Supplementary figures

Supplementary Figure 1. Correlation between PD-L1 level in macrophages and PD-L1, CD8, CD68 levels. PD-L1 level in macrophages and its correlation with CD8 level, CD68 level and PD-L1 level in tumor.

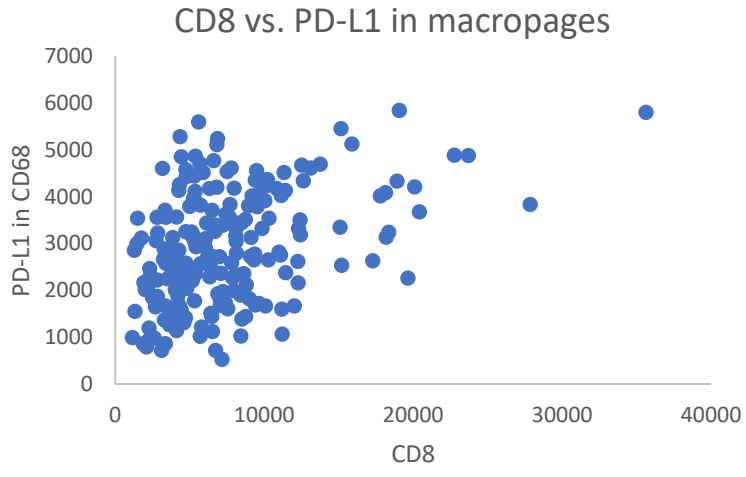
Supplementary Figure 2. Identification of the significant change point of the trend of conventional therapy treated control arm.

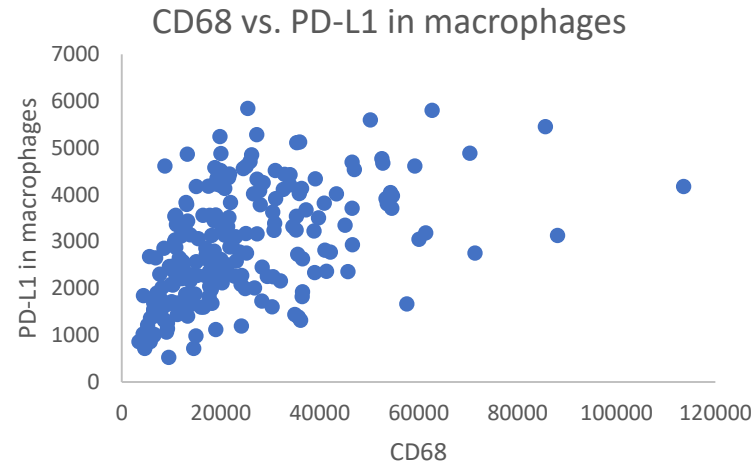
Supplementary Figure 3. PD-L1 expression in CD68 does not carry prognostic value with joinpoint determined cut-off point.

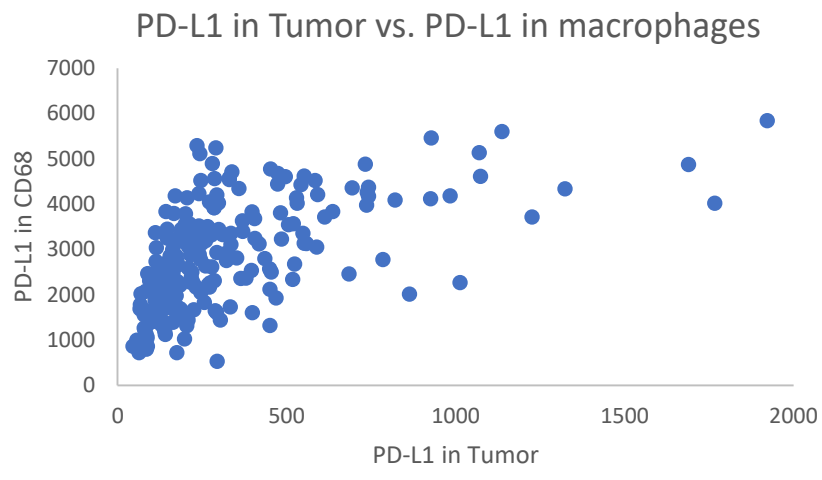
Supplementary Figure 4. No difference of PD-L1/CD68 double positive phenotype cell count was found between clinical benefit and non-clinical benefit group.

