HARMONi-2
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Overall Survival Analysis From HARMONi-2: Ivonescimab vs Pembrolizumab as First-line Treatment for PD-L1-Positive NSCLC

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Abbreviations: NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1.

Ivonescimab is an investigational therapy not presently approved by any regulatory authority other than China's National Medical Products Administration (NMPA).
It is currently being investigated in phase 3 clinical studies. Data generated and analyzed by Akeso.

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Disclosure

Caicun Zhou

- Honoraria as a speaker: Eli Lilly, Sanofi, BI, Roche, MSD, Qilu, Hengrui, Innovent Biologics, C-Stone, LUYE Pharma, TopAlliance Biosciences Inc, Amoy Diagnositics, Allist, Dizal
- Advisor: Innovent Biologics, Hengrui, Qilu, TopAlliance Biosciences Inc.

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Background

- Pembrolizumab is a standard of care for patients with PD-L1–positive advanced non–small cell lung cancer (NSCLC)
- **HARMONi-2 trial previously demonstrated a statistically significant progression-free survival (PFS) benefit with ivonescimab** compared with pembrolizumab in this population [1]
- Here, we report **overall survival (OS), the key secondary endpoint of HARMONi-2**, to further characterize the benefit of **ivonescimab as a chemo-free regimen in PD-L1–positive NSCLC**

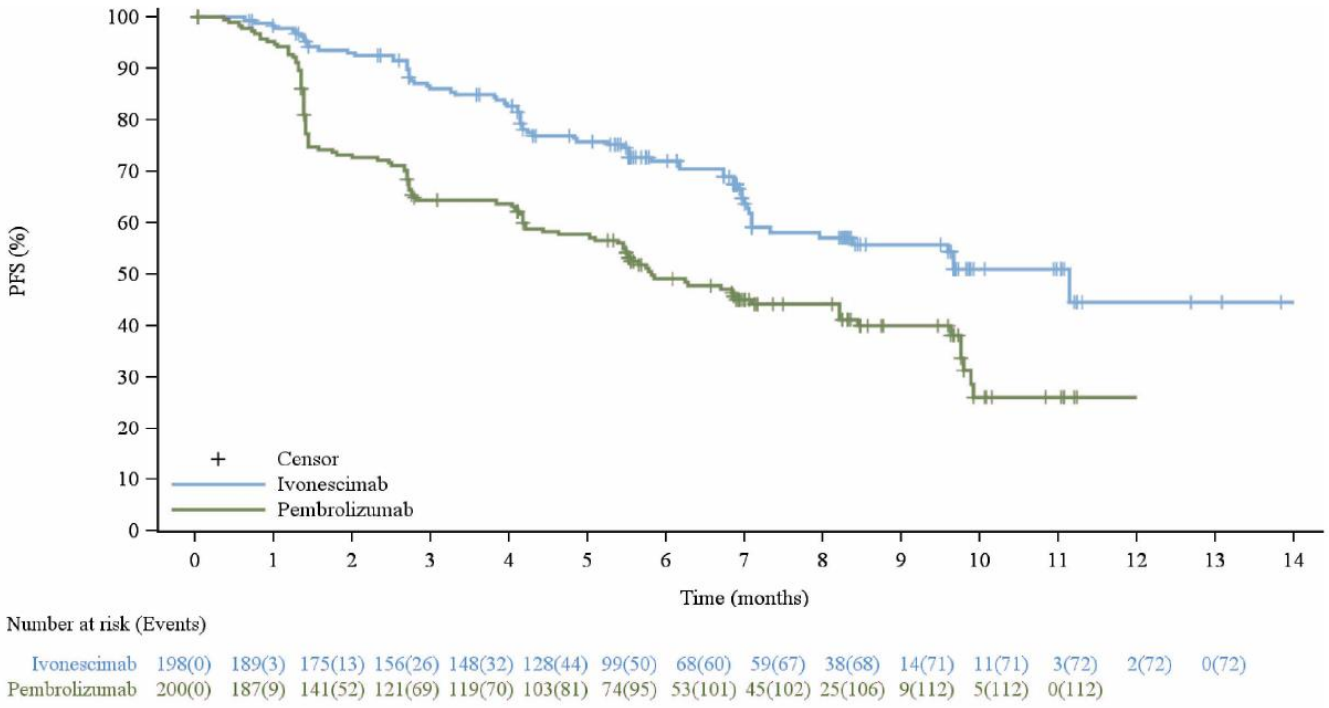
1. Xiong A, et al. *Lancet*. 2025;405(10481):839-849.
Abbreviations: PD-L1=programmed death-ligand 1

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Background (PFS interim analysis results)

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➢ **Ivonescimab demonstrated a statistically significant improvement in PFS vs pembrolizumab**



	Ivonescimab (n = 198)	Pembrolizumab (n = 200)
ORR, % (95% CI)	**50.0** (42.8, 57.2)	**38.5** (31.7, 45.6)
DCR, % (95% CI)	**89.9** (84.8, 93.7)	**70.5** (63.7, 76.7)
mPFS, mo (95% CI)	**11.1** (7.3, NE)	**5.8** (5.0, 8.2)
Stratified HR (95% CI)	**0.51** (0.38, 0.69)	
***P*-value**	**<0.0001**	

Median follow-up: 8.7 months
Data cutoff: January 29, 2024

Xiong A, et al. *Lancet*. 2025;405(10481):839-849.
Abbreviations: CI=confidence interval; DCR=disease control rate; HR=hazard ratio; IRRC=independent radiology review committee; mPFS=median progression-free survival; NE=not estimable; PFS=progression-free survival; ORR=overall response rate.

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Study Design

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HARMONi-2: A randomized, double-blind, phase 3 trial

Patient Population
Locally advanced or metastatic (IIIB-IV) NSCLC

Key Eligibility Criteria

- PD-L1 TPS ≥1%
- No prior systemic therapy
- No *EGFR* mutations or *ALK* alterations
- ECOG PS 0 or 1

R 1:1

N=398

Ivonescimab
20 mg/kg Q3W (n=198)

Pembrolizumab
200 mg Q3W (n=200)

Treatment until no clinical benefit, unacceptable toxicity or up to 24 months

Stratification Factors

- Clinical stage (IIIB/C vs IV)
- Histology (SQ vs non-SQ)
- PD-L1 TPS (≥50% vs 1-49%)

Endpoints

- **Primary endpoint**: PFS by blind IRRC per RECIST v1.1
- **Key Secondary endpoint : OS**
- **Secondary endpoints**: PFS assessed by INVs, ORR, DoR, TTR and safety

Abbreviations: ALK=anaplastic lymphoma kinase; DoR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance score; EGFR=epidermal growth factor receptor; INV=investigator; IRRC=independent radiology review committee; NSCLC=non-small cell lung cancer; non-SQ=non-squamous; ORR=overall response rate; OS=overall survival; PD-L1=programmed death-ligand 1; PFS=progression-free survival; Q3W=every 3 weeks; SQ=squamous; TPS=tumor proportion score; TTR=time to response.

