The Potential Role of PD-1 x VEGF Bispecific Antibodies in the Management of Non-Small Cell Lung Cancer: Translating Emerging Evidence into Community Oncology Practice

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Learning Objectives

- Appraise the scientific rationale for the development of bispecific antibodies directed at PD-1 and VEGF, and understand the mechanism of action and the similarities and differences among the various investigational agents in this class.
- Evaluate the documented efficacy of PD-1 x VEGF bispecific antibodies in combination with chemotherapy for patients with progressive EGFR-mutated metastatic non-small cell lung cancer (NSCLC), and consider the potential role of these agents.
- Review published research findings with PD-1 x VEGF bispecific antibodies alone and in combination with chemotherapy as first-line therapy for patients with metastatic NSCLC without actionable genomic alterations, and reflect on ongoing trials attempting to further validate the effectiveness of these strategies.
- Recognize the spectrum, frequency and severity of toxicities associated with PD-1 x VEGF bispecific antibodies, and appreciate management strategies to facilitate the safe and effective administration of these agents.

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Dr Ready — Disclosures
Faculty

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Agenda

Module 1: Ivonescimab for Previously Untreated Metastatic Non-Small Cell Lung Cancer (mNSCLC)

Module 2: Ivonescimab for Relapsed/Refractory EGFR-Mutated mNSCLC

Module 3: Other Novel PD-1/PD-L1 x VEGF Bispecific Antibodies Under Investigation

Agenda

Module 1: Ivonescimab for Previously Untreated Metastatic Non-Small Cell Lung Cancer (mNSCLC)

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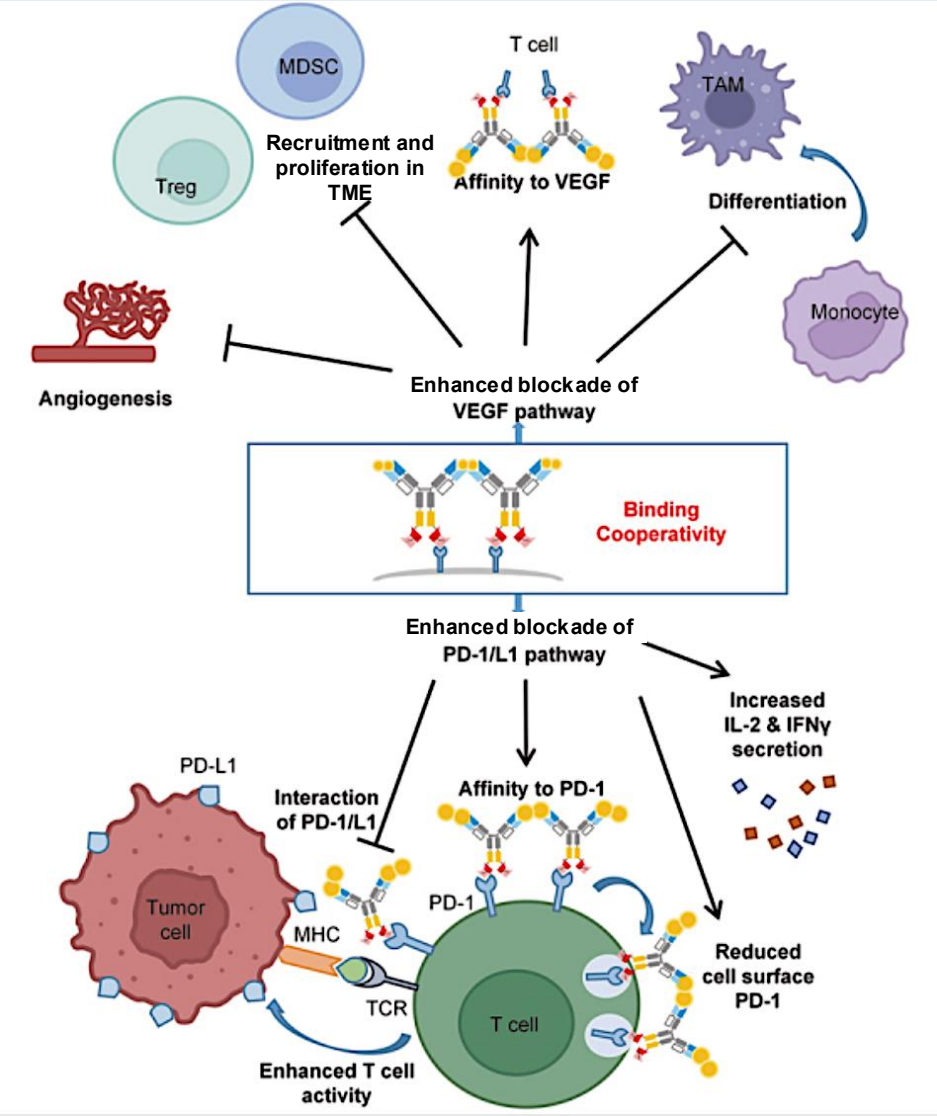
Module 3: Other Novel PD-1/PD-L1 x VEGF Bispecific Antibodies Under Investigation

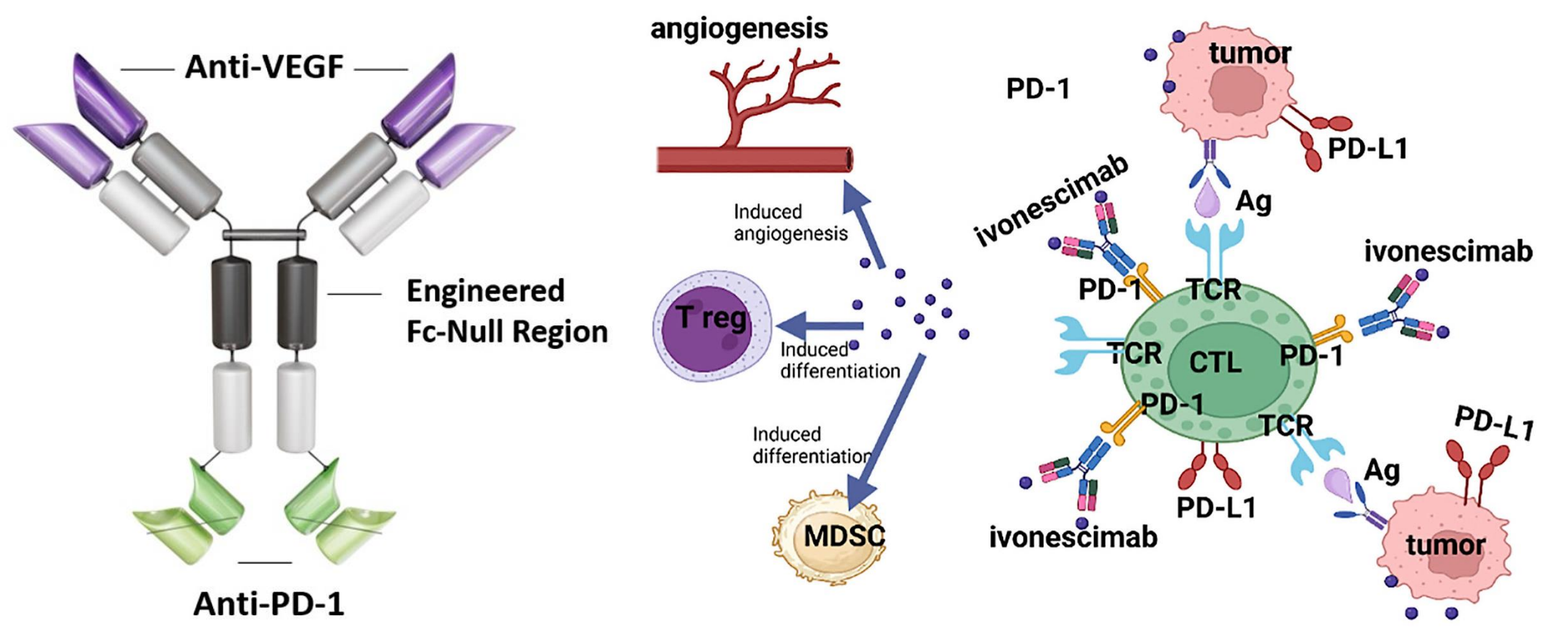
Rationale for Dual Targeting of PD-1/PD-L1 and VEGF



- By blocking both PD-1/PD-L1 and VEGF in the tumor microenvironment (TME), bispecific antibodies have the potential to drive synergistic antitumor activity through higher binding affinity and increased activity of T cells
- In vitro studies have demonstrated that the presence of VEGF increased PD-1 binding strength more than tenfold

Zhong T et al. *iScience* 2024;28(3):111722.
Zhang J et al. ASCO 2025;Abstract TPS8664.

Ivonescimab Mechanism of Action



Zhang L et al. ASCO 2024;Abstract 8508.

Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small-cell lung cancer (HARMONi-6): a randomised, double-blind, phase 3 trial

Zhiwei Chen, Fang Yang*, Zhou Jiang*, Longhua Sun*, Lin Wu*, Zhengxiang Han, Yun Fan, Yanqiu Zhao, Xingya Li, Haipeng Xu, Xiangjiao Meng, Ying Liu, Zhiye Zhang, Hui Luo, Xuelei Ma, Xuezhen Ma, Qin Shi, Zhongmin Zhang, Runxiang Yang, Pingli Wang, Pinhua Pan, Xiaohong Ai, Jie Li[1], Xingxiang Pu, Zhiwu Wang, Jian Fang, Ming He, Yong He, Shuliang Guo, Juan Li, Hongbiao Wang, Jungiang Zhang, Qian Chu, Xuewen Liu, Shenpeng Ying, Hongcheng Wu, Hongmei Sun, Yinghua Ji, Ming Zhou, Jianya Zhou, Hongzhong Yang, Yingying Du, Hui Yang, Jian Shi, Hualin Baiyong Li, Michelle Xia, Shun Lu*

Lancet 2025;406:2078-88.

2026 ASCO ANNUAL MEETING

Abstract LBA4

Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy in previously untreated advanced squamous non-small cell lung cancer: Overall survival results of the Phase 3 HARMONi-6 trial

Presented by: Shun Lu, MD, PhD

Chen Zhiwei[1], Fang Yang[2], Yongzhong Luo[3], Longhua Sun[4], Lin Wu[3], Zhengxiang Han[5], Yun Fan[6], Yanqiu Zhao[7], XingYa Li[8], Haipeng Xu[9], Xiangjiao Meng[10], Ying Liu[11], Zhiye Zhang[12], Hui Luo[13], Qin Shi[14], Xuelei Ma[15], Xuezhen Ma[16], Zhongmin Zhang[17], Michelle Y. Xia[18], Shun Lu[1]

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2026 ASCO® ANNUAL MEETING

What's Old is New Again

VEGF inhibition's role with immunotherapy for squamous NSCLC

Julie R Brahmer, MD, MSc, FASCO, FAIO

The Marilyn Meyerhoff Professor of Thoracic Oncology

Johns Hopkins Kimmel Cancer Center, Baltimore, Maryland

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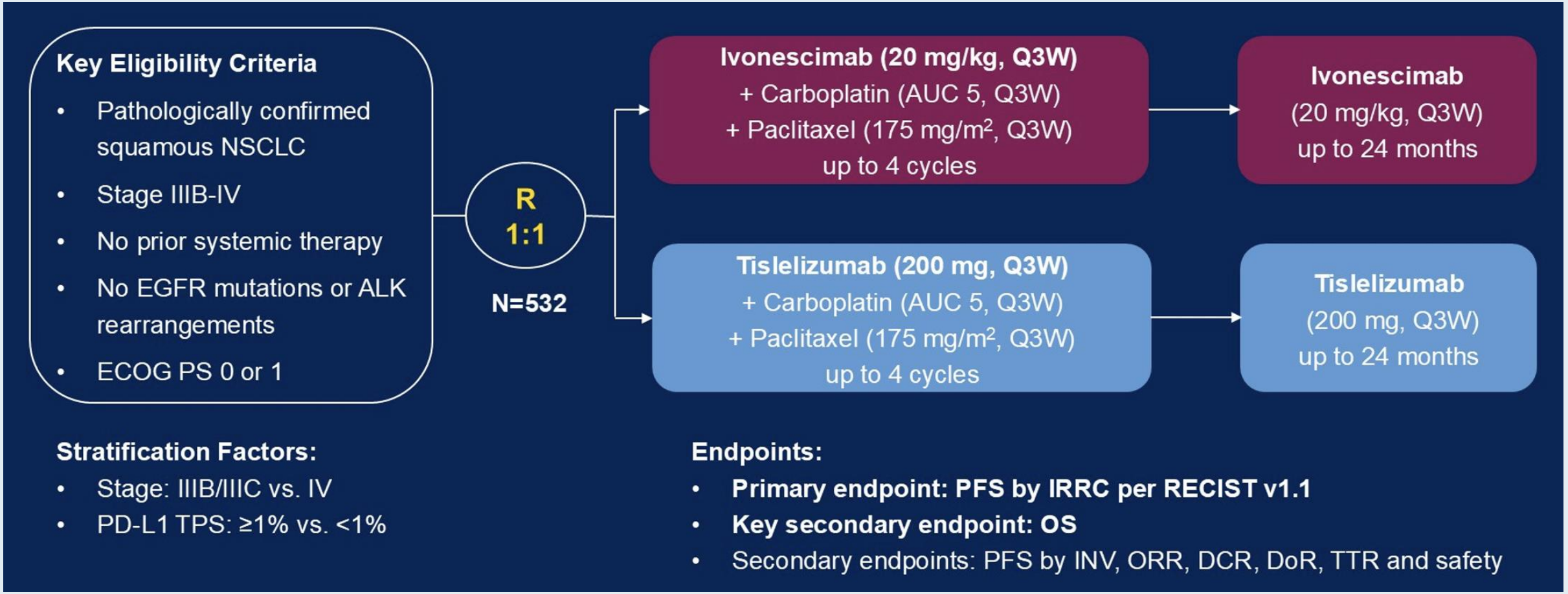
Will PD-1/VEGF Bispecific Antibodies Replace Immune Checkpoint Inhibitors in NSCLC?

Immune checkpoint inhibitor	Approval date
Nivolumab	2015
Pembrolizumab	2015
Atezolizumab	2016
Durvalumab	2018
Ipilimumab	2020
Cemiplimab	2021
Tremelimumab	2022

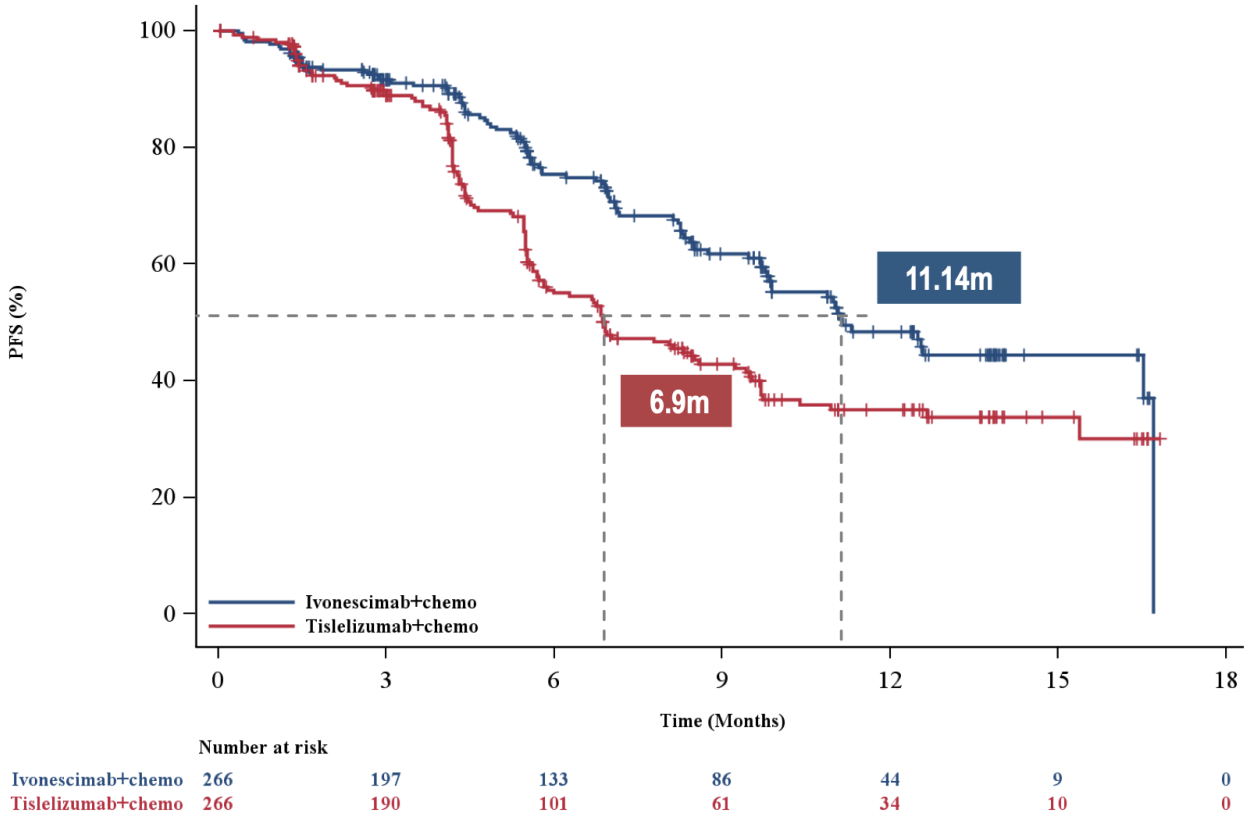
HARMONi-6 Chinese Phase III Study Design



Zhiwei C et al. ASCO 2026;Abstract LBA4.