Supplementary Figure 5. Identification of the significant change point of the trend. Joinpoint regression identified the marker score that is the significant change point of the trend for total PD-L1/CK cell count and PD-L1/CD68 cell count. Supplementary Figure 6. CD8 level predicts patients' overall survival to anti-PD-1 axis blockade therapy. With Ultimapper method, top 1/4 CD8 level was predicting better overall survival of patients treated with single immunotherapy.

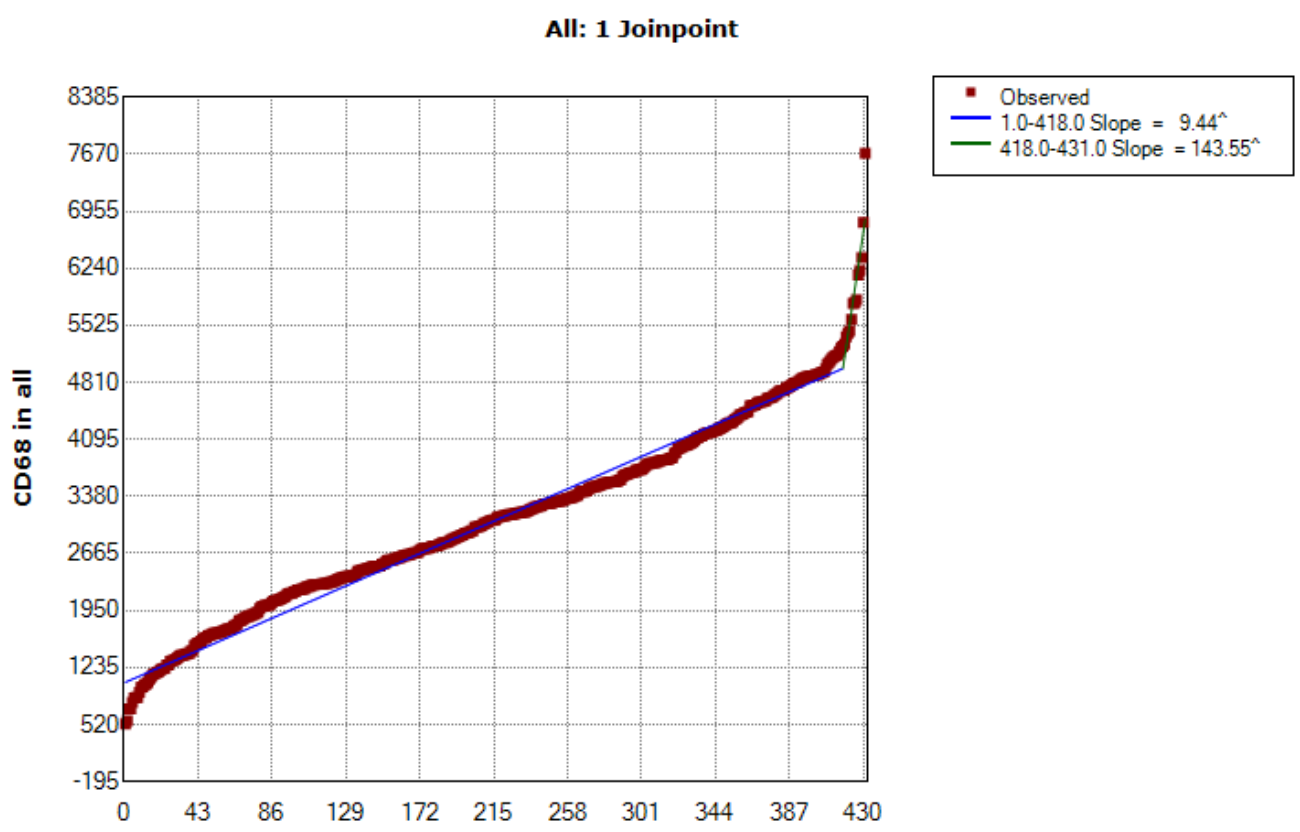
Supp Figure 1. Correlation between PD-L1 level in macrophages and PD-L1 level in Tumor, CD8 and CD68 levels



