

SUPPLEMENTARY MATERIAL

First-Line Tislelizumab Plus Chemotherapy for Esophageal Squamous Cell Carcinoma with Programmed Death-Ligand 1 Expression $\geq$ 1%: A Retrospective Analysis of RATIONALE-306

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List of ethics committees by site number

Site No.	Name/address of ethics committee	Approval number
61028 61052	St. Vincent's Hospital Melbourne Human Research Ethics Committee, Melbourne, Australia	HREC 042/19
32001 32011 32013 32015 32017 32018	Ethische Commissie Onderzoek, Leuven, Belgium	EudraCT No.: 2018-000587-28
86001	Beijing Cancer Hospital, Beijing, China	2018YW37
86006	Henan Cancer Hospital – Oncology, Zhengzhou, China	2018109
86007	Jiangsu Province Hospital, Nanjing, China	2018-MD-173; 2018-MD-173.A1
86009	Peking Union Medical College, Beijing, China	KS2019018
86014	The First Affiliated Hospital, Hangzhou, China	2018伦审第(155)号
86018	Subei People's Hospital, Yangzhou, China	2018025-1
86020	The Affiliated Hospital of Xuzhou, Xuzhou, China	XYFY2018-YL056-01
86022	Harbin Medical University Cancer Hospital, Xuzhou, China	2018-59
86029	Anhui Provincial Hospital – Oncology, Anhui, China	2018伦审第152号; 2018伦审第168号
86031	The Second Hospital of Anhui, Anhui, China	YW2018-032(F1)]号
86033	Fudan University Cancer Hospital, Shanghai, China	1904199-9
86036	Fujian Provincial Cancer Hospital, Fuzhou, China	2018-035-01
86037	The Second Affiliated Hospital, Nanchang, China	药临审[2019]第(1)号
86038	Sir Run Run Shaw Hospital, Zhejiang, China	20181106-3
86042	Chinese PLA General Hospital, Beijing, China	C2021-040-01

Site No.	Name/address of ethics committee	Approval number
86048	Tianjin Cancer Hospital – Gastroenterology and Hepatology, Tianjin, China	E2018207
86049	Hunan Cancer Hospital – GCP Office, Hunan, China	2018年药审[158]号; 2018年快审[265]号
86053	The First Affiliated Hospital, Weihui, China	[2018]伦药审字(35)号
86054	The First Affiliated Hospital, Fuzhou, China	LY2018-010-01; LY2018-010-02
86056 86132	The First Affiliated Hospital, Guangzhou, China	086056 2018-046-01 2018-046-02 086132 ZYYEC[2018]012
86068	The First Affiliated Hospital, Xiamen, China	[2018]药伦审字(022)号
86055	Hubei Cancer Hospital, Hubei, China	[2018]第25号
86057	Xiangyang Central Hospital, Hubei, China	XYSZXYY-LL-PJ-2018-016
86058	Shandong Linyi Tumor Hospital, Linyi, China	XY1824
86059	Cancer Hospital of Shantou University, Shantou, China	2018009
86066	Shanxi Provincial People's Hospital, Taiyuan, China	(2018)省医药伦审字第30号
86075	Liaoning Cancer Hospital & Institute, Shenyang, China	20180942
86083	Nantong Tumor Hospital, Nantong, China	通肿伦审药试[2018-013]号
86089	Hainan General Hospital, Hainan, China	医伦[2018]第71号
86101	Zhejiang Cancer Hospital, Hangzhou, China	IRB-[2018]236号; IRB-[2018]289号
86102	Shandong Cancer Hospital, Jinan, China	SD2LEC2018-069-01
86103	First Affiliated Hospital of Zhengzhou University, Zhengzhou, China	药-2018-83
86108	Guangxi Medical University Affiliated Cancer Hospital, Nanning, China	CS2018(42)