HARMONi-6: Progression-Free Survival (PFS) Outcomes

Ivonescimab + chemo demonstrated a statistically significant improvement in PFS vs. tislelizumab + chemo with HR = 0.60, representing a 4.2-month improvement in mPFS.



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mPFS, months (95% CI)	**11.14** (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95% CI)	**0.60** (0.46, 0.78)	
p-value	**<0.0001**	

Median Follow-up: 10.28 months

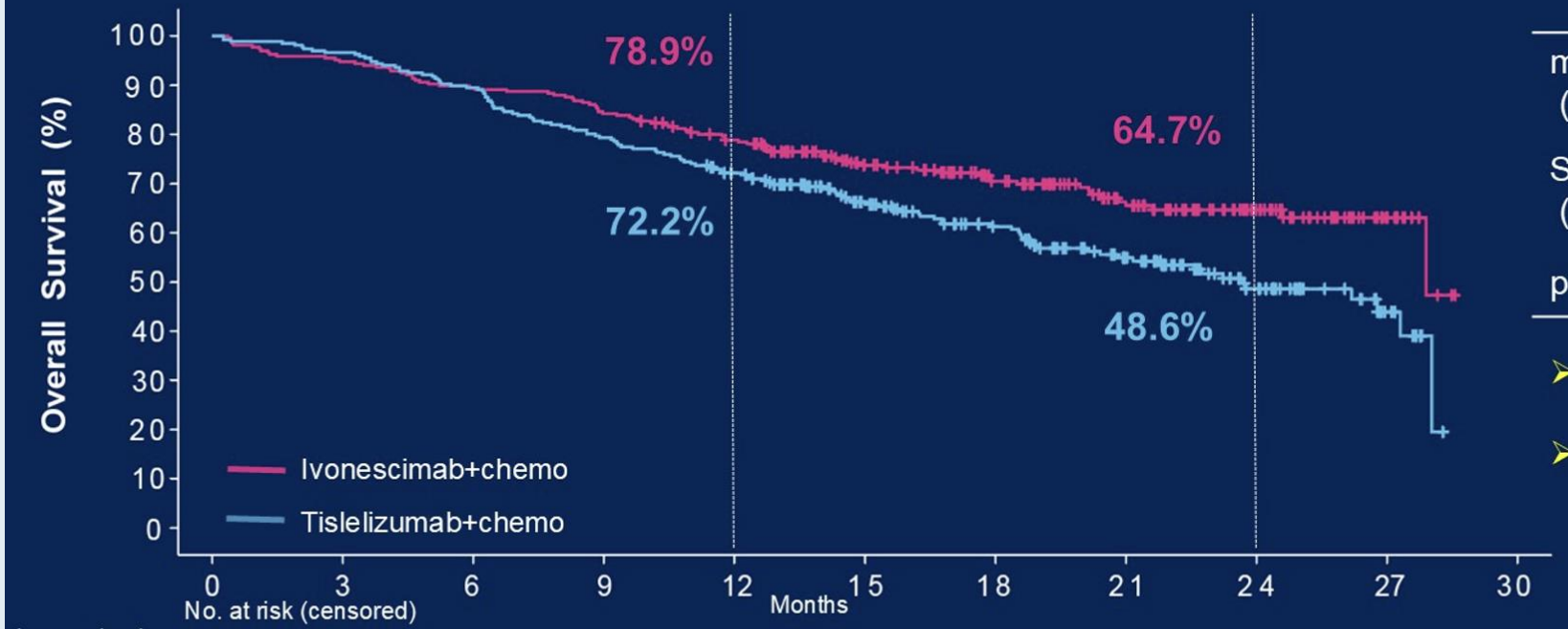
Consistent PFS benefit by investigator-assessment: HR = 0.64 (95% CI: 0.50, 0.84)

mPFS = median PFS

Lu S et al. ESMO 2025;Abstract LBA4.

HARMONi-6: Interim Overall Survival (OS) Analysis

✓ Ivonescimab with chemotherapy significantly improved OS



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mOS, months (95% CI)	27.89 (27.89, NE)	23.69 (20.11, NE)
Stratified HR (95% CI)	**0.66** (0.50, 0.87)	
p-value	**0.0017**	

- OS significance boundary: 0.0049
- The median OS in the ivonescimab group would have not been reached without the last single event

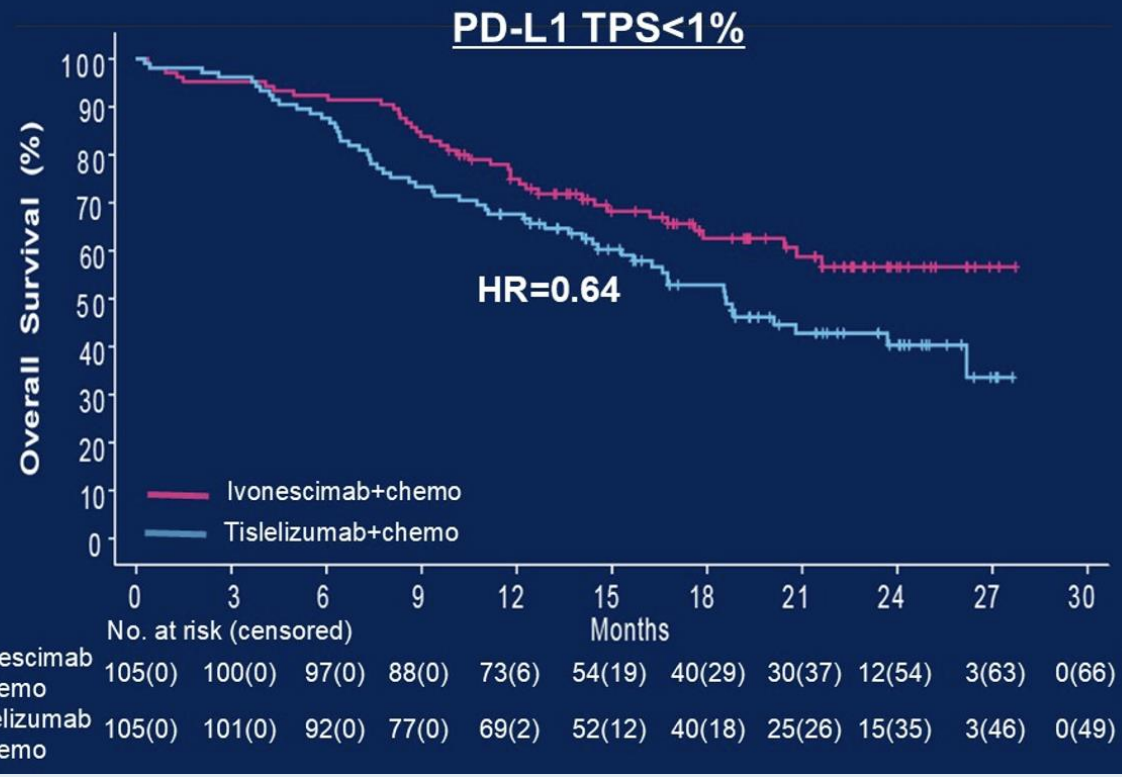
- Data cutoff date: Feb 27, 2026
- Median Follow-up: 21.36 months

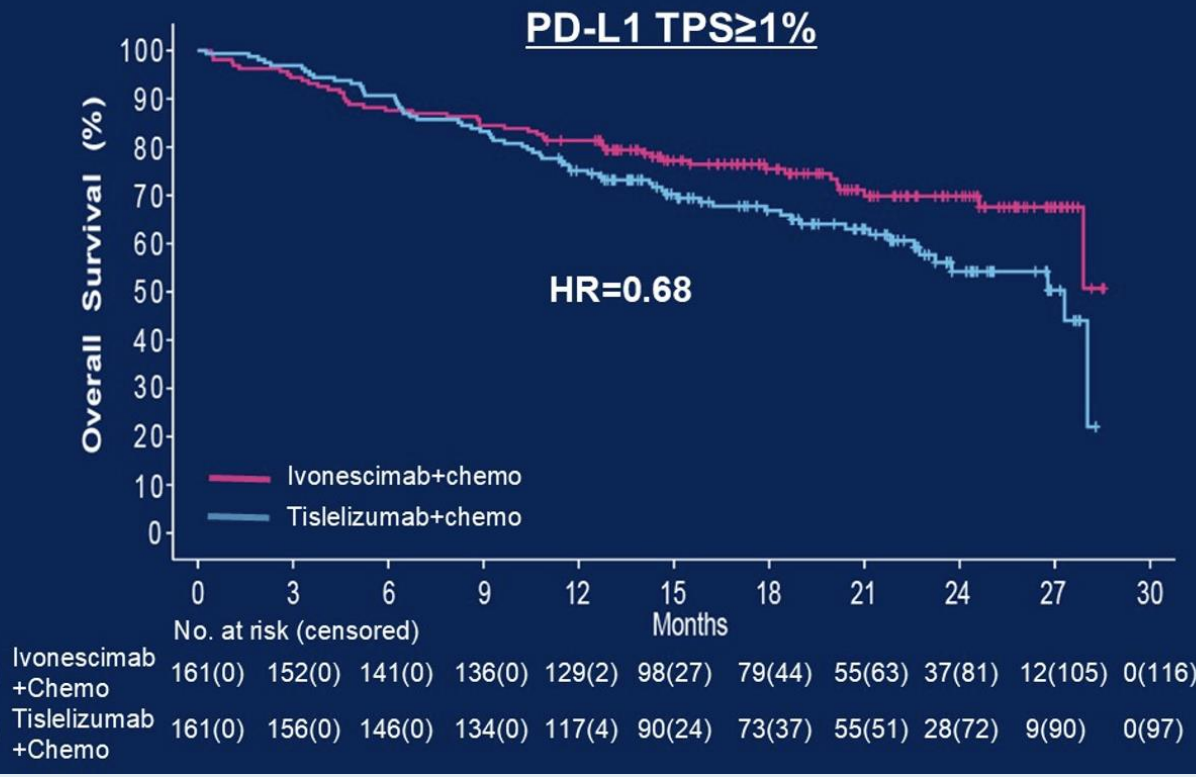
Abbreviation: mOS, median overall survival; NE, not estimable; HR, hazard ratio; CI, confidence interval

Zhiwei C et al. ASCO 2026;Abstract LBA4.

HARMONi-6: OS by PD-L1 Expression Levels

✓ Ivonescimab with chemotherapy showed consistent OS improvement across PD-L1 expression subgroups

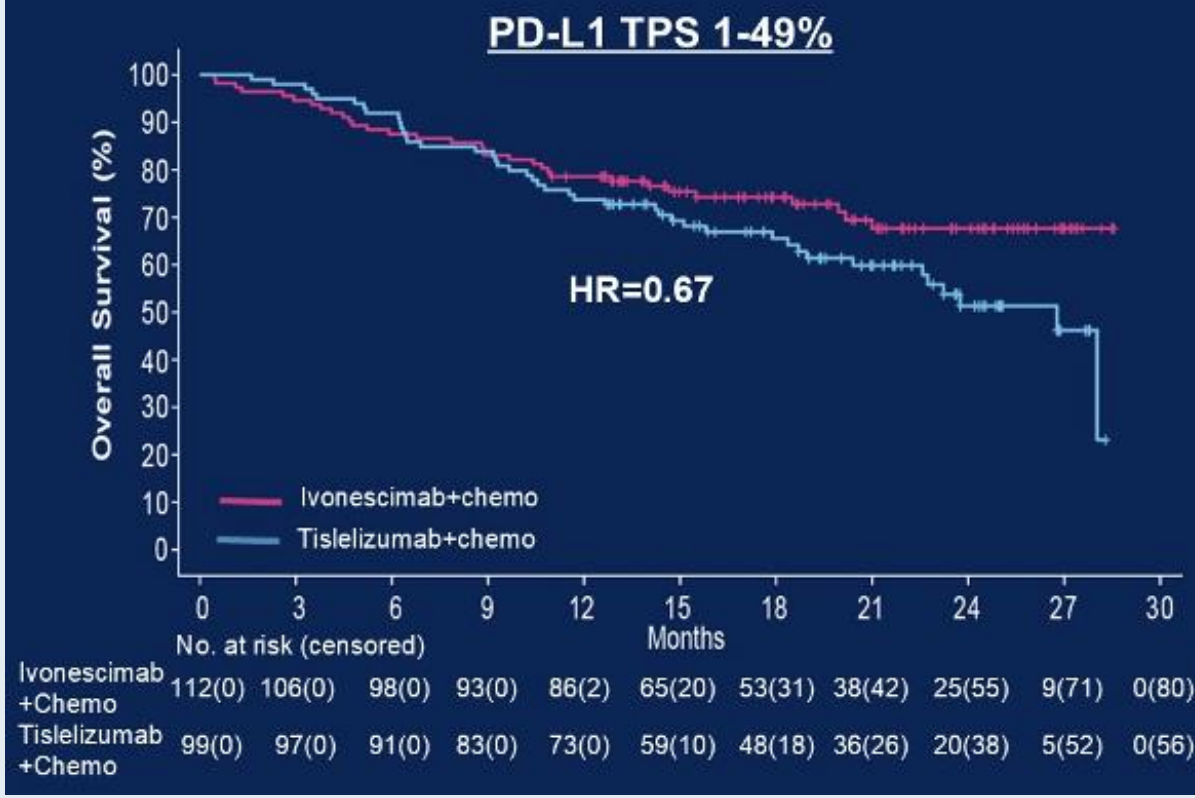


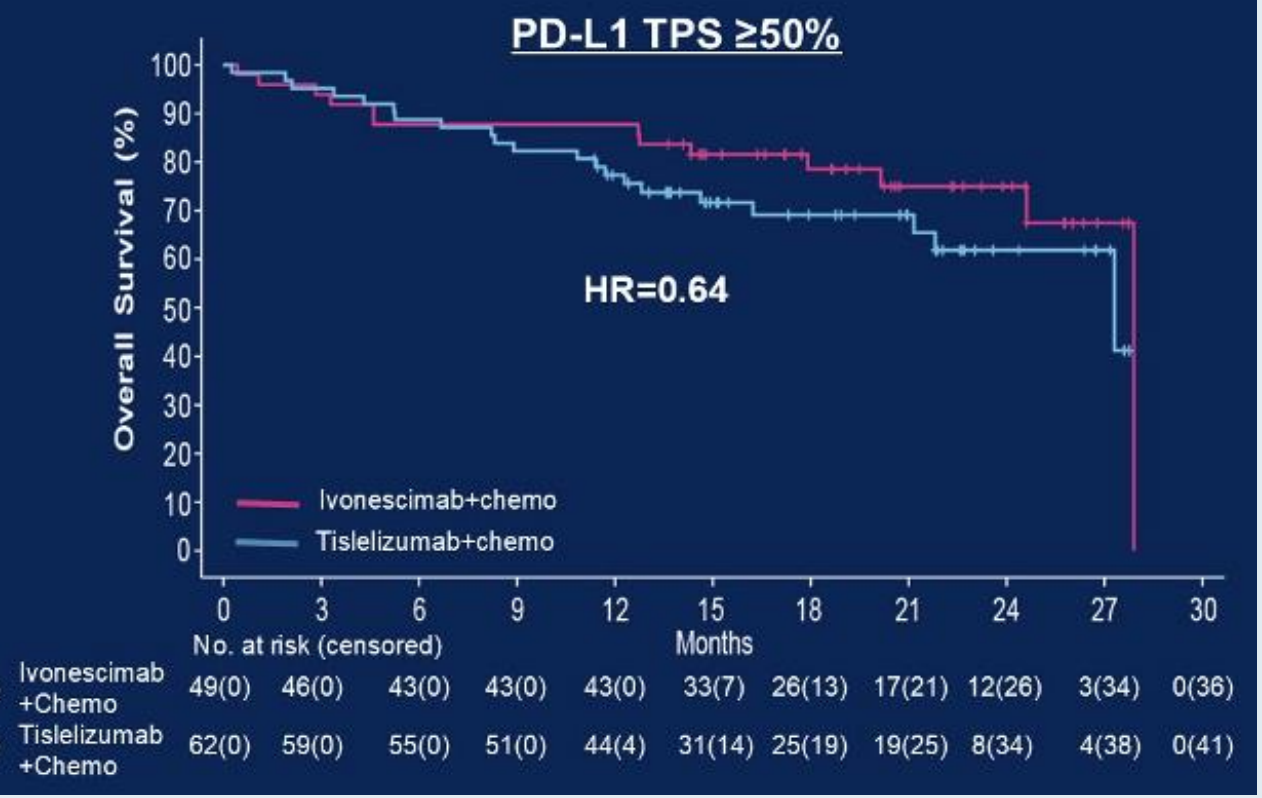


Zhiwei C et al. ASCO 2026;Abstract LBA4.

