HARMONi-6

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

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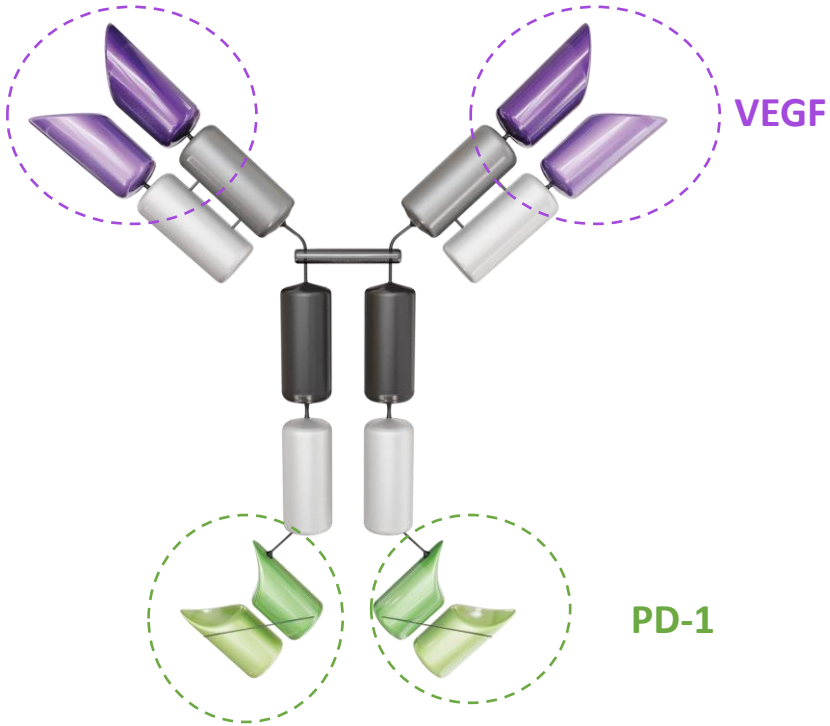
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Ivonescimab is an investigational therapy not presently approved by any regulatory authority other than China's National Medical Products Administration (NMPA).

Key takeaway points HARMONi-6

Ivonescimab is the first PD-1/VEGF dual-target bispecific antibody approved in China

Ivonescimab plus chemotherapy significantly improved overall survival (OS) in previously untreated advanced squamous NSCLC compared with tislelizumab plus chemotherapy, with a manageable safety profile



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Background

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- For patients with advanced squamous NSCLC, PD-(L)1 inhibitor plus chemotherapy is an established first-line regimen, however few studies were powered for OS and reported significant improvement
- HARMONi-6 (NCT05840016) is a randomized phase 3 study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy in patients with advanced squamous NSCLC
  - In the interim analysis of progression-free survival (PFS), ivonescimab plus chemotherapy significantly improved PFS (median PFS, 11.1 vs 6.9 months; P<0.0001)[1]
- Can the bispecific antibody-based regimen significantly improve overall survival (OS)? Here, we report results from the prespecified OS interim analysis of HARMONi-6

Abbreviations: NSCLC, non-small cell lung cancer; OS, overall survival; PD-(L)1, programmed death-(ligand) 1.

[1]Chen Z, et al. Lancet. 2026 Jan 17;407(10525):226.

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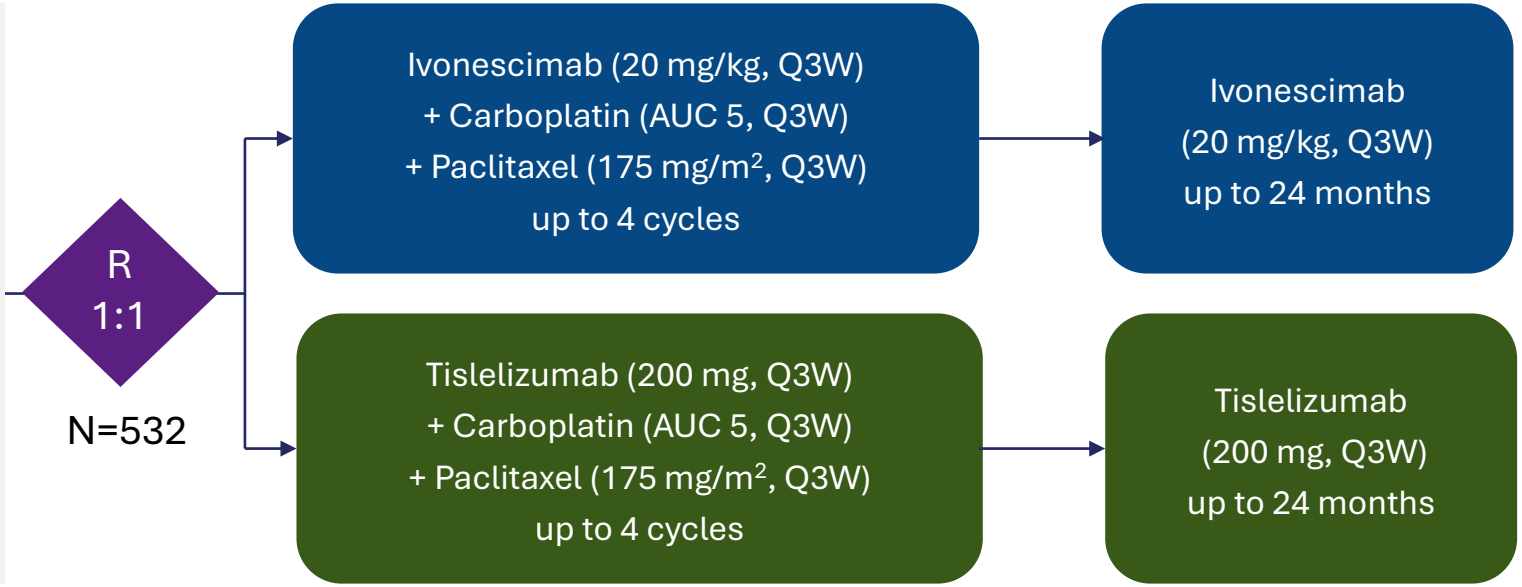
Study Design