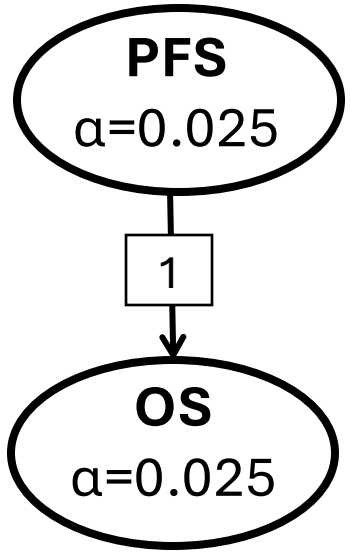
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Statistical Considerations

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Hierarchical testing:

PFS tested first, followed by OS, to control the overall type I error at a one-sided α=0.025



- PFS was statistically significant at interim analysis (mPFS 11.1 vs 5.8 months; stratified HR 0.51 [95% CI 0.38–0.69]; one-sided *p*<0.0001), enabling formal OS testing
- The prespecified interim OS analysis
  - ✓ The first IA was conducted at 157 events (HR 0.777, nominal α=0.0001*)
  - ✓ The second IA was conducted at **234 events**, with **one-sided alpha of 0.0141** based on the pre-specified O'Brien-Flemming spending function

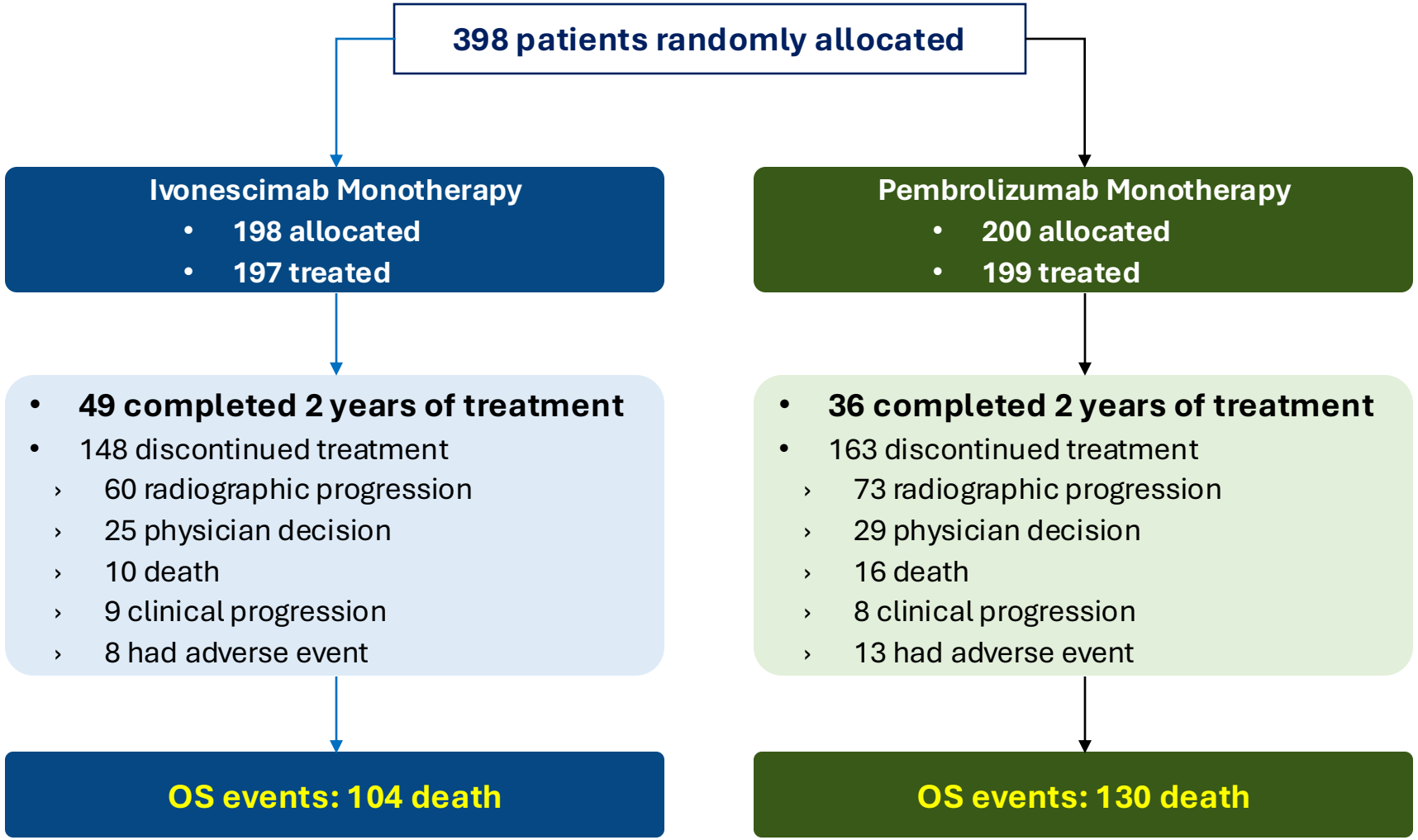
** Minimal alpha allocated to the first IA of OS to provide preliminary OS information to support regulatory approval*

Abbreviations: CI=confidence interval; HR=hazard ratio; IA=interim analysis; mPFS=median progression-free survival; OS=overall survival; PFS=progression-free survival.

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Disposition of Study Treatment

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Abbreviations: OS=overall survival.

