Figure S1. Comparative analysis of the response of A2780 and A2780ADR cells to treatment with anticancer drugs (Doxo, Eto and CisPt). Logarithmically growing parental A2780 and drug resistant A2780ADR variant cells were treated with the anticancer drugs Doxo, Eto or CisPt at the indicated concentrations. 24 h after addition of the drug cell viability was monitored as described in methods. Data shown are the mean ± SD from three independent experiments each performed in biological quadruplicates (n=3; n=4). Dashed lines indicate inhibitory concentrations (IC_{20} and IC_{50}). Doxo, doxorubicin; Eto, etoposide; CisPt, cisplatin.

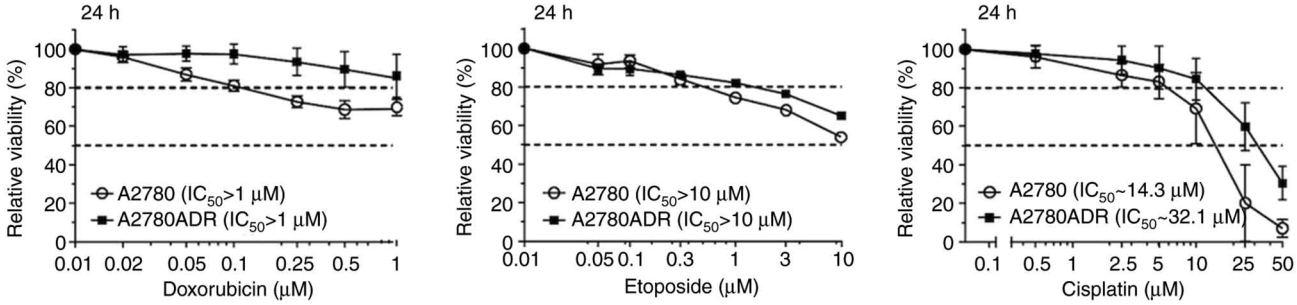

Figure S2. Comparative analysis of the protein expression of selected transporters in parental A2780 and Doxo-resistant A2780ADR cells. Protein expression of selected drug transporters (left panel) and Topo II-related factors (right panel) was analyzed under basal situation and 72 h after treatment with Doxo (0.1 μM, 1.0 μM). Data shown are from a representative western blotting. GAPDH protein expression was used as protein loading control. Doxo, doxorubicin; MDR1, multi-drug resistance gene 1; ATP7A, copper transporting ATPase; OCT2, organic cation transporter-2; CTR1, copper uptake protein 1; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; Topo IIa, topoisomerase IIα; pTopo IIa (S1106), Ser 1106 phosphorylated topoisomerase IIα; TOPBP1, topoisomerase binding protein 1, ERK2, extracellular regulated kinase 2.

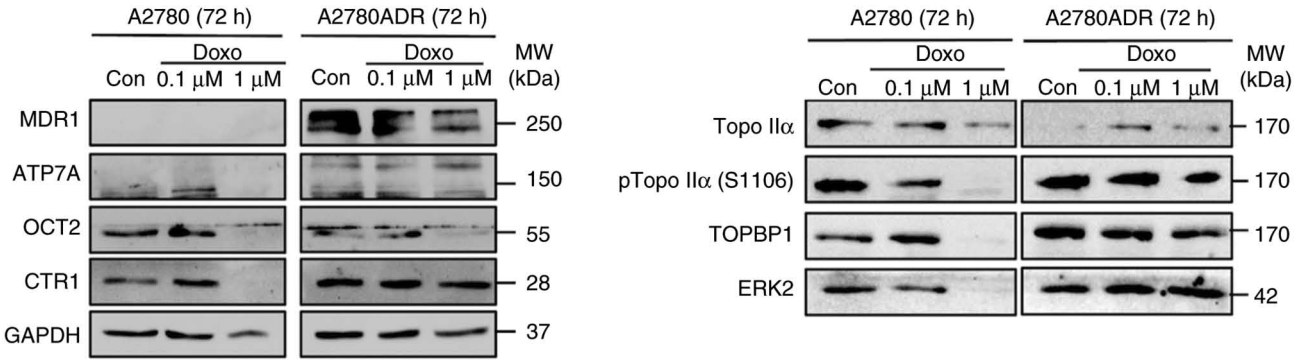

Figure S3. Effect of Eto on the activation of DDR-related mechanisms in A2780 cells. Logarithmically growing A2780 cells were treated with the indicated concentrations of Eto for 24 h. Afterwards, the protein expression of DDR-related factors (γH2AX, p21, pp53) was analyzed by western blotting using GAPDH protein expression as loading control. Eto, etoposide; DDR, DNA damage response; γH2AX, Ser139 phosphorylated histone H2AX; pp53, Ser15 phosphorylated p53 protein.