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A multicenter, randomized, double-blind, parallel-controlled phase III study

Key Eligibility Criteria

- Pathologically confirmed sq-NSCLC
- Stage IIIB-IV
- No prior systemic therapy
- No EGFR mutations or ALK rearrangements
- ECOG PS 0 or 1



Stratification Factors:

- Stage: IIIB/IIIC vs. IV
- PD-L1 TPS: ≥1% vs. <1%

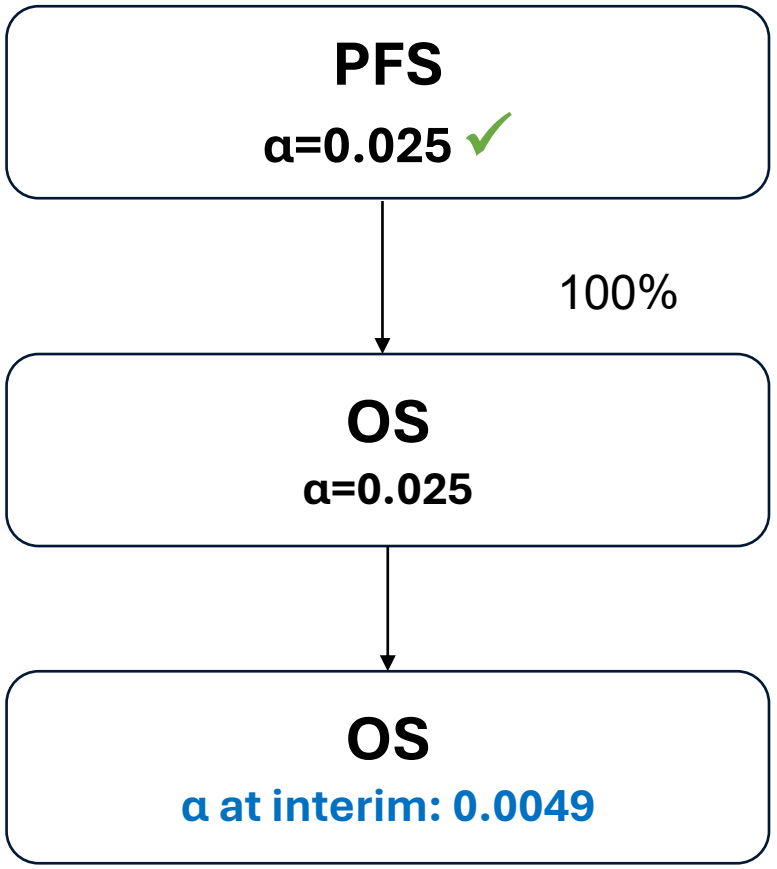
Endpoints:

- **Primary endpoint: PFS by IRRC per RECIST v1.1**
- Key secondary endpoint: OS
- Secondary endpoints: PFS by INV, ORR, DCR, DoR, TTR and safety

Abbreviations: ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance score; R, randomization; AUC, area under the curve; Q3W, every three weeks; IRRC, independent radiology review committee; RECIST v1.1, response evaluation criteria in solid tumors version 1.1; PFS, progression-free survival; OS, overall survival; INV, investigator; ORR, overall response rate; DCR, disease control rate; DoR, duration of response; TTR, time to response.

