



Prognostic factors in patients receiving pembrolizumab with biliary tract cancer

Min je Sung, Hee Seung Lee, Moon Jae Chung, Seungmin Bang, Seung Woo Park, Si Young Song, Jeong Youp Park*.

Division of Gastroenterology, Department of Internal Medicine,
Gastric Cancer Center, Severance Hospital,
Yonsei University College of Medicine

* Corresponding author

Severance



Background

- Biliary tract cancers are aggressive neoplasms that arise from the epithelial lining of bile ducts and gallbladder and have poor prognosis.
- The benefit of second-line chemotherapy over standard first-line gemcitabine plus cisplatin chemotherapy in advanced biliary tract cancer is unclear.
- Among many second-line chemotherapy, immune check point inhibitors are used, especially pembrolizumab.

Aim

- Our aim was to identify prognostic factors for overall survival (OS) with pembrolizumab in advanced biliary tract cancer.

Method

- 44 cases with pembrolizumab in advanced biliary tract cancer
- Between December 2017 and April 2019
- at the Yonsei University Medical Center

Result

● Table 1. Baseline characteristics

Variables	N = 44					
Age, year	66 (59-74)	Prior resection of primary tumor	25 / 43 (56.8%)	AST, IU/L (13.0~34.0)	23.5 (18.3-36.0)	
Female gender	18 (40.9%)	PD-L1 Tumor Proportion Score		ALT, IU/L (5.0~46.0)	18.0 (12.0-31.8)	
Weight, kg	56 (50.0-70.7)	≤ 5	34 (77.3%)	Total bilirubin, mg/dL (0.5~1.8)	0.6 (0.4-0.9)	
Height, cm	159.2 (152.4-169.0)	6~49	7 (15.9%)	ALP, IU/L (50~151)	120 (84-281)	
BMI, kg/m ²	22.5 (20.4-25.1)	≥ 50	3 (6.8%)	Albumin, g/dl	3.8 (3.3-4.1)	
Performance status		Previous chemotherapy period, month	4.43 (2.17-6.73)	CA 19-9, U/ml (0.0~34.0)	361 (31-3129)	
0	27 (61.4%)	Best response		Overall Survival, month	5.9 (2.5-10.1)	
1	15 (34.1%)	CR	0	Progression Free Survival, month	1.9 (1.4-2.8)	
2	2 (4.5%)	PR	5 (11.4%)			
Bile tract cancer		SD	9 (20.5%)			
Intrahepatic CCC	18 (40.9%)	PD	27 (61.4%)			
Extrahepatic CCC	21 (47.7%)	Unknown	3 (6.8%)			
GB cancer	5 (11.4%)	Tumor size (sum of diameters), cm	4.4 (2.0-6.2)			
Stage		< 4	19/39 (48.7%)			
Locally advanced	5 (11.4%)	≥ 4	20/39 (51.3%)			
Metastatic	39 (88.6%)	WBC, 10 ³ /uL	6.38 (5.01-8.97)			
Distant metastasis	38/44 (86.4%)	Neutrophil, 10 ³ /uL	4.46 (3.06-6.60)			
Liver	21 (47.7%)	Lymphocyte, 10 ³ /uL	1.46 (1.02-1.81)			
Abd.LN	19 (43.2%)	Platelet, 10 ³ /uL	162 (133-237)			
Lung	0	NLR	3.11 (2.04-6.38)			
Bone	3 (6.8%)	LMR	2.04 (1.44-3.00)			
Carcinomatosis	18 (40.9%)	PLR	143 (92-186)			

* Abbreviation: NLR; neutrophil-lymphocyte ratio, LMR; lymphocyte-monocyte ratio. PLR; platelet-lymphocyte ratio, AST; alanine transaminase, ALT; alanine aminotransferase, ALP; Alkaline phosphatase

** median (Interquartile range) or n (%)

Result

● Table 2. Prognostic factors with overall survival in univariate analysis

Variables	Number of Patients	Number of events	HR	95% CI	p-value								
Performance status	0	27	20	1	-	-	WBC, 10 ³ /uL	< 10.8	39	31	1	-	-
	1	15	14	1.407	0.704-2.814	0.334		≥ 10.8	5	5	5.868	2.033-16.940	0.001
	2	2	2	6.175	1.335-28.557	0.020		NLR	< 3	17	12	1	-
Bile tract cancer	Intrahepatic CCC	18	15	1	-	-	≥ 3		19	18	3.324	1.521-7.266	0.003
	Extrahepatic CCC	21	16	0.932	0.460-1.889	0.846	LMR	< 2.5	22	20	3.109	1.392-6.943	0.006
	GB cancer	5	5	2.465	0.884-6.871	0.085		≥ 2.5	14	10	1	-	-
Bone	No	41	33	1	-	-	Total bilirubin, mg/dL (0.5~1.8)	< 1.8	41	33	1	-	-
	Yes	3	3	3.540	1.026-12.217	0.045		≥ 1.8	3	3	5.619	1.336-23.629	0.018
Number of metastasis sites	< 3	40	32	1	-	-	ALP, IU/L (50~151)	< 151	21	17	1	-	-
	≥ 3	4	4	2.716	0.933-7.907	0.067		≥ 151	20	19	2.224	1.112-4.450	0.024
Prior resection of primary tumor	No	18	17	1	-	-	Albumin, g/dl	< 3.3	9	9	1	-	-
	Yes	25	18	0.545	0.279-1.068	0.077		≥ 3.3	35	27	0.358	0.165-0.778	0.010
PD-L1 Tumor Proportion Score	≤ 5	34	27	1	-	-	CA 19-9, U/ml	< 500	23	16	1	-	-
	6~49	7	7	2.234	0.951-5.249	0.065		≥ 500	21	20	1.940	0.993-3.790	0.052
	≥ 50	3	2	0.945	0.224-3.998	0.939	Tumor size (sum of diameters), cm	< 4	19	13	1	-	-
BMI, kg/m ²								≥ 4	20	19	2.781	1.344-5.753	0.006
								< 18.5	41	33	1	-	-
								≥ 18.5	3	3	5.902	1.575-22.116	0.008

* Abbreviation: NLR; neutrophil-lymphocyte ratio, LMR; lymphocyte-monocyte ratio. ALP; Alkaline phosphatase

Result

● Table 3. Prognostic factors with overall survival in multivariate analysis

Variables	Number of Patients	Number of events	HR	95% CI	p-value
NLR					
< 3	17	12	1	-	-
≥ 3	19	18	3.031	1.163-7.897	0.023
Albumin, g/dl					
< 3.3	9	9	1	-	-
≥ 3.3	35	27	0.169	0.063-0.458	< 0.001
Tumor size (sum of diameters), cm					
< 4	19	13	1	-	-
≥ 4	20	19	2.947	1.104-7.867	0.043

* Abbreviation: NLR; neutrophil-lymphocyte ratio

Conclusion

- The more number of metastatic sites, higher neutrophil-lymphocyte ratio, leukocytosis, higher serum albumin level, and larger tumor size is associated with poorer outcomes in advanced biliary tract cancer patients with pembrolizumab.



YONSEI UNIVERSITY
COLLEGE OF MEDICINE