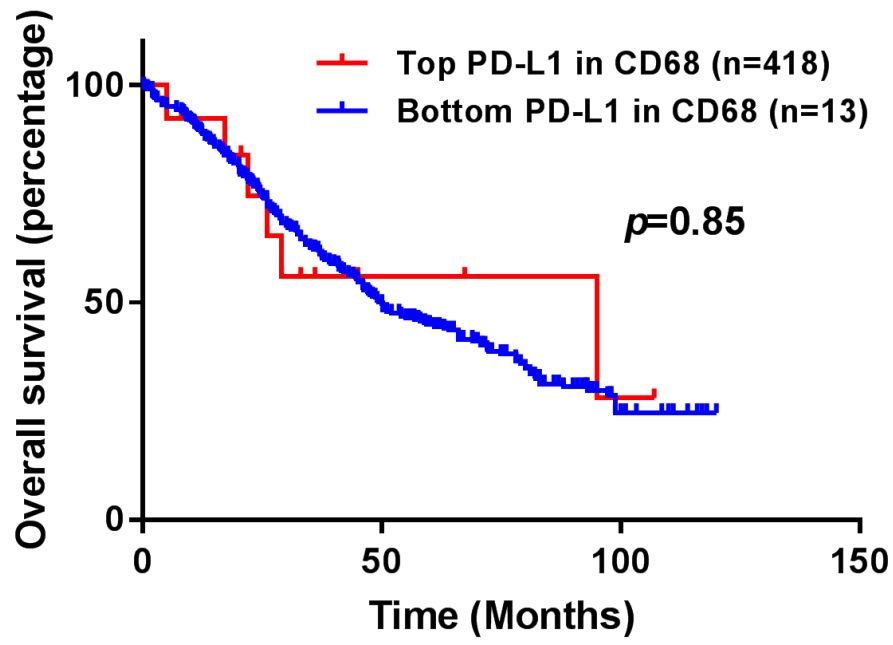




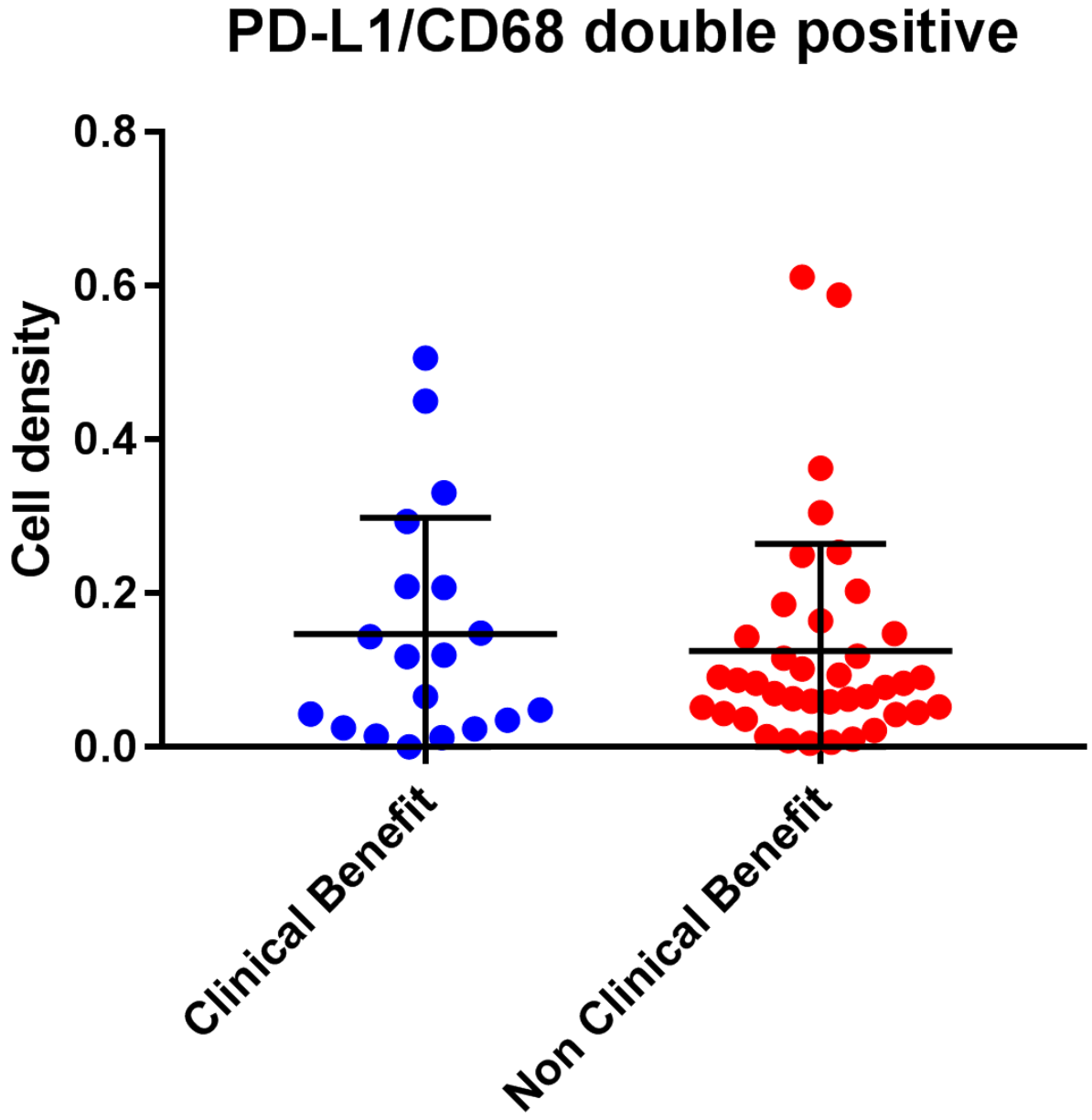
Supp Figure 2. Identification of the significant change point of the trend of conventional therapy treated control arm.