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Statistical Considerations



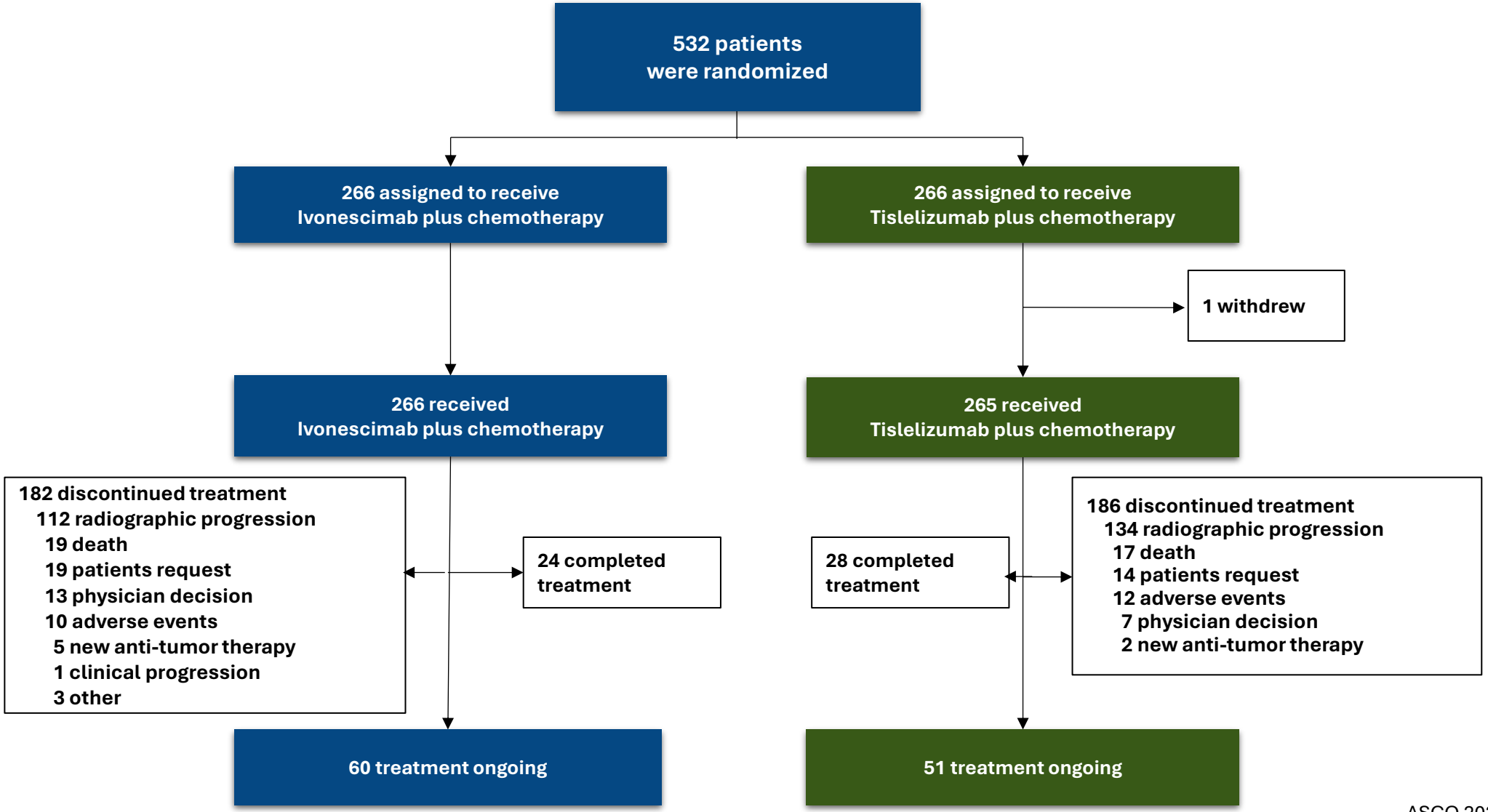
- Hierarchical testing was applied with PFS tested first, followed by OS at a one-sided α=0.025
- PFS was statistically significant at interim analysis (mPFS 11.1 vs 6.9 months; HR 0.60 [95% CI 0.46–0.78]; p<0.0001; boundary 0.0094), enabling formal OS testing
- The prespecified interim OS analysis was conducted at 204 events (boundary 0.0049)

Abbreviations: CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; OS, overall survival.

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Patient Disposition

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Baseline Characteristics

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Characteristics, n(%)		Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
Age, years	< 65	135 (50.8)	139 (52.3)
	≥ 65	131 (49.2)	127 (47.7)
Sex	Male	256 (96.2)	238 (89.5)
	Female	10 (3.8)	28 (10.5)
ECOG PS*	0	42 (15.8)	42 (15.8)
	1	224 (84.2)	222 (83.5)
Smoking history	Never	21 (7.9)	37 (13.9)
	Current/Former	245 (92.1)	229 (86.1)
Disease stage	IIIB/IIIC	21 (7.9)	20 (7.5)
	IV	245 (92.1)	246 (92.5)
Tumor characteristics	Central type	178 (66.9)	158 (59.4)
	Major blood vessel encasement	49 (18.4)	44 (16.5)
	With cavity	24 (9.0)	23 (8.6)
	With hemoptysis history	86 (32.3)	79 (29.7)
PD-L1 TPS	<1%	105 (39.5)	105 (39.5)
	≥ 1%	161 (60.5)	161 (60.5)
	1-49%	112 (42.1)	99 (37.2)
	≥ 50%	49 (18.4)	62 (23.3)
Metastases sites	≥3 metastatic sites	42 (15.8)	39 (14.7)
	Liver metastases	28 (10.5)	45 (16.9)
	Brain metastases	9 (3.4)	17 (6.4)

