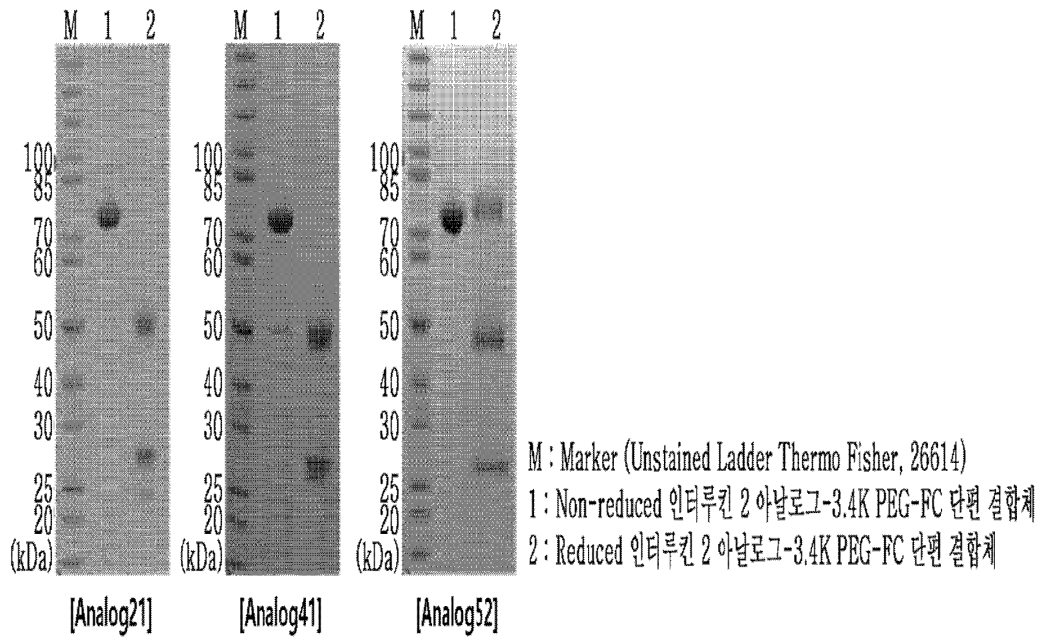
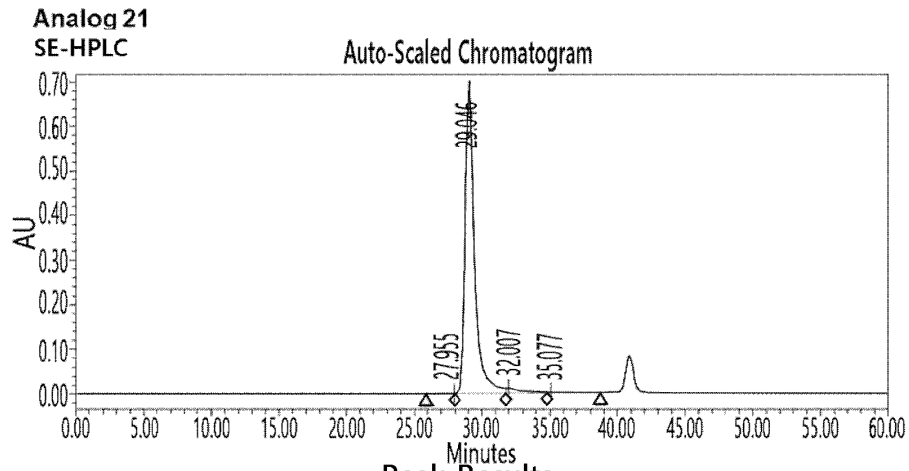