HARMONi-6: OS by PD-L1 Expression Levels

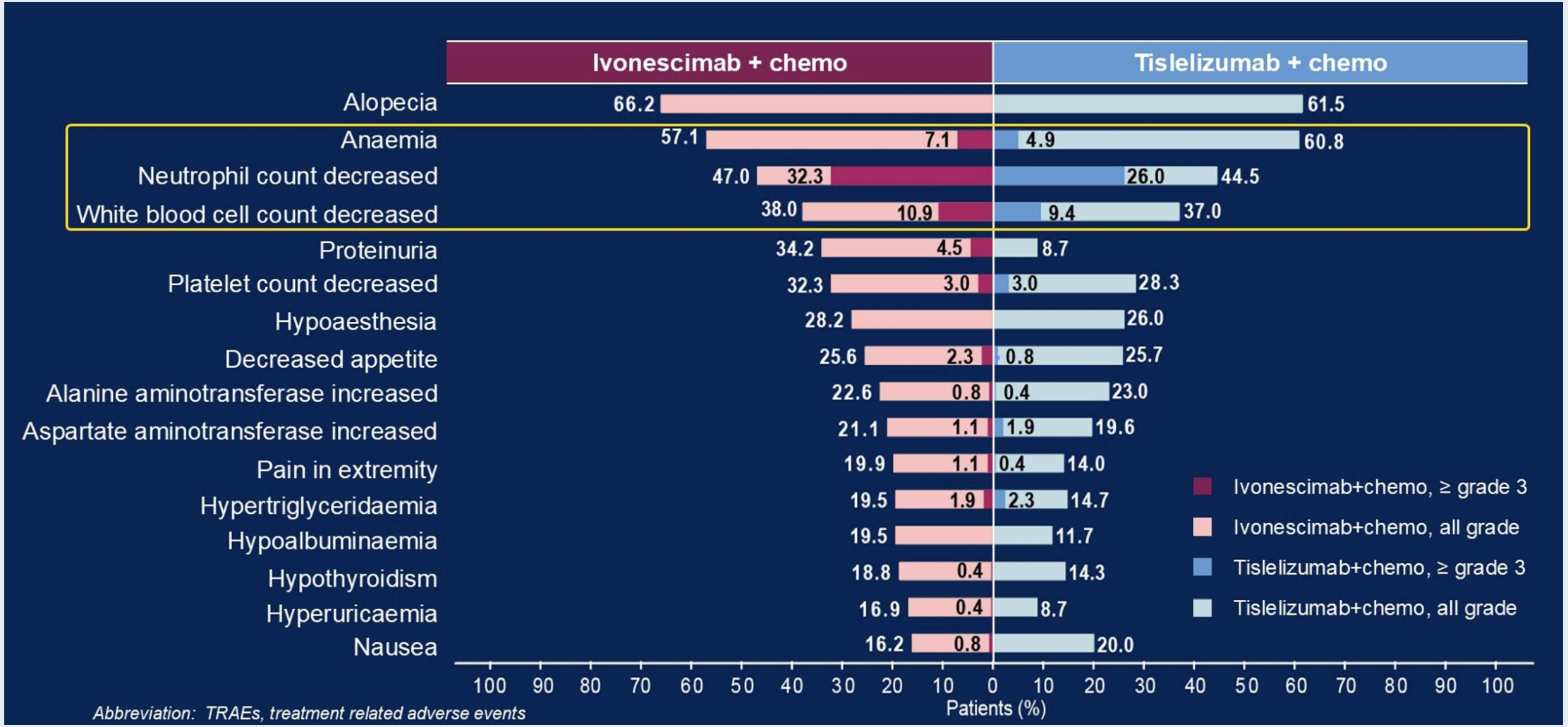
✓ Ivonescimab with chemotherapy showed consistent OS improvement across PD-L1 expression subgroups





Zhiwei C et al. ASCO 2026;Abstract LBA4.

HARMONi-6: Safety Profile



- Grade ≥3 immune-related adverse events (AEs) were observed in 34 (14%) of patients receiving ivonescimab/chemotherapy and in 36 (14%) of patients receiving tislelizumab/chemotherapy.

Zhiwei C et al. ASCO 2026;Abstract LBA4.

HARMONi-6: Possibly VEGF-Related Adverse Events (AEs)

- **Possibly VEGF-related AEs occurred more frequently in the ivonescimab arm, most of which were grade 1-2**

Possibly VEGF-Related AEs#	Ivonescimab + chemo (N=266)				Tislelizumab + chemo (N=265)			
	Any Grade	Grade 1	Grade 2	Grade ≥3	Any Grade	Grade 1	Grade 2	Grade ≥3
Proteinuria	113 (42.5)	35 (13.2)	60 (22.6)	**18 (6.8)**	34 (12.8)	26 (9.8)	8 (3.0)	**0**
Haemorrhage	**66 (24.8)**	**39 (14.7)**	**20 (7.5)**	**7 (2.6)**	**32 (12.1)**	**24 (9.1)**	**6 (2.3)**	**2 (0.8)**
Hypertension	39 (14.7)	7 (2.6)	22 (8.3)	**10 (3.8)**	15 (5.7)	3 (1.1)	7 (2.6)	**5 (1.9)**
Arterial thromboembolism	4 (1.5)	1 (0.4)	0	**3 (1.1)**	0	0	0	**0**
Venous thromboembolism	2 (0.8)	0	2 (0.8)	**0**	3 (1.1)	0	2 (0.8)	**1 (0.4)**
Fistula	1 (0.4)	0	1 (0.4)	**0**	0	0	0	**0**

- # AE terms were grouped terms
- Data are n (%)

Zhiwei C et al. ASCO 2026;Abstract LBA4.

Key Takeaway Points

Ivonescimab plus taxane/carboplatin chemotherapy **is effective for Chinese patients with advanced squamous NSCLC based on the interim overall survival advantage.**

Ivonescimab **results in VEGF-related AEs, and there is some uncertainty regarding patient selection.**

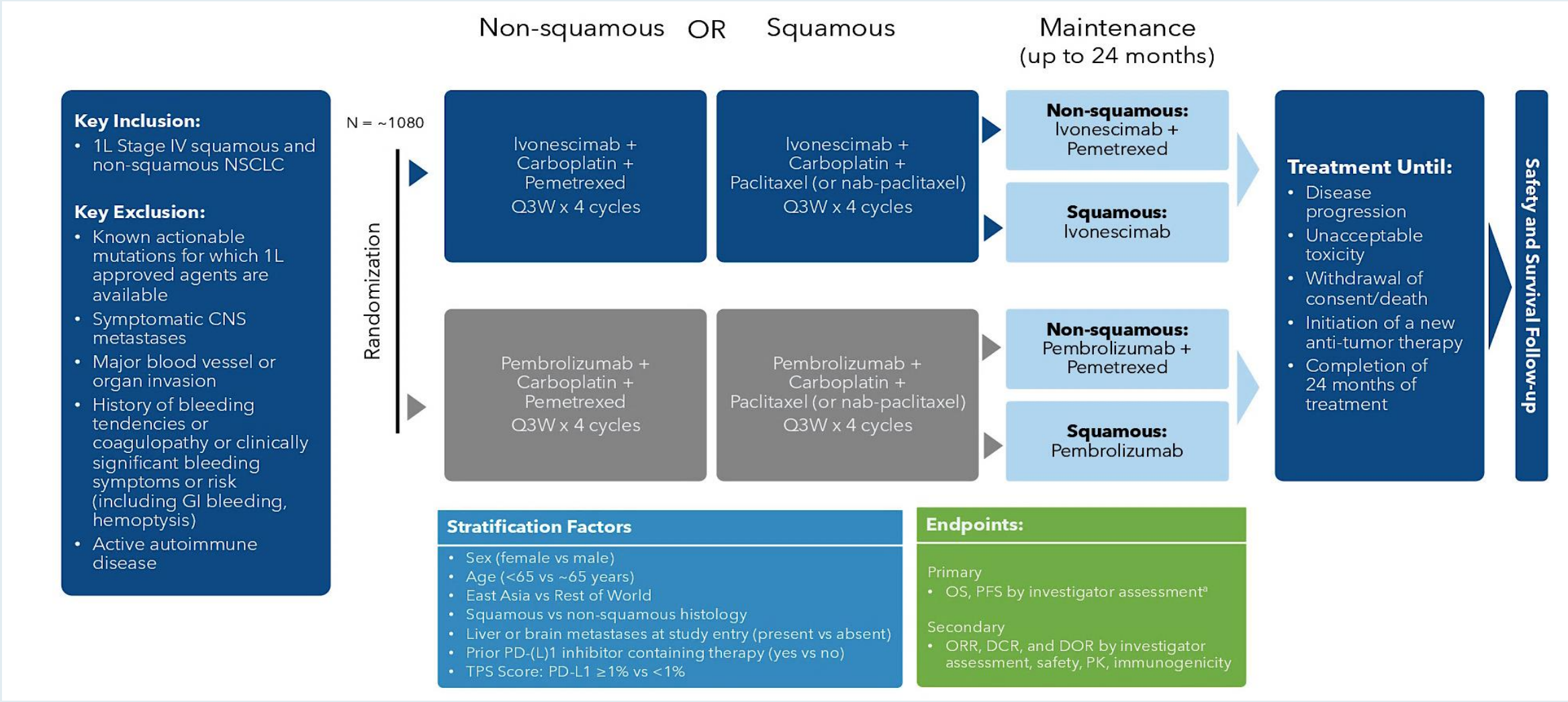
Applicability to the global, generally older, squamous lung cancer population is unclear.

“We have to wait and see if ivonescimab will be approved in squamous cell. If they approve it in the EU based on HARMONi-6 and we don’t, and then years down the line, it turns out to be the same in the US, we will regret that, and our patients would have been getting inferior care, which has never happened. We’re always the first, so how can we be the last? So that’s a big deal.”

Stephen V Lui, MD

Oncology Today with Dr Neil Love

HARMONi-3: An Ongoing Phase III Study of Ivonescimab/Chemotherapy versus Pembrolizumab/Chemotherapy for Previously Untreated mNSCLC



Zhang J et al. ASCO 2025;Abstract TPS8664.

HARMONi-2 Chinese Phase III Study Design

A randomized, double-blind, phase 3 study[a]

Patient Population

- Stage IIIB-IV aNSCLC
- No prior systemic therapy
- No *EGFR* mutations or *ALK* rearrangements
- ECOG PS 0 or 1
- PD-L1 TPS ≥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

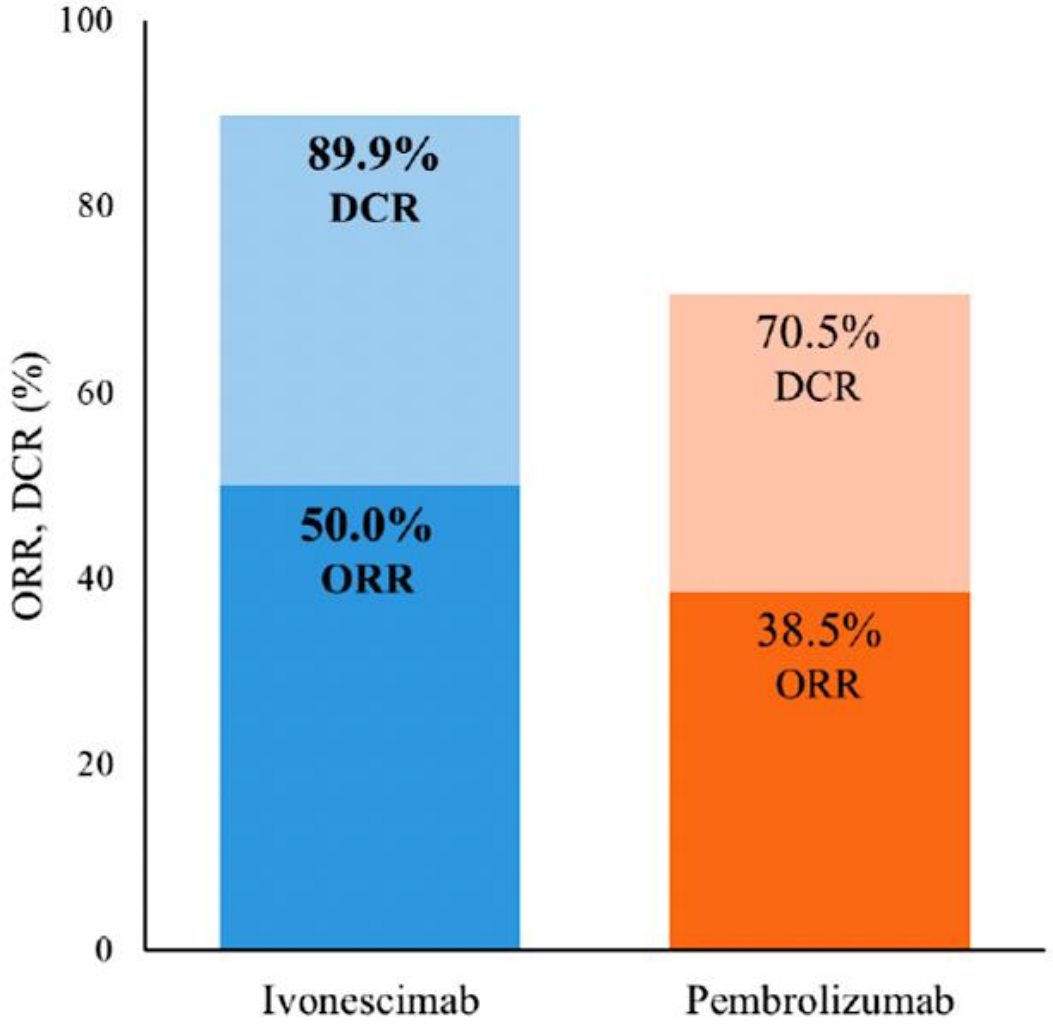
- Clinical stage (IIIB/C vs. IV)
- Histology (SQ vs. non-SQ)
- PD-L1 TPS (≥50% vs. 1-49%)

Endpoints

Primary: PFS by blind IRRC per RECIST v1.1
Secondary: OS, PFS assessed by INVs, ORR, DoR, TTR and safety
Exploratory: QoL

Zhou C et al. WCLC 2024;Abstract PL02.04.

HARMONi-2: Response Data



	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)
Median DoR, mos **(95% CI)**	**NR** (NE, NE)	NR (8.28, NE)

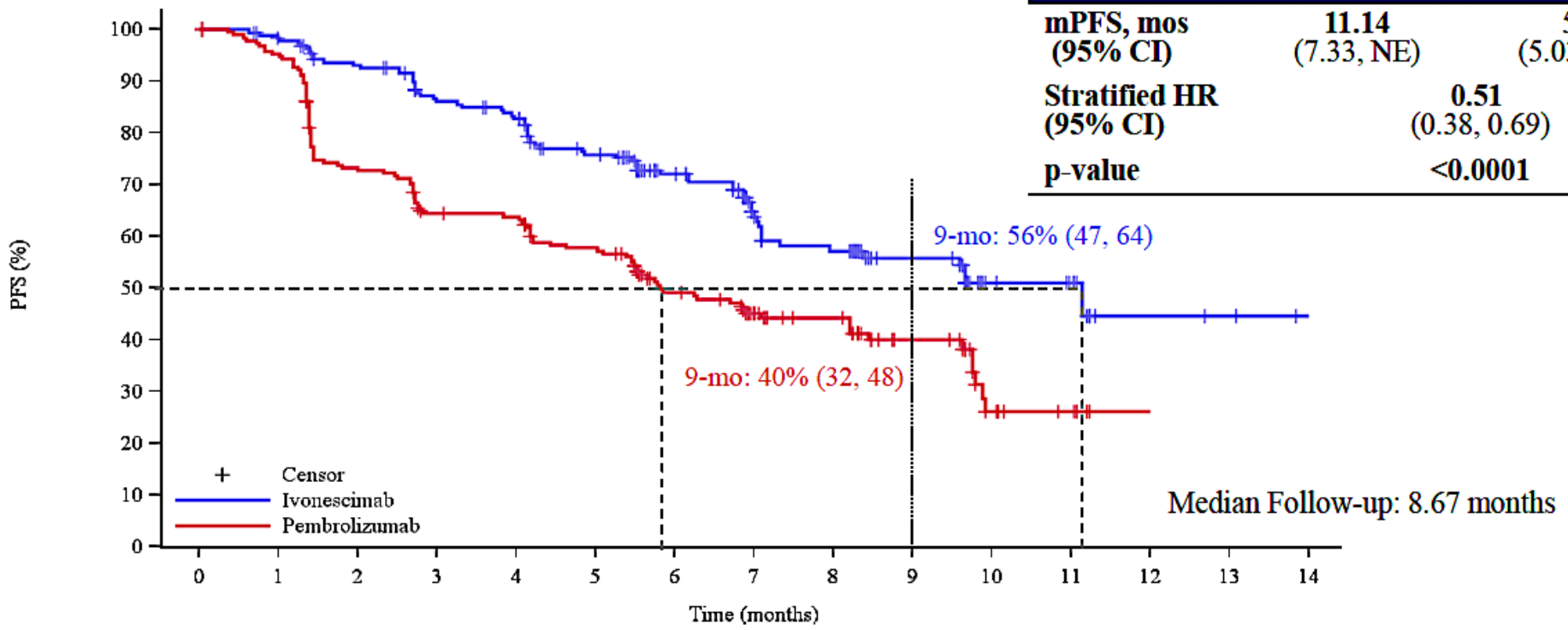
ORR and DCR were higher with ivonescimab vs. pembrolizumab.

ORR = objective response rate; DCR = disease control rate; DoR = duration of response

Zhou C et al. WCLC 2024;Abstract PL02.04.