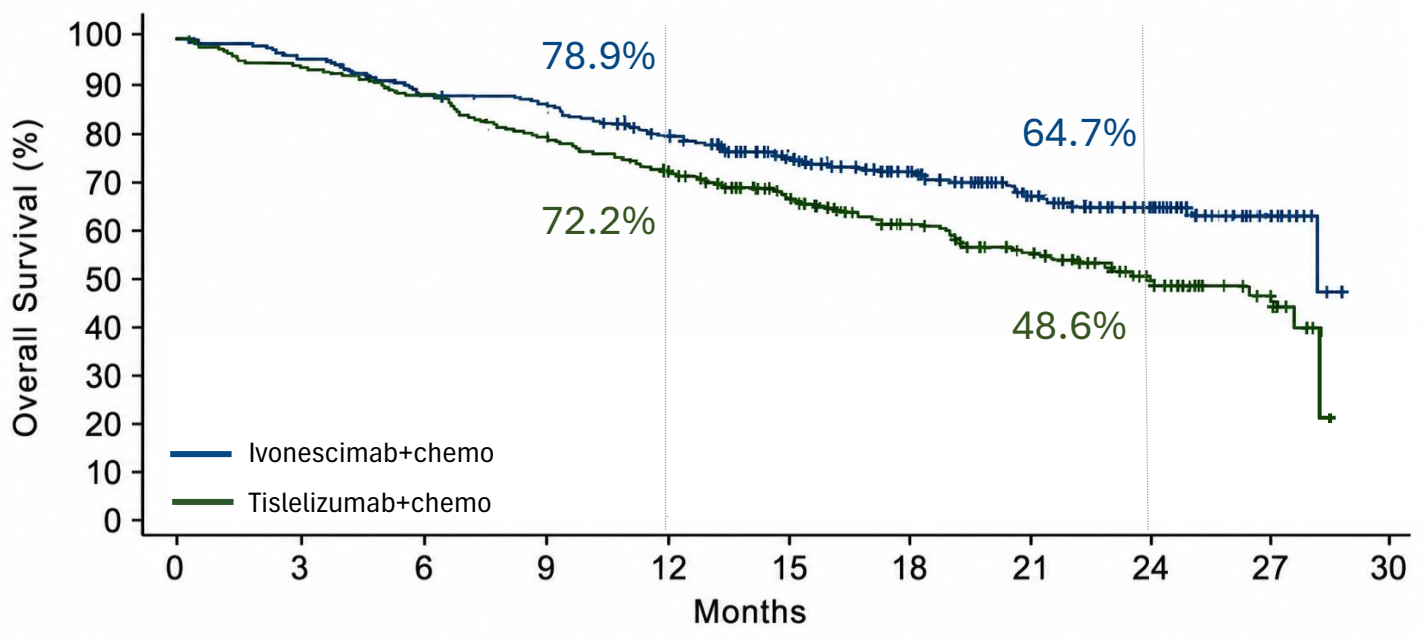
*Two patients' ECOG PS were missing in the tislelizumab plus chemotherapy arm.

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Overall Survival (interim analysis)

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Ivonescimab with chemotherapy significantly improved OS



No. at risk (censored)

Ivonescimab +Chemo	266(0)	252(0)	238(0)	224(0)	202(8)	152(46)	119(73)	85(100)	49(135)	15(168)	0(182)
Tislelizumab +Chemo	266(0)	257(0)	238(0)	211(0)	186(6)	142(36)	113(55)	80(77)	43(107)	12(136)	0(146)

	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

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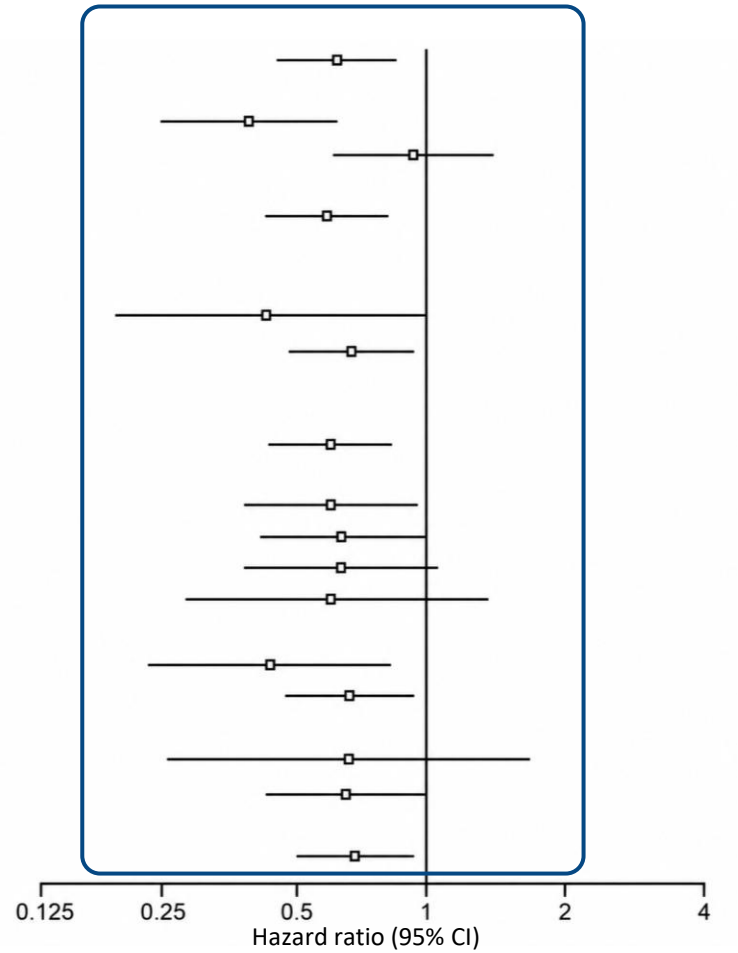
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Subgroup Analysis of Overall Survival

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OS benefit was consistent across key subgroups