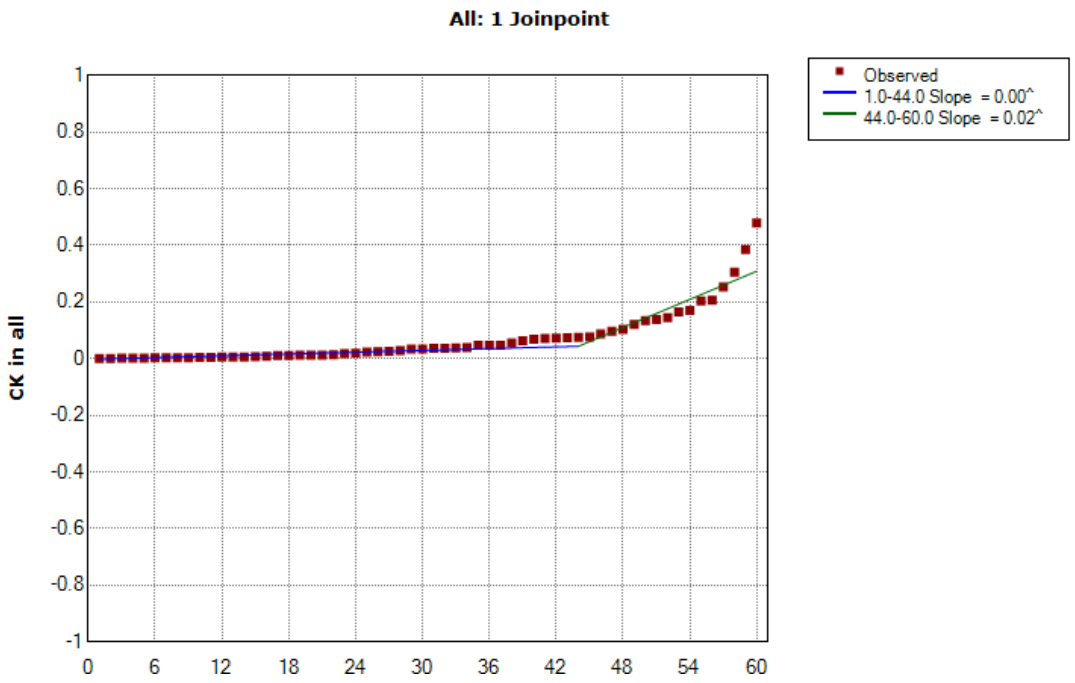
Supp Figure 3. PD-L1 expression in CD68 does not carry prognostic value with joinpoint determined cut-off point.