HARMONi-2: PFS Outcomes

	Ivonescimab (n = 198)	Pembrolizumab (n = 200)
mPFS, mos (95% CI)	**11.14** (7.33, NE)	5.82 (5.03, 8.21)
Stratified HR (95% CI)	**0.51** (0.38, 0.69)	
p-value	**<0.0001**	



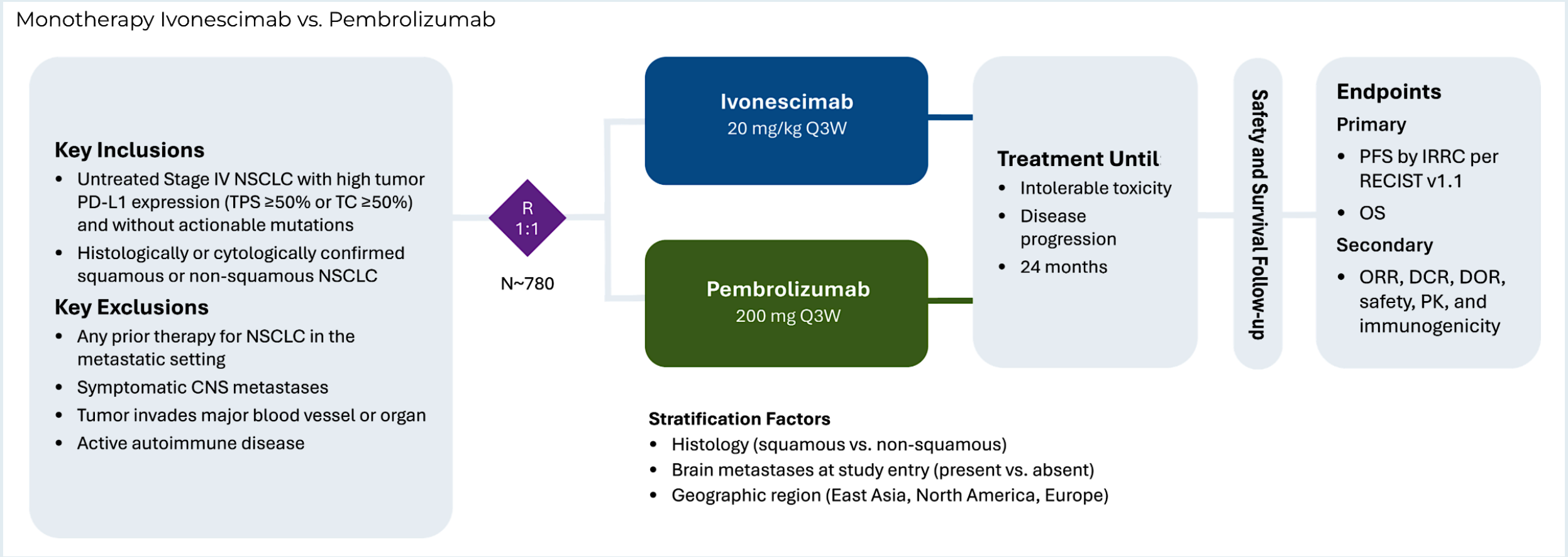
Number at risk (Events)

Ivonescimab	198(0)	189(3)	175(13)	156(26)	148(32)	128(44)	99(50)	68(60)	59(67)	38(68)	14(71)	11(71)	3(72)	2(72)	0(72)
Pembrolizumab	200(0)	187(9)	141(52)	121(69)	119(70)	103(81)	74(95)	53(101)	45(102)	25(106)	9(112)	5(112)	0(112)		

Ivonescimab demonstrated a statistically significant improvement in PFS vs. pembrolizumab with HR = 0.51, and a 5.3 months improvement in mPFS.

Zhou C et al. WCLC 2024;Abstract PL02.04.

HARMONi-7: An Ongoing Phase III Study of Ivonescimab versus Pembrolizumab for mNSCLC with High PD-L1 Expression



Passaro A et al. ELCC 2025;Abstract 133TiP.

Do you anticipate that ivonescimab/chemotherapy will yield superior efficacy outcomes compared to pembrolizumab/chemotherapy in previously untreated advanced NSCLC in a global population?

 Dr Baik	Yes
 Dr Goldman	Yes
 Dr Paik	Yes
 Prof Passaro	I’m not sure
 Dr Piotrowska	Yes
 Dr Rotow	Yes

Do you anticipate that ivonescimab monotherapy will yield superior efficacy outcomes compared to pembrolizumab monotherapy in previously untreated advanced NSCLC with high PD-L1 expression in a global population?

 Dr Baik	Yes
 Dr Goldman	Yes
 Dr Paik	Yes
 Prof Passaro	I'm not sure
 Dr Piotrowska	Yes
 Dr Rotow	Yes

According to clinical trial data and/or your clinical experience, how much of a concern are treatment-related adverse events for patients receiving ivonescimab?

 Dr Baik	A minor concern; the majority of patients experience low-grade side effects related to VEGF pathway inhibition
 Dr Goldman	A minor concern; the majority of patients experience low-grade side effects related to VEGF pathway inhibition
 Dr Paik	A minor concern; the majority of patients experience low-grade side effects related to VEGF pathway inhibition
 Prof Passaro	Minimal concern; the majority of patients experience no side effects
 Dr Piotrowska	A minor concern; the majority of patients experience low-grade side effects related to VEGF pathway inhibition
 Dr Rotow	A minor concern; the majority of patients experience low-grade side effects related to VEGF pathway inhibition

How would you indirectly compare the spectrum and severity of VEGF-related toxicities associated with ivonescimab to those experienced by patients with NSCLC receiving VEGF/VEGFR-targeted monoclonal antibodies?

 Dr Baik	VEGF-related toxicities are about the same
 Dr Goldman	VEGF-related toxicities are more common/severe with VEGF/VEGFR-targeted monoclonal antibodies
 Dr Paik	VEGF-related toxicities are more common/severe with VEGF/VEGFR-targeted monoclonal antibodies
 Prof Passaro	VEGF-related toxicities are about the same
 Dr Piotrowska	VEGF-related toxicities are more common/severe with VEGF/VEGFR-targeted monoclonal antibodies
 Dr Rotow	VEGF-related toxicities are about the same

How would you indirectly compare the spectrum and severity of immune-related toxicities associated with ivonescimab to those experienced by patients with NSCLC receiving PD-1/PD-L1-targeted monoclonal antibodies?

 Dr Baik	Immune-related toxicities are about the same
 Dr Goldman	Immune-related toxicities are about the same
 Dr Paik	Immune-related toxicities are more common/severe with PD-1/PD-L1-targeted monoclonal antibodies
 Prof Passaro	Immune-related toxicities are about the same
 Dr Piotrowska	Immune-related toxicities are about the same
 Dr Rotow	Immune-related toxicities are about the same

Agenda

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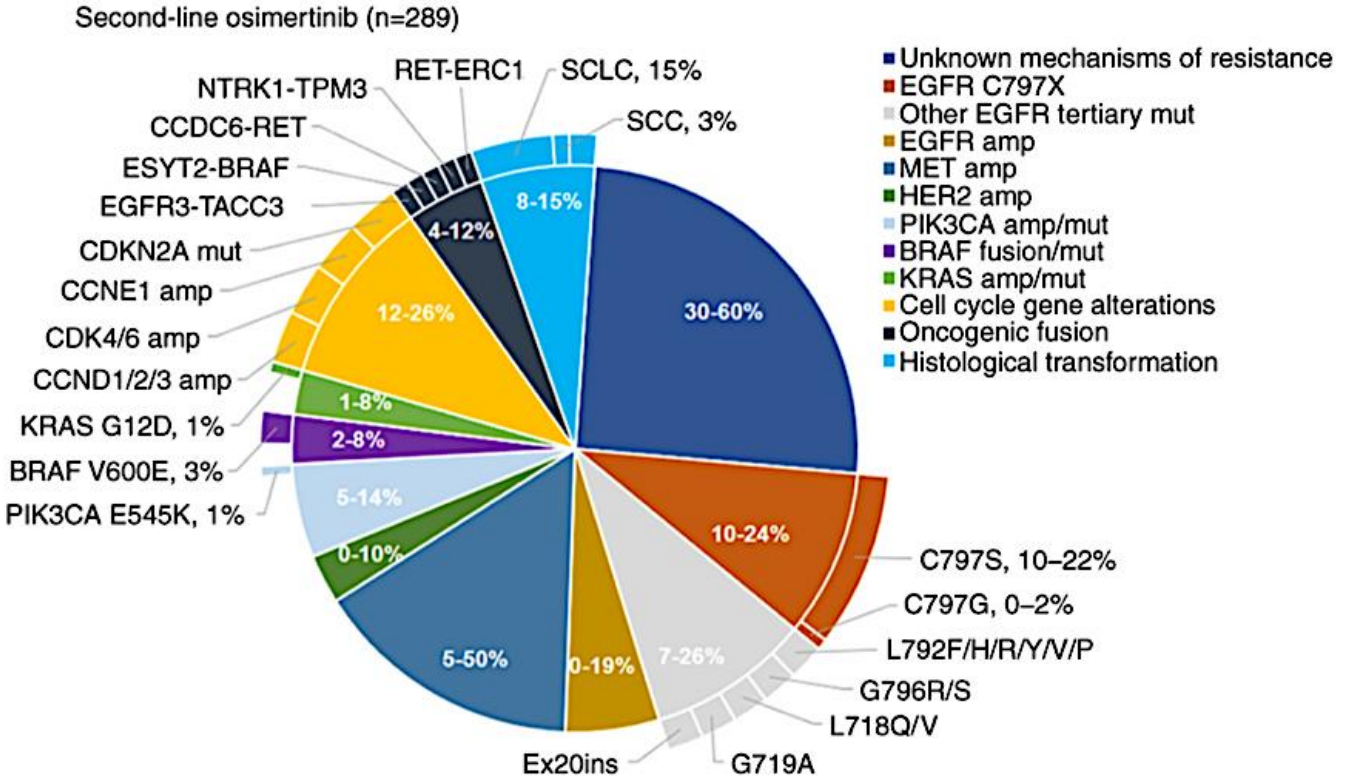
Module 2: Ivonescimab for Relapsed/Refractory EGFR-Mutated mNSCLC

Module 3: Other Novel PD-1/PD-L1 x VEGF Bispecific Antibodies Under Investigation

Acquired Resistance in EGFR-Mutated NSCLC

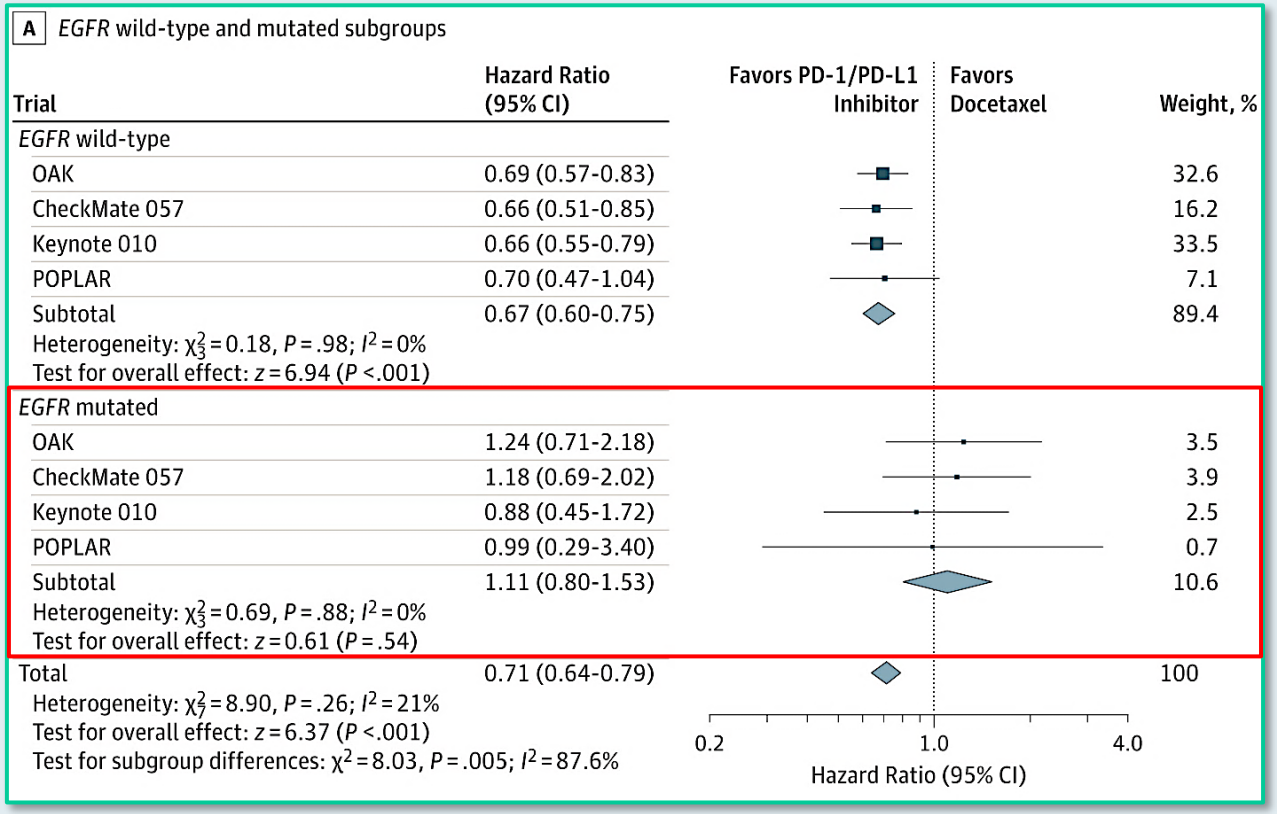


- The occurrence of acquired resistance is inevitable, and the mechanisms of third-generation EGFR tyrosine kinase inhibitor (TKI) resistance are complex and incompletely understood
- The mechanisms of acquired resistance to third-generation EGFR TKIs include an altered EGFR signaling pathway, aberrant activation of bypass and downstream signaling pathways and histological transformation

He J et al. *Int J Oncol* 2021;59(5):90.

Poor Immunotherapy Response in EGFR-Mutated NSCLC

Overall survival hazard ratios



Mechanisms

- Low tumor mutational burden
- Immunosuppressive tumor microenvironment
- Disrupted helper T-cell signaling
- EGFR-mediated suppression of IFN-γ
- TGF-β upregulation

Content courtesy of Jonathan Goldman, MD

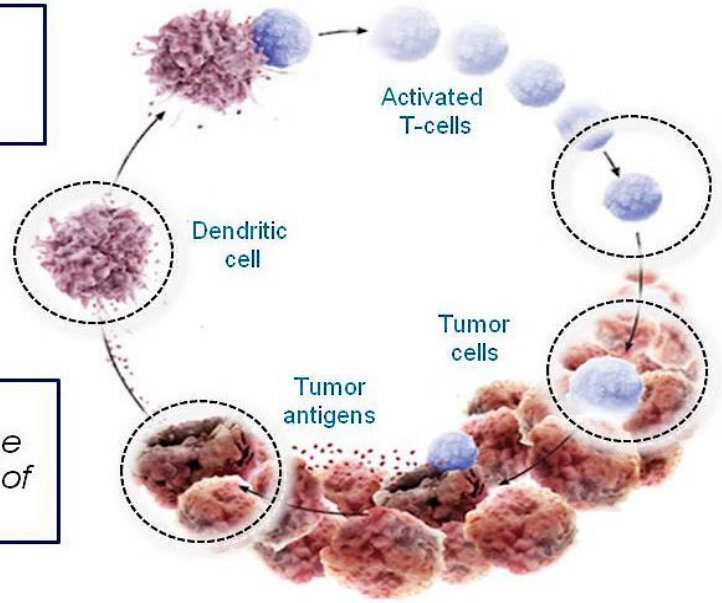
Lee et al. *JAMA Oncology* 2018. Yang et al. *J Clin Oncol* 2024. Mok et al. *J Clin Oncol* 2024. Lu et al. *Lancet Oncol* 2022 and *Lancet Respir Med* 2023. Shi et al. *Cancer Medicine* 2021.

RTP RESEARCH TO PRACTICE

Rationale for the Combination of Atezolizumab + Bevacizumab + Chemotherapy

- In addition to its known anti-angiogenic effects[1], bevacizumab's inhibition of VEGF has immune modulatory effects[2]

Inhibition of VEGF can promote T-cell priming and activation via dendritic cell maturation[2-4]



Normalization of the tumor vasculature through VEGF inhibition increases T-cell tumor infiltration[2,5-8]

Tumor cell killing by chemotherapy may expose the immune system to high levels of cancer cell antigens[9]

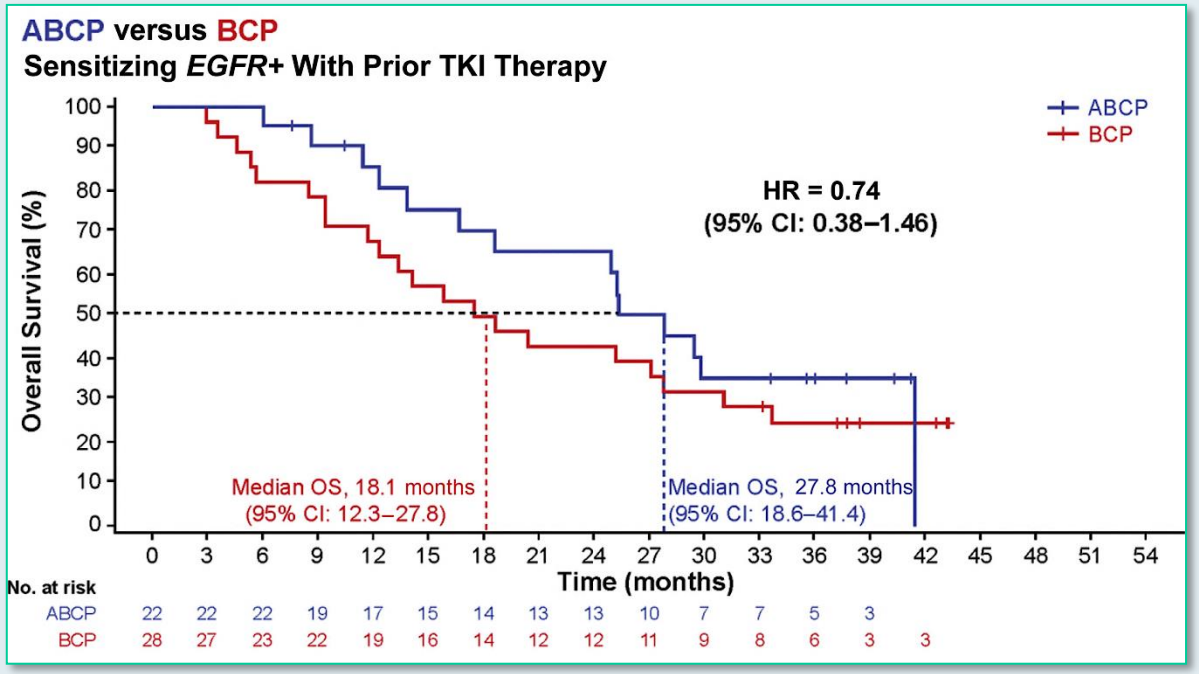
VEGF blockade can establish an immune-permissive tumor microenvironment by decreasing myeloid-derived suppressor cell and regulatory T cell populations[2,8,10-13]