Site No.	Name/address of ethics committee	Approval number
86110	The Sixth Affiliated Hospital, Guangzhou, China	意见函2018-107; 2018ZSLYEC-080
86113	Beijing Friendship Hospital, Beijing, China	2018-P1-药017-01
86115	Anhui Provincial Cancer Hospital, Hefei, China	2018-伦理审查-24
86117	The First People's Hospital of Changzhou, Changzhou, China	(2018)药第22号
86133	The People's Library Arm No. 307 Hospital, Beijing, China	2018-5-24-1; 2018-5-24-2
86134	Weifang People's Hospital, Weifang, China	2018-020-01
86135	Guangdong Province Traditional Chinese Medical Hospital, Shenzhen, China	广东省中医院伦理委员会AF2018-091-01
86139	Quanzhou First Hospital, Quanzhou, China	泉一伦[2018]25号 ; 泉一伦[2018]29号
86142	Zhongshan Hospital Xiamen University, Zhongshan, China	XMZSIRB2018第031号; 2018伦审第(17)号
86157	Wuxi Fourth People's Hospital, Wuxi, China	2018-019-001
420004	Fakultni nemocnice Olomouc, Olomouc, Czech Republic	EudraCT No.: 2018-000587-28
420011	Fakultni Thomayerova nemocnice, Prague, Czech Republic	EudraCT No.: 2018-000587-28
33011 33030 33035 33036 33038 33039 33042 33050 33057 33059	Comité de Protection des Perso, France	EudraCT No.: 2018-000587-28
49011 49012 49021 49031	Ethikkommission der Landesärztl, Stuttgart, Germany	EudraCT No.: 2018-000587-28

Site No.	Name/address of ethics committee	Approval number
39029	Comitato Etico Di Area Vasta R, Modena, Italy	EudraCT No.: 2018-000587-28
39035	Comitato Etico Degli Irccs Ist, Italy	EudraCT No.: 2018-000587-28
39054	Azienda Ospedaliera Di Padova, Padova, Italy	EudraCT No.: 2018-000587-28
39056	Comitato Etico Regionale (C.E.R), Bologna, Italy	EudraCT No.: 2018-000587-28
39063	Comitato Etico IRCCS Pascale, Napoli, Italy	EudraCT No.: 2018-000587-28
81001	Osaka University Hospital, Osaka, Japan	File No.: No. 180047-B
81003	Saitama Cancer Center, Saitama, Japan	File No.: AA019-04
81005	Kyushu Medical Center, Kyushu, Japan	File No.: 19C10
81006	Kumamoto University Hospital, Kumamoto, Japan	File No.: 2019011
81009 81015	National Cancer Center Hospital, Chuo City, Tokyo, Japan	File No.: K0846
81016	Kanagawa Cancer Center, Yokohama, Japan	File No.: 290
81017	Akita University Hospital, Akita, Japan	File No.: 19008
81021	University Hospital, Kyoto Prefectural University of Medicine, Kyoto, Japan	File No.: 2019-012
81026	Hiroshima University Hospital, Hiroshima, Japan	File No.: 00951
81029	Kyoto University Hospital, Kyoto, Japan	File No.: 2095
81030	National Hospital Organization, Japan	File No.: 527
81031	Osaka International Cancer Institute, Osaka, Japan	File No.: A-2019-05-0367
81033	Kagawa University Hospital, Miki, Japan	File No.: 20191000117101
81035	Hyogo Cancer Center, Akashi, Japan	File No.: HCC255
81056	Kansai Rosai Hospital, Amagasaki, Japan	File No.: 19A011a
81062	Niigata Cancer Center Hospital, Niigata, Japan	File No.: NA, IRB approval date 11Oct2019
82012	Irb Of Dongsan Hospital, Daegu, Republic of Korea	IRB file number: DSMC2019-02-015 Document number:

Site No.	Name/address of ethics committee	Approval number
		DSMC201902015-HE002
82015	Gachon University Gil Medical, Incheon, Republic of Korea	IRB No.: GFIRB2019-101 Document No.: GilHos IRB-2019-0748
82016	Korea University Guro Hospital, Seoul, Republic of Korea	IRB No.: 2019GR0120 Document No.: K2018-2180-001
82019	The Catholic University of Korea, Seoul, Republic of Korea	Study No.: KC19MDGT0133 Receipt No.: 2019-0347-0001 Document No.: KIRB-Full 20190305-010
82023	CHA University – Bundang Medical Center, Seongnam, Republic of Korea	IRB File No.: CHAMC 2019-02-006-001 Document No.: CHAMC201902006-HE001
82024	SMG-SNU Boramae Medical Center, Republic of Korea	IRB No.: 20190425 / 30 - 2019 - 33 /053
82031	Seoul National University Bund, Republic of Korea	IRB No.: B-1902 /522-007
82032	Asan Medical Center, Republic of Korea	Study No.: 2018-1497 Receipt No.: S2018-2164-0001
82034	Chonnam National University, Gwangju, Republic of Korea	IRB No.: HTMP-2019-028
82035	Samsung Medical Center, Republic of Korea	IRB File No.: SMC 2019-01-164-002 Document No.: SMC201901164002-HE001
48009 48013 48019 48030 48041	Komisja Bioetyczna przy NIO, Poland	EudraCT No.: 2018-000587-28

