

SUPPLEMENTAL DATA

RESEARCH ARTICLE

Wang et al: Neoadjuvant immunochemotherapy for EC

Neoadjuvant immunochemotherapy for resectable esophageal cancer: A study on efficacy and safety

Xiaomin Wang¹, Bingxu Li¹, Zhiyong Zheng¹, Weijie Wang^{2*}

¹Department 1st of Radiation Oncology, Anyang Tumor Hospital, Anyang City, Henan Province, China.

²Department Thoracic Surgery, Anyang Tumor Hospital, Anyang City, Henan Province, China.

*Correspondence to Weijie Wang: wwjjw9009@163.com

DOI: <https://doi.org/10.17305/bb.2025.11806>

Full article is available at the following link:

<https://www.bjbms.org/ojs/index.php/bjbms/article/view/11806>

Table S1. Pathologic information after treatment

Characteristics	Sintilimab group (n=75)	Other drug group (n=24)	P value
Surgical residuals (n, %)			1.000
R0	74 (98.7)	24 (100.0)	
R1	1 (1.3)	0	
ypT (n, %)			0.393
T0	19 (25.3)	7 (29.2)	
T1	20 (26.7)	2 (8.3)	
T2	17 (22.7)	6 (25.0)	
T3	17 (22.7)	8 (33.3)	
T4	2 (2.7)	1 (4.2)	
ypN (n, %)			0.107
N0	50 (66.7)	13 (54.2)	
N1	20 (26.7)	6 (25.0)	
N2	5 (6.7)	3 (12.5)	
N3	0	2 (8.3)	
CAP grading			0.454
Grade 0	19 (25.3)	7 (29.2)	
Grade 1	32 (42.7)	6 (25.0)	
Grade 2	12 (16.0)	5 (20.8)	
Grade 3	12 (16.0)	6 (25.0)	
Induction therapy response assessment			0.454
TRG1	19 (25.3)	7 (29.2)	
TRG2	32 (42.7)	6 (25.0)	
TRG3	12 (16.0)	5 (20.8)	
TRG4	12 (16.0)	6 (25.0)	

Table S2. Comparison of AE in different PD-1 drug subgroups

AE	Sintilimab group (n=75)	Other drug group (n=24)	P value
Neoadjuvant therapy-related grade ≥3 AEs	12 (16.0)	5 (20.8)	0.756
Digestive tract reaction	11 (14.7)	5 (20.8)	
Bone marrow suppression	2 (2.7)	2 (8.3)	
Dermatitis	1 (1.3)	0	
Surgery-related grade ≥3 AEs	10 (13.3)	1 (4.2)	0.287
Anastomotic leak	6 (8.0)	0	
Lung infection	1 (1.3)	0	
Incisional fat liquefaction	0	1 (4.2)	
Pleural effusion	1 (1.3)	0	
Stress ulcers	1 (1.3)	0	
Others	1 (1.3)	0	

Table S3. Comparison of AE in different PD-1 drug subgroups			
AE	Cisplatin group (n=66)	Other drug group (n=33)	P value
Neoadjuvant therapy-related grade ≥3 AEs	11 (16.7)	6 (18.2)	1.000
Digestive tract reaction	10 (15.2)	6 (18.2)	
Bone marrow suppression	2 (3.0)	2 (6.1)	
Dermatitis	1 (1.5)	0	
Surgery-related grade ≥3 AEs	8 (12.1)	3 (9.1)	0.747
Anastomotic leak	5 (7.6)	1 (3.0)	
Lung infection	0	1 (3.0)	
Incisional fat liquefaction	1 (1.5)	0	
Pleural effusion	1 (1.5)	0	
Stress ulcers	0	1 (3.0)	
Others	1 (1.5)	0	

Table S4. Pathologic information after treatment			
Characteristics	Cisplatin group (n=66)	Other drug group (n=33)	P value
Surgical residuals (n, %)			0.333
R0	66 (100.0)	32 (97.0)	
R1	0	1 (3.0)	
ypT (n, %)			0.632
T0	18 (27.3)	8 (24.2)	
T1	17 (25.8)	5 (15.2)	
T2	14 (21.2)	9 (27.3)	
T3	16 (24.2)	9 (27.3)	
T4	1 (1.5)	2 (6.1)	
ypN (n, %)			0.401
N0	44 (66.7)	19 (57.6)	
N1	18 (27.3)	8 (24.2)	
N2	3 (4.5)	5 (15.2)	
N3	1 (1.5)	1 (3.0)	
CAP grading			0.257
Grade 0	18 (27.3)	8 (24.2)	
Grade 1	29 (43.9)	9 (27.3)	
Grade 2	9 (13.6)	8 (24.2)	
Grade 3	10 (15.2)	8 (24.2)	
Induction therapy response assessment			0.257
TRG1	18 (27.3)	8 (24.2)	
TRG2	29 (43.9)	9 (27.3)	
TRG3	9 (13.6)	8 (24.2)	
TRG4	10 (15.2)	8 (24.2)	

