Summit Therapeutics Update Call from WCLC

September 9, 2024

Forward-Looking Statements

Any statements in this presentation about the Company's future expectations, plans and prospects, including but not limited to, statements about the clinical and preclinical development of the Company's product candidates, entry into and actions related to the Company's partnership with Akeso Inc., including the expected benefits of the amendment to the collaboration and license agreement, the intended use of the net proceeds from the private placement, the Company's anticipated spending and cash runway, the therapeutic potential of the Company's product candidates, the potential commercialization of the Company's product candidates, the timing of initiation, completion and availability of data from clinical trials, the potential submission of applications for marketing approvals, potential acquisitions, statements about the previously disclosed At-The-Market equity offering program ("ATM Program"), the expected use of proceeds and uses thereof, and other statements containing the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the results of our evaluation of the underlying data in connection with the development and commercialization activities for ivonescimab, the outcome of discussions with regulatory authorities, including the Food and Drug Administration, the uncertainties inherent in the initiation of future clinical trials, availability and timing of data from ongoing and future clinical trials, the results of such trials, and their success, and global public health crises that may affect timing and status of our clinical trials and operations, whether preliminary results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials or preclinical studies will be indicative of the results of later clinical trials, whether business development opportunities to expand the Company's pipeline of drug candidates, including without limitation, through potential acquisitions of, and/or collaborations with, other entities occur, expectations for regulatory approvals, laws and regulations affecting government contracts and funding awards, availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements and other factors discussed in the "Risk Factors" section of filings that the Company makes with the Securities and Exchange Commission. Any change to our ongoing trials could cause delays, affect our future expenses, and add uncertainty to our commercialization efforts, as well as to affect the likelihood of the successful completion of clinical development of ivonescimab. Accordingly, the audience should not place undue reliance on forward-looking statements or information. In addition, any forward-looking statements included in this presentation represent the Company's views only as of the date of this presentation and should not be relied upon as representing the Company's views as of any subsequent date. The Company specifically disclaims any obligation to update any forward-looking statements included in this presentation.

Summit therapeutics

HARMONi-2: Study Design

Akeso Sponsored Study Conducted in China

A double-blind, randomized Phase III study comparing ivonescimab with pembrolizumab for patients with advanced or metastatic PD-L1-positive NSCLC (PD-L1 TPS ≥1%)[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

[a] Patients were randomized from November 2022 to August 2023. Data cut off: January 29, 2024.

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

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

HARMONi-2 Baseline Characteristics

Characteristics, n (%)		Ivonescimab (n = 198[a])	Pembrolizumab (n = 200[a])	Total (n = 398[a])
Age (years)	<65	97 (49.0)	85 (42.5)	182 (45.7)
	≥65	101 (51.0)	115 (57.5)	216 (54.3)
Sex	Male	164 (82.8)	169 (84.5)	333 (83.7)
	Female	34 (17.2)	31 (15.5)	65 (16.3)
ECOG PS	0	25 (12.6)	26 (13.0)	51 (12.8)
	1	173 (87.4)	174 (87.0)	347 (87.2)
Smoker	Never	39 (19.7)	38 (19.0)	77 (19.3)
	Current	39 (19.7)	42 (21.0)	81 (20.4)
	Former	120 (60.6)	120 (60.0)	240 (60.3)
Clinical stage	IIIB/C	15 (7.6)	16 (8.0)	31 (7.8)
	IV	183 (92.4)	184 (92.0)	367 (92.2)
Pathology	SQ	90 (45.5)	91 (45.5)	181 (45.5)
	Tumor centrally located[b]	65 (72.2)	57 (62.6)	122 (67.4)
	Tumor with cavitation/necrosis[b]	9 (10.0)	7 (7.7)	16 (8.8)
	Tumor encasing large blood vessel[b]	6 (6.7)	1 (1.1)	7 (3.9)
	Non-SQ	108 (54.5)	109 (54.5)	217 (54.5)
PD-L1 TPS	≥50%	83 (41.9)	85 (42.5)	168 (42.2)
	1-49%	115 (58.1)	115 (57.5)	230 (57.8)
Liver metastases	Yes	25 (12.6)	28 (14.0)	53 (13.3)
	No	173 (87.4)	172 (86.0)	345 (86.7)
Brain metastases	Yes	33 (16.7)	39 (19.5)	72 (18.1)
	No	165 (83.3)	161 (80.5)	326 (81.9)