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Baseline Characteristics

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Characteristics, n (%)		Ivonescimab (n = 198 [a])	Pembrolizumab (n = 200 [a])
Age (years)	<65	97 (49.0)	85 (42.5)
	≥65	101 (51.0)	115 (57.5)
Sex	Male	164 (82.8)	169 (84.5)
	Female	34 (17.2)	31 (15.5)
ECOG PS	0	25 (12.6)	26 (13.0)
	1	173 (87.4)	174 (87.0)
Smoker	Never	39 (19.7)	38 (19.0)
	Current	39 (19.7)	42 (21.0)
	Former	120 (60.6)	120 (60.0)
Pathology	Non-Squamous	108 (54.5)	109 (54.5)
	Squamous	90 (45.5)	91 (45.5)
	Tumor centrally located [b]	**65 (72.2)**	**57 (62.6)**
	Tumor with cavitation/necrosis [b]	**9 (10.0)**	**7 (7.7)**
	Tumor encasing large blood vessel [b]	**6 (6.7)**	**1 (1.1)**
Clinical stage	IIIB/C	15 (7.6)	16 (8.0)
	IV	183 (92.4)	184 (92.0)
PD-L1 TPS	1-49%	115 (58.1)	115 (57.5)
	≥50%	83 (41.9)	85 (42.5)
Distant metastases	Liver metastases	25 (12.6)	28 (14.0)
	Brain metastases	33 (16.7)	39 (19.5)
	≥ 3 sites	49 (24.7)	51 (25.5)

[a] Patients who were randomized. [b] In 181 patients with squamous cell carcinoma.

Abbreviations: ECOG PS=Eastern Cooperative Oncology Group performance score; PD-L1=programmed death-ligand 1; TPS=tumor proportion score.

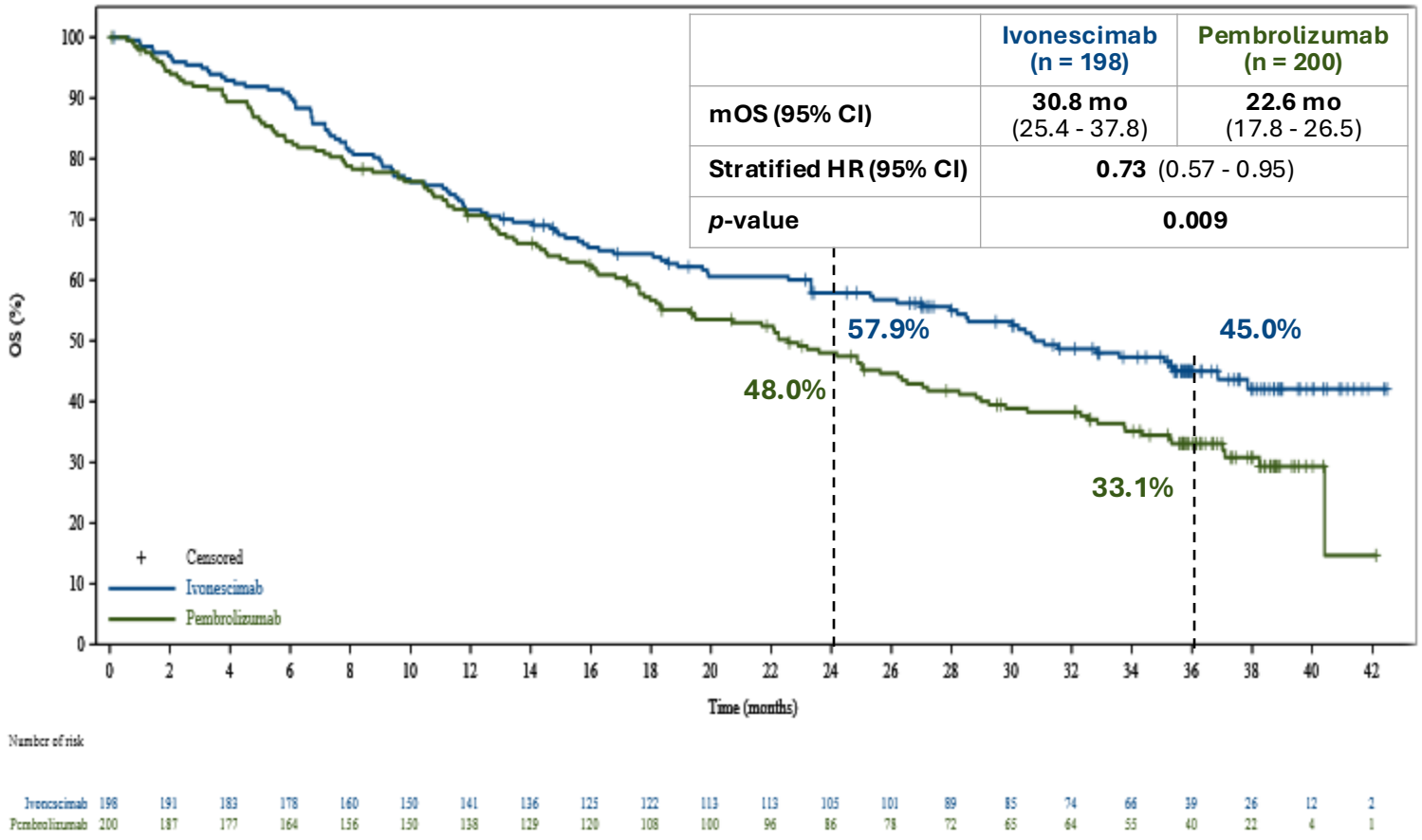
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Overall Survival

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➢ Ivonescimab demonstrated a statistically significant improvement in OS with a median follow-up of 36.0 mo

Data cutoff: August 20, 2026



	Ivonescimab (n = 198)	Pembrolizumab (n = 200)
mOS (95% CI)	**30.8 mo** (25.4 - 37.8)	**22.6 mo** (17.8 - 26.5)
Stratified HR (95% CI)	**0.73** (0.57 - 0.95)	
p-value	**0.009**	

OS rate (%)	HARMONi-2		KN-042 China study [1]
	Ivonescimab (n = 198)	Pembrolizumab (n = 200)	Pembrolizumab (n = 128)
24-mo	57.9%	48.0%	43.8%
36-mo	45.0%	33.1%	28.1%

1. Wu Y, et al. *Int J Cancer*. 2026;158:2429–2439 (KEYNOTE-042 China study, pembrolizumab in PD-L1 TPS ≥1% NSCLC).
Abbreviations: CI=confidence interval; HR=hazard ratio; mOS=median OS; OS=overall survival.