Table S5. COX regression analysis to determine risk factors affecting OS

Characteristics	Level	HR	Univariate 95%CI	P value	HR	Multivariate 95%CI	P value
Sex	Male	Reference			-	-	-
	Female	1.589	0.616~4.100	0.338	-	-	-
Age	≤68	Reference			-	-	-
	>68	0.411	0.135~1.248	0.117	-	-	-
KPS score	<85	Reference			-	-	-
	>85	1.204	0.429~3.379	0.725	-	-	-
Tumor site	Upper segment	Reference			-	-	-
	Middle segment	0.658	0.238~1.816	0.419	-	-	-
	Lower segment	0.383	0.99~1.481	0.164	-	-	-
Tumor length	<7.5	Reference			-	-	-
	>7.5	0.466	0.107~2.031	0.309	-	-	-
cT	T2	Reference			-	-	-
	T3	0.595	0.129~2.756	0.507	-	-	-
	T4	1.515	0.315~7.296	0.604	-	-	-
cLN	N0	Reference			-	-	-
	N1	0.556	0.126~2.457	0.438	-	-	-
	N2	0.538	0.076~3.821	0.535	-	-	-
Type of PD-1 inhibitor	Sintilimab	Reference			Reference		
	Camrelizumab	2.430	0.844~6996	0.100	8.440	0.989~72.053	0.051
	Pembrolizumab	1.119	0.144~8.709	0.914	3.670	0.047~287.124	0.559
	Penpulimab	4.435	0.554~35.470	0.160	5259.326	50.875~543692.346	<0.001
	Toripalimab	0	0	0.992	0.002	-	0.995
	Tislelizumab	0	0	0.989	0.006	0~5.42E53	0.938
Chemotherapy regimens-1	Paclitaxel + platinum	Reference			Reference		
	Others	3.860	1.102~13.523	0.035	0.110	0~2.7518E108	0.986
Type of paclitaxel in chemotherapy	Paclitaxel	Reference			-	-	-
	Albumin-bound paclitaxel	2.695	0.354~20.498	0.338	-	-	-
Chemotherapy regimens-2	Platinum-based chemotherapy	Reference			-	-	-
	Others	0.049	0~4663850.039	0.747	-	-	-
Type of platinum drugs in	Cisplatin	Reference			Reference		
	Nedaplatin	0.916	0.292~2.877	0.880	0.684	0.087~5.364	0.718

chemotherapy	Oxaliplatin	10.309	2.728~38.961	0.001	100203.837	0~2.495E114	0.929
	Others	0	0	0.986	0.120	-	0.998
Course of chemotherapy	≤2	Reference			-	-	-
	>2	1.773	0.583~5.389	0.313	-	-	-
Neoadjuvant therapy-related grade ≥3 AEs	No	Reference			-	-	-
	Yes	0.869	0.251~3.002	0.824	-	-	-
Number of preoperative immunizations	≤2	Reference			-	-	-
	>2	1.558	0.554~4.380	0.401	-	-	-
Surgical method	Cavascopes	Reference			Reference		
	Left thoracotomy	1.414	0.375~5.334	0.609	17.755	2.065~152.642	0.009
	Right thoracotomy	1.153	0.346~3.841	0.816	6.438	0.566~73.228	0.133
	Others	6.771	1.773~25.866	0.005	-	-	-
Surgery-related grade ≥3 AEs	No	Reference			-	-	-
	Yes	1.075	0.247~4.683	0.923	-	-	-
Time interval between last dose and surgery	≤34 d	Reference			Reference		
	>34 d	3.448	0.997~11.922	0.050	75.740	1.920~1987.609	0.021
Surgical residuals	R0	Reference			-	-	-
	R1	0.049	0~1608260.675	0.732	-	-	-
Number of lymph nodes removed	<10	Reference			-	-	-
	>10	23.427	0.021~26278.233	0.379	-	-	-
Positive lymph nodes	No	Reference			Reference		
ypT	Yes	6.987	2.296~21.261	0.001	0.052	0~6.338E96	0.980
	T0	Reference			Reference		
	T1	4.080	0.422~39.408	0.224	0.498	0.010~25.623	0.729
	T2	7.148	0.832~61.434	0.073	2.808	0.096~81.976	0.549
	T3	9.862	1.210~80.381	0.033	0.825	0.021~32.340	0.918
	T4	45.464	3.962~521.646	0.002	0.001	0~1.438	0.062
ypN	N0	Reference			Reference		
	N1	5.779	1.779~18.773	0.004	295.437	0~3.492E100	0.961
	N2	16.877	4.463~63.821	<0.001	738.858	0~8.875E100	0.954
	N3	0	0	0.988	0.001	-	0.995
CAP/TRG assessment	Grade 0/TRG1	Reference			Reference		
	Grade 1/TRG2	5.292	0.648~43.203	0.120	0.538	0.059~4.901	0.582
	Grade 2/TRG3	5.900	0.612~56.890	0.125	0.164	0.005~5.250	0.307