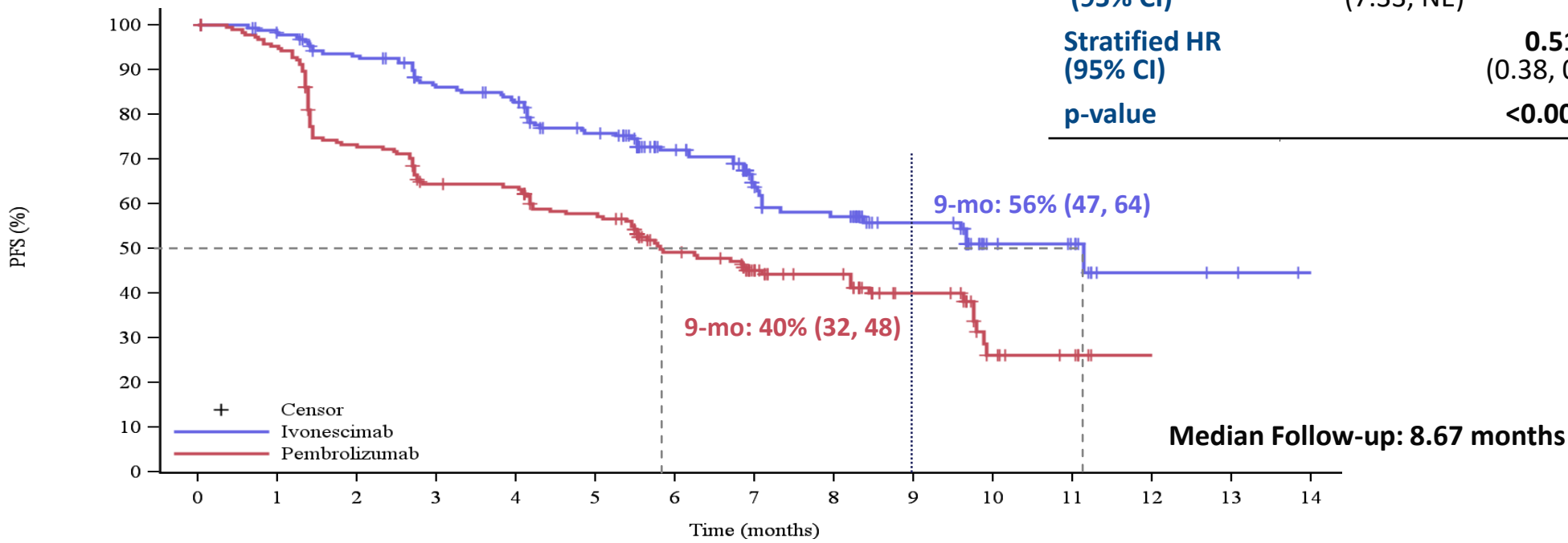
[a] Patients who received randomization. [b] In 181 patients with SQ.

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance score; PD-L1, programmed death ligand 1; TPS, tumor proportion score; SQ, squamous cell carcinoma.

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

HARMONi-2 Primary endpoint: PFS per IRRC

	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**	



Median Follow-up: 8.67 months

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)		

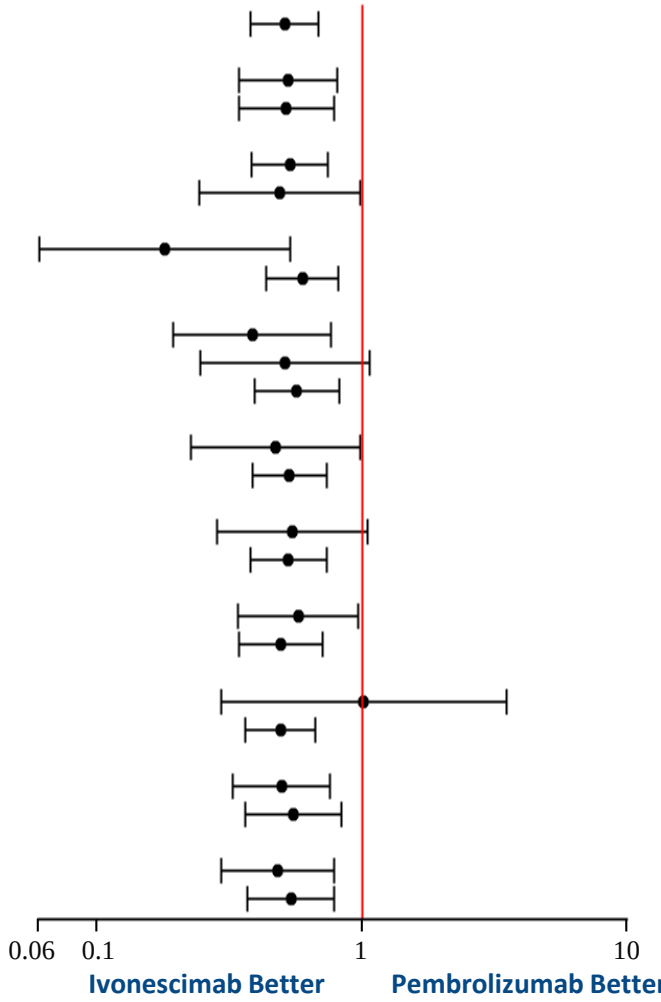
Ivonescimab is the first compound to demonstrate a statistically significant improvement in PFS vs. pembrolizumab with HR = 0.51, and 5.3 months improvement in mPFS.