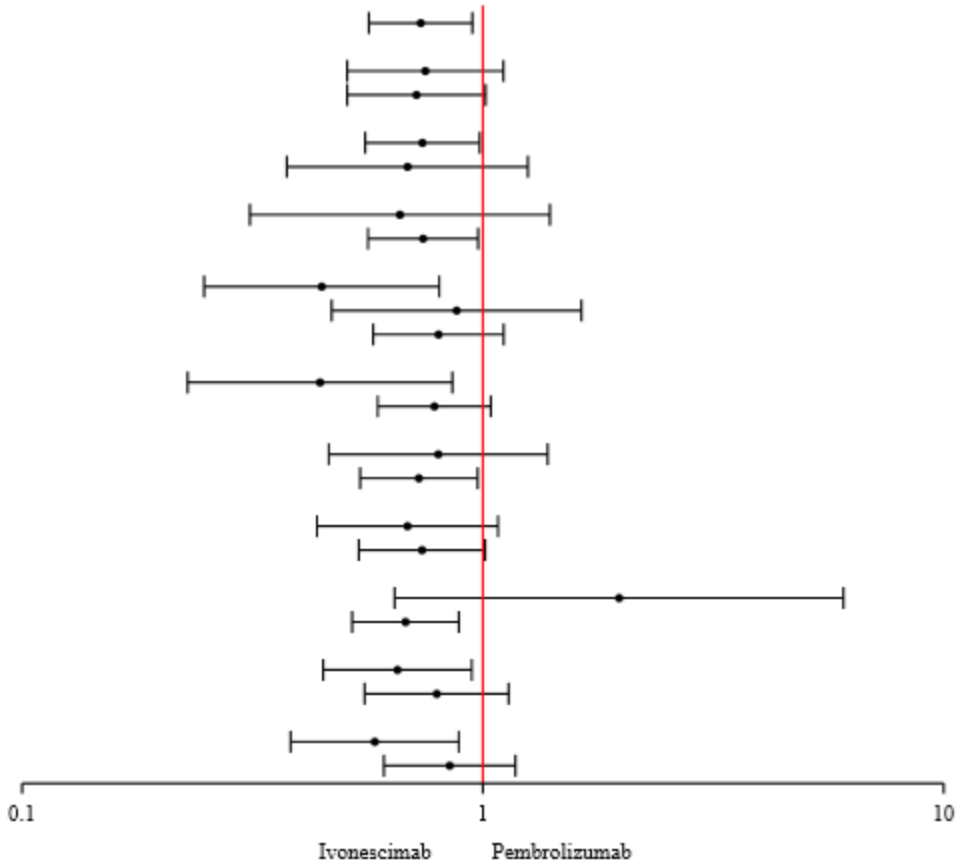
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Subgroup Analysis of Overall Survival

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➢ **OS benefit with ivonescimab was observed across prespecified subgroups**

	Ivonescimab (n/N)	Pembrolizumab (n/N)	HR (95% CI)
Overall	104/198	130/200	0.73 (0.57, 0.95)
Age, years			
< 65	49/97	52/85	0.75 (0.51, 1.11)
≥ 65	55/101	78/115	0.72 (0.51, 1.01)
Sex			
Male	85/164	106/169	0.74 (0.56, 0.98)
Female	19/34	24/31	0.69 (0.38, 1.25)
Baseline ECOG			
0	12/25	16/26	0.66 (0.31, 1.40)
1	92/173	114/174	0.74 (0.56, 0.98)
Smoking Status			
Never	18/39	30/38	0.45 (0.25, 0.80)
Current smoker	18/39	22/42	0.88 (0.47, 1.64)
Former smoker	68/120	78/120	0.80 (0.58, 1.11)
Liver metastases			
Yes	15/25	25/28	0.44 (0.23, 0.86)
No	89/173	105/172	0.78 (0.59, 1.04)
Brain metastases			
Yes	22/33	31/39	0.80 (0.46, 1.38)
No	82/165	99/161	0.73 (0.54, 0.97)
≥ 3 metastases sites			
Yes	34/49	43/51	0.69 (0.44, 1.08)
No	70/149	87/149	0.74 (0.54, 1.01)
Disease stage			
IIIB/IIIC	8/15	5/16	1.98 (0.64, 6.06)
IV	96/183	125/184	0.68 (0.52, 0.89)
Histological type			
Squamous	50/90	64/91	0.65 (0.45, 0.95)
Non-squamous	54/108	66/109	0.79 (0.55, 1.14)
PD-L1 tumor proportion score			
≥ 50%	37/83	54/85	0.58 (0.38, 0.89)
1-49%	67/115	76/115	0.85 (0.61, 1.18)



Abbreviations: CI=confidence interval; ECOG=Eastern Cooperative Oncology Group; OS=overall survival; PD-L1=programmed death-ligand 1.

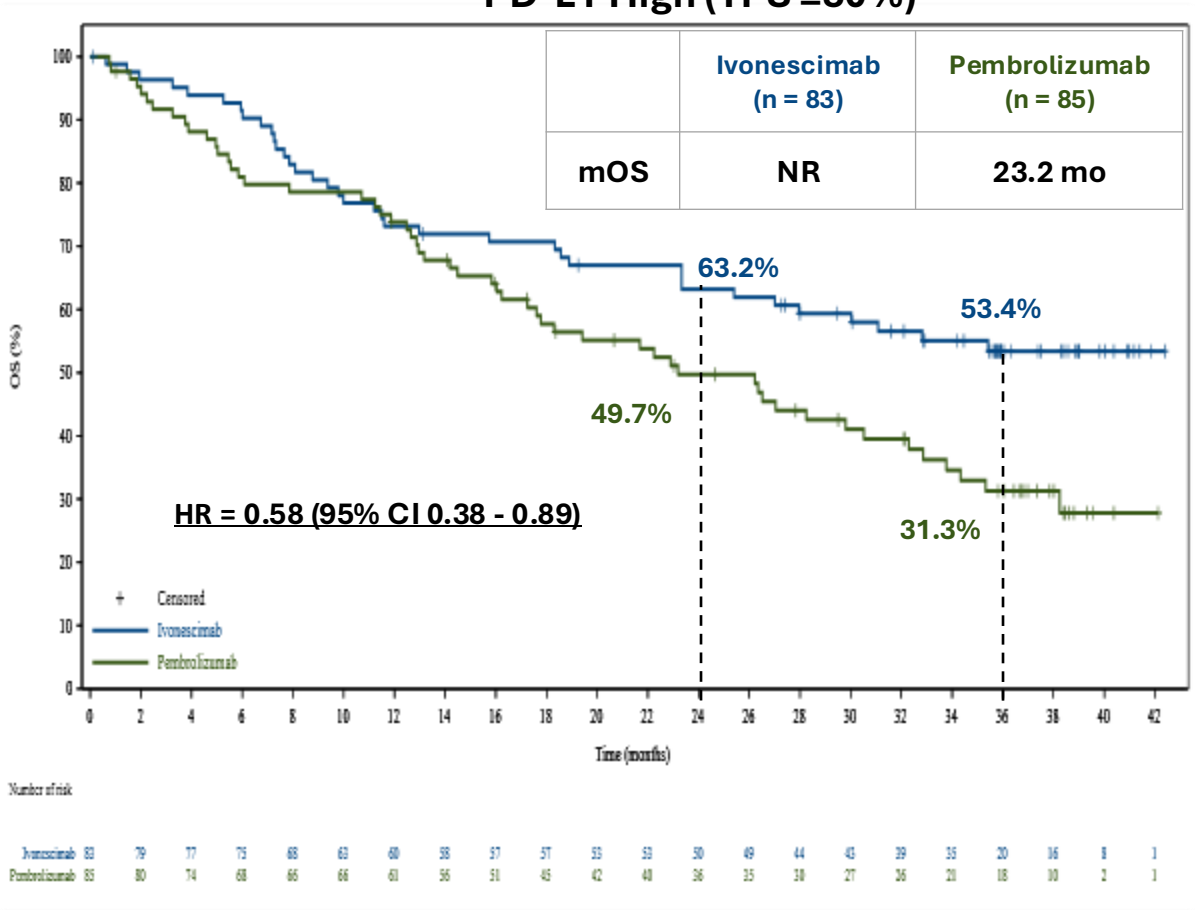
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Overall Survival by PD-L1 Expression Level