Charecteristic	Ivonescimab+chemo	Tislelizumab+chemo	Hazard ratio (95% CI)
	Events/Number of subjects	Events/Number of subjects	
Overall Age, Years	84/266	120/266	0.66 (0.50, 0.87)
<65	31/135	63/139	0.43 (0.28, 0.67)
≥65	53/131	57/127	0.93 (0.64, 1.36)
Sex			
Male	79/256	110/238	0.63 (0.47, 0.84)
Female	5/10	10/28	
ECOG PS			
0	10/42	21/42	0.47 (0.22, 0.99)
1	74/224	99/222	0.71 (0.52, 0.96)
Disease Stage			
IIIB/IIIC	7/21	8/20	
IV	77/245	112/246	0.63 (0.48, 0.86)
PD-L1 TPS			
<1%	39/105	56/105	0.64 (0.43, 0.96)
≥1%	45/161	64/161	0.68 (0.46, 0.99)
1 – 49%	32/112	43/99	0.67 (0.42, 1.05)
≥50%	13/49	21/62	0.64 (0.32, 1.31)
≥3 metastases sites			
Yes	18/42	28/39	0.47 (0.26, 0.85)
No	66/224	92/227	0.70 (0.51, 0.97)
Liver metastases			
Yes	11/28	25/45	0.69 (0.34, 1.41)
No	73/238	95/221	0.68 (0.50, 0.92)
Brain metastases			
Yes	2/9	12/17	
No	82/257	108/249	0.71 (0.53, 0.95)



Median OS and HR will not be reported for subgroups with fewer than 10 events

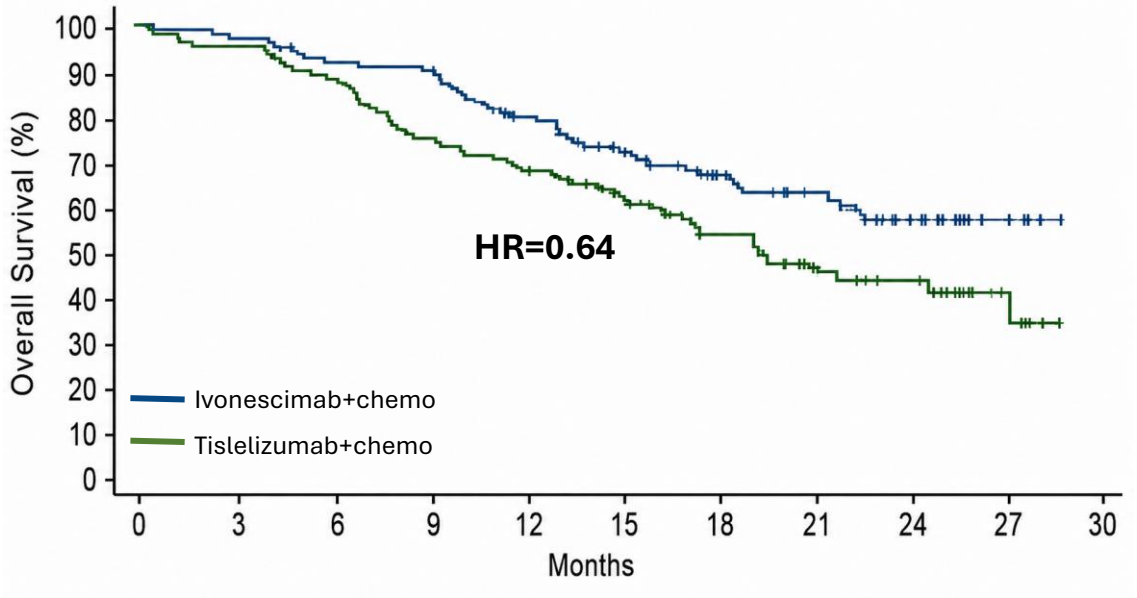
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Overall survival by PD-L1 expression levels

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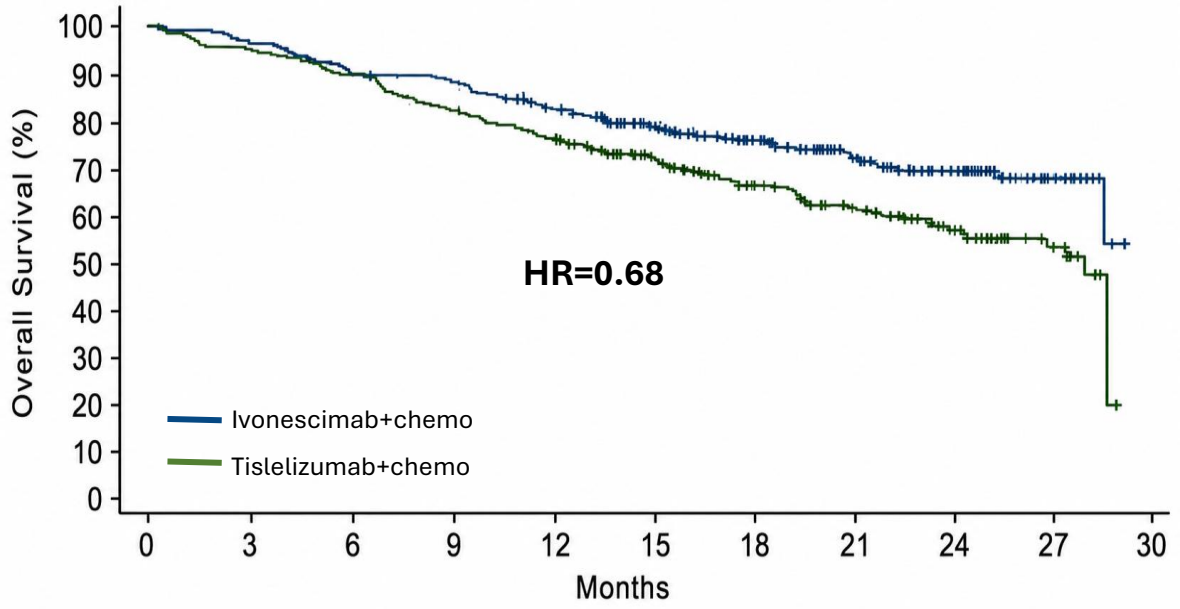
Ivonescimab with chemotherapy showed consistent OS improvement across subgroups stratified by PD-L1 expression levels