Site No.	Name/address of ethics committee	Approval number
40002 40004 40007 40012 40013 40014	Comisia de Bioetica, Romania	Reg. no. 4 S / 22 .01 .2019
7020	Arkhangelsk Regional Clinical, Russian Federation	Minutes No. 801 Meeting of the Ethics Committee of the Arkhangelsk Clinical Oncological Dispensary
7025	Leningrad Regional Oncology Dispensary, Leningrad, Russian Federation	Meeting of the Local Ethics Committee at the GBUZ LOKOD No. 04-01 /2019
7027	Ivanovo Regional Oncological Dispensary, Ivanovo, Russian Federation	Minutes No. 05 /19 of the meeting of the Committee on Ethical Matters at the OBUZ
7044	The First Saint-Petersburg Sta, Russian Federation	Minutes No. 218 of the Meeting of the Local Ethics Committee at FGBOU VO
7045	Petrov Research Institute of O, Russian Federation	No. 3 /50 from Minutes No. 8 of the Regular meeting of the Ethics Committee at the FGBU
7047	Rostov Research Institute of O, Russian Federation	MINUTES No. 17 of the meeting of the Ethics Board at FGBU
7048	Orenburg Regional Clinical Oncology Center, Orenburg, Russian Federation	Minutes No.92 of the meeting of the Local Ethics Committee at the GBUZ

Site No.	Name/address of ethics committee	Approval number
34017 34018 34026 34028 34033 34034 34039	CEIm Regional Madrid, Madrid, Spain	EudraCT No.: 2018-000587-28 Ref: 07 /674294 .9 /19
886004 886009	Chi Mei Medical Center, Taiwan	886004: IRB Seial No.: 10804—L03 886009: IRB Seial No.: 10804—005
886012	Kaohsiung Veterans General Hospital, Taiwan	IRB No.: VGHKS19-CT5-14
886044	Chang Gung Medical Foundation, Taiwan	IRB No.: 201802166A0
886048	China Medical University Hospital, Taiwan	CMUH REC No.: CMUH108-REC2-078
44011 44012 44015 44034 44045	East of England – Essex Research, United Kingdom	IRAS project ID: 252786 EudraCT number: 2018-000587-28
1159 1161 1235	Advarra, United States	1159: SSU00082455 1161: SSU00089440 1235: SSU00080807

Supplementary Tables

Supplementary Table 1. Patient demographic and baseline characteristics in the PD-L1 CPS ≥ 1 population

Demographic/characteristics	Tislelizumab plus ICC (<i>n</i> = 233)	Placebo plus ICC (<i>n</i> = 247)
Age		
Median (range)	63.0 (38.0–81.0)	65.0 (40.0–84.0)
≥ 65 years, <i>n</i> (%)	100 (42.9)	125 (50.6)
Sex, <i>n</i> (%)		
Female	35 (15.0)	30 (12.1)
Male	198 (85.0)	217 (87.9)
ECOG performance status, <i>n</i> (%)		
0	78 (33.5)	86 (34.8)
1	155 (66.5)	161 (65.2)
Tobacco consumption, <i>n</i> (%)		
Never	43 (18.5)	58 (23.5)
Former	141 (60.5)	140 (56.7)
Current	38 (16.3)	40 (16.2)
Missing	11 (4.7)	9 (3.6)
Region, <i>n</i> (%)		
Asia	177 (76.0)	190 (76.9)
China including Taiwan	132 (56.7)	149 (60.3)
Japan	26 (11.2)	26 (10.5)
Korea	19 (8.2)	15 (6.1)
Rest of the world	56 (24.0)	57 (23.1)
Europe	54 (23.2)	55 (22.3)
Australia	2 (0.9)	2 (0.8)
US	0	0
Race, <i>n</i> (%)		
Asian	177 (76.0)	190 (76.9)
Chinese	132 (56.7)	149 (60.3)
Japanese	26 (11.2)	26 (10.5)
Korean	19 (8.2)	15 (6.1)
White	54 (23.2)	53 (21.5)
Not reported	1 (0.4)	2 (0.8)
Unknown	1 (0.4)	1 (0.4)
American Indian or Alaska Native	0	1 (0.4)
Time from initial diagnosis to study entry, median (range), months	2.0 (0.1–152.7)	1.9 (0.2–116.8)
Disease status at study entry, <i>n</i> (%)		
Metastatic	202 (86.7)	217 (87.9)
Locally advanced	31 (13.3)	30 (12.2)