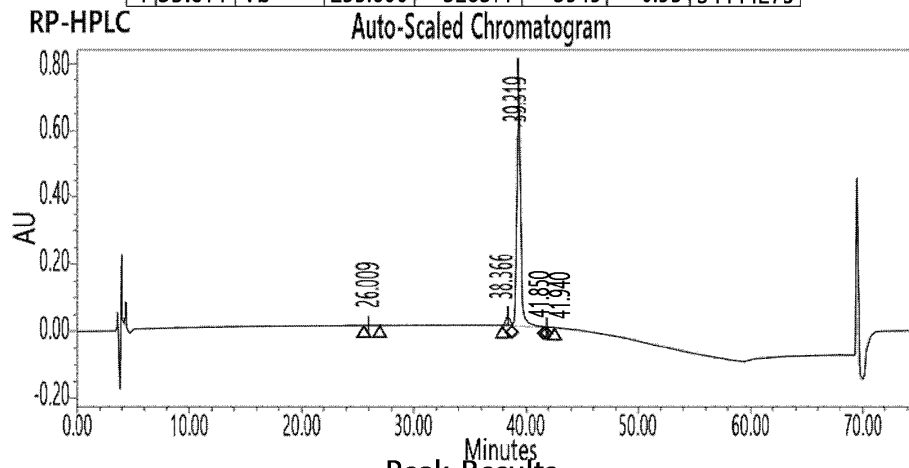
[도1]



[도 2a]

**Peak Results**

	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	27.955	bv	127.200	50410	945	0.15	34444275
2	29.046	vv	228.800	32900952	682750	95.52	34444275
3	32.007	vv	181.200	1164536	11799	3.38	34444275
4	35.077	vb	235.600	328377	3549	0.95	34444275

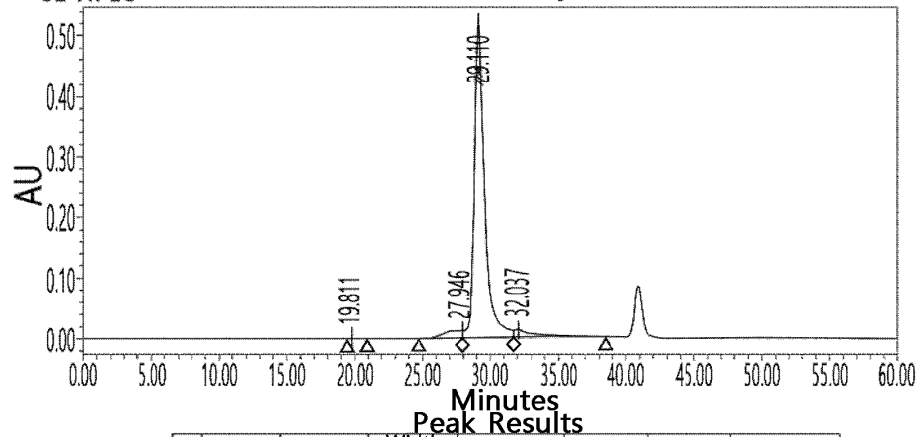
**Peak Results**

	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	26.009	Bb	83.600	51066	1429	0.28	18317715
2	38.366	bv	52.400	708275	32497	3.87	18317715
3	39.319	vv	173.600	17478553	777242	95.42	18317715
4	41.850	vv	11.200	27638	2585	0.15	18317715
5	41.840	vb	42.000	52183	3089	0.28	18317715

[도 2b]

Analog 41
SE-HPLC

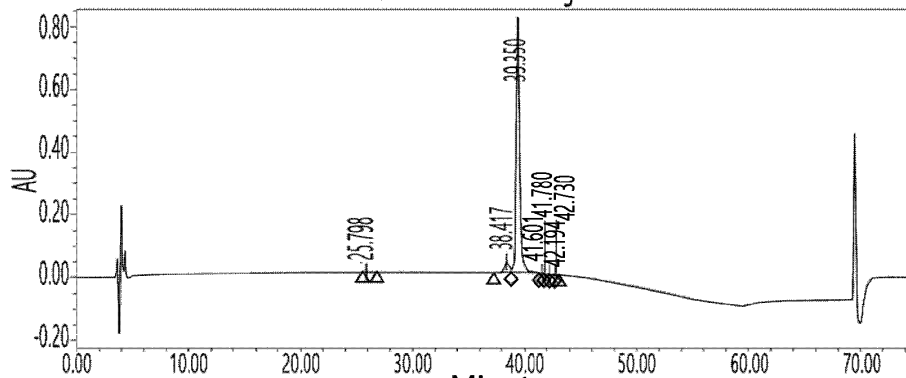
Auto-Scaled Chromatogram

Minutes
Peak Results

	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	19.811	bb	87.200	25933	1206	0.09	30049290
2	27.946	bv	194.000	1177831	12306	3.92	30049290
3	29.110	vv	227.200	27297055	520812	90.84	30049290
4	32.037	vb	404.400	1548471	13016	5.15	30049290