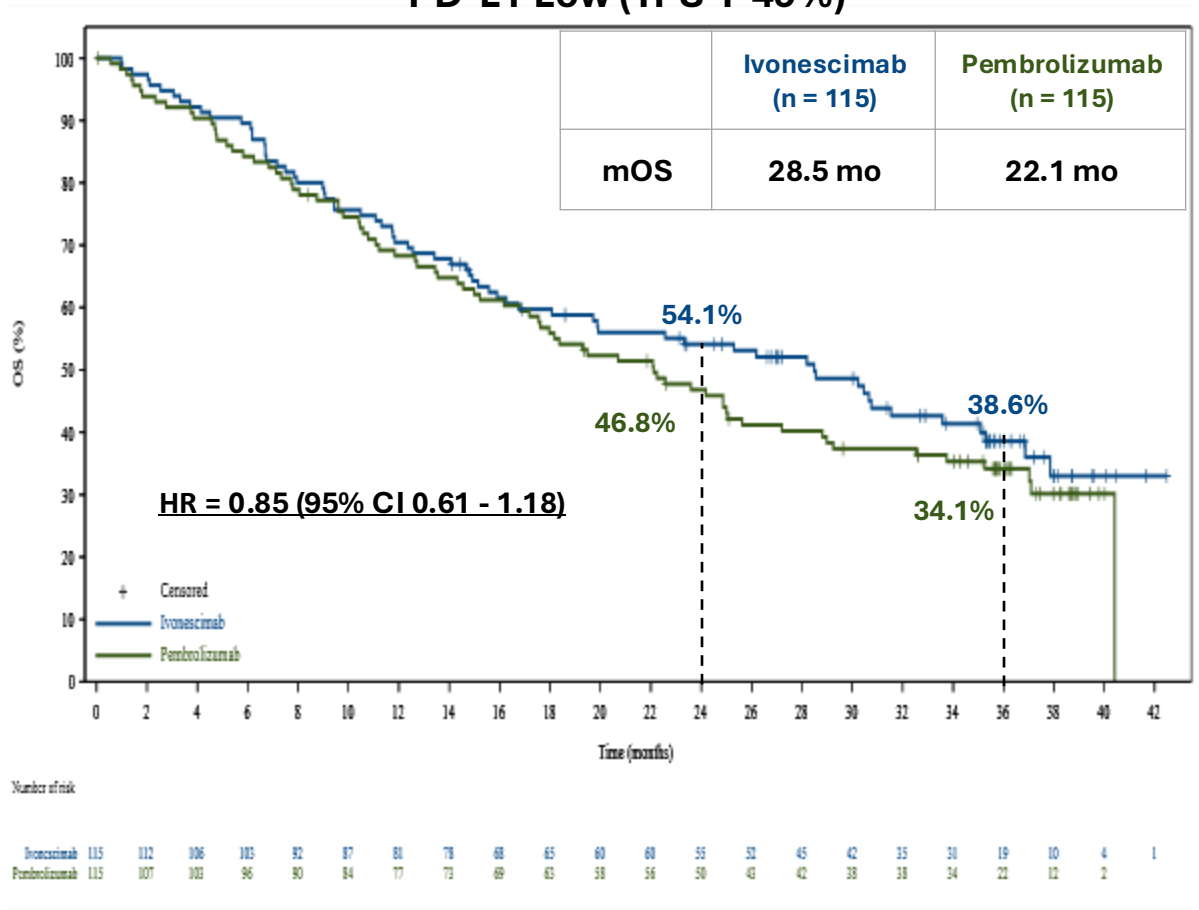
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➢ **OS benefit with ivonescimab was consistent in both PD-L1 High and PD-L1 Low expressors**

PD-L1 High (TPS ≥50%)



PD-L1 Low (TPS 1-49%)



The subgroup analysis was descriptive and not formally powered.

Abbreviations: CI=confidence interval; HR=hazard ratio; mOS=median overall survival; NR=not reached; PD-L1=programmed death-ligand 1; TPS=tumor proportion score.