	Grade 3/TRG4	21.785	2.612~181.704	0.004	-	-	-
Postoperative regional recurrence	No	Reference			Reference		
	Yes	6.051	2.396~15.278	<0.001	34.919	3.959~308.013	0.001
Postoperative distant metastasis	No	Reference			Reference		
	Yes	3.264	1.073~9.929	0.037	8.097	0.142~462.241	0.311

Table S6. The pairwise comparison between multiple groups

Figure	Survival time (95%CI)	Log-rank P
Figure 3-A		
Sintilimab vs. Camrelizumab	24.599 (23.258~25.940) vs. 25.974 (20.323~31.525)	0.085
Sintilimab vs. Pembrolizumab	24.599 (23.258~25.940) vs. 23.250 (21.977~24.523)	0.940
Sintilimab vs. Penpulimab	24.599 (23.258~25.940) vs. 13.000 (6.599~19.401)	0.155
Sintilimab vs. Toripalimab	-	0.721
Sintilimab vs. Tislelizumab	-	0.655
Camrelizumab vs. Pembrolizumab	25.974 (20.323~31.525) vs. 23.250 (21.977~24.523)	0.439
Camrelizumab vs. Penpulimab	25.974 (20.323~31.525) vs. 13.000 (6.599~19.401)	0.596
Camrelizumab vs. Toripalimab	-	0.571
Camrelizumab vs. Tislelizumab	-	0.480
Pembrolizumab vs. Penpulimab	23.250 (21.977~24.523) vs. 13.000 (6.599~19.401)	0.197
Pembrolizumab vs. Toripalimab	-	-
Pembrolizumab vs. Tislelizumab	-	0.617
Penpulimab vs. Toripalimab	-	0.414
Penpulimab vs. Tislelizumab	-	0.564
Toripalimab vs. Tislelizumab	-	-
Figure 3-C		
Cisplatin vs. Nedaplatin	29.781 (27.512~32.051) vs. 24.433 (22.070~26.796)	0.879
Cisplatin vs. Oxaliplatin	29.781 (27.512~32.051) vs. 14.000 (7.117~20.883)	<0.001
Cisplatin vs. Others	-	0.654
Nedaplatin vs. Oxaliplatin	24.433 (22.070~26.796) vs. 29.781 (27.512~32.051)	<0.001
Nedaplatin vs. Others	24.433 (22.070~26.796) vs. 14.000 (7.117~20.883)	0.609
Oxaliplatin vs. Others	29.781 (27.512~32.051) vs. 14.000 (7.117~20.883)	0.414
Figure 3-D		
Cavascopie vs. Left thoracotomy	30.346 (28.004~32.688) vs. 23.678 (20.255~27.101)	0.636
Cavascopie vs. Right thoracotomy	30.346 (28.004~32.688) vs. 24.444 (22.060~26.827)	0.826
Cavascopie vs. Others	30.346 (28.004~32.688) vs. 15.500 (10.576~20.424)	0.002
Left thoracotomy vs. Right thoracotomy	23.678 (20.255~27.101) vs. 24.444 (22.060~26.827)	0.736
Left thoracotomy vs. Others	23.678 (20.255~27.101) vs. 15.500 (10.576~20.424)	0.048
Right thoracotomy vs. Others	24.444 (22.060~26.827) vs. 15.500 (10.576~20.424)	0.007
Figure 3-G		
T0 vs. T1	26.333 (25.054~27.612) vs. 23.155 (24.360~26.961)	0.240
T0 vs. T2	26.333 (25.054~27.612) vs. 23.232 (20.316~26.148)	0.041
T0 vs. T3	26.333 (25.054~27.612) vs. 26.506 (21.998~31.014)	0.010
T0 vs. T4	26.333 (25.054~27.612) vs. 15.500 (10.600~20.400)	<0.001
T1 vs. T2	23.155 (24.360~26.961) vs. 23.232 (20.316~26.148)	0.501
T1 vs. T3	23.155 (24.360~26.961) vs. 26.506 (21.998~31.014)	0.161
T1 vs. T4	23.155 (24.360~26.961) vs. 15.500 (10.600~20.400)	0.002
T2 vs. T3	23.232 (20.316~26.148) vs. 26.506 (21.998~31.014)	0.599