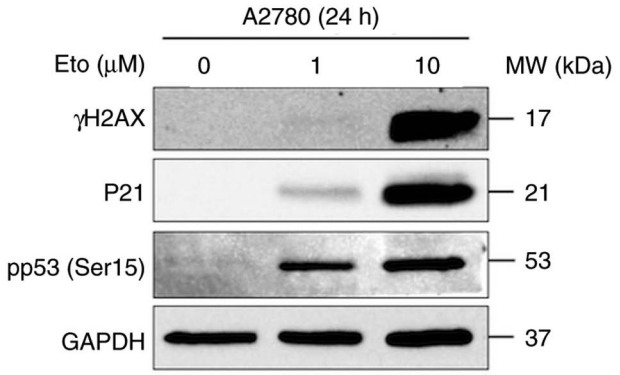

Figure S4. Cross-sensitivity of A2780 and A2780ADR cells to selected inhibitors of drug transport, DDR- and DNA repair-related mechanisms. Logarithmically growing parental A2780 and Doxo-resistant A2780ADR variant cells were treated with selected pharmacological inhibitors at the indicated concentrations. 24 h after drug treatment viability was monitored as described in methods. Data shown are the mean ± SD from three independent experiments each performed in biological quadruplicates (n=3; N=4). Dashed lines indicate inhibitory concentrations (i.e. IC_{20} and IC_{50}). Doxo, doxorubicin; DDR, DNA damage response; SD, standard deviation; EHT1864, Ras-related 3 botulinum C3 substrate 1 (Rac1) inhibitor; Ehop16, Rac1 guanine exchange inhibitor.