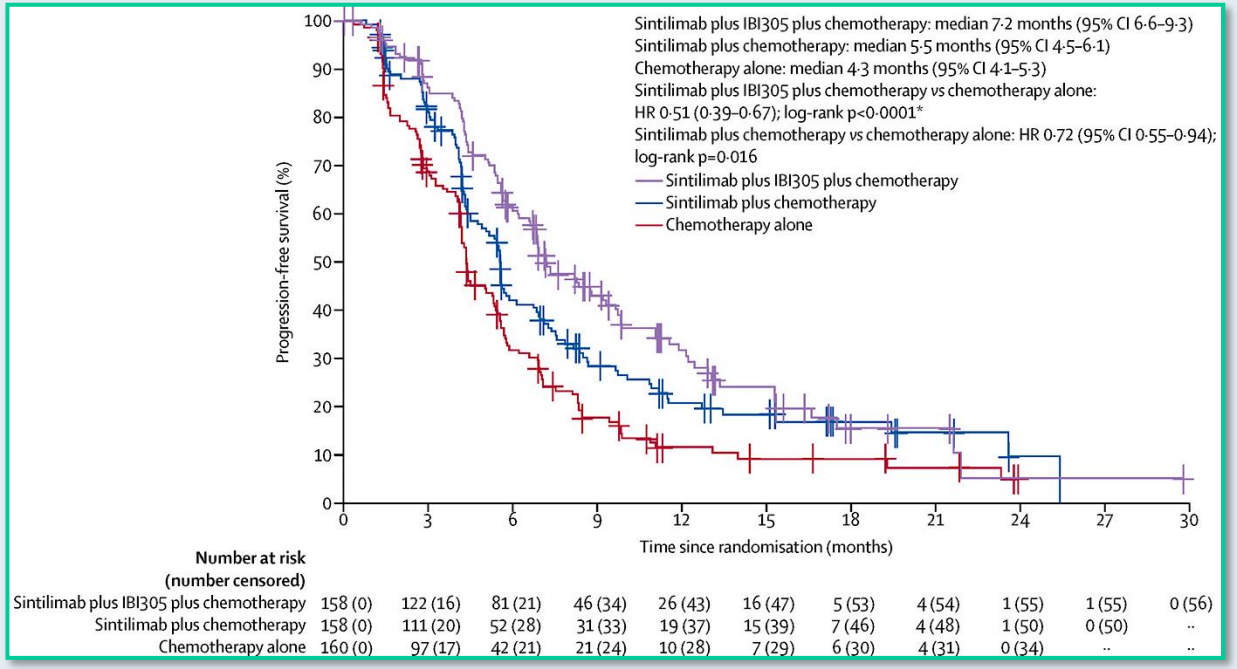
- Atezolizumab's T-cell mediated cancer cell killing may be enhanced through bevacizumab's reversal of VEGF-mediated immunosuppression

1. Ferrara N, et al. *Nat Rev Drug Discov*, 2004. 2. Hegde PS, et al. *Semin Cancer Biol*. 2017 . 3. Gabrilovich DI, et al. *Nat Med*, 1996. 4. Oyama T, et al. *J Immunol*, 1998. 5. Goel S, et al. *Physiol Rev*, 2011. 6. Motz GT, et al. *Nat Med*, 2014. 7. Hodi FS, et al. *Cancer Immunol Res*, 2014. 8. Wallin JJ, et al. *Nat Commun*, 2016. 9. Zitvogel L, et al. *Immunity*, 2013. 10. Gabrilovich DI, Nagaraj S. *Nat Rev Immunol*, 2009. 11. Roland CL, et al. *PLoS One*, 2009. 12. Facciabene A, et al. *Nature*, 2011. 13. Voron T, et al. *J Exp Med*, 2015. Figure adapted from Chen DS, Mellman I. *Immunity*, 2013.

Content courtesy of Jonathan Goldman, MD
Socinski M et al. ASCO 2018.

Combination Chemotherapy with VEGF Inhibition and Immunotherapy (IO)





IMpower150 trial: Chemo + VEGFi vs chemo + VEGFi + IO

- Exploratory analysis in 123 patients with EGFRm.
  - For all pt, OS HR 0.60.
  - For those treated with previous TKI, HR 0.74.

ORIENT-31 trial: Chemo vs chemo + IO vs chemo + VEGFi + IO

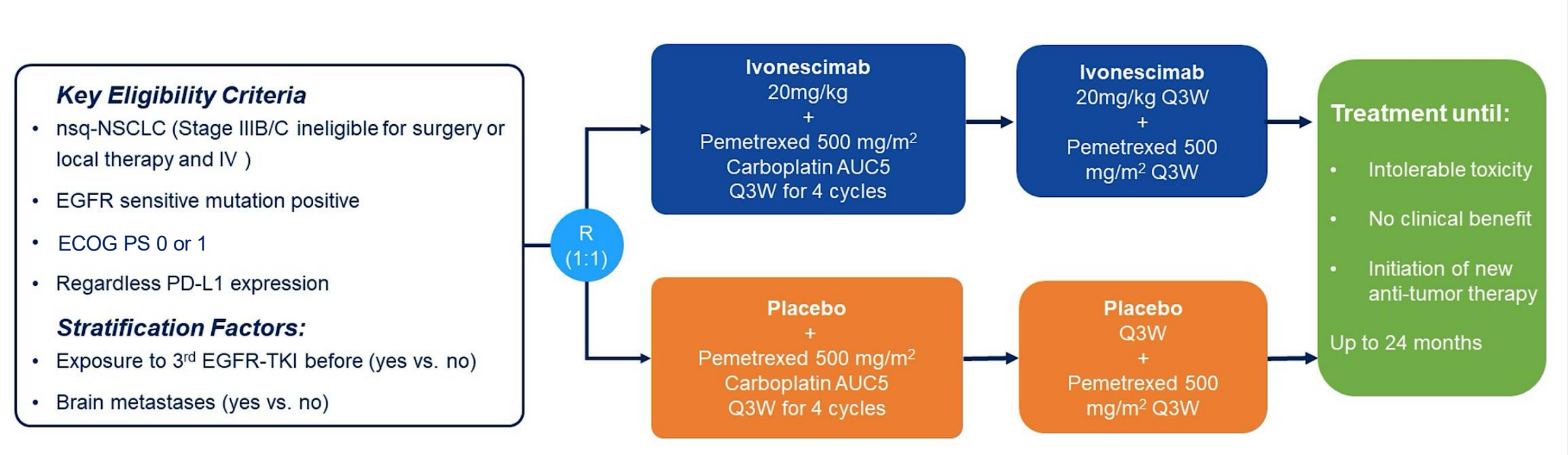
- PFS 4.3 vs 5.5 vs 7.2 months.
- OS curves are overlapping.

Content courtesy of Jonathan Goldman, MD

Socinski et al. *New Eng J Med* 2018. Reck et al. *Lancet Respir Med* 2019 and Nogami et al. *J Thor Oncol* 2022. Lu et al. *Lancet Respir Med* 2023.

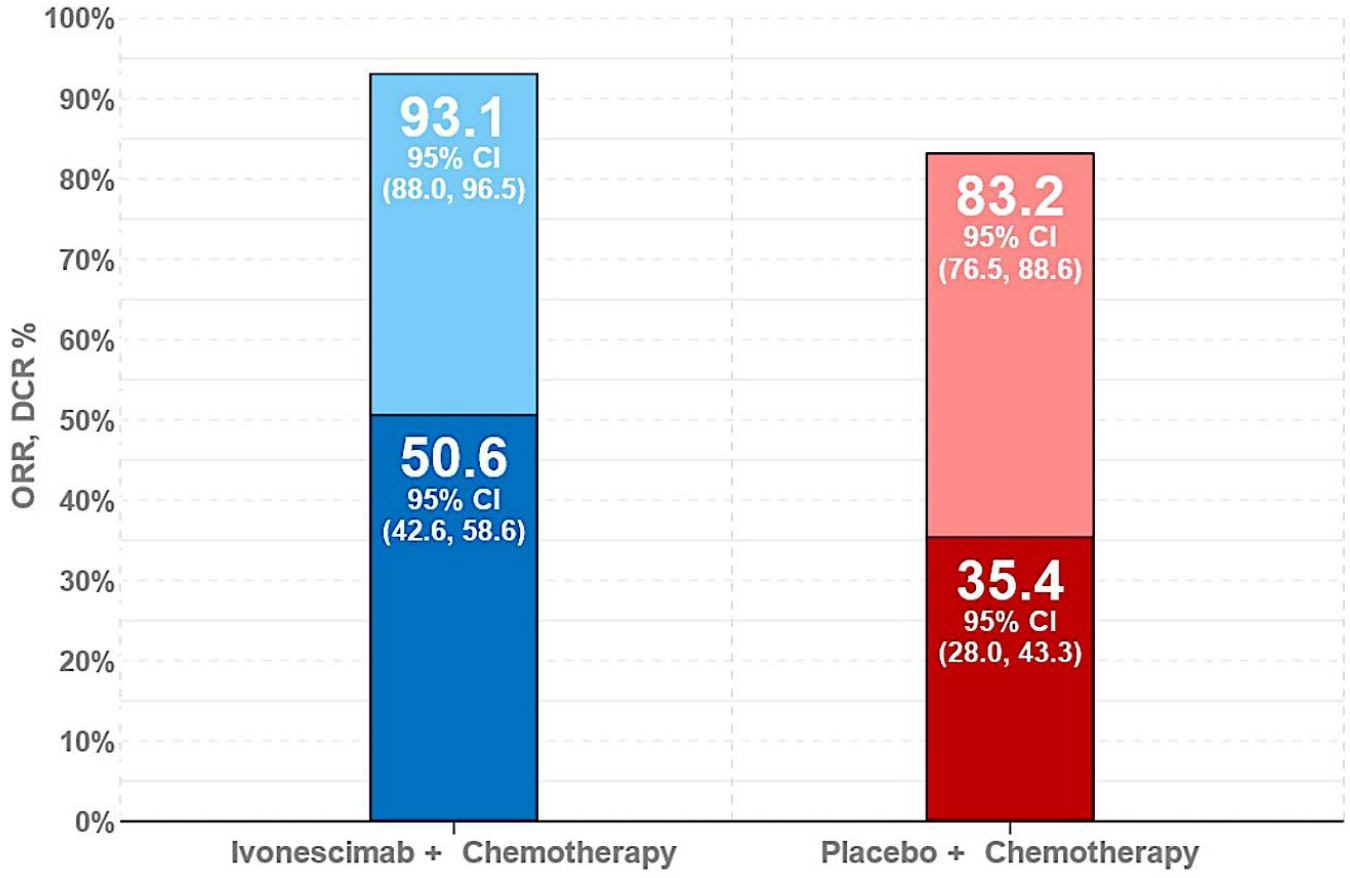
RTP RESEARCH TO PRACTICE

HARMONi-A Chinese Phase III Study Design



Zhang L et al. ASCO 2024;Abstract 8508.

HARMONi-A: Response Data

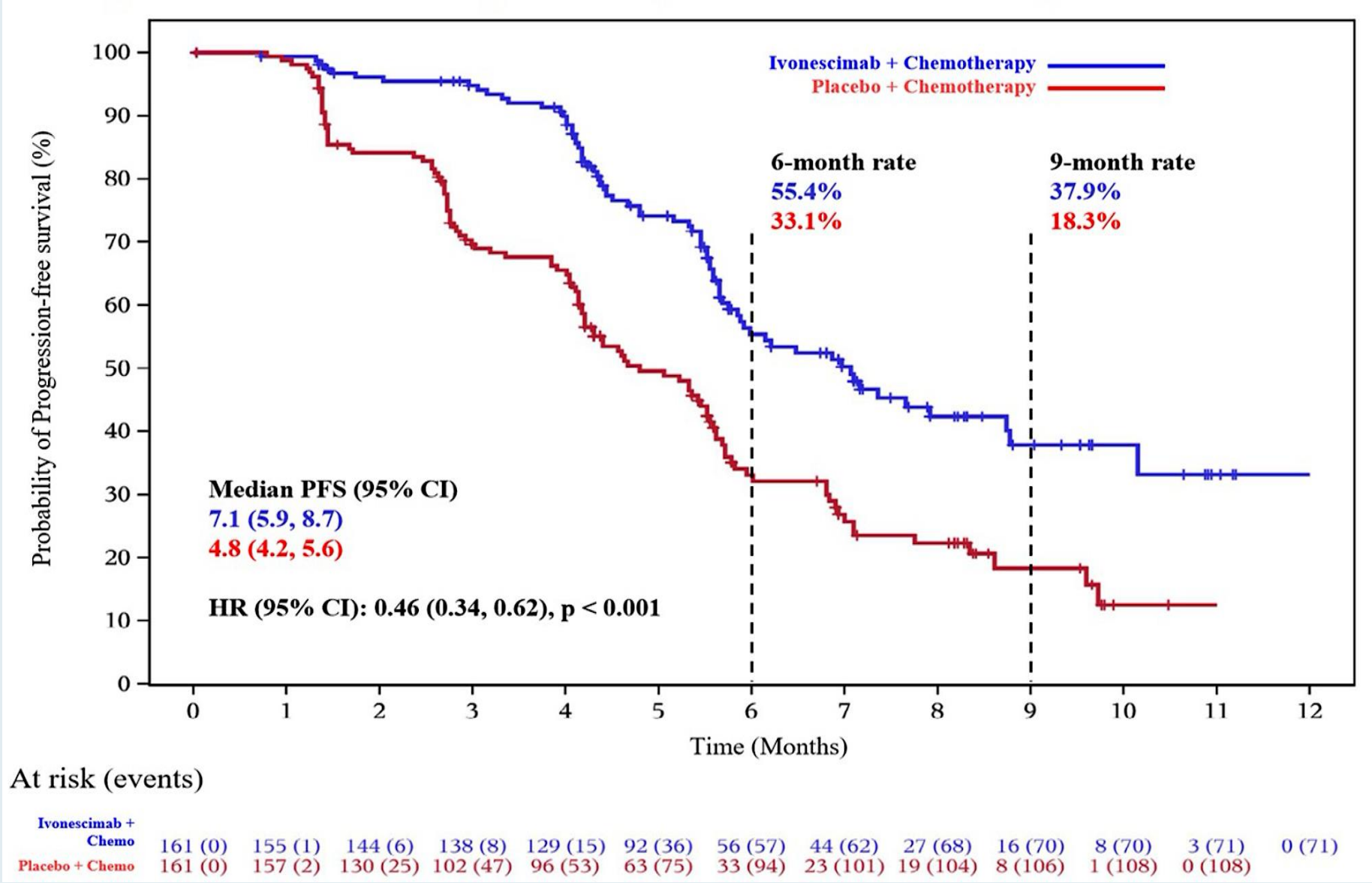


	Ivonescimab + Chemo	Placebo + Chemo
ORR, % (95% CI)	**50.6** (42.6, 58.6)	**35.4** (28.0, 43.3)
DCR, % (95% CI)	**93.1** (88.0, 96.5)	**83.2** (76.5, 88.6)
Median DoR, month (95% CI)	**6.6** (4.3, 7.6)	**4.2** (3.0, 4.7)

ORR = objective response rate; DCR = disease control rate; DoR = duration of response

Zhang L et al. ASCO 2024;Abstract 8508.