Abbreviations: mPFS, median progression-free survival; IRRC, independent radiology review committee; mo, month; NE, not estimable; HR: hazard ratio; CI, confidence interval.

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

HARMONi-2 PFS Subgroup Analyses

	Ivonescimab Events/Patients	Pembrolizumab Events/Patients	Unstratified Hazard Ratio (95% CI)
Overall	72/198	112/200	0.51 (0.38, 0.69)
Age			
<65	37/97	50/85	0.53 (0.34, 0.81)
≥65	35/101	62/115	0.52 (0.34, 0.79)
Sex			
Male	58/164	94/169	0.53 (0.38, 0.74)
Female	14/34	18/31	0.49 (0.24, 0.99)
ECOG PS			
0	4/25	19/26	0.18 (0.06, 0.54)
1	68/173	93/174	0.60 (0.44, 0.82)
Smoking Status			
Never	13/39	22/38	0.39 (0.19, 0.77)
Current smoker	12/39	20/42	0.51 (0.24, 1.07)
Former smoker	47/120	70/120	0.57 (0.39, 0.74)
Liver metastases			
Yes	12/25	18/28	0.47 (0.23, 0.98)
No	60/173	94/172	0.53 (0.39, 0.74)
Brain metastases			
Yes	14/33	25/39	0.55 (0.28, 1.05)
No	58/165	87/161	0.53 (0.38, 0.74)
Distant metastatic sites			
≥3	25/49	33/51	0.58 (0.34, 0.97)
<3	47/149	79/149	0.49 (0.34, 0.71)
Clinical stage			
IIIB/C	5/15	5/16	1.01 (0.29, 3.51)
IV	67/183	107/184	0.49 (0.36, 0.67)
Pathology			
Squamous	35/90	56/91	0.50 (0.33, 0.76)
Non-Squamous	37/108	56/109	0.55 (0.36, 0.84)
PD-L1 TPS			
≥50%	25/83	45/85	0.48 (0.29, 0.79)
1-49%	47/115	67/115	0.54 (0.37, 0.78)



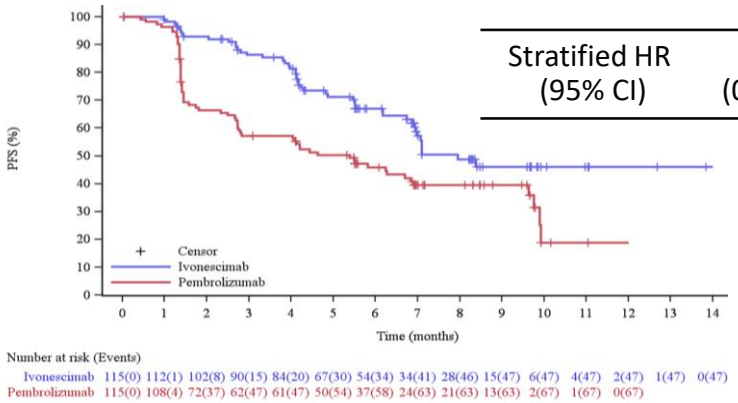
Abbreviations: PFS, progression-free survival; ECOG PS, Eastern Cooperative Oncology Group performance score; PD-L1, programmed death ligand 1; TPS, tumor proportion score; SQ, squamous cell carcinoma; CI, confidence interval; aNSCLC, advanced non-small cell lung cancer.