PD-L1 TPS<1%



	No. at risk (censored)										
Ivonescimab +Chemo	105(0)	100(0)	97(0)	88(0)	73(6)	54(19)	40(29)	30(37)	12(54)	3(63)	0(66)
Tislelizumab +Chemo	105(0)	101(0)	92(0)	77(0)	69(2)	52(12)	40(18)	25(26)	15(35)	3(46)	0(49)

PD-L1 TPS≥1%



	No. at risk (censored)										
Ivonescimab +Chemo	161(0)	152(0)	141(0)	136(0)	129(2)	98(27)	79(44)	55(63)	37(81)	12(105)	0(116)
Tislelizumab +Chemo	161(0)	156(0)	146(0)	134(0)	117(4)	90(24)	73(37)	55(51)	28(72)	9(90)	0(97)

- The subgroup analysis was descriptive and not formally powered

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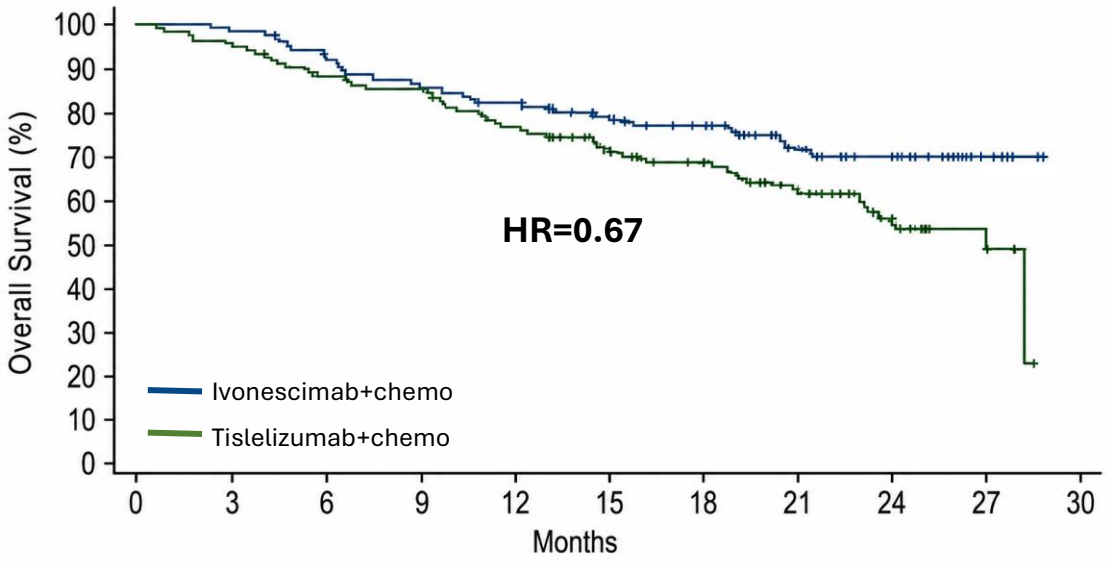
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Overall survival by PD-L1 expression levels

HARMONi-6

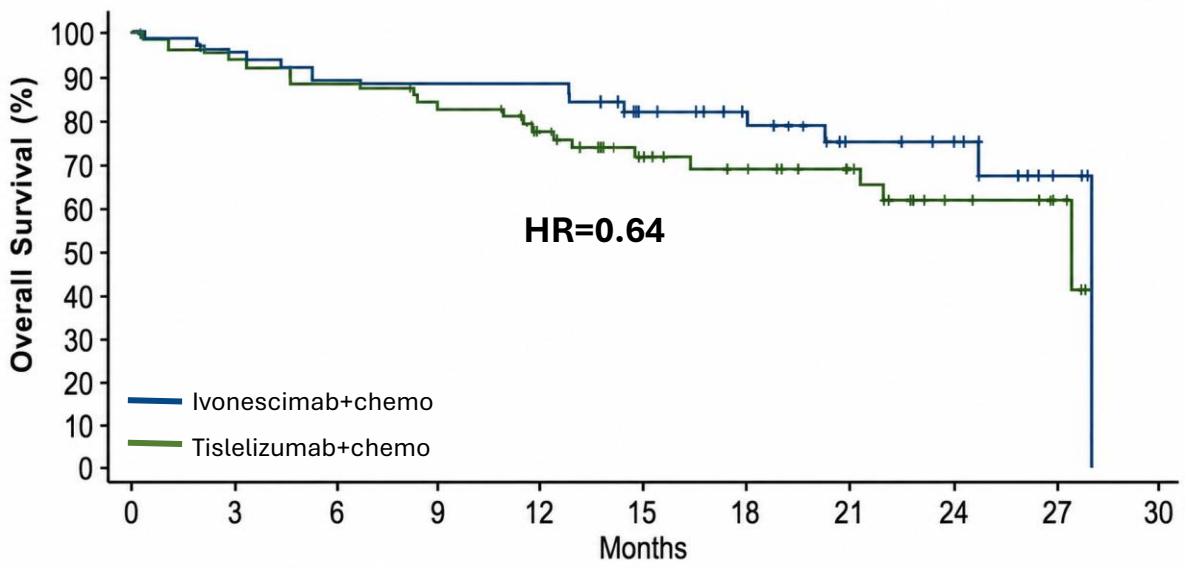
Ivonescimab with chemotherapy showed consistent OS improvement across subgroups stratified by PD-L1 expression levels