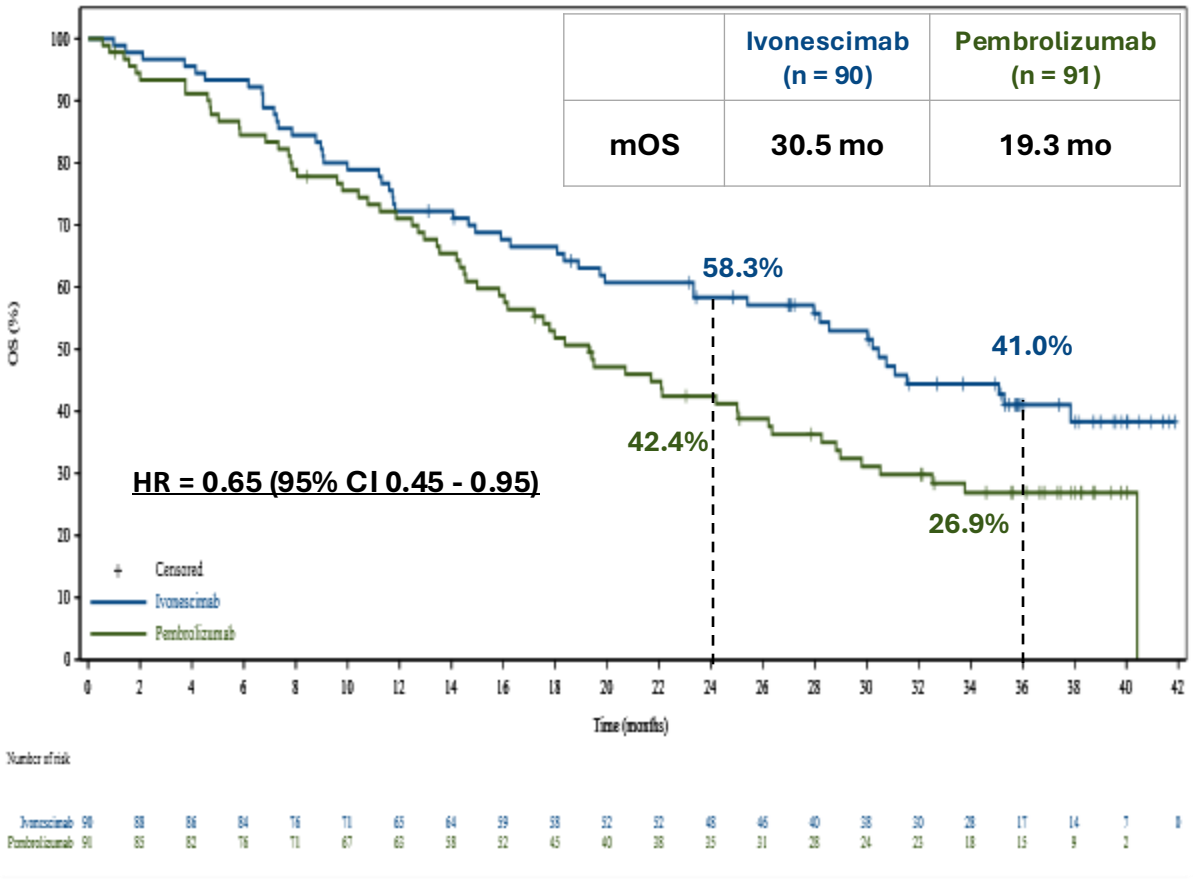
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Overall Survival by Histology

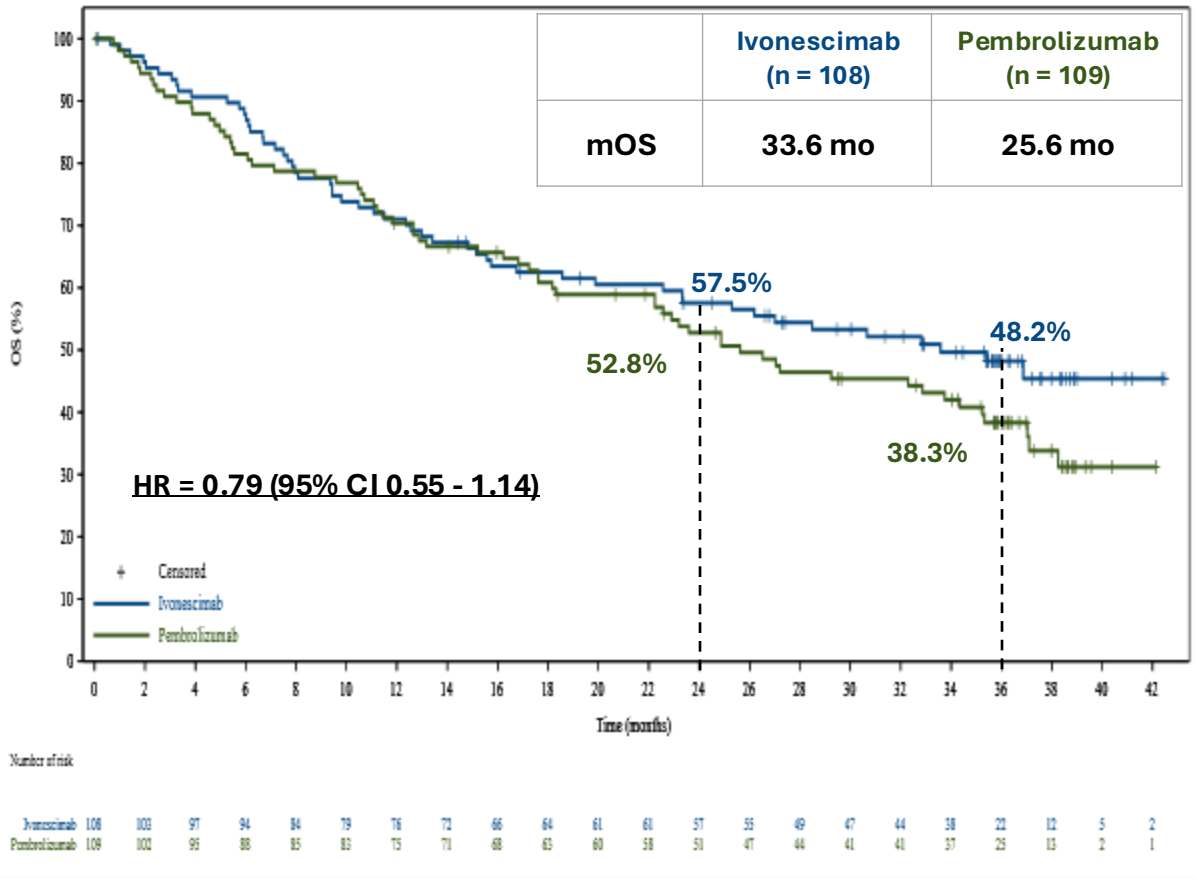
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➢ **OS benefit with ivonescimab was consistent in both squamous and non-squamous histology**

Squamous



Non-Squamous



The subgroup analysis was descriptive and not formally powered.

Abbreviations: CI=confidence interval; HR=hazard ratio; mOS=median overall survival.