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

HARMONi-2 Key PFS Subgroup Analyses

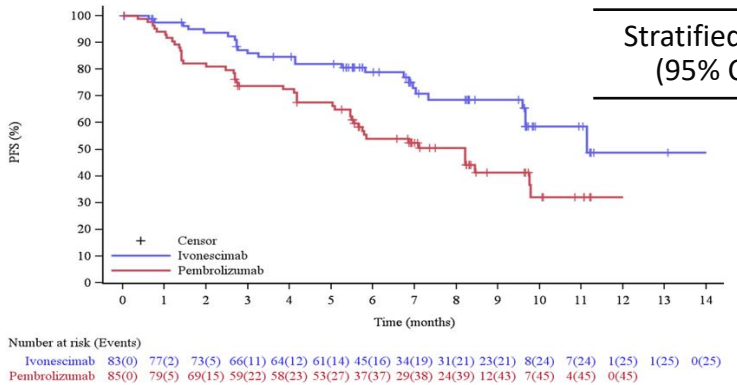
PD-L1 expression

PD-L1 Low (TPS 1-49%)



Stratified HR (95% CI)	0.54 (0.37, 0.79)

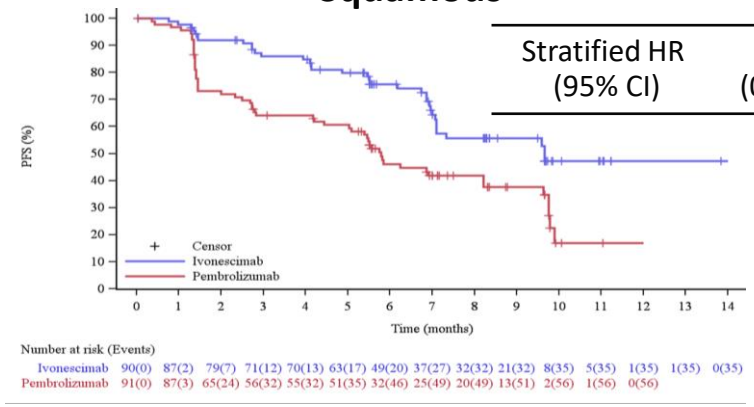
PD-L1 High (TPS ≥50%)



Stratified HR (95% CI)	0.46 (0.28, 0.75)

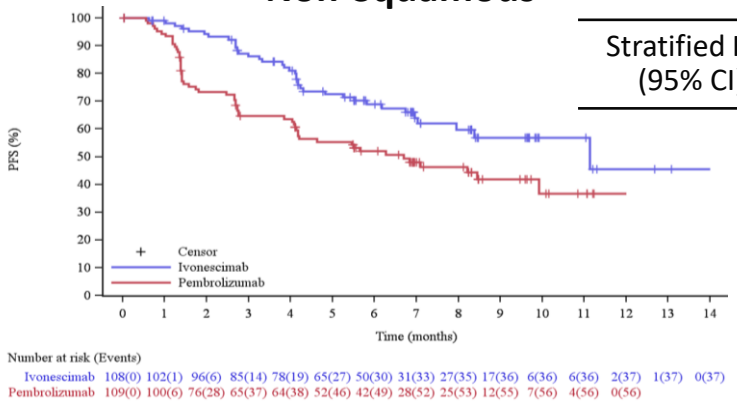
NSCLC Histology

Squamous



Stratified HR (95% CI)	0.48 (0.31, 0.74)