PD-L1 TPS 1-49%



	No. at risk (censored)										
Ivonescimab +Chemo	112(0)	106(0)	98(0)	93(0)	86(2)	65(20)	53(31)	38(42)	25(55)	9(71)	0(80)
Tislelizumab +Chemo	99(0)	97(0)	91(0)	83(0)	73(0)	59(10)	48(18)	36(26)	20(38)	5(52)	0(56)

PD-L1 TPS ≥50%



	No. at risk (censored)										
Ivonescimab+ Chemo	49(0)	46(0)	43(0)	43(0)	43(0)	33(7)	26(13)	17(21)	12(26)	3(34)	0(36)
Tislelizumab+ Chemo	62(0)	59(0)	55(0)	51(0)	44(4)	31(14)	25(19)	19(25)	8(34)	4(38)	0(41)

The subgroup analysis was descriptive and not formally powered

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Subsequent anti-tumor therapy

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The subsequent anti-tumor therapy was similar between the two arms

	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
Systemic therapy	**95 (35.7)**	**97 (36.5)**
Chemotherapy	64 (24.1)	60 (22.6)
Immunotherapy	**37 (13.9)**	**51 (19.2)**
Targeted therapy	33 (12.4)	46 (17.3)
Traditional Chinese Medicine	12 (4.5)	14 (5.3)
ADC	12 (4.5)	15 (5.6)
Blinded Investigational Agents Therapy	2 (0.8)	6 (2.3)
Other	3 (1.1)	2 (0.8)
Surgery	3 (1.1)	1 (0.4)
Radiotherapy	25 (9.4)	26 (9.8)

- Data are n (%)
- # immune-related adverse events were assessed by investigators

Abbreviation: TRAE, treatment-related adverse events.

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Safety Summary

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Ivonescimab plus chemotherapy showed a manageable safety profile in squamous NSCLC

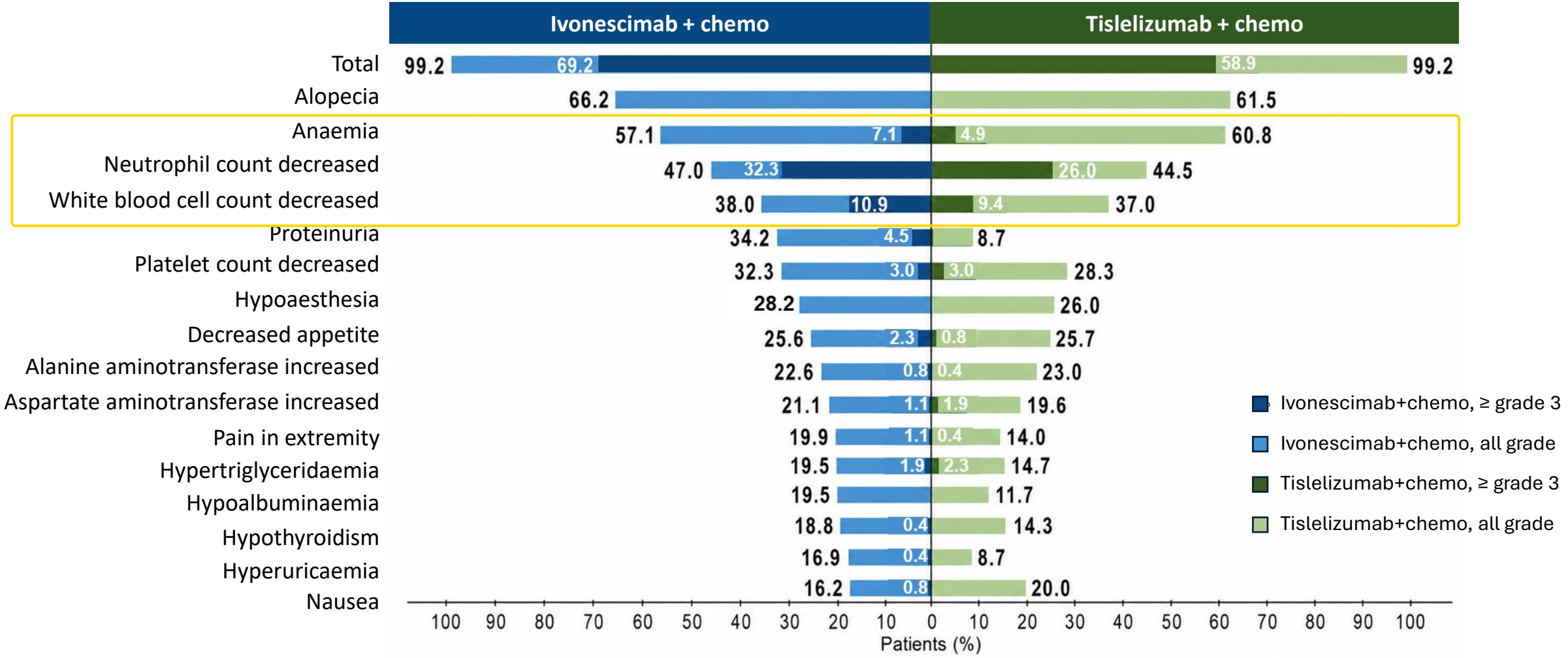
	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=265)
TRAE	264 (99.2)	263 (99.2)
Grade ≥ 3 TRAE	184 (69.2)	156 (58.9)
Serious TRAE	110 (41.4)	91 (34.3)
Leading to ivonescimab or tislelizumab discontinuation	14 (5.3)	12 (4.5)
Leading to death	10 (3.8)	11 (4.2)
Grade ≥ 3 irAE#	34 (14)	36 (14)