T2 vs. T4	23.232 (20.316~26.148) vs. 15.500 (10.600~20.400)	0.024
T3 vs. T4	26.506 (21.998~31.014) vs. 15.500 (10.600~20.400)	0.020
Figure 3-H		
N0 vs. N1	26.074 (25.191~26.958) vs. 25.475 (20.972~29.978)	0.001
N0 vs. N2	26.074 (25.191~26.958) vs. 15.026 (10.786~19.266)	<0.001
N0 vs. N3	-	-
N1 vs. N2	25.475 (20.972~29.978) vs. 15.026 (10.786~19.266)	0.053
N1 vs. N3	-	0.538
N2 vs. N3	-	0.445
Figure 4		
cT2 vs. cT3	14.333 (11.089~17.578) vs. 14.243 (10.633~17.853)	0.981
cT2 vs. cT4	14.333 (11.089~17.578) vs. 7.167 (3.910~10.424)	0.122
cT3 vs. cT4	14.243 (10.633~17.853) vs. 7.167 (3.910~10.424)	0.028

Table S7. COX regression analysis to determine risk factors affecting DFS							
Characteristics	Level	HR	Univariate 95%CI	P value	HR	Multivariate 95%CI	P value
Sex	Male	Reference			-	-	-
	Female	1.138	0.409~3.169	0.805	-	-	-
Age	≤66	Reference			-	-	-
	>66	1.177	0.402~3.449	0.767	-	-	-
KPS score	<85	Reference			-	-	-
	>85	0.979	0.329~2.090	0.969	-	-	-
Tumor site	Upper segment	Reference			-	-	-
	Middle segment	0.427	0.128~1.424	0.166	-	-	-
	Lower segment	0.602	0.142~2.554	0.491	-	-	-
Tumor length	<4.5	Reference			-	-	-
	>4.5	0.850	0.282~2.563	0.772	-	-	-
cT	T2	Reference			-	-	-
	T3	0.967	0.199~4.689	0.967	-	-	-
	T4	3.524	0.681~18.230	0.133	-	-	-
cLN	N0	Reference			-	-	-
	N1	0.786	0.172~3.604	0.757	-	-	-
	N2	0.609	0.082~4.515	0.628	-	-	-
Type of PD-1 inhibitor	Sintilimab	Reference			-	-	-
	Camrelizumab	1.370	0.457~4.103	0.574	-	-	-
	Pembrolizumab	0	0	0.985	-	-	-
	Penpulimab	4.700	0.530~41.654	0.165	-	-	-
	Toripalimab	-	-	-	-	-	-
	Tislelizumab	-	-	-	-	-	-
Chemotherapy regimens-1	Paclitaxel + platinum	Reference			-	-	-
	Others	2.252	0.615~8.249	0.220	-	-	-
Type of paclitaxel in chemotherapy	Paclitaxel	Reference			-	-	-
	Albumin-bound paclitaxel	0.536	0.060~4.806	0.577	-	-	-