Non-Squamous

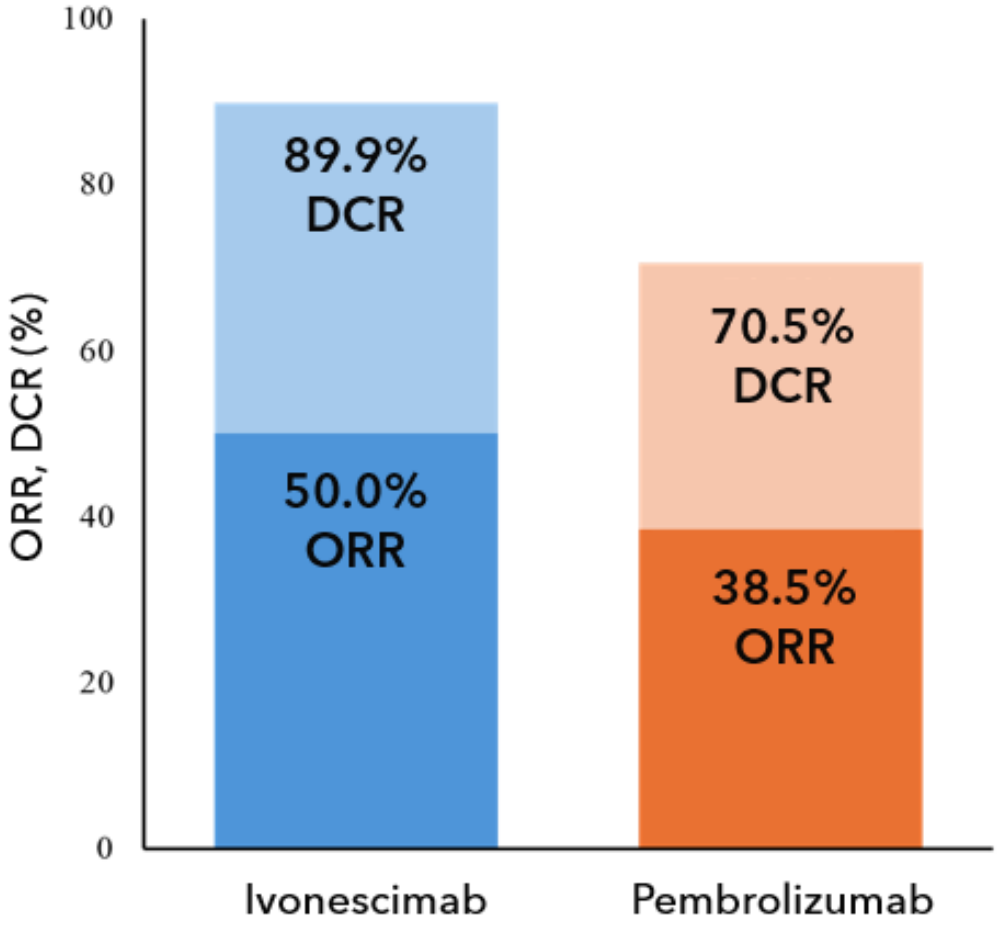


Stratified HR (95% CI)	0.54 (0.36, 0.82)

Ivonescimab showed meaningful improvement in PFS vs. pembrolizumab in patients with both low and high PD-L1, with squamous or non-squamous advanced NSCLC.

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

HARMONi-2 ORR, DCR and DoR per IRRC



	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.

Data cut off: January 29, 2024.

Abbreviations: ORR, overall response rate; DCR, disease control rate; DoR, duration of response; IRRC, independent radiology review committee; CI, confidence interval; mo, month; NR, not reached; NE, not estimable.

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

HARMONi-2 Safety Summary

TRAEs

Safety Summary, n (%)	Ivonescimab (n = 197[a])	Pembrolizumab (n = 199[a])
TRAEs (all grades)	177 (89.8)	163 (81.9)
Grade≥3	58 (29.4)	31 (15.6)
Serious TRAEs	41 (20.8)	32 (16.1)
Leading to discontinuation	3 (1.5)	6 (3.0)
Leading to death	1 (0.5)	2 (1.0)

Ivonescimab showed a manageable safety profile, which was consistent with previous studies.