Number of metastatic sites at study entry, *n*
(%)

0	31 (13.3)	30 (12.1)
1	102 (43.8)	112 (45.3)
2	62 (26.6)	62 (25.1)
> 2	38 (16.3)	43 (17.4)
Patients with ≥ 1 prior definitive therapy, <i>n</i> (%)	103 (44.2)	102 (41.3)
ICC option		
Platinum with fluoropyrimidine	102 (43.8)	117 (47.4)
Platinum with paclitaxel	131 (56.2)	130 (52.6)

CPS combined positive score, *ECOG* Eastern Cooperative Oncology Group, *ICC* investigator-chosen chemotherapy, *US* United States

Supplementary Table 2. ORR and PFS in the PD-L1 CPS ≥ 1 population at the primary analysis

	Tislelizumab plus ICC (n = 233)	Placebo plus ICC (n = 247)
ORR, n	134	89
% (95% CI) ^a	57.5 (50.9–63.9)	36.0 (30.0–42.4)
Stratified odds ratio for ORR (95% CI) ^b	2.41 (1.67–3.49)	
Two-sided nominal <i>p</i> -value ^b	< 0.0001	
PFS		
Events, n (%)	153 (65.7)	195 (78.9)
Median (95% CI)	7.1 (6.8–8.3)	5.5 (4.5–5.8)
HR (95% CI) ^c	0.58 (0.46–0.72)	

The data cutoff was February 28, 2022. ORR is confirmed and defined as the proportion of patients with a partial response or complete response per Response Evaluation Criteria In Solid Tumors v1.1

^aTwo-sided 95% CI was calculated using Clopper-Pearson method

^bOdds ratio and *p*-value between arms were calculated using the Cochran-Mantel-Haenszel method stratified by pooled geographic region (Asia vs. rest of the world), prior definitive therapy (yes vs. no), and ICC option (platinum with fluoropyrimidine vs. platinum with paclitaxel)

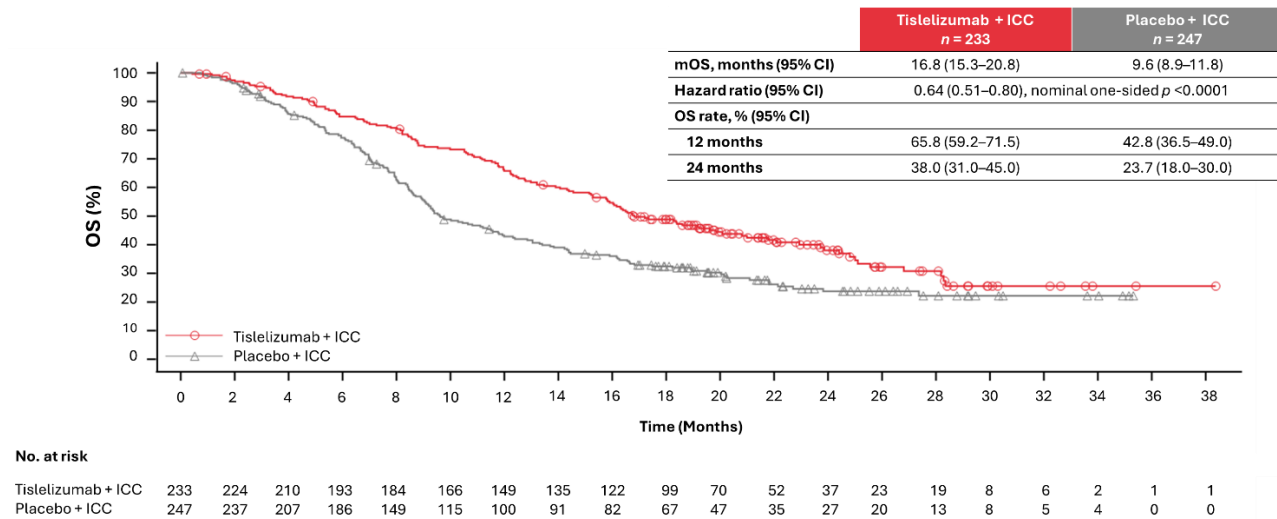
^cHR (tislelizumab plus ICC vs. placebo plus ICC) was based on Cox regression model including treatment as covariate, and pooled geographic region (Asia vs. rest of the world), prior definitive therapy (yes vs. no), and ICC option (platinum with fluoropyrimidine vs. platinum with paclitaxel) as strata