HARMONi-A: PFS Outcomes



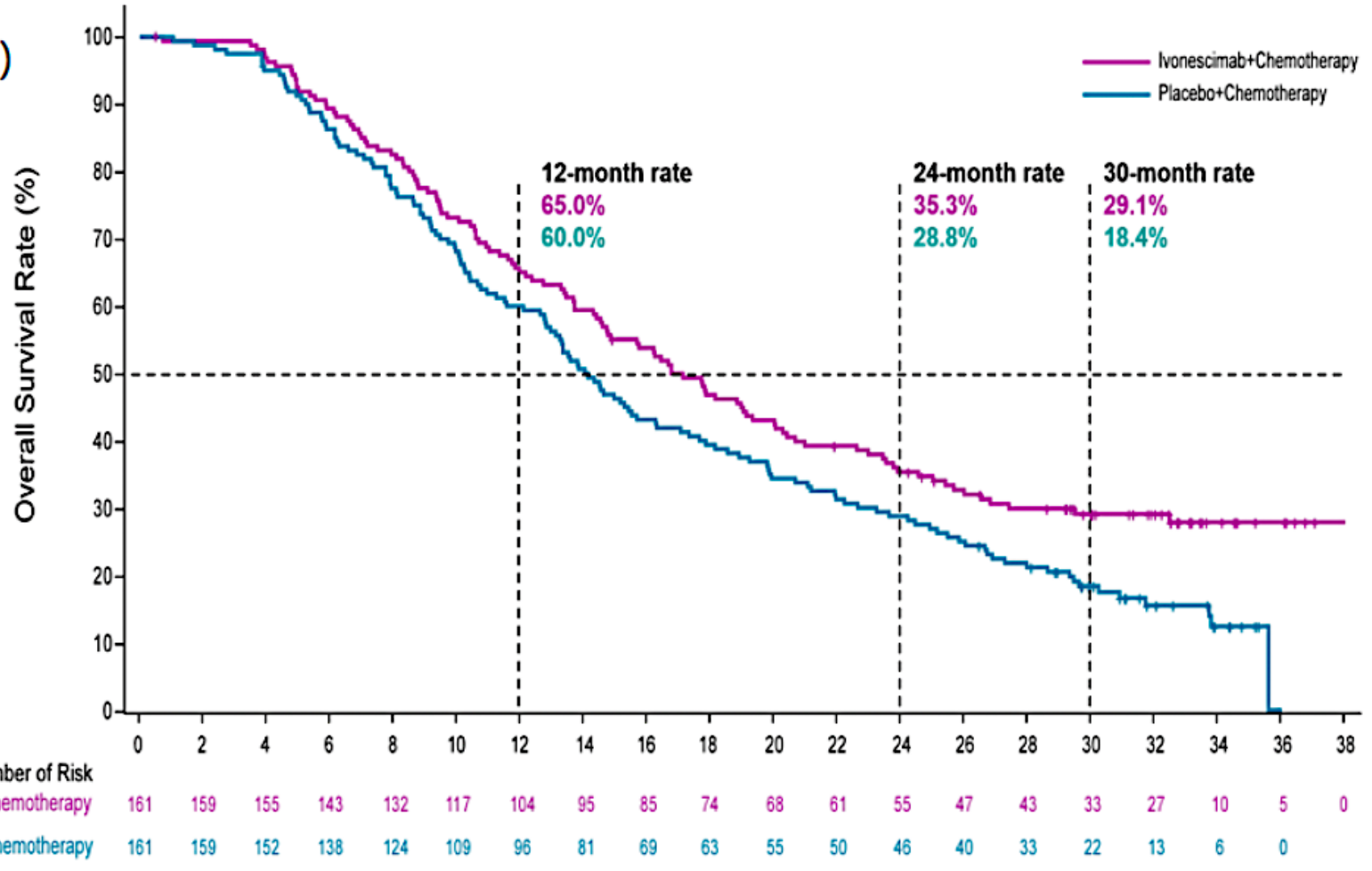
Zhang L et al. ASCO 2024;Abstract 8508.

HARMONi-A: Final OS Analysis

Data cut-off date: April 2025
(median follow-up of 32.5 months)

	Ivonescimab + chemotherapy	Placebo + chemotherapy
ORR[1], % (95% CI)	**50.6** (42.6, 58.6)	**35.4** (28.0, 43.3)
DCR[1], % (95% CI)	**93.1** (88.0, 96.5)	**83.2** (76.5, 88.6)
mPFS[1], months (95% CI)	**7.1** (5.9, 8.7)	**4.8** (4.2, 5.6)
PFS HR[1] (95% CI)	**0.46** (0.34, 0.62) **p<0.001**	
mOS[2], months (95% CI)	**16.8** (14.5, 20.0)	**14.1** (12.8, 16.3)
OS HR[2] (95% CI)	**0.74** (0.58, 0.95) **p=0.019** (two-side)	

[1]Interim analysis
[2]Final analysis



Zhang L et al. SITC 2025;Abstract 1348.

HARMONi Study Design (Asia and Western Populations)

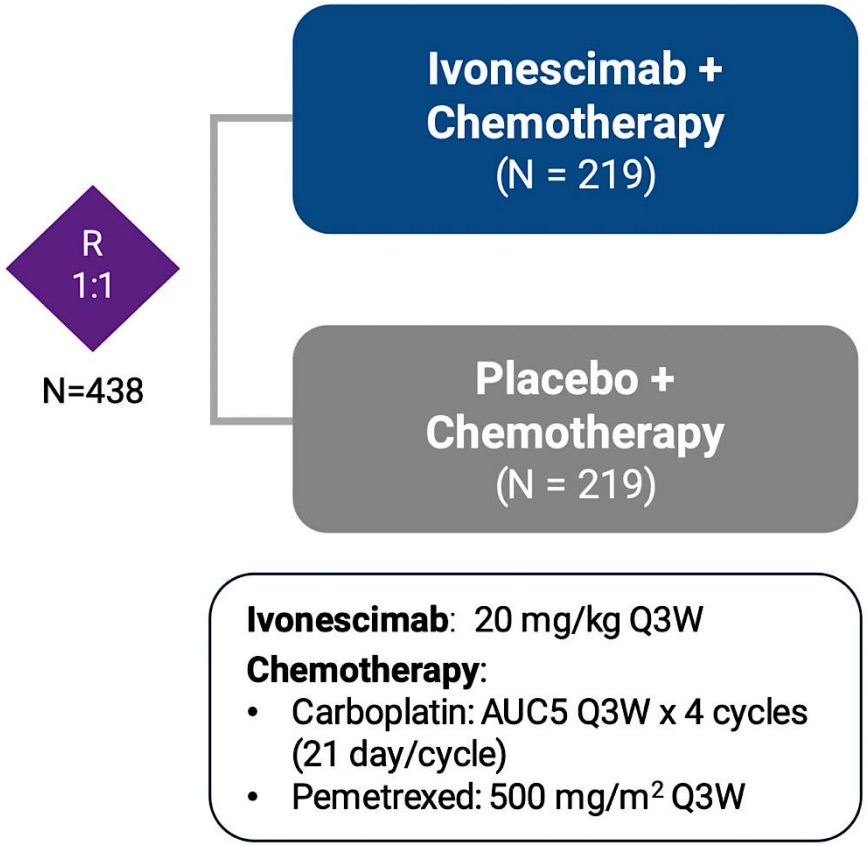
Key Eligibility Criteria

Locally advanced or metastatic NSCLC:

- EGFR sensitizing mutation+
- Progressed on 3rd gen EGFR-TKI
- ECOG 0 or 1
- Any PD-L1 expression

Stratification factor by geographic region:

- Brain metastases (yes or no)



Ivonescimab: 20 mg/kg Q3W

Chemotherapy:

- Carboplatin: AUC5 Q3W x 4 cycles (21 day/cycle)
- Pemetrexed: 500 mg/m^2 Q3W

Endpoints:

Primary

- OS, PFS by IRRC per RECIST 1.1

Secondary

- ORR by IRRC, DoR, safety and tolerability

Planned Efficacy Analyses

- PFS primary (at ~231 events) & OS interim analyses
- OS final analysis (at ~261 events)

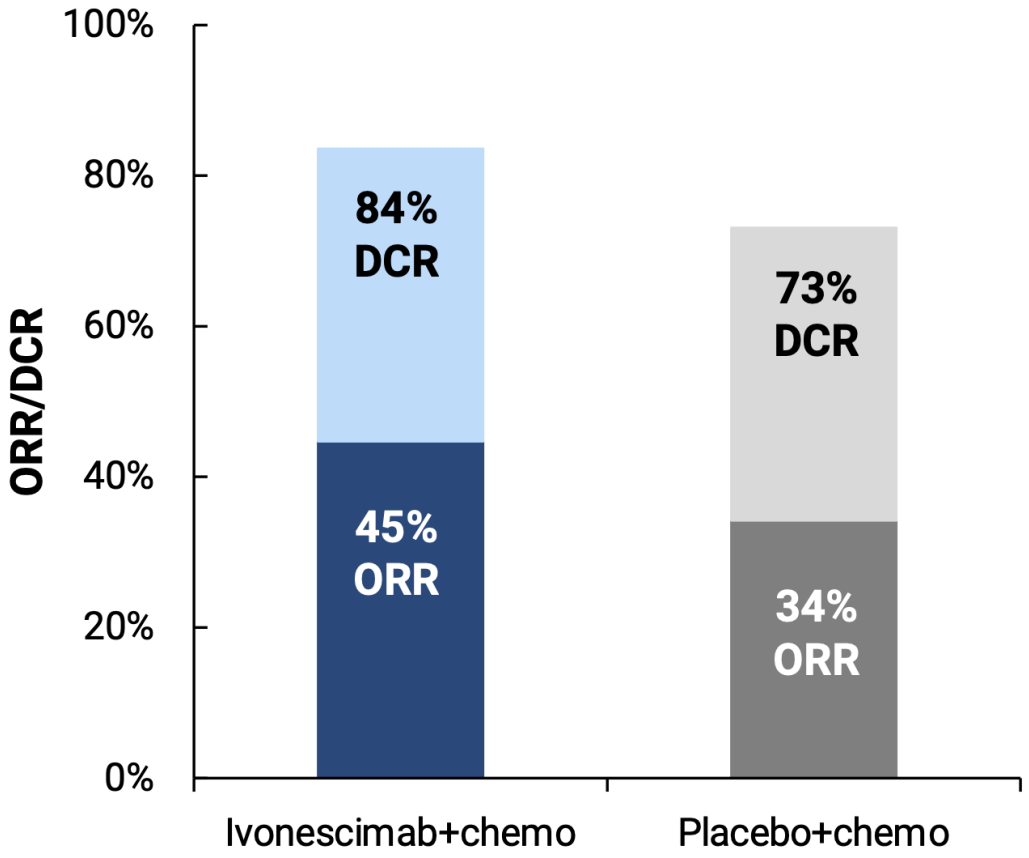
FPI: Jan 2022 (overall)
LPI Asia: Nov 2022
LPI NA & EU (and overall): Oct 2024

Note: Positive outcomes were reported from the single-region (Asia) study HARMONi-A, with PFS as the primary endpoint.

DoR=duration of response; ECOG=eastern cooperative oncology group; EGFR= Epidermal growth factor receptor; EU=Europe; FPI=first patient in; IRRC= independent radiology review committee; LPI=last patient in; mets=metastases; NA=North America; ORR=overall response rate; OS=overall survival; NSCLC=non-small cell lung cancer; TKI=tyrosine kinase inhibitor; PD-L1= programmed cell death ligand; PFS=progression-free survival; Q3W=every 3 weeks; RECIST=response evaluation criteria in solid tumors.

Goldman J et al. WCLC 2025;Abstract PL02.12.

HARMONi: Response Data

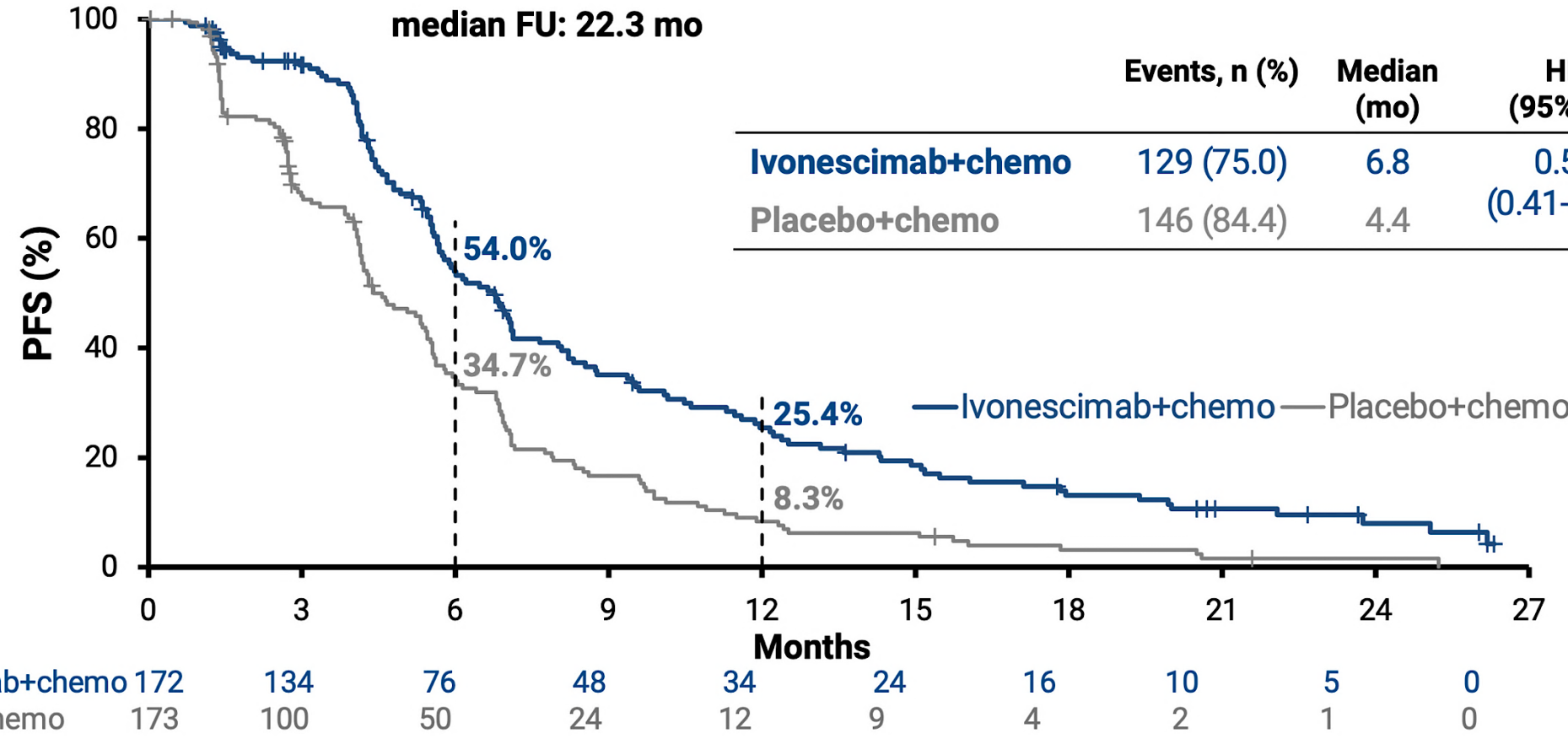


DoR (mo)	Ivonescimab + chemo	Placebo + chemo
n	98	75
Median (95% CI)	**7.6** (5.5-10.6)	**4.2** (2.9-4.7)

ORR = overall response rate

Goldman J et al. WCLC 2025;Abstract PL02.12.

HARMONi: PFS Outcomes

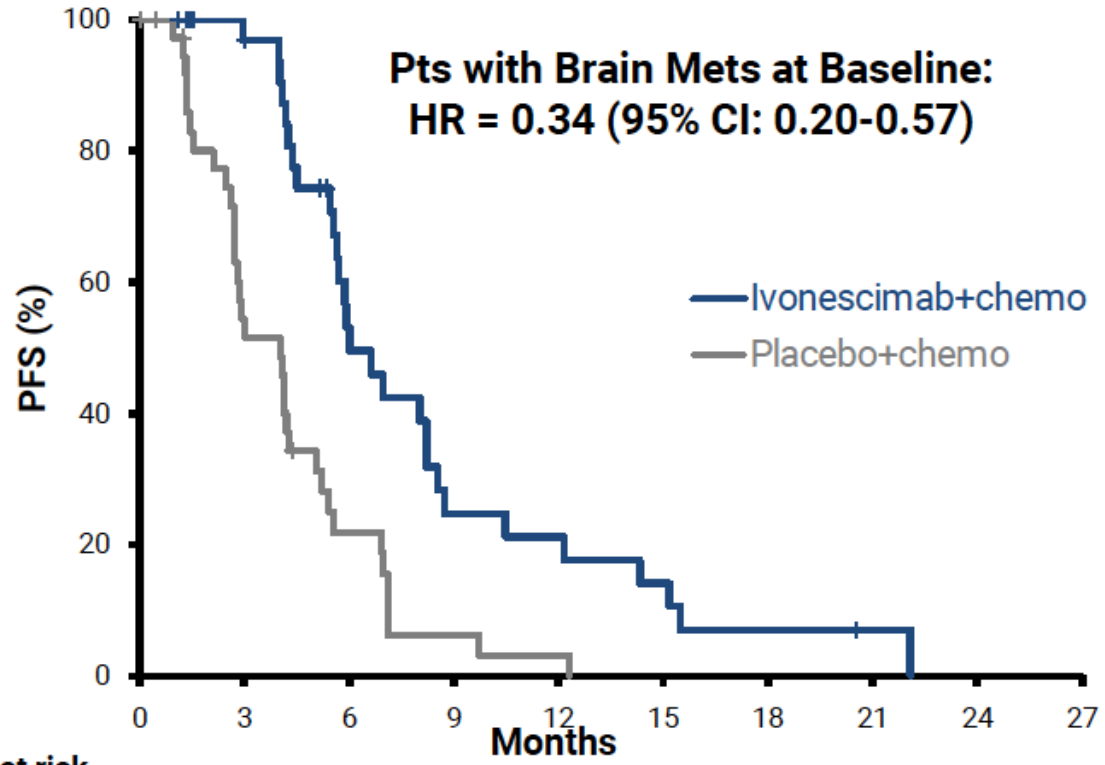


	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab+chemo	129 (75.0)	6.8	0.52 (0.41-0.66)	<0.0001
Placebo+chemo	146 (84.4)	4.4		

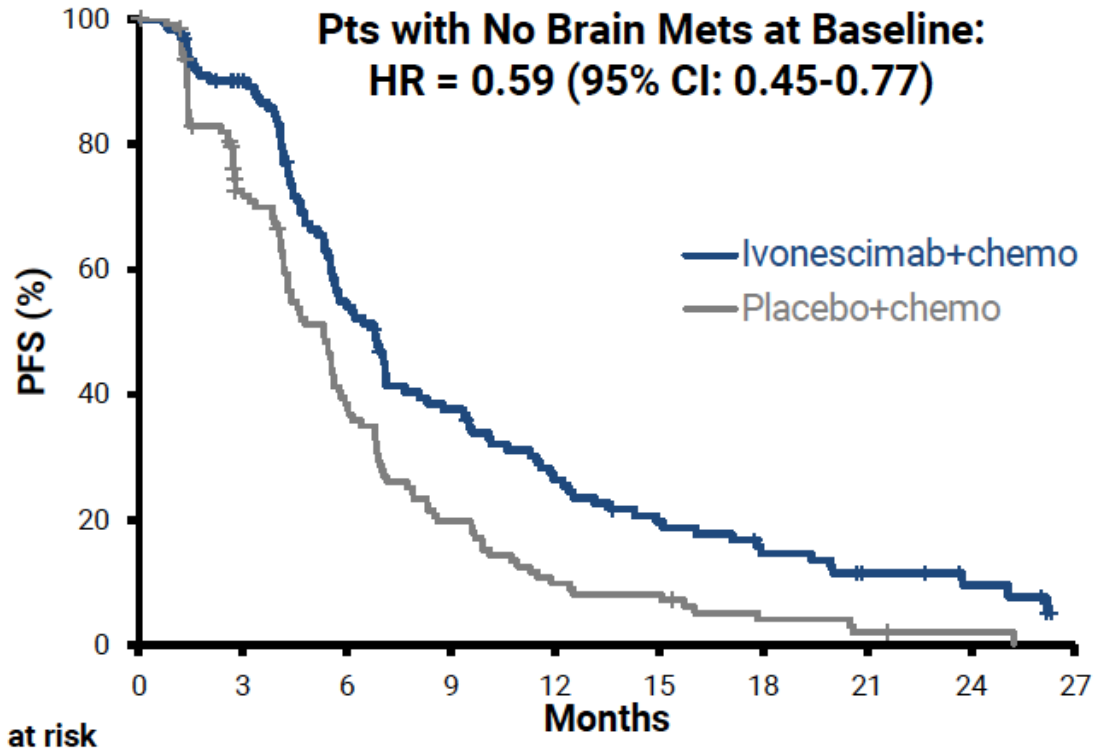
Consistent PFS benefit by investigator: HR = 0.58 (95% CI: 0.45-0.73)

Goldman J et al. WCLC 2025;Abstract PL02.12.