TRAEs in SQ Subgroup

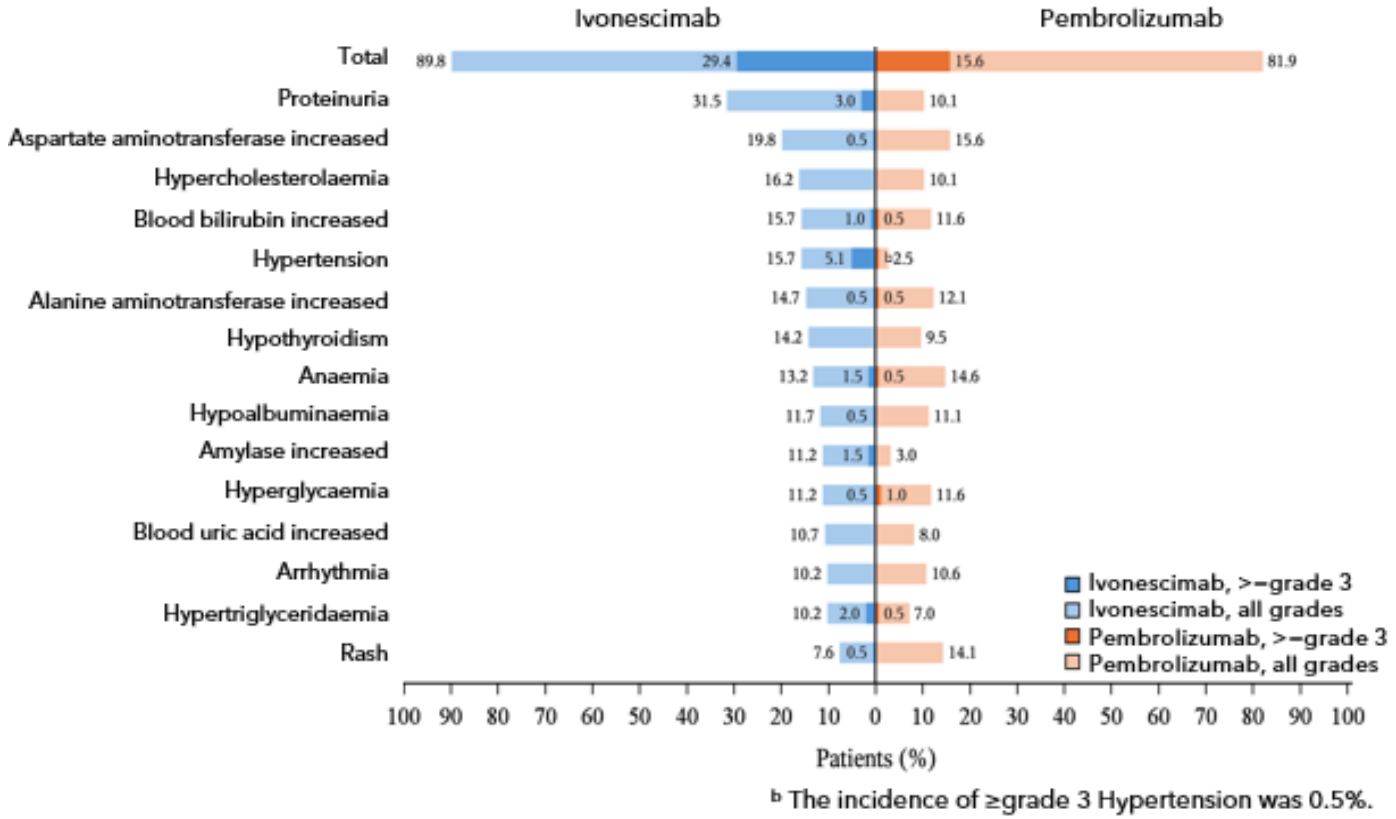
Safety Summary, n (%)	Ivonescimab (n = 90[a])	Pembrolizumab (n = 91[a])
TRAEs (all grades)	77 (85.6)	73 (80.2)
Grade≥3	20 (22.2)	17 (18.7)
Serious TRAEs	17 (18.9)	17 (18.7)
Leading to discontinuation	2 (2.2)	3 (3.3)
Leading to death	0	1 (1.1)

Ivonescimab also demonstrated a tolerable safety profile in SQ patients.

[a] Patients who received ≥1 dose of study treatment.

Abbreviations: AEs, adverse events; TRAEs, treatment-related adverse events; SQ, squamous cell carcinoma.

Most Common TRAEs (incidence ≥10%)



[b] The incidence of ≥grade 3 Hypertension was 0.5%.

The differences in AEs were predominantly proteinuria, hypertension, and laboratory abnormalities.

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

HARMONi-2 irAEs and Possible VEGF-Related AEs

irAEs

Safety Summary, n (%)	Ivonescimab (n = 197[a])	Pembrolizumab (n = 199[a])
irAEs (all grades)	59 (29.9)	56 (28.1)
Grade≥3	14 (7.1)	16 (8.0)
Serious irAEs	11 (5.6)	22 (11.1)
Leading to discontinuation	0	5 (2.5)
Leading to death	0	0

Ivonescimab exhibited similar irAEs to that of pembrolizumab.