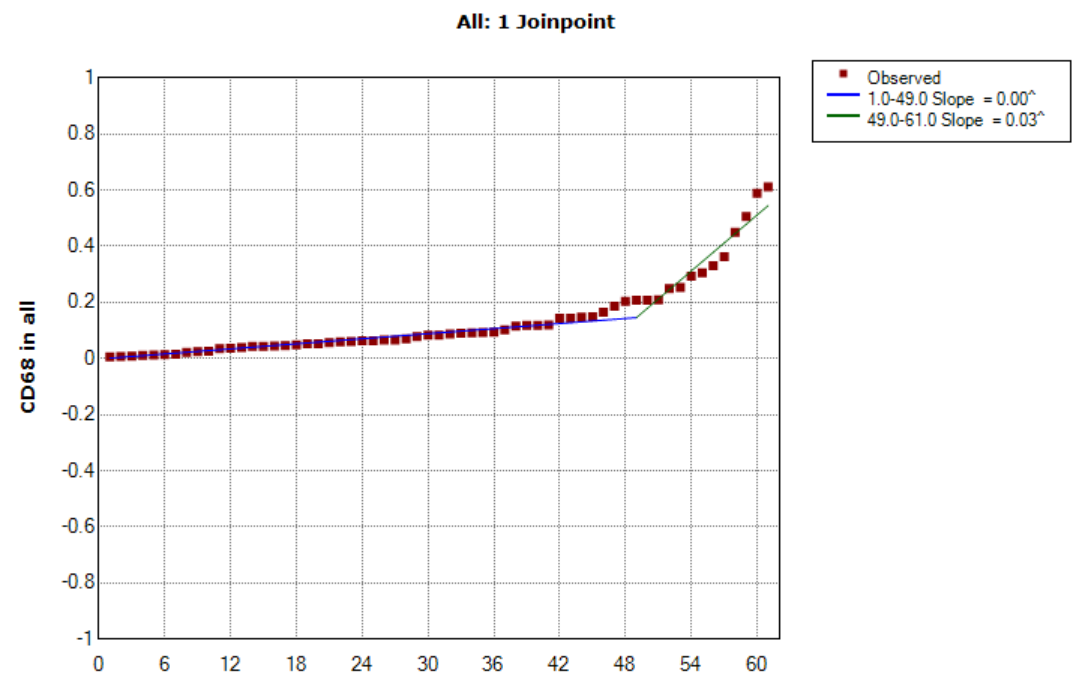


Supp Figure 4. No difference of PD-L1/CD68 double positive phenotype cell count was found between clinical benefit and non-clinical benefit group