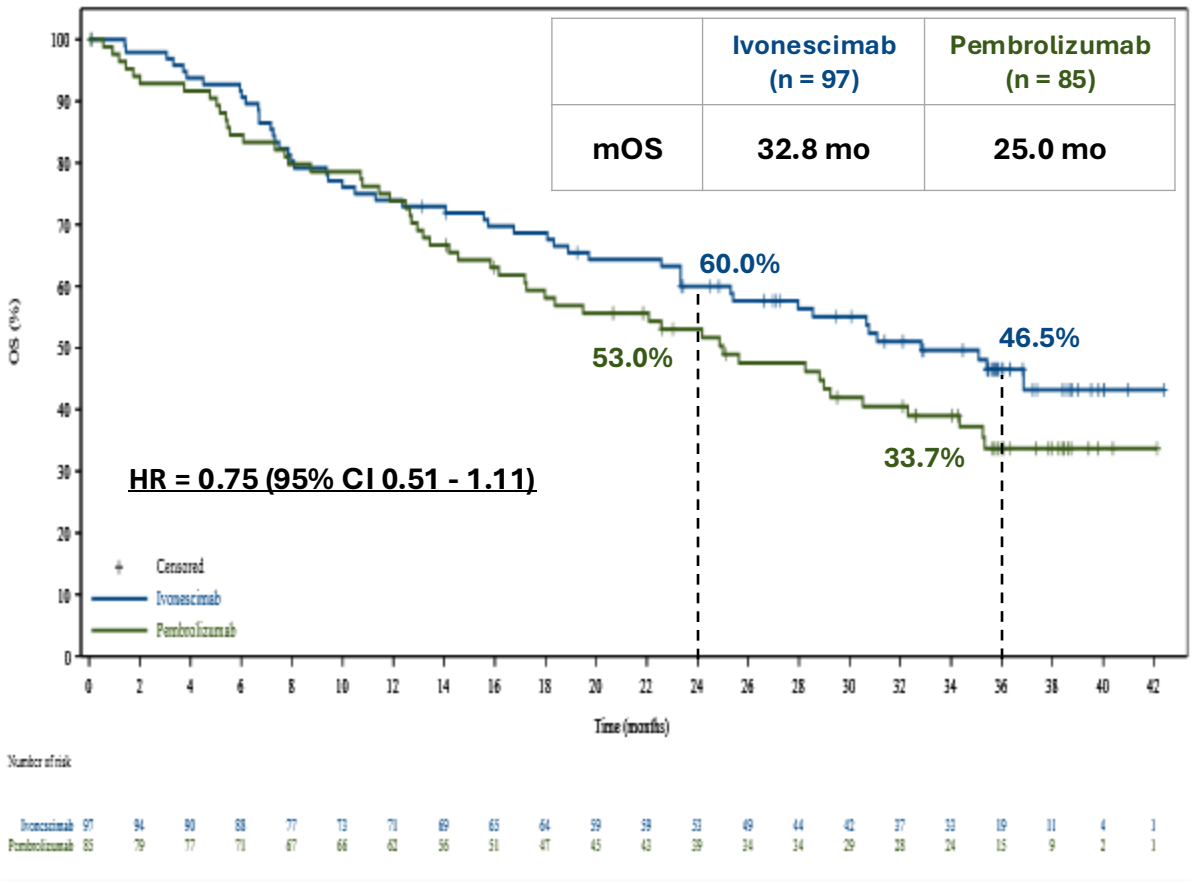
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Overall Survival by Age Subgroups

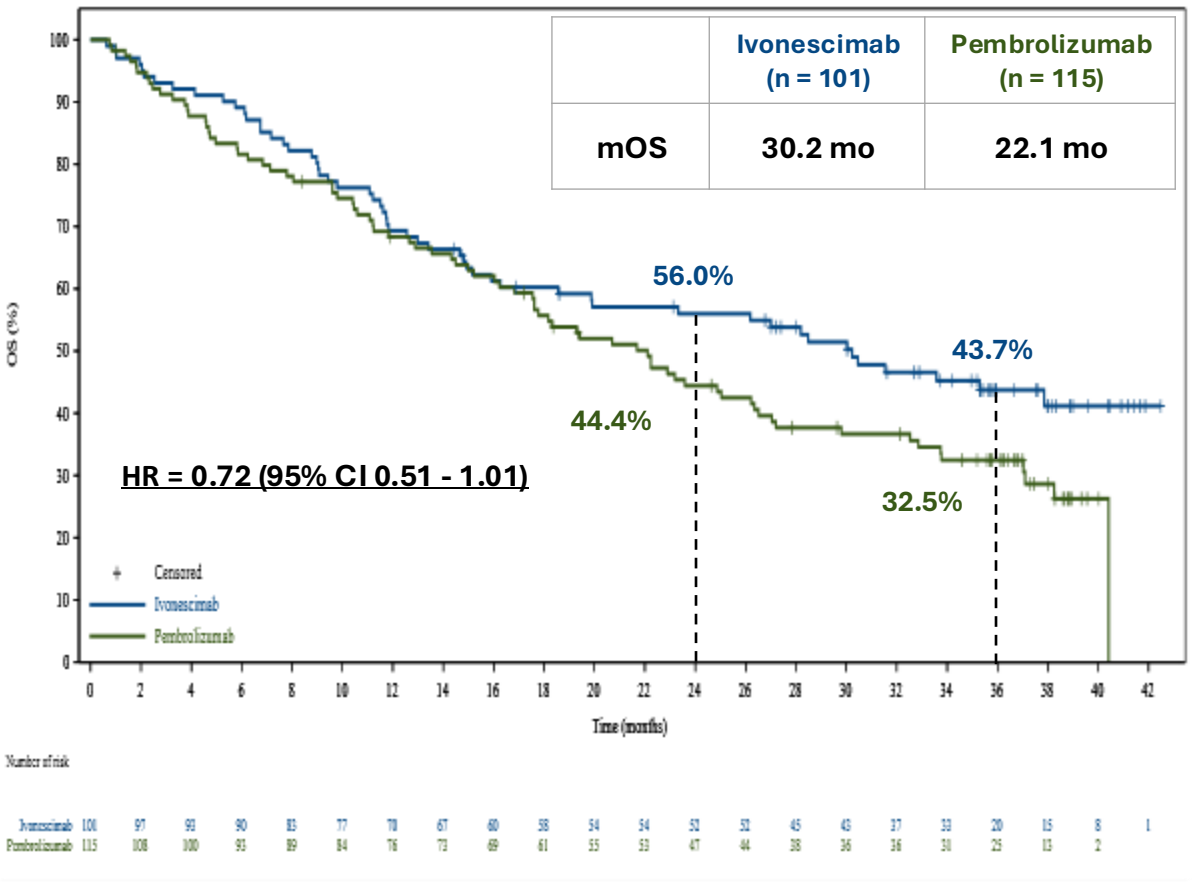
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➢ **OS benefit with ivonescimab was consistent in both age subgroups (< 65 years vs ≥ 65 years)**

< 65 years



≥ 65 years



The subgroup analysis was descriptive and not formally powered.

Abbreviations: CI=confidence interval; HR=hazard ratio; mOS=median overall survival.