Possible VEGF-Related AEs

Safety Summary, n (%)	Ivonescimab (n = 197[a])	Pembrolizumab (n = 199[a])
Possible VEGF-Related AEs (all grades)	94 (47.7)	42 (21.1)
Grade≥3	20 (10.2)	2 (1.0)

Safety Summary by Classification, n (%)	Ivonescimab (n = 197[a])		Pembrolizumab (n = 199[a])	
	All Grade	Grade≥3	All Grade	Grade≥3
Proteinuria	62 (31.5)	6 (3.1)	20 (10.1)	0
Hypertension	31 (15.7)	10 (5.1)	5 (2.5)	1 (0.5)
Haemorrhage	29 (14.7)	2 (1.0)	22 (11.1)	1 (0.5)
Arterial thromboembolism	2 (1.0)	2 (1.0)	1 (0.5)	0
Venous thromboembolism	0	0	1 (0.5)	0

- All VEGF-related AEs were grades 1-3 in both arms.
- Grade 3 haemorrhage was observed in two patients with non-SQ and was not reported in SQ patients in the ivonescimab arm.

[a] Patients who received ≥1 dose of study treatment.
Abbreviations: VEGF, vascular endothelial growth factor; irAEs, immune-related AEs; AEs, adverse events; SQ, squamous cell carcinoma.

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

Additional Promising Phase II Data for Ivonescimab (Ivo)

Akeso Sponsored Phase II Studies Conducted in China – Study Designs Contained in Appendix

Perioperative Resectable NSCLC	Ivonescimab (n=11)	Ivo + Chemo (n=49)
pCR (n = 10; n = 39; respectively)	30.0%	43.6%
MPR (n = 10; n = 39; respectively)	60.0%	71.8%
12-month EFS	81.8%	80.3%

No TRAEs led to cancelled / delayed surgery or wound healing complications.

1L Triple Negative Advanced Breast Cancer (TNBC)	Ivo + Chemo CPS <10% (n=23)	Ivo + Chemo CPS ≥10% (n=6)
Overall Response Rate	69.6%	83.3%
Disease Control Rate	100%	100%
6-month PFS Rate	68.4%	
TRAE-Led Discontinuations	0	

1L MSS Metastatic Colorectal Cancer (mCRC)	Ivo + Chemo (n = 22)	Ivo + CD47 + Chemo (n = 17)
Overall Response Rate	81.8%	88.2%
Disease Control Rate	100%	100%
9-month PFS Rate	81.4%	86.2%
TRAE-Led Discontinuations	0	1

1L PD-L1-positive Head-and-Neck SCC (R/M HNSCC)	Ivonescimab (n =10)	Ivo + CD47 (n=20)
Overall Response Rate	30.0%	60.0%
Disease Control Rate	80.0%	90.0%
Median PFS Rate	5 mos	7.1 mos
TRAE-Led Discontinuations	0	

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

Ivonescimab Global Clinical Trials

Indication	Study	Treatment Population	Regimen	Phase	Status
NSCLC	HARMONi	2L EGFRm+	+ Chemo vs. chemo	III	Ongoing
	HARMONi-3	1L Squamous	+ Chemo vs. pembrolizumab (PD-1) + chemo	III	Ongoing
	HARMONi-7	1L PD-L1 TPS ≥50%	Monotherapy vs. pembrolizumab (PD-1)	III	Planned

These ivonescimab clinical trials are being conducted in China and / or Australia and are fully sponsored and managed by Akeso.

Indication	Study	Treatment Population	Regimen	Phase	Status
NSCLC	HARMONi-A	2L EGFRm+	+ Chemo vs. Chemo		Approved
	HARMONi-2	1L PD-L1 TPS ≥1%	Monotherapy vs. pembrolizumab (PD-1)	III	Primary Analysis
	HARMONi-6	1L Squamous	+ Chemo vs. tislelizumab (PD-1) + chemo	III	Ongoing
	AK112-205	Neoadjuvant/Adjuvant	+/- Chemo	II	Ongoing
	AK112-208	1L advanced or metastatic	+ PD-1/CTLA-4 bsAb + chemo	II	Ongoing
Biliary Tract CA	TBD	1L	+ Chemo	III	Planned
Head & Neck CA	TBD	1L PD-L1 CPS ≥1%	+ CD47 vs. pembrolizumab (PD-1)	III	Planned
Pancreatic CA	TBD	1L PDAC	+ Chemo	III	Planned
Ovarian CA	AK112-211	PSOC	+ Chemo +/- PARP inhibitor	II	Ongoing
Colorectal CA	AK112-206	Metastatic MSS CRC	+/- CD47, +/- chemo	II	Ongoing
Hepatocellular CA	AK112-207	BCLC Stage B or C	Monotherapy	II	Ongoing
Ovarian CA	AK104-221	Recurrent	+/- Chemo, PD-1/CTLA-4 bsAb	II	Ongoing
G/GEJ CA	AK117-202	HER2 negative	+/- CD47 + chemo	II	Ongoing
Breast CA	AK117-203	TNBC	+ Chemo, CD47 + chemo	II	Ongoing
SCLC	AK112-103	Extensive Stage	+ Chemo	I	Completed