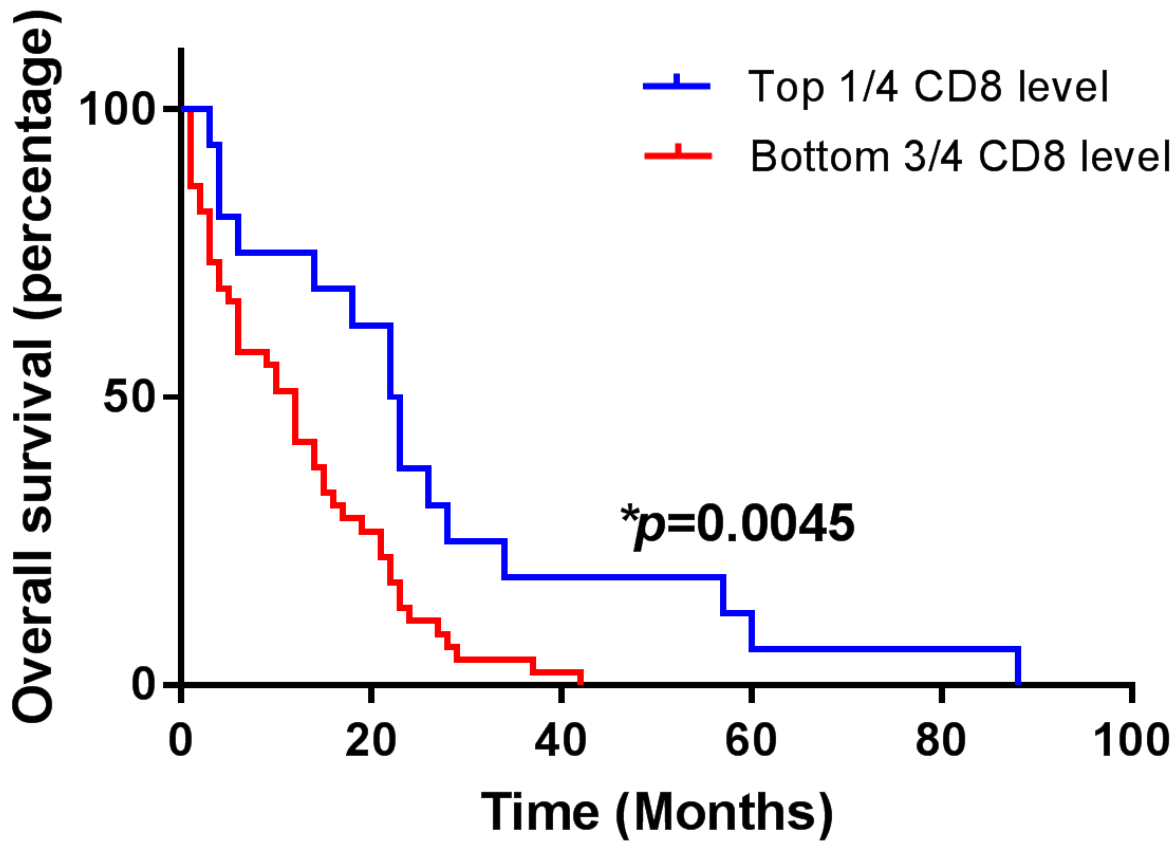


Supp Figure 5. Identification of the significant change point of the trend of immunotherapy treated cohort





Supp Figure 6. CD8 level predicts patients' overall survival to anti-PD-1 axis blockade therapy.



Supp Table 1. Clinicopathological characteristics of YTMA250

Characteristic	N (%)
Total	249
Gender	
Male	108 (43.4)
Female	141 (56.6)
Age	
< 70 yo	145 (58.2)
>= 70 yo	104 (41.8)
Stage	
I-II	198 (79.5)
III-IV	48 (19.3)
Unknown	3
Histology	
ADC	165 (66.3)
SCC	66 (26.5)
Other	48 (19.2)
Smoking History	
Non smoker	40 (16.1)
Current/Former	194 (78.0)
Unknown	15

Supp Table 2. Clinicopathological characteristics of YTMA79

Characteristic	N (%)
Total	176
Gender	
Male	84 (47.7)
Female	92 (52.3)
Age	
< 70 yo	114 (64.8)
>= 70 yo	62 (35.2)
Stage	
0	14 (8.0)
I-II	119 (67.7)
III-IV	41 (23.3)
Unknown	2
Histology	
ADC	106 (60.2)
SCC	35 (20.0)
LCC	22 (12.5)
Other	13
Smoking History	
Non smoker	8 (4.5)
Current/Former	167 (94.9)
Unknown	1

Supp Table 3. Multivariate analysis indicates that PD-L1 in CD68+ macrophages and CD8 level are independent predictive factors to overall survival

Variables	**HR**	**95%CL**	**P-value**
Age, years (<70 vs. ≥70)	0.89	0.45-1.71	0.73
Gender (Female vs. Male)	0.94	0.49-1.80	0.87
Stage (I&II vs. III&IV) *	-	-	-
Smoking (Non-smoker vs. Smoker)	0.15	0.04-0.48	0.0004
PD-L1/CD68 (Low vs. High)	2.56	1.09-7.10	0.0291
CD8 (Low vs High)	3.18	1.37-8.60	0.0056

*All patients are stage III and IV