

## Supplementary Information

Range of CI	Graded symbol	Drug effect
<0.1	+ + + + +	Very strong synergism
0.1-0.3	+ + + +	Strong synergism
0.3-0.7	+ + +	Synergism
0.7-0.85	+ +	Moderate synergism
0.85-0.90	+	Slight synergism
0.90-1.10	±	Nearly additive
1.10-1.20	–	Slight antagonism
1.20-1.45	– –	Moderate antagonism
1.45-3.3	– – –	Antagonism
3.3-10	– – – –	Strong antagonism
>10	– – – – –	Very strong antagonism

### Supplementary Table S1. Categorization of combination index (CI) of drug combination to corresponding drug effect and grading

This table is adapted from the paper published by Chou [17].

Cell line	B16-F10		
Drug sequential order of combination treatment	CI values and gradings		
	ED <sub>50</sub>	ED <sub>75</sub>	ED <sub>90</sub>
<b>Combination</b> (Simultaneous combined treatment of VPA and ETO)	0.57  + + +	0.73  + +	1.42  - -
<b>V→E</b> (Sequential combined treatment that pre-treated with VPA)	1.77  - - -	3.52  - - - -	10.58  - - - - -
<b>E→V</b> (Sequential combined treatment that pre-treated with ETO)	0.21  + + + +	1.15  -	9.55  - - - -

Cell line	SK-MEL-2-Luc		
Drug sequential order of combination treatment	CI values and gradings		
	ED <sub>50</sub>	ED <sub>75</sub>	ED <sub>90</sub>
<b>Combination</b> (Simultaneous combined treatment of VPA and ETO)	0.30  + + +	0.39  + + +	0.68  + + +
<b>V→E</b> (Sequential combined treatment that pre-treated with VPA)	1.17  —	11.38  — — — — —	147.31  — — — — —
<b>E→V</b> (Sequential combined treatment that pre-treated with ETO)	0.32  + + +	0.43  + + +	0.77  + +

**Supplementary Table S2. Combination index (CI) values and synergism/antagonism grading of simultaneous and sequential combined treatments of VPA and ETO on B16-F10 and SK-MEL-2-Luc cells**