- Data are n (%)
- # immune-related adverse events were assessed by investigators

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Most common TRAEs (incidence ≥15%)



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Possibly VEGF-related adverse events

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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 (%)

Abbreviation: VEGF, vascular endothelial growth factor; AEs, adverse events; irAEs, immune-related adverse events.

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Conclusions

- Ivonescimab with chemotherapy significantly improved OS in advanced squmous NSCLC first-line treatment compared with tislelizumab with chemotherapy
  - mOS: 27.89 vs. 23.69, HR=0.66 (95%CI: 0.50, 0.87), p=0.0017
- Ivonescimab with chemotherapy showed comparable safety profile to tislelizumab with chemotherapy
  - ≥ G3 TRAE: 69.2% vs. 58.9%
  - Similar rates of AEs leading to discontinuation or death between the two arms

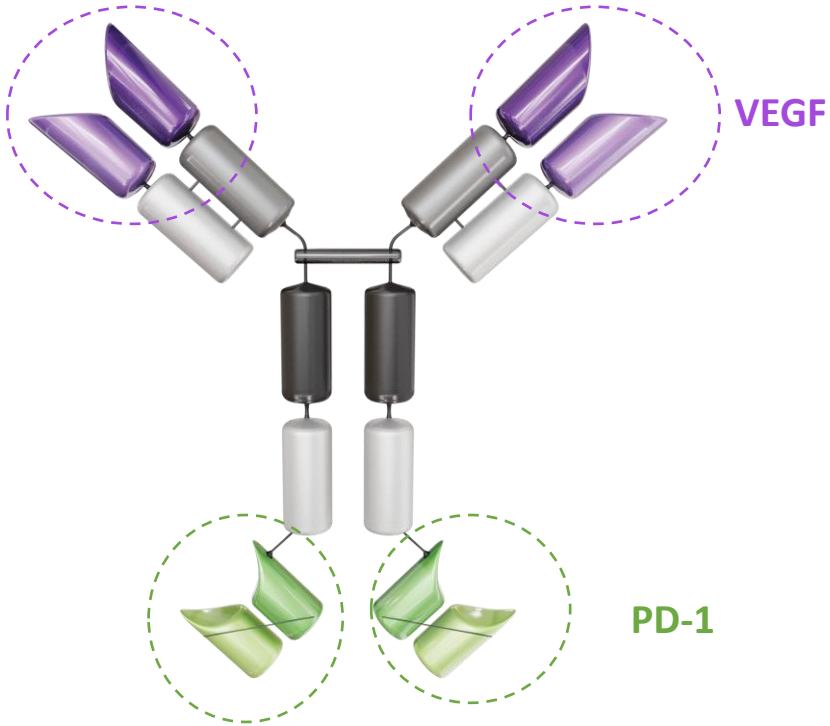
- **HARMONi-6 supports adoption of ivonescimab with chemotherapy as a new standard for patients with advanced squamous NSCLC in first-line treatment in China**
- **A global phase 3 study (HARMONi-3, NCT05899608) is underway**

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Key takeaway points HARMONi-6

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Patient Summary

The full manuscript has been published concurrently in *The Lancet*

Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy in advanced squamous non-small cell lung cancer (HARMONi-6): interim overall survival analysis of a randomised, double-blind, phase 3 trial in China

Shun Lu, Baogang Liu*, Yongzhong Luo*, 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, Junqiang Zhang, Qian Chu, Xuewen Liu, Shenpeng Ying, Hongcheng Wu, Hongmei Sun, Yinghua Ji, Ming Zhou, Chao Cao, Kejing Tang, Zhengguo Li, Dairong Li, Zhihong Zhang, Jie Li[2], Jianya Zhou, Hongzhong Yang, Yingying Du, Hui Yang, Jian Shi, Hualin Chen, Zhiwei Chen, Wenting Li, Dongmei Lu, Mingxiu Hu, Zhongmin Maxwell Wang, Baiyong Li, Michelle Y Xia*

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