CPS combined positive score, CI confidence interval, IRT interactive response technology, ORR objective response rate, PFS progression-free survival

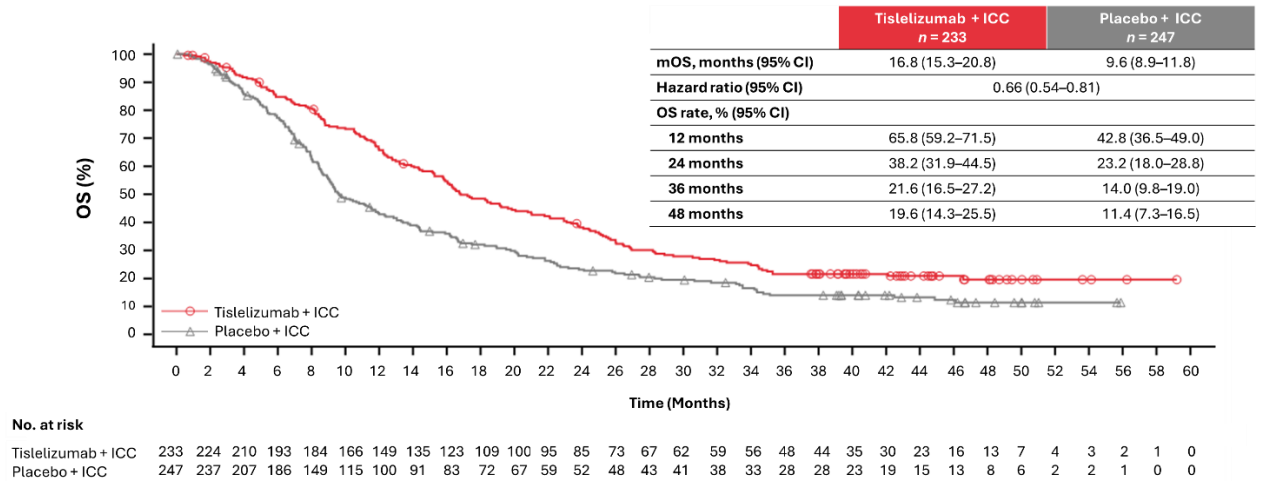
Supplementary Figures

Supplementary Fig. S1. Kaplan–Meier curve of OS by baseline PD-L1 CPS ≥ 1 at the primary analysis (A) and 3-year follow-up (B) (efficacy-evaluable population)