HARMONi: PFS by Brain Metastases Status



No. at risk									
Ivonescimab +chemo	41	30	15	7	6	4	2	1	0
Placebo +chemo	42	19	7	2	1	0			

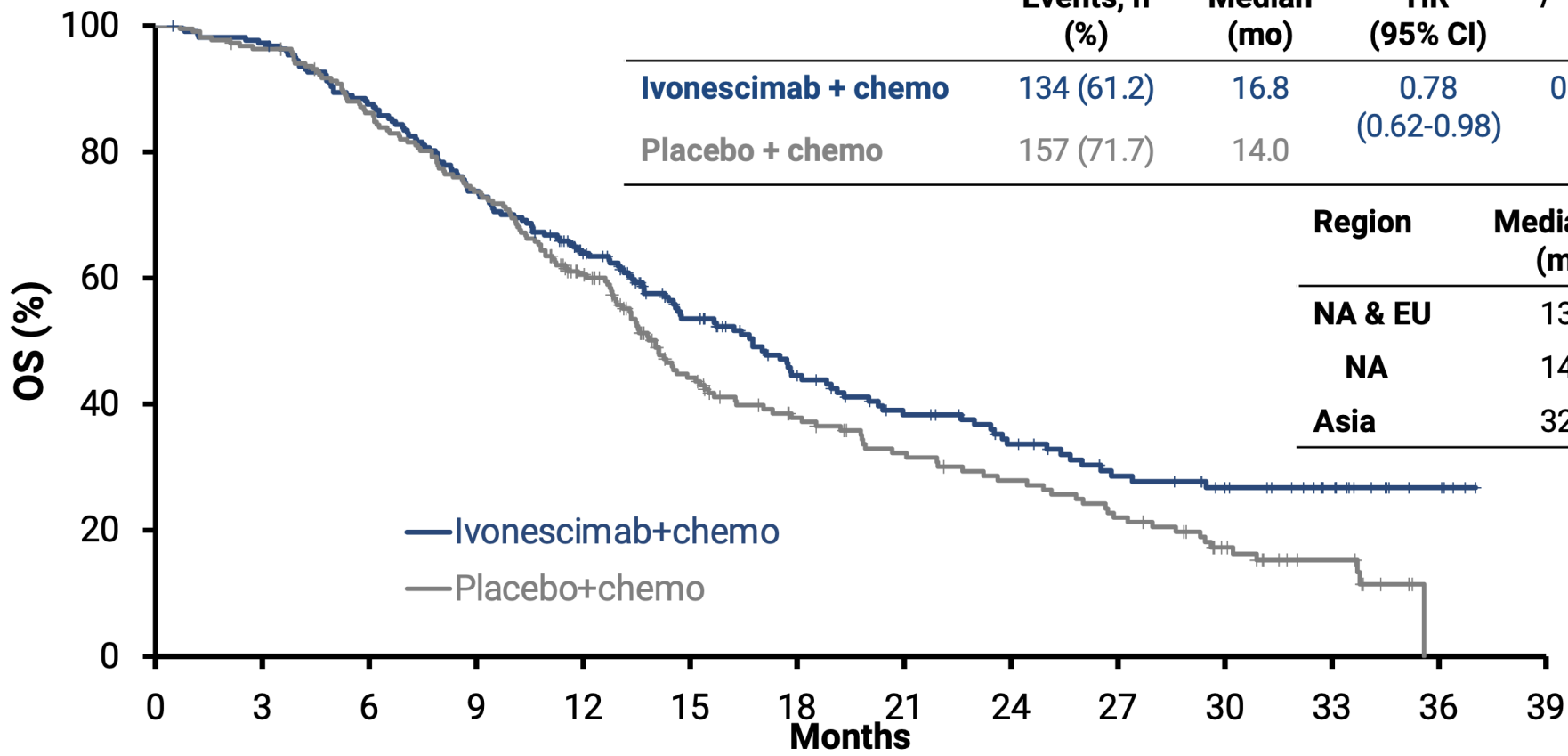


No. at risk										
Ivonescimab +chemo	131	104	61	41	28	20	14	9	5	0
Placebo +chemo	131	81	43	22	11	9	4	2	1	0

Goldman J et al. WCLC 2025;Abstract PL02.12.

HARMONi: OS Outcomes

OS stable with longer term Western data, nominal p=0.0332



	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab + chemo	134 (61.2)	16.8	0.78 (0.62-0.98)	0.0332
Placebo + chemo	157 (71.7)	14.0		

Region	Median FU (mo)	Median OS (mo)
NA & EU	13.7	17.0 vs. 14.0
NA	14.6	NR vs. 14.0
Asia	32.7	16.7 vs. 14.0

Data cutoff
NA&EU: Sep 2025
Asia: Apr 2025

No. at risk

Ivonescimab+chemo	219	212	190	160	127	92	68	53	43	33	26	16	5	0
Placebo+chemo	219	210	186	159	119	74	56	45	38	30	18	9	0	

Goldman J et al. WCLC 2025;Abstract PL02.12.

FDA Acceptance of Biologics License Application Seeking Approval for Ivonescimab in Combination with Chemotherapy in the Treatment of EGFR-Mutated NSCLC After Tyrosine Kinase Inhibitor Therapy

Press Release: January 29, 2026

"The US Food & Drug Administration (FDA) has accepted for filing a Biologics License Application (BLA) seeking approval for ivonescimab in combination with chemotherapy in patients with epidermal growth factor receptor (EGFR)-mutated locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) post-tyrosine kinase inhibitor (TKI) therapy.

The FDA provided a Prescription Drug User Fee Act (PDUFA) goal action date of **November 14, 2026**.

The BLA was submitted based on the overall results of the Phase III HARMONi trial, which evaluated ivonescimab plus platinum-doublet chemotherapy compared to placebo plus platinum-doublet chemotherapy in patients with EGFR-mutated, locally advanced or metastatic NSCLC who were previously treated with a 3rd generation EGFR TKI."

https://smmttx.com/news/press-releases/news-details/2026/Summit-Therapeutics-Announces-U-S--FDA-Acceptance-of-Biologics-License-Application-BLA-Seeking-Approval-for-Ivonescimab-in-Combination-with-Chemotherapy-in-Treatment-of-Patients-with-EGFRm-NSCLC-Post-TKI-Therapy/default.aspx

RTP RESEARCH TO PRACTICE

Do you believe VEGF inhibition yields enhanced antitumor activity in EGFR-mutant NSCLC relative to EGFR wild-type disease?

 Dr Baik	Yes
 Dr Goldman	Yes
 Dr Paik	Yes
 Prof Passaro	I'm not sure
 Dr Piotrowska	Yes
 Dr Rotow	No

Do you believe the risk-benefit ratio with ivonescimab/chemotherapy in previously treated EGFR-mutated NSCLC supports its clinical use?

 Dr Baik	Yes, for select patients for whom chemotherapy makes sense
 Dr Goldman	Yes
 Dr Paik	I'm not sure
 Prof Passaro	Yes
 Dr Piotrowska	I'm not sure
 Dr Rotow	Yes

Would you like to be able to access ivonescimab/chemotherapy today for your patients with previously treated EGFR-mutated NSCLC?

 Dr Baik	No
 Dr Goldman	Yes
 Dr Paik	I’m not sure
 Prof Passaro	Yes
 Dr Piotrowska	Yes
 Dr Rotow	Yes

In what line of therapy do you envision ivonescimab/chemotherapy will be employed for patients with EGFR-mutated NSCLC?

 Dr Baik	Third line or later
 Dr Goldman	Second line and beyond, but most likely in third line
 Dr Paik	Probably around fourth line
 Prof Passaro	Second-line setting
 Dr Piotrowska	Possibly in second line for patients with a smoking history, higher PD-L1 status and limited benefit from EGFR TKIs
 Dr Rotow	Second-line platinum doublet competing with COMPEL and MARIPOSA-2

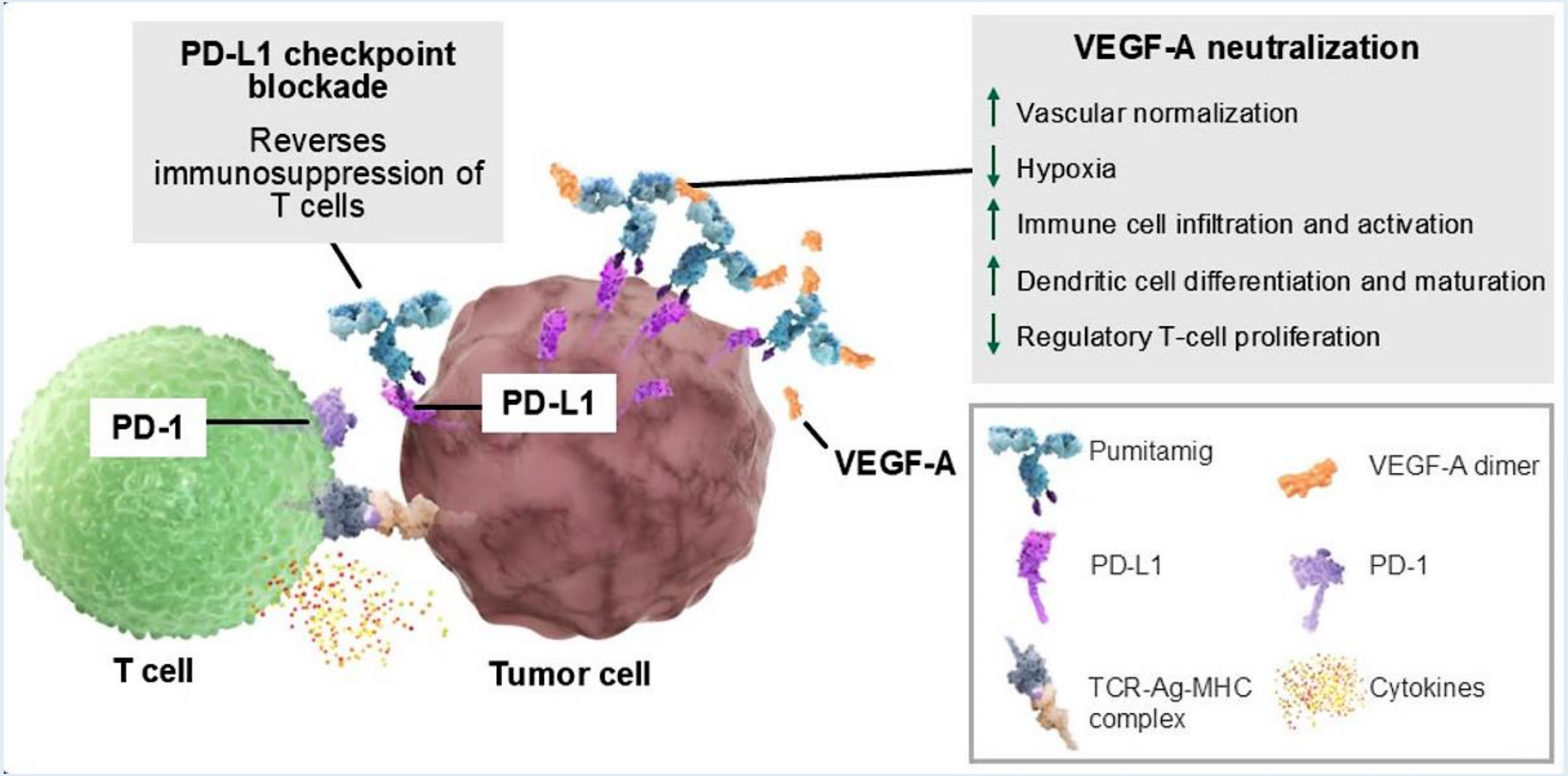
Agenda

Module 1: Ivonescimab for Previously Untreated Metastatic Non-Small Cell Lung Cancer (mNSCLC)

Module 2: Ivonescimab for Relapsed/Refractory EGFR-Mutated mNSCLC

Module 3: Other Novel PD-1/PD-L1 x VEGF Bispecific Antibodies Under Investigation

Pumitamig: Mechanism of Action



Peters S et al. ASCO 2026;Abstract 8513.

2026 ASCO ANNUAL MEETING

Abstract 8513

ROSETTA LUNG-02

Phase 2 data from ROSETTA Lung-02

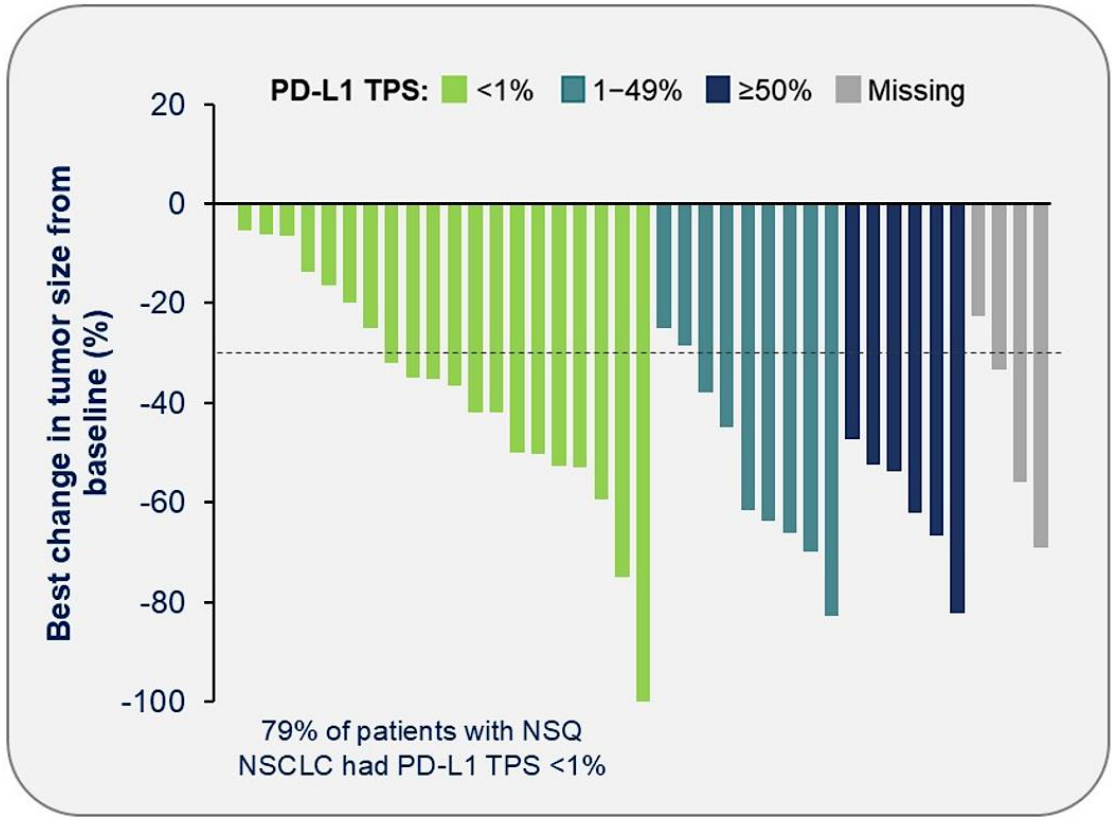
A global, randomized, phase 2/3 trial of pumitamig (PD-L1 × VEGF-A bsAb) + chemotherapy in 1L NSCLC

Solange Peters,[1] Youngjoo Lee,[2] Mustafa Erman,[3] Stephen V. Liu,[4] Benjamin Solomon,[5] Terufumi Kato,[6] Shun Lu,[7] Sanjay Popat,[8] Ulug Mutlu Gunaydin,[9] René Bartz,[10] Vikesh Patel,[11] Kevin Tsai,[9] Li Li,[9] Uchechukwu Dimkpa,[10] Claudia-Nanette Gann,[10] Aurora O'Brate,[12] Ilhan Celik,[10] Özlem Türeci,[10] Ugur Sahin,[10] Byoung Chul Cho[13]

