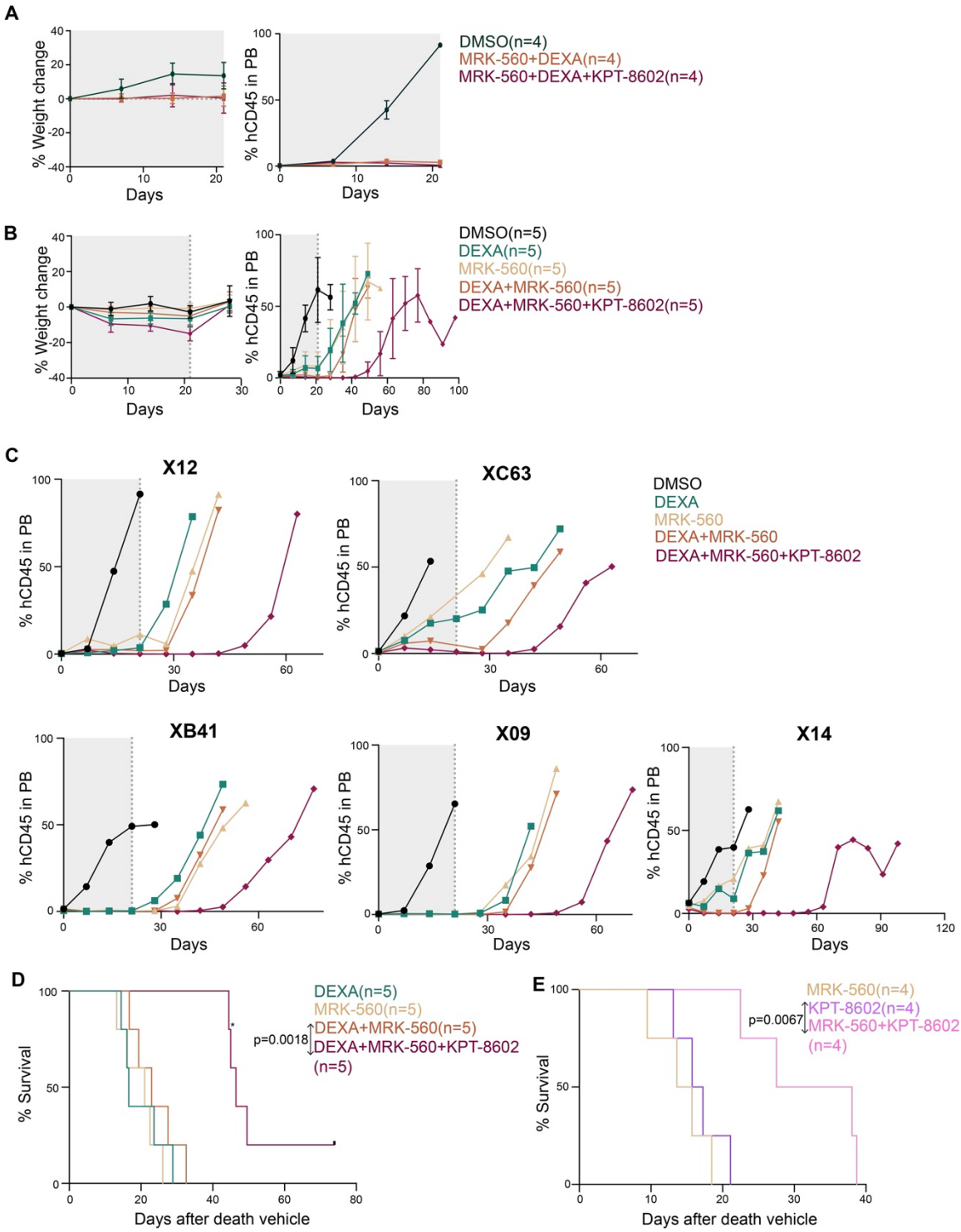


Supplemental Figure S1. Other chemotherapeutic compounds (doxorubicin and vincristine) have an additive effect with MRK-560 on cell viability.
The effect of MRK-560 treatment was visible after 5-7 days and therefore, cells were always pretreated with DMSO/MRK-560 for 5 days, followed by 48h treatment with DMSO/MRK-560 alone or in combination with dexamethasone/doxorubicin/vincristine. **(A)** Dose response curve and synergy plot of a NOTCH1-independent B-ALL cell line (697). The relative viability was calculated based on the DMSO condition of each pretreatment group (DMSO/MRK-560). **(B)** Dose response curves and synergy plots of DND-41 and SUPT-1 cells for the combination of MRK-560 with doxorubicin. **(C)** Dose response curves and synergy plots of DND-41 and SUPT-1 cells for the combination of MRK-560 with vincristine. All graphs show mean and standard deviation (error bars) of 3 replicates. MSS: maximum synergy score for a specific drug combination. ASS: Average synergy score for all drug combinations.

Supplemental Table S1. Mutations of PDX T-ALL samples

PDX sample	Mutations
X10-Luc	NOTCH1 (F1617P, P1618R) TLX1 overexpression
X12	FBXW7 (G557R) NUP214-ABL1 TLX3 overexpression
X09	NOTCH1 (F1606insTP) SPI1-TCF7 NRAS
XC63	NOTCH1 (L1678P, D1698D) JAK3 (M511I) TAL1 overexpression
X14	NOTCH1 (L1579M, D1698D, S2533T) PTEN (R233_fs) RPL10 (R98S)
XB41	NOTCH1 (L1600P) TAL1 overexpression RPL10 (R98S) TCRG deletion



Supplemental Figure S2. Treatment efficiency varies along different T-ALL PDX models.
(A) Percentage of weight changes compared to initial weight at start treatment and percentage of human CD45⁺ cells in peripheral blood (PB) of all treatment groups at different time points. This data belongs to the *in vivo* experiment of Figure 3A. **(B)** Percentage of weight changes compared to initial weight at start treatment and percentage of human CD45⁺ cells in peripheral blood of all treatment groups at different time points. This data belongs to the *in vivo* experiment of Figure 3E. **(C)** Percentage of human CD45+ cells in peripheral blood for each PDX model during (grey) and after treatment. Each dot represent one mice. **(D)** Kaplan-Meier survival plots, normalized to death of vehicle, for 5 different PDX samples (X09, X14, XB41, XC63, X12). *XC63 mouse was treated with 2.5mg/kg KPT-8602 instead of 5mg/kg. The experiment was stopped after 98 days, the last triplet combination mice was sacrificed and leukemia was detected in bone marrow. **(E)** Kaplan-Meier survival plots, normalized to death of vehicle, from Govaerts *et al.* for X09, X14, XB41, XC63.