RP-HPLC

Auto-Scaled Chromatogram

Minutes
Peak Results

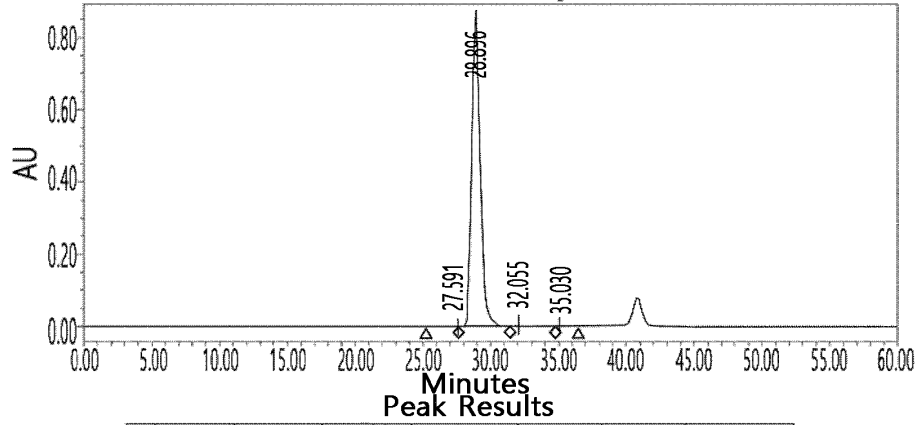
	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	25.798	BB	75.600	47777	1788	0.24	19600965
2	38.417	bv	94.000	962823	36778	4.91	19600965
3	39.350	vv	159.600	18335061	790978	93.54	19600965
4	41.601	vv	18.000	76997	4518	0.39	19600965
5	41.790	vv	25.600	81262	4246	0.41	19600965
6	42.194	vv	22.400	41294	2181	0.21	19600965
7	42.730	vb	28.800	55751	3954	0.28	19600965

[E-2c]

Analog 52

SE-HPLC

Auto-Scaled Chromatogram

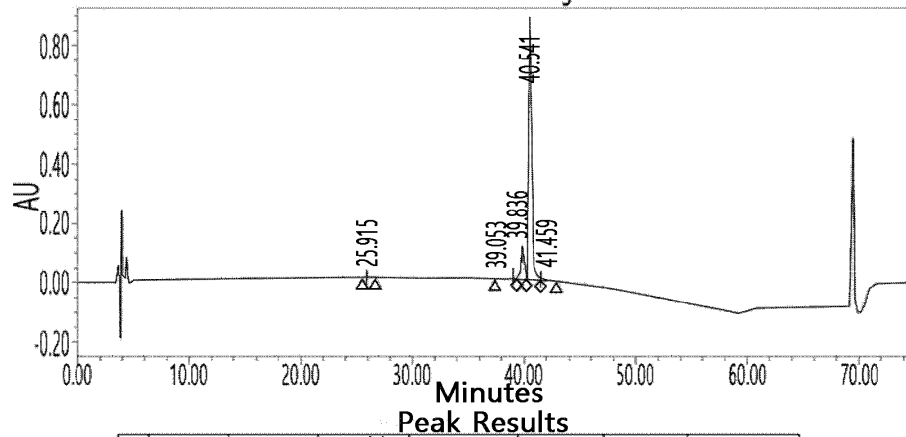


Peak Results

	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	27.591	bv	144.000	24021	348	0.06	37263781
2	28.896	vv	230.000	37016396	851448	99.34	37263781
3	32.055	vv	197.200	212592	3662	0.57	37263781
4	35.030	vb	104.000	10772	250	0.03	37263781