RTP RESEARCH TO PRACTICE

ROSETTA Lung-02: Response Data

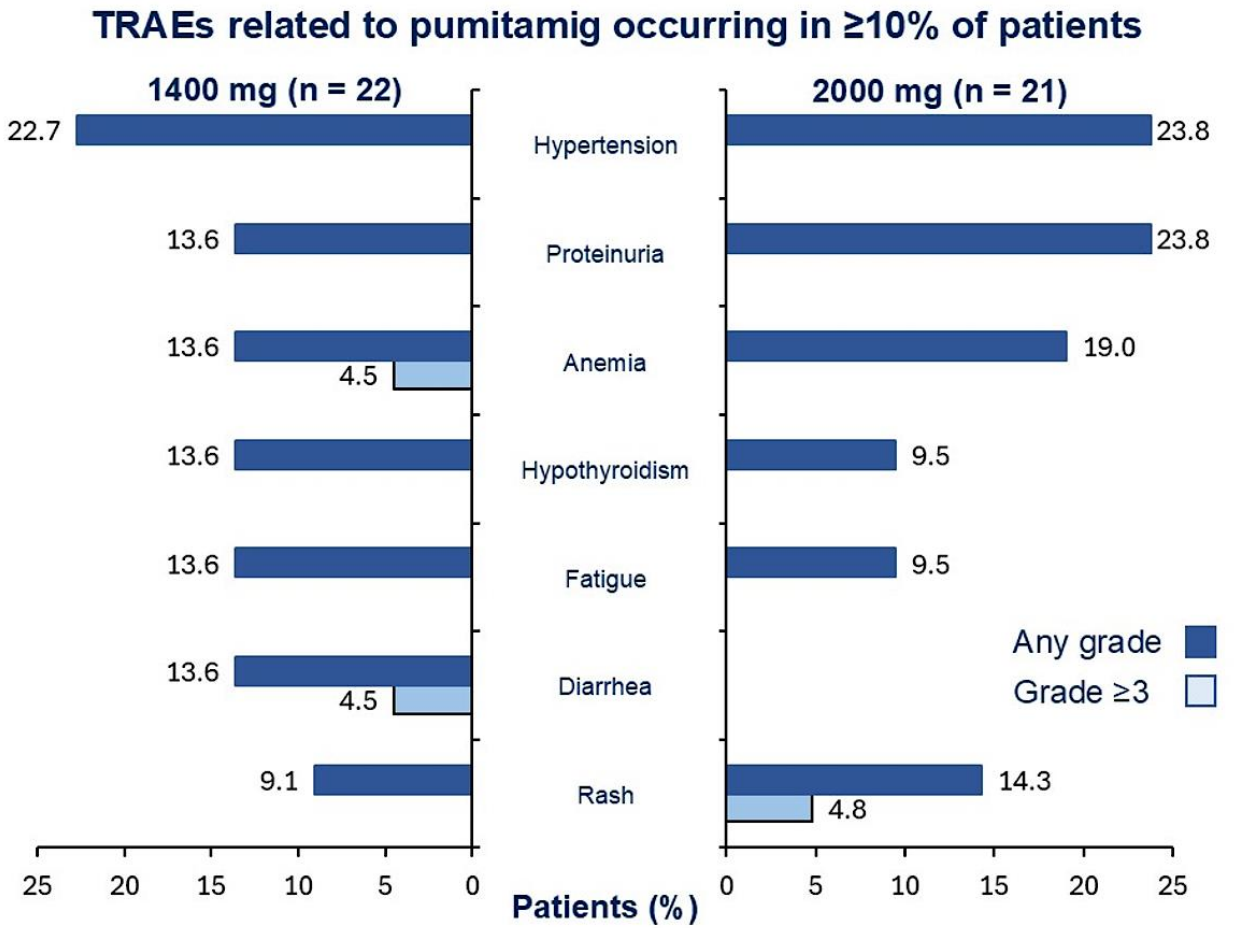
	Overall NSCLC (NSQ + SQ)				
	TPS <1% (n = 21)	TPS 1–49% (n = 9)	TPS ≥50% (n = 6)	Missing* (n = 4)	Overall (N = 40)
uORR, % (95% CI)	61.9 (38.4–81.9)	77.8 (40.0–97.2)	100.0 (54.1–100.0)	75.0 (19.4–99.4)	72.5 (56.1–85.4)
cORR, % (95% CI)	**47.6** (25.7–70.2)	77.8 (40.0–97.2)	100.0 (54.1–100.0)	50.0 (6.8–93.2)	62.5 (45.8–77.3)
cBOR, n (%)					
CR	0	1 (11.1)	0	0	1 (2.5)
PR	10 (47.6)	6 (66.7)	6 (100.0)	2 (50.0)	24 (60.0)
SD	11 (52.4)	2 (22.2)	0	2 (50.0)	15 (37.5)



Peters S et al. ASCO 2026;Abstract 8513.

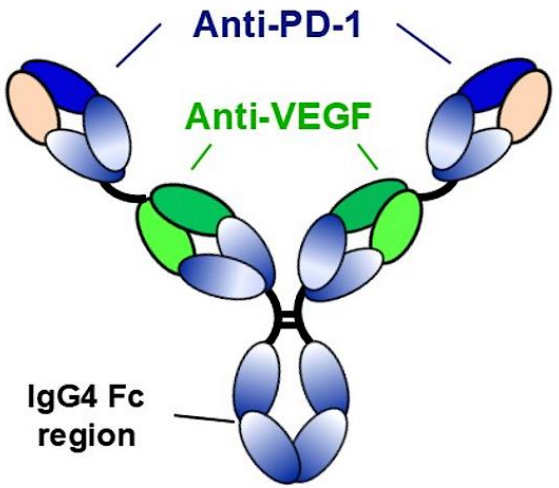
ROSETTA Lung-02: Safety Summary

	NSQ (n = 22)	SQ (n = 21)	Overall (N = 43)
Any TRAE, n (%)	19 (86.4)	21 (100.0)	40 (93.0)
Grade ≥3	8 (36.4)	13 (61.9)	21 (48.8)
Pumitamig-related TRAE, n (%)	14 (63.6)	19 (90.5)	33 (76.7)
Grade ≥3	4 (18.2)	6 (28.6)	10 (23.3)
TRAE leading to discontinuation, n (%)	3 (13.6)	5 (23.8)	8 (18.6)
Pumitamig-related	1 (4.5)	3 (14.3)	4 (9.3)
TRAE leading to death, n (%)	0	1 (4.8)*	1 (2.3)*
Pumitamig-related	0	1 (4.8)*	1 (2.3)*
Any irAE TEAE , n (%)	8 (36.4)	8 (38.1)	16 (37.2)
Grade ≥3	1 (4.5)	1 (4.8)	2 (4.7)
VEGF-related TEAEs, n (%)	10 (45.5)	14 (66.7)	24 (55.8)
Grade ≥3	1 (4.5)	1 (4.8)	2 (4.7)
Hemorrhage/bleeding TEAEs, n (%)	2 (9.1)	7 (33.3)	9 (20.9)
Grade ≥3	0	1 (4.8)‡	1 (2.3)‡



Peters S et al. ASCO 2026;Abstract 8513.

SSGJ-707 (PF-08634404) Mechanism of Action



PF-08634404

Bispecific Antibody with Unique Tetravalent Structure:

VEGF and PD-1 binding arms in linear, stacked orientation

Simultaneous Binding of PD-1 and VEGF Amplifies Therapeutic Potential Through:

Cooperative binding and Improved PD-1 Inhibition[1]

In the presence of VEGF, PF'4404 forms multimers to enhance binding and inhibition of PD-1

Augmented VEGF Inhibition[1]

Functionally enhanced VEGF Fab arm normalizes tumor vasculature and reduces VEGF-related immune suppression

IgG4 backbone[2,3]

IgG4 backbone is consistent with approved anti-PD-1 therapeutics

Wu L et al. ASCO 2026;Abstract 8514.

Abstract 8514

2026 ASCO ANNUAL MEETING

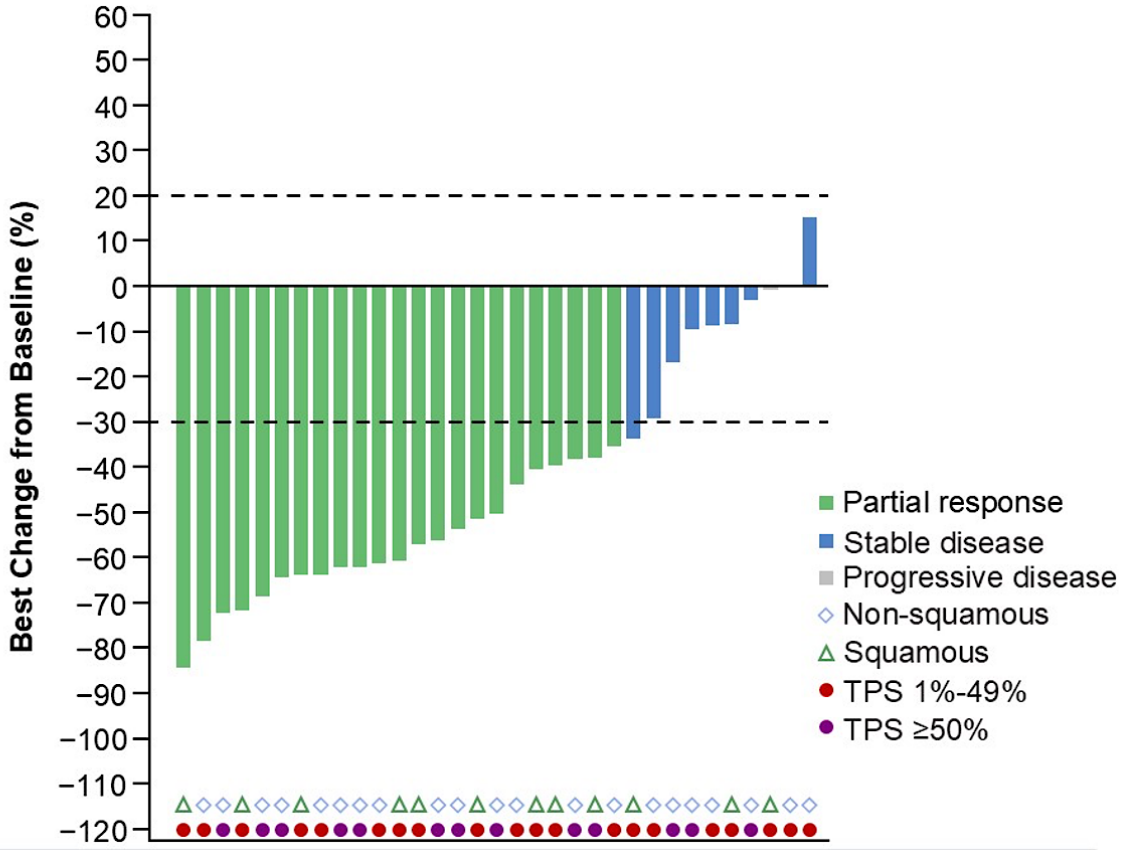
A phase 2 trial of PF-08634404 (SSGJ-707), a PD-1/VEGF bispecific antibody, as monotherapy in patients with advanced non-small cell lung cancer: updated results

Lin Wu,[1] Jun Yao,[2] Yulan Sun,[3] Ruoyu Wang,[4] Xiang Li,[4] Bolin Chen,[1] Qian Chu,[5] Qing Bu,[6] Yong Fang,[7] Jun Zhao,[8] Weizhen Huang,[9] Jin Zhou,[10] Qiming Wang,[11] Jie Li,[12] Yongzhong Luo,[1] Yan Yu,[13] Michael Burns,[14] Tienan Yi[15]

A Phase II Study of SSGJ-707 (PF-08634404) Monotherapy for PD-L1-Positive mNSCLC – Response Data

Endpoint	10 mg/kg (n=34)
Confirmed ORR, % (95% CI)	**67.6** (49.5-82.6)
Best overall response, n (%)	
Partial response	23 (67.6)
Stable disease	10 (29.4)
Progressive disease	1 (2.9)
Disease control rate, % (95% CI)	**97.1** (84.7-99.9)
Duration of response, median (95% CI), months	**18.0** (10.9-NE)

CI, confidence interval; cORR, confirmed objective response rate; NE, not estimable; Q3W, every 3 weeks; TPS, tumor proportion score.

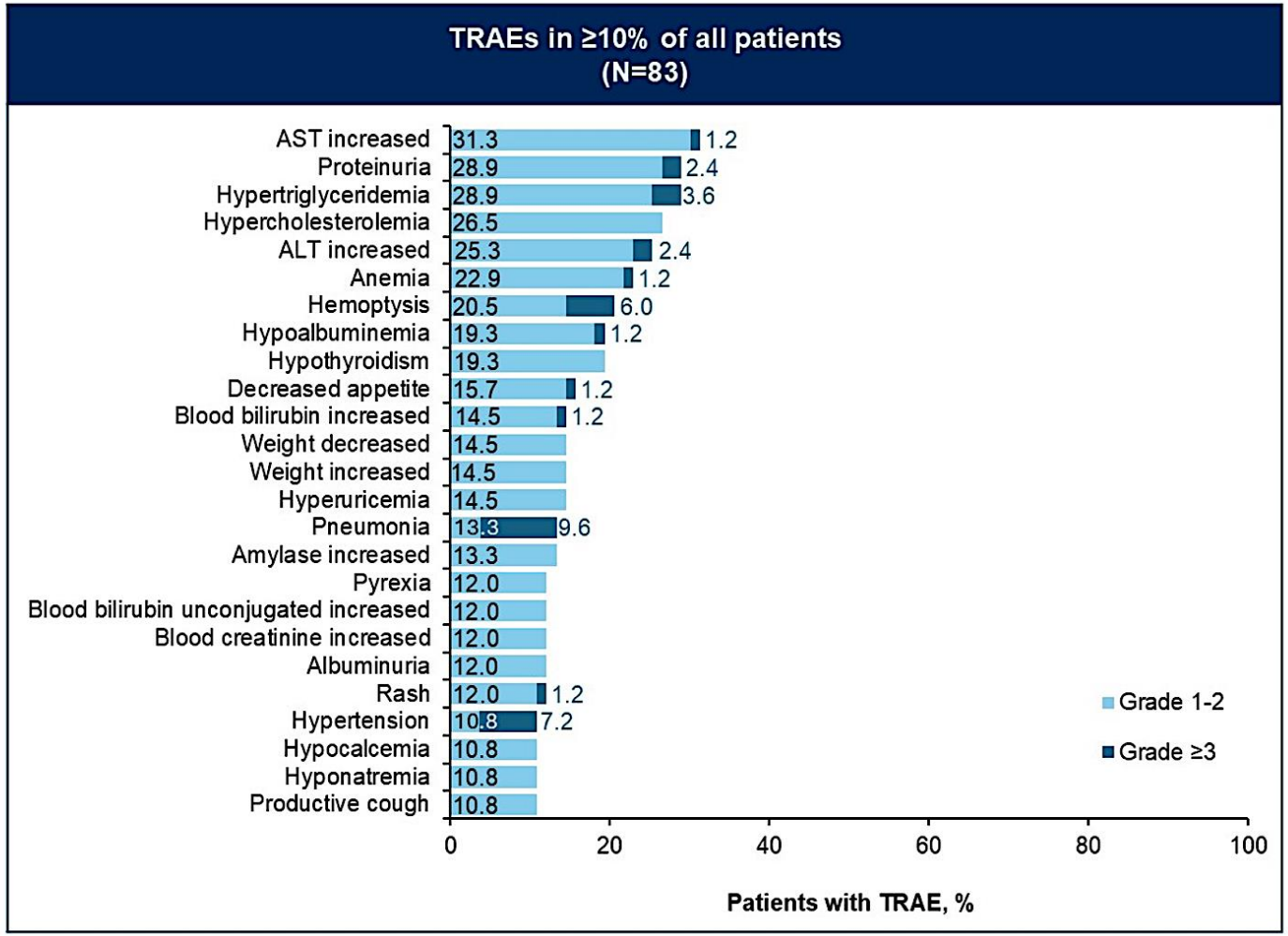


Wu L et al. ASCO 2026;Abstract 8514.

A Phase II Study of SSGJ-707 (PF-08634404) Monotherapy for PD-L1-Positive mNSCLC – Safety Summary

	All patients (N=83)	10 mg/kg (n=34)
TRAEs, n (%)[a]		
Any grade	77 (92.8)	34 (100)
Grade ≥3	36 (43.4)	15 (44.1)
Grade 5	2 (2.4)[b]	0
SAE	31 (37.3)	10 (29.4)
Leading to discontinuation	7 (8.4)[c]	1 (2.9)[d]
VEGF-related AEs, n (%)[e]		
Any grade	52 (62.7)	25 (73.5)
Grade ≥3	15 (18.1)	5 (14.7)
irAEs, n (%)[f]		
Any grade	32 (38.6)	17 (50.0)
Grade ≥3	7 (8.4)	2 (5.9)[g]

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; irAE, immune-related adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; VEGF, vascular endothelial growth factor.
[a]Defined as a TEAE that was "related" to PF'4404, "most possibly related" to PF'4404, or "possibly related" to PF'4404, or for which relationship to PF'4404 was missing. [b]Grade 5 TRAEs consisted of hemoptysis (n=1) and death from unknown cause (n=1). No grade 4 events occurred. [c]Hemoptysis (n=4), pneumonia (n=1), increased alanine transferase (n=1), diabetic ketoacidosis (n=1). [d]Hemoptysis. [e]Defined as gastrointestinal perforation and fistula, hemorrhage, thromboembolic event, hypertension, or proteinuria. [f]Defined as any TEAE that was potentially immune mediated and categorized as "related," "most possibly related," or "possibly related" to PF'4404. [g]Abnormal hepatic function (n=1), rash (n=2)



Wu L et al. ASCO 2026;Abstract 8514.

Thank you for your attention!

Questions?

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