Type of platinum drugs in chemotherapy	Cisplatin	Reference			-	-	-
	Nedaplatin	0.560	0.172~1.826	0.336	-	-	-
	Oxaliplatin	1.807	0.468~6.975	0.391	-	-	-
	Others	-	-	-	-	-	-
Course of chemotherapy	<3	Reference			-	-	-
	≥3	1.114	0.340~3.652	0.858	-	-	-
Neoadjuvant therapy-related grade ≥3 AEs	No	Reference			-	-	-
	Yes	0.501	0.113~2.221	0.363	-	-	-
Number of preoperative immunizations	<3	Reference			-	-	-
	≥3	0.785	0.268~2.299	0.659	-	-	-
Surgical method	Cavascopie	Reference			-	-	-
	Left thoracotomy	1.050	0.220~5.009	0.952	-	-	-
	Right thoracotomy	1.238	0.323~4.748	0.756	-	-	-
	Others	2.383	0.606~9.361	0.214	-	-	-
Surgery-related grade ≥3 AEs	No	Reference			-	-	-
	Yes	1.977	0.425~9.187	0.384	-	-	-
Time interval between last dose and surgery	≤41 d	Reference			-	-	-
	>41 d	1.573	0.438~5.646	0.487	-	-	-
Number of lymph nodes removed	<15	Reference			-	-	-
	>15	2.201	0.755~6.413	0.148	-	-	-
Positive lymph nodes	No	Reference			-	-	-
	Yes	2.038	0.572~7.269	0.272	-	-	-
ypT	T0	Reference			-	-	-
	T1	1.621	0.165~15.900	0.678	-	-	-
	T2	2.643	0.262~26.691	0.410	-	-	-
	T3	1.682	0.201~14.103	0.632	-	-	-
	T4	3.044	0.271~34.226	0.367	-	-	-
ypN	N0	Reference			-	-	-
	N1	1.769	0.455~6.871	0.410	-	-	-
	N2	2.642	0.625~11.172	0.187	-	-	-
	N3	0	0	0.991	-	-	-
CAP/TRG assessment	Grade 0/TRG1	Reference			-	-	-
	Grade 1/TRG2	1.586	0.184~13.645	0.674			
	Grade 2/TRG3	0.615	0.050~7.601	0.705			
	Grade 3/TRG4	3.777	0.451~31.636	0.220			

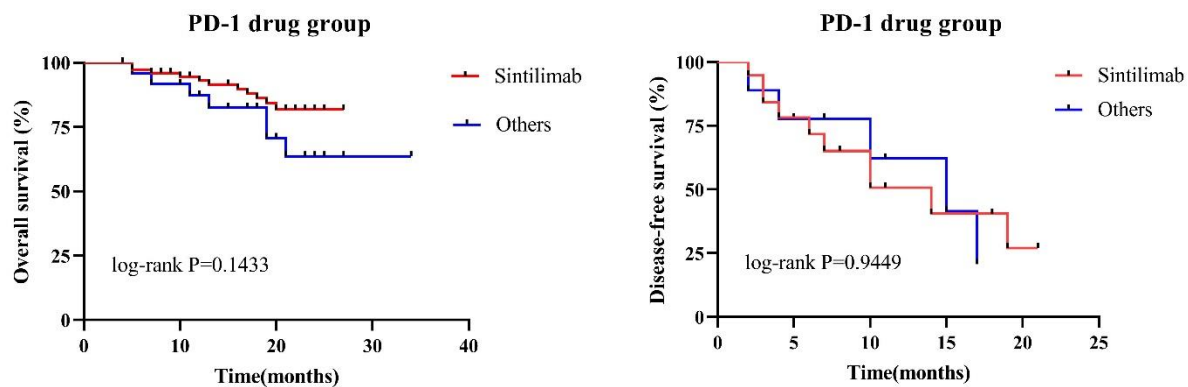


Figure S1.

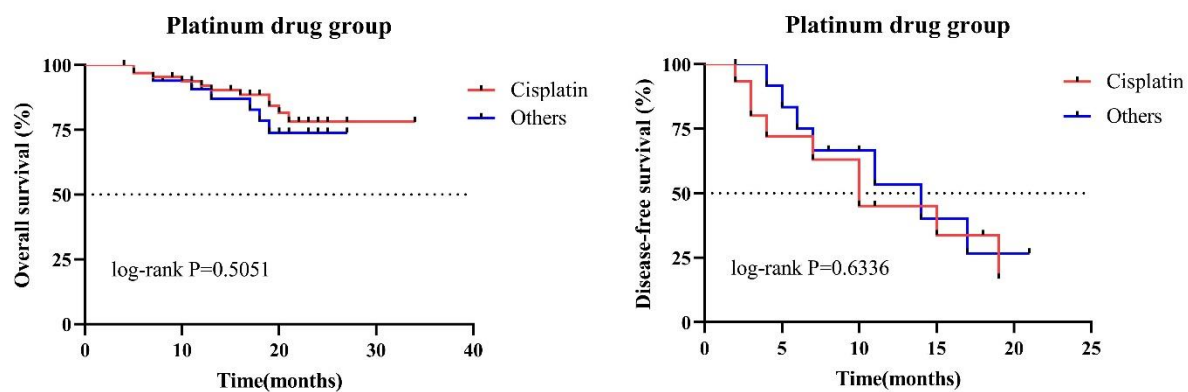


Figure S2.