A



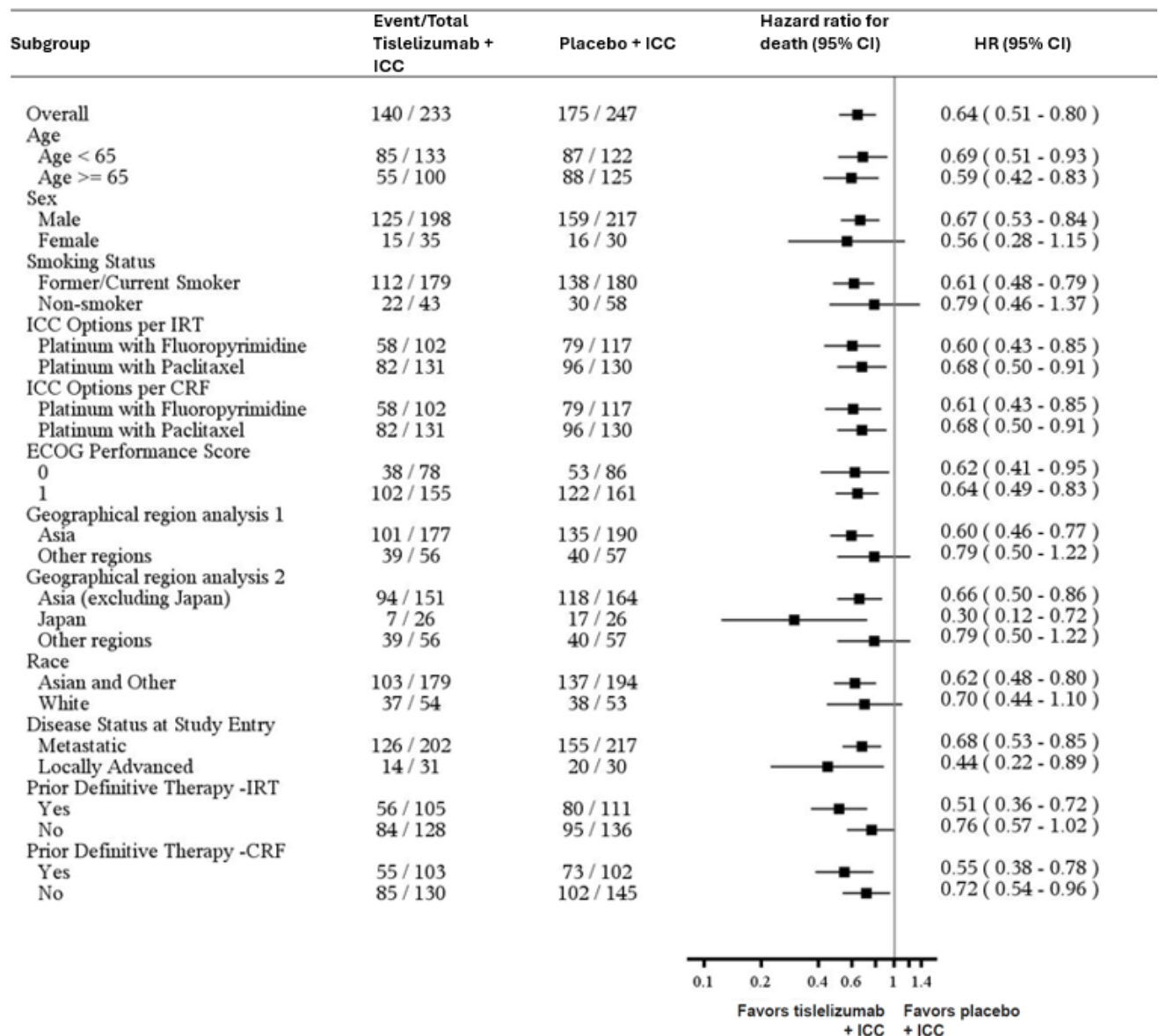
B



Stratified HRs were based on a Cox regression model including treatment as a covariate and pooled geographic region (Asia vs. rest of world) per interactive response technology (IRT), prior definitive therapy (yes vs. no), and ICC option (platinum with fluoropyrimidine vs. platinum with paclitaxel) as strata. The red circles and grey triangles represent censored patients. (A) The data cutoff was February 28, 2022. (B) The data cutoff was November 24, 2023.

CI confidence interval, *CPS combined positive score*, *ICC* investigator-chosen chemotherapy, *mOS* median overall survival, *OS* overall survival, *PD-L1* programmed death-ligand 1

Supplementary Fig. S2. Subgroup analysis of OS by baseline PD-L1 CPS ≥ 1 at the primary analysis (efficacy-evaluable population)



The data cutoff was February 28, 2022. The HR was analyzed using an unstratified Cox regression model including treatment as a covariate. The race subcategory “Other” includes American Indian or Alaska Native, not reported, and unknown. “Unknown” refers to patients without sample collection or not evaluable at baseline

CI confidence interval, CPS combined positive score, CRF case report form, ECOG Eastern Cooperative Oncology Group, HR hazard ratio, ICC investigator-chosen chemotherapy, IRT interactive response technology