RP-HPLC

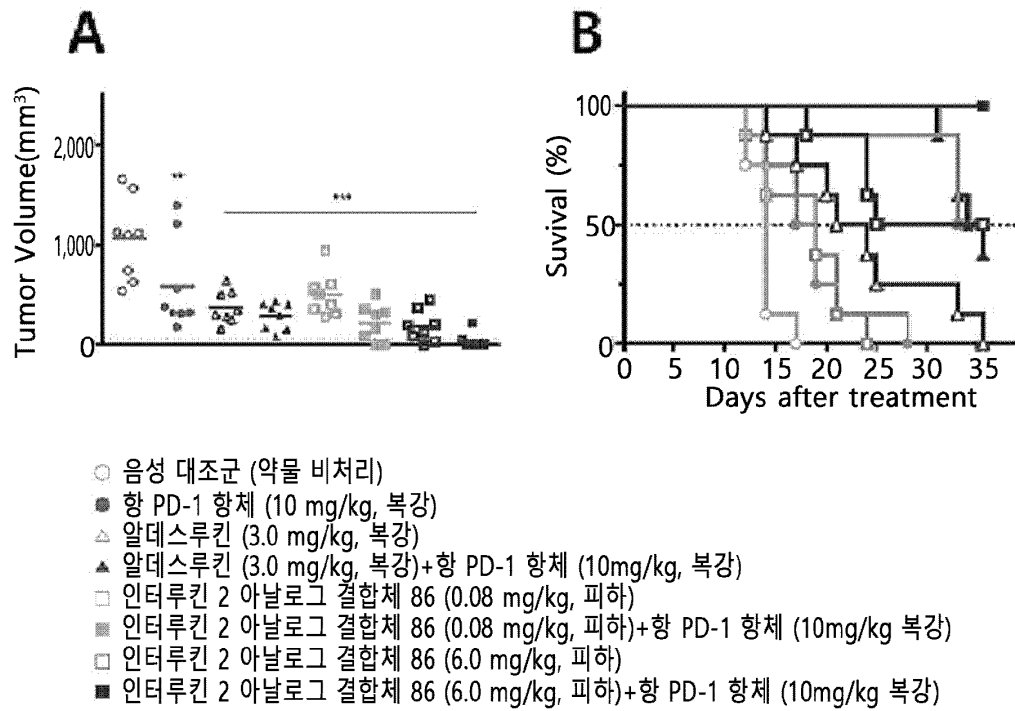
Auto-Scaled Chromatogram



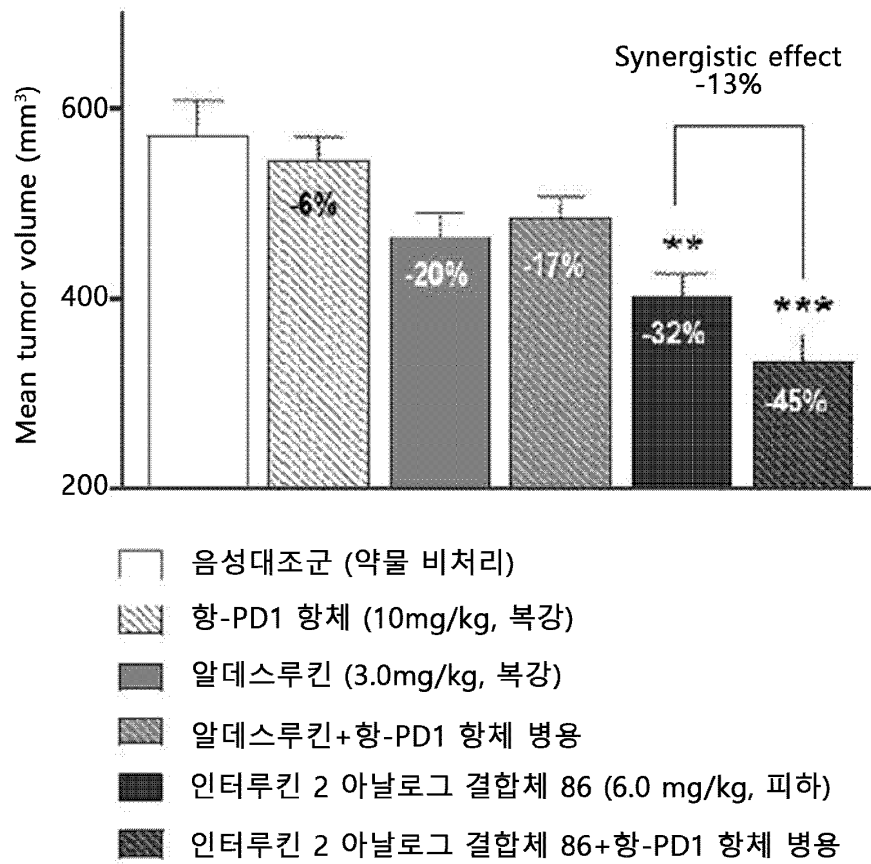
Peak Results

	RT	Int Type	Width (sec)	Area	Height	% Area	Total Area
1	25.915	Bb	70.400	34022	1272	0.18	19021437
2	39.053	bv	122.800	386132	8859	2.03	19021437
3	39.836	vv	47.600	1921333	88063	10.10	19021437
4	40.541	vv	77.600	16466179	864067	86.57	19021437
5	41.459	vb	87.200	213771	6643	1.12	19021437

[도3]

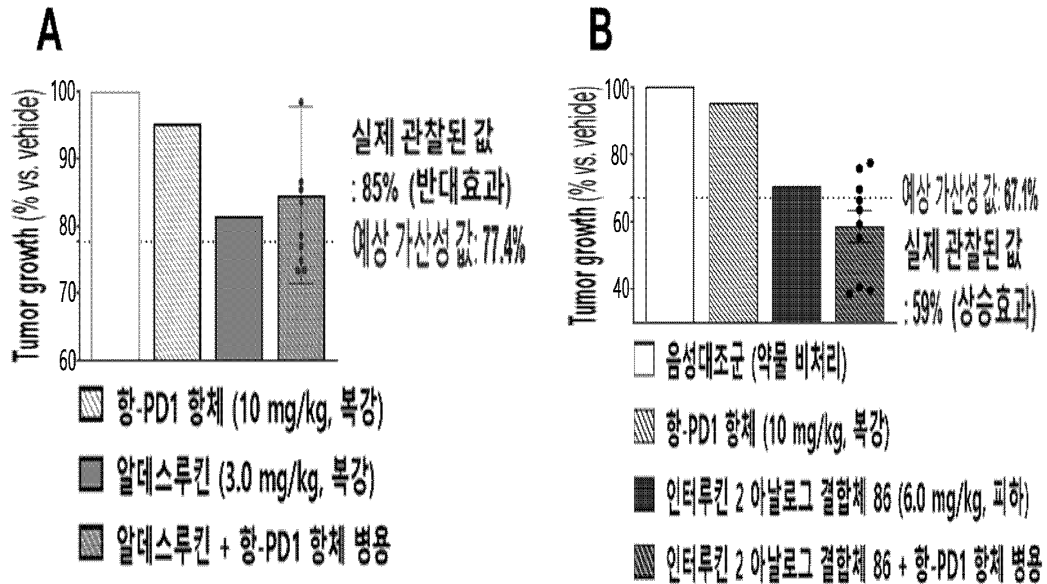


[도4]



***p<0.001, **p<0.01, *p<0.05vs vehicle group by one-way ANOVA test

[도5]



*Bliss 독립모형의 분석 예시

1) 항-PD1 단클론항체 단독 투약에 따른, 중앙 억제 효능: 95.24% (vs. 음성대조군)

2) 알데스루킨 단독 투약에 따른 중앙 억제 효능: 81.55% (vs. 음성대조군)

- 두약물의 병용에 따른 예상 가산성 값: $(0.9524 \times 0.8155) \times 100 = 77.7\%$

실제 두 약물의 병용 투약군에서 관찰된 값이 예상 가산성 값(< 77.7%) 보다 적은 경우 경우: 상승 효과

실제 두 약물의 병용 투약군에서 관찰된 값이 예상 가산성 값(< 77.7%) 보다 큰 경우 경우: 반대 효과

Bliss independence was conducted based on reference (J Cheminform. 2015 Feb 26;7:7)

[도6]