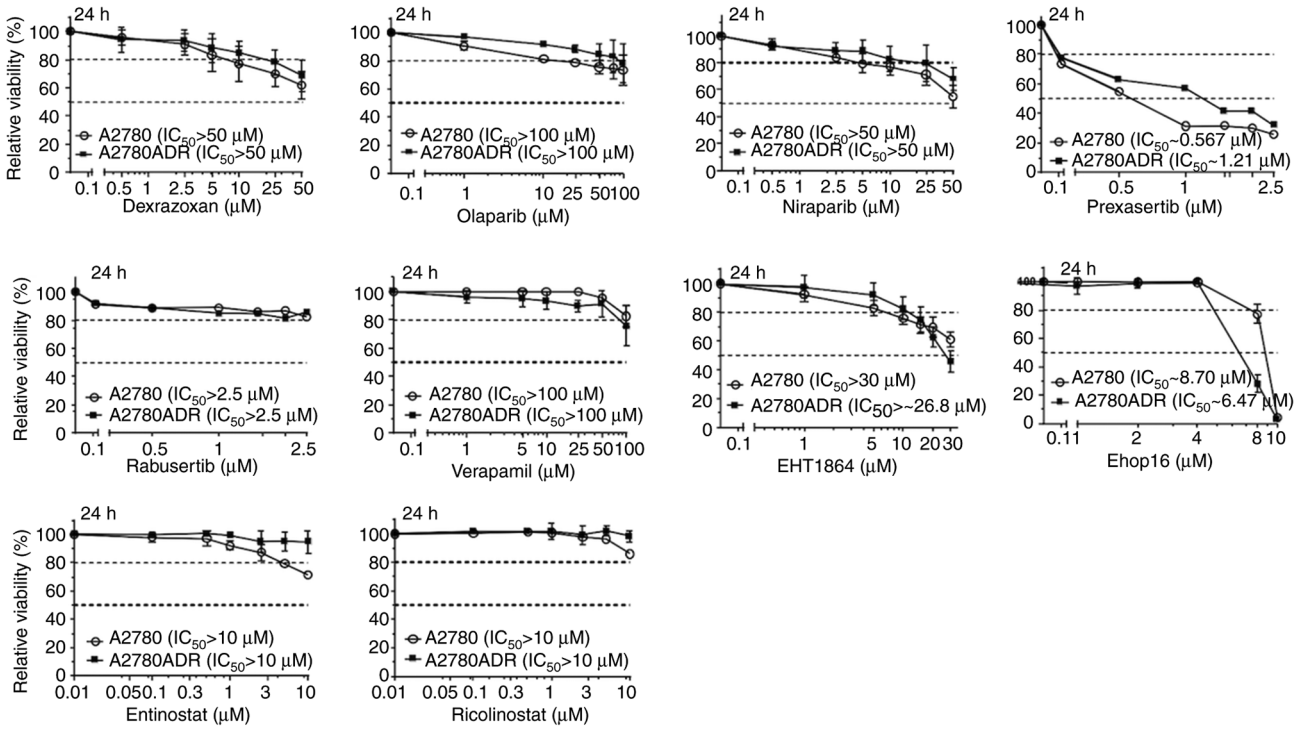

Figure S5. Cytotoxic effects of mono- and combined treatment of parental A2780 and doxorubicin resistant ovarian A2780ADR cells with Topo II poisons and inhibitors. Logarithmically growing A2780 and A2780ADR cells were co-treated with the topoisomerase II poison (A) Doxo or (B) Eto, respectively, in combination with selected pharmacological inhibitors (Ver, Dex, EST, EHT, Rab) using the indicated concentrations. 72 h after drug treatment, viability was monitored by use of the AlamarBlue assay as described in methods. Data shown are the mean ± SD from biological quadruplicate determinations. Doxo, doxorubicin; Eto, etoposide; Ver, verapamil; Dex, dexrazoxane; EST, entinostat; EHT, Rac1 inhibitor EHT1864; Rab, rabusertib; SD, standard deviation.

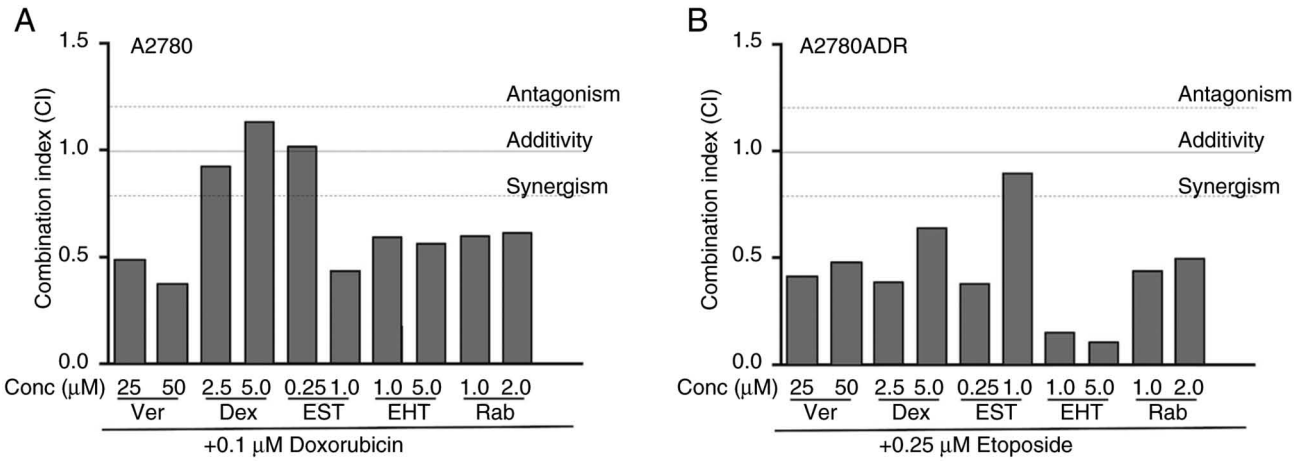

Figure S6. Cytotoxic effects of mono- and combined treatment of CisPt resistant ovarian A2780CisR cells with CisPt and selected inhibitors. Logarithmically growing CisPt resistant A2780CisR cells were co-treated with CisPt in combination with selected pharmacological inhibitors (Ver, EHT, EST) using the indicated concentrations. 72 h after drug treatment viability was monitored by use of the AlamarBlue assay as described in methods. Data shown are the mean ± SD from biological quadruplicate determinations. CisPt cisplatin; Ver, verapamil; EHT, Rac1 inhibitor EHT1864; EST, entinostat; SD, standard deviation.