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Subsequent Anti-Tumor Therapy

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➢ **Higher subsequent therapy rate with pembrolizumab**

	Ivonescimab (n = 198)	Pembrolizumab (n = 200)
Systemic therapy, n (%)	**72 (36.4)**	**92 (46.0)**
Chemotherapy	**55 (27.8)**	**76 (38.0)**
Immunotherapy	**38 (19.2)**	**55 (27.5)**
Targeted therapy	**31 (15.7)**	**35 (17.5)**
Antibody-drug conjugate	**5 (2.5)**	**2 (1.0)**
Other	**1 (0.5)**	**0**
Surgery, n (%)	**0**	**1 (0.5)**
Radiotherapy, n (%)	**4 (2.0)**	**1 (0.5)**

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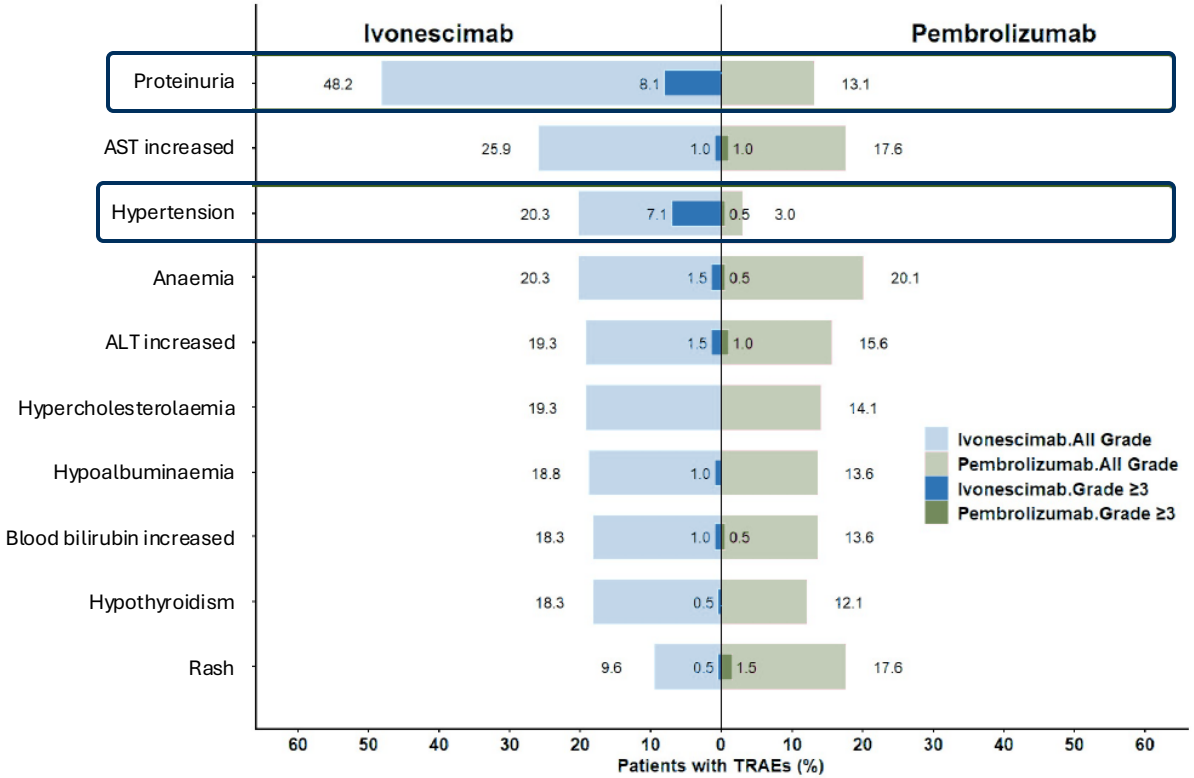
Safety Summary

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TRAE summary, n (%)	Ivonescimab (n = 197 [a])	Pembrolizumab (n = 199 [a])
TRAEs (all grade)	184 (93.4)	169 (84.9)
Grade ≥ 3 TRAEs	82 (41.6)	43 (21.6)
Serious TRAEs	59 (29.9)	43 (21.6)
Leading to discontinuation	8 (4.1)	10 (5.0)
Leading to death	1 (0.5)	3 (1.5)

Possible VEGF-related AEs [b], n (%)	Ivonescimab (n = 197 [a])		Pembrolizumab (n = 199 [a])	
	All grade	Grade ≥ 3	All grade	Grade ≥ 3
Proteinuria	95 (48.2)	16 (8.1)	26 (13.1)	0
Hypertension	40 (20.3)	14 (7.1)	6 (3.0)	1 (0.5)
Haematuria	18 (9.1)	0	17 (8.5)	0
Haemoptysis	13 (6.6)	0	7 (3.5)	1 (0.5)
Epistaxis	3 (1.5)	0	0	0
Gingival bleeding	2 (1.0)	0	0	0
Cerebral infarction	2 (1.0)	2 (1.0)	1 (0.5)	0

Most common TRAEs (incidence ≥15%)



The median duration of exposure:

14.0 cycles (ivonescimab) vs **10.0 cycles (pembrolizumab)**

- ✓ **No new safety signals**
- ✓ **No apparent increase in bleeding risk**

[a] Patients who received ≥1 dose of study treatment. [b] Possible VEGF-related AEs occurring in ≥1% of patients in either arm are presented.

Abbreviations: AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; TRAEs=treatment-related adverse events; VEGF=vascular endothelial growth factor

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Conclusions

- Ivonescimab significantly improved clinical outcomes in PD-L1-positive advanced NSCLC
  - **mOS:** **30.8 mo vs 22.6 mo (HR 0.73; *p*=0.009)**
  - **3-years OS rate:** **45.0% vs 33.1%**
  - **mPFS:** **11.1 mo vs 5.8 mo (HR 0.51; *p*<0.0001)**
  - **ORR:** **50.0% vs 38.5%**
- With longer follow-up, ivonescimab maintained a favorable and manageable safety profile, with no new safety signals
- **The findings support ivonescimab as a standard-of-care in first-line PD-L1+ NSCLC in China**
- A global phase 3 trial of ivonescimab versus pembrolizumab in PD-L1–high metastatic NSCLC (HARMONi-7) is ongoing, to provide a potential chemo-free regimen for patients worldwide

Abbreviations: HR=hazard ratio; mOS=median overall survival; mPFS=median progression-free survival; NSCLC=non-small cell lung cancer; ORR=overall response rate; PD-L1=programmed death-ligand 1.

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Acknowledgments

- We are deeply grateful to the patients and their families who participated in the HARMONi-2 trial for their invaluable contributions to this study
- We sincerely thank the investigators, study coordinators, and research staff at all participating sites for their unwavering dedication to patient care and meticulous data collection
- We also appreciate the independent data monitoring committee (IDMC) for their vigilant oversight of participant safety throughout the trial
- Finally, we acknowledge Akeso Biopharma for sponsoring this study

Thank You!

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