Abbreviations: Abbreviations: 1L=first-line; 2L=second-line; Adeno CA=adenocarcinoma; BCLC=Barcelona clinic liver cancer; BRAC=breast cancer gene; bsAb=bispecific antibody; Chemo=chemotherapy; CD47=cluster of differentiation 47; CTLA-4=cytotoxic T lymphocyte antigen-4; CPS=combined positive score; CRC=colorectal cancer; EGFRm+=epidermal growth factor receptor mutant positives; G/GEJ=gastroesophageal junction; HER2=human epidermal growth factor receptor 2; NSCLC=non-small-cell lung cancer; PARPi=poly(ADP-ribose) polymerase inhibitors; PD-L1=programmed cell death ligand 1; PD-1=Programmed Cell Death Protein 1; TNBC=triple negative breast cancer; TPS=tumor proportion score; SCLC=Extensive Stage Small Cell Lung Cancer; PDAC=pancreatic ductal adenocarcinoma

Ivonescimab

More Than 25 Clinical Trials Across 17 Indications[1]

1,800+ Patients Treated in Clinical Trials

8 Phase III Trials Completed or Ongoing[1]

1 Approved Cancer Indication in China[1]

4 Head-to-Head Studies vs. PD-1

9 Dedicated Trials Outside NSCLC[1]

China

1. Akeso's 2024 First Half Interim Results (prnewswire.com)

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

Q&A

Summit Therapeutics Update Call from WCLC

September 9, 2024

Appendix

Study Designs for Additional Phase II for Ivonescimab (Ivo)

Akeso Sponsored Phase II Studies Conducted in China

- **1L MSS Metastatic Colorectal Cancer (mCRC):**
- *This was an open-label, multicenter, phase II randomized study. Untreated mCRC patients (pts) were randomly assigned (1:1) to receive FOLFOXIRI + ivonescimab (group A) or FOLFOXIRI + ivonescimab + ligufalimab (CD47) (group B) for up to 8 cycles, followed by maintenance with 5-fluoruracil + ivonescimab with (group B) or without ligufalimab (group A). The primary endpoints were objective response rate (ORR) by RECIST v1.1 and safety.*

Deng, et. al., *ESMO, 2024*

- **1L Triple Negative Advanced Breast Cancer (TNBC):**
- *This was an open-label, multicenter phase II study in patients (pts) with locally advanced unresectable or metastatic TNBC. Pts received ivonescimab at 20 mg/kg Q2W and paclitaxel at 90 mg/m2 or nab-paclitaxel at100 mg/m2 on the 1st, 8th, and 15th day of each four-week treatment cycle. The primary endpoints were safety and objective response rate (ORR) by RECIST v1.1. The secondary endpoints included duration of response (DoR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).*

Ouyang, et. al., *ESMO, 2024*

- **Perioperative Resectable NSCLC:**
- *This was an open-label, multi-center phase II study, pts diagnosed with resectable stage II, IIIA or IIIB (N2) NSCLC per AJCC 8th edition were enrolled into two cohorts. Pts received neoadjuvant ivonescimab (20 mg/kg) monotherapy in cohort 1 or ivonescimab (20 mg/kg or 30 mg/kg) plus cisplatin/carboplatin and paclitaxel in cohort 2 once every 3 weeks for 3-4 cycles, followed by surgery and adjuvant ivonescimab once every 3 weeks for up to 16 cycles. Primary endpoints were safety and major pathological response (MPR).*

Wang, et. al., *WCLC, 2024*

- **1L PD-L1-Positive Head-and-Neck SCC (R/M HNSCC)**:
- *In this open-label, multi-center phase II study, eligible R/M HNSCC pts with PD-L1 positive disease (CPS≥1) were enrolled, including oropharynx, hypopharynx, larynx or oral cavity cancer. Patients were treated with ivonescimab (10 mg/kg Q3W) monotherapy or in combination with ligufalimab (CD47) (45 mg/kg Q3W). The primary endpoint was objective response rate (ORR) per RECIST v1.1 assessed by investigator.*

Chen, et. al., *ESMO, 2024*

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