Lung Cancer
UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Iniciativa científica de:
GECP
lung cancer research

Inmunoterapia en enfermedad avanzada en CPNCP.

Dra. Karla Medina

Hospital Universitario Nuestra Señora de Candelaria, Tenerife

Inmunoterapia en enfermedad avanzada.

Abstract: LBA:8502

2025 ASCO ANNUAL MEETING

CAMPASS: Benmelstobart in combination with anlotinib vs pembrolizumab in the first-line treatment of PD-L1 positive, advanced non-small cell lung cancer (aNSCLC): A randomized, blind, multicenter phase 3 study

Authors: Baohui Han[1], Kai Li[2], Runxiang Yang[3], Yongzhong Luo[4], Wei Zuo[5], Chao Xie[6], Qingshan Li[7], Xingxiang Xu[8], Qiang Liu[9], Yan Yu[10], Qiming Wang[11], Tienan Yi[12], Yongxing Chen[13], Hongmei Sun[14], Xuhong Min[15], Huaqiu Shi[16], Hualin Chen[17], Jianhua Shi[18], Jinsheng Shi[19], Junzhen Gao[20]

1. Shanghai Chest Hospital, Shanghai, China; 2. Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; 3. Internal Medicine Department 2, Yunnan Cancer Hospital (The Third Affiliated Hospital of Kunming Medical University), Kunming, China; 4. Hunan Cancer Hospital & The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; 5. The First Affiliated Hospital of Nanchang University, Nanchang, China; 6. Cancer Hospital of Shandong First Medical University, Jinan, China; 7. Chengde Medical College Affiliated Hospital, Chengde, China; 8. Northern Jiangsu People's Hospital Affiliated to Yangzhou University, Yangzhou, China; 9. Department of Oncology, China Shenyang The Tenth People's Hospital,China Shenyang Chest Hospital, Shenyang, China; 10. Respiratory Medicine Ward 3, Harbin Medical University Cancer Hospital, Harbin, China; 11. The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; 12. Xiangyang Central Hospital, Xiangyang, China; 13. Hainan Provincial People's Hospital, Haikou, China; 14. Jiamusi cancer and tuberculosis hospital, Jiamusi, China; 15. Anhui Chest Hospital, Hefei, China; 16. First Affiliated Hospital of Gannan Medical University, Ganzhou, China; 17. Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; 18. Linyi Cancer Hospital, Linyi, China; 19. Cangzhou People's Hospital, Cangzhou, China; 20. Affiliated Hospital of Inner Mongolia Medical University, Huhehaote, China

Baohui Han MD
Shanghai Chest Hospital, Shanghai, China

Methods

Randomized, blind, multicenter phase 3 study (NCT04964479)

Key enrollment criteria

- Locally advanced or recurrent/metastatic NSCLC
- TPS ≥ 1%
- Age: 18-75; ECOG PS: 0-1
- Previous systemic treatment naïve
- No EGFR mutations, no ALK or ROS1 rearrangements
- No prior exposure of anti-angiogenic agents or immune checkpoint inhibitors

2:1
N = 531

- Benmelstobart 1200mg iv D1
- Anlotinib 12mg po, QD D1~D14
- 3 weeks / cycle

- Pembrolizumab 200mg iv D1
- Placebo 0mg po, QD D1~D14
- 3 weeks / cycle

Primary endpoint

Progression-free survival (PFS) per RECIST 1.1 assessed by IRC

Secondary endpoints

- Overall survival (OS)
- Objective response rate (ORR)
- PFS per RECIST 1.1 by INV
- Disease control rate (DCR)
- Safety

Stratification factors:

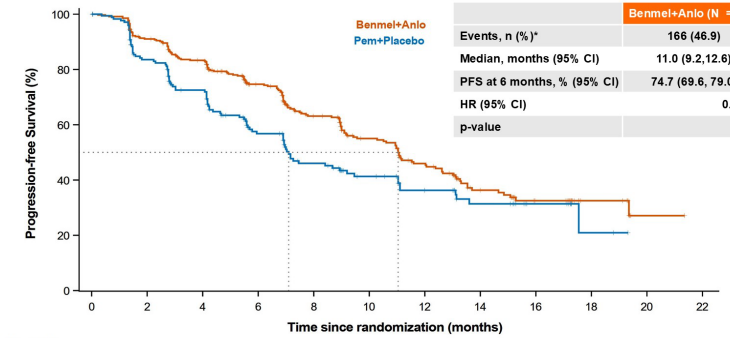
- Histology: squamous vs. non-squamous
- Brain metastases: yes vs. no
- PD-L1 expression (TPS): ≥ 50% vs. 1-49%

Abbreviation: IRC: independent review committee, INV: investigator, TPS: tumor proportion score

Inmunoterapia en enfermedad a

Results

Primary endpoint: PFS by IRC



	Benmel+Anlo (N = 354)	Pem+Placebo (N = 177)
Events, n (%)*	166 (46.9)	95 (53.7)
Median, months (95% CI)	11.0 (9.2,12.6)	7.1 (5.8, 9.5)
PFS at 6 months, % (95% CI)	74.7 (69.6, 79.0)	56.8 (48.6, 64.2)
HR (95% CI)	0.70 (0.54, 0.90)	
p-value	0.0057	

*Median follow-up:
Benmel+Anlo: 11.4 months
Pem+Placebo: 10.6 months

Benmelstobart in combination with anlotinib vs pembrolizumab in the 1L

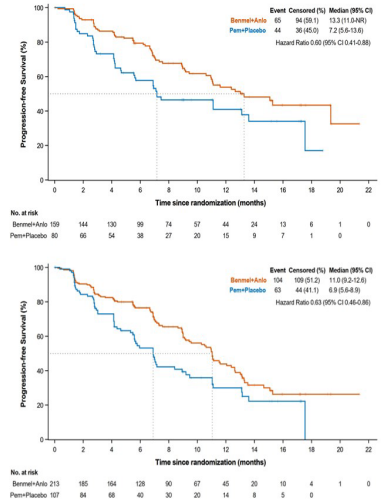
- **Key findings: Efficacy & Safety**
  - mPFS subgroup analysis: Squamous mPS 11 mo (HR 0.6); PD-L1 ≥ 50% 13.3 mo (HR 0.63)
  - Higher ORR 57 vs 40%
  - Safety: higher rates of grade ≥ 3 toxicities, but no increased rates of IRAEs or discontinuation

Han B et al. ASCO 2025

Abstract: LBA8502

Results

Key Pre-specified PFS Subgroup Analyses



TPS ≥ 50%	Benmel+Anlo	Pem+Placebo
N (%)	159 (44.9)	80 (45.2)
Median, months (95% CI)	13.3 (11.0, NE)	7.2 (5.6, 13.6)
HR (95% CI)	0.60 (0.41, 0.88)	

Squamous	Benmel+Anlo	Pem+Placebo
N (%)	213 (60.2)	107 (60.5)
Median, months (95% CI)	11.0 (9.2, 12.6)	6.9 (5.6, 8.9)
HR (95% CI)	0.63 (0.46, 0.86)	

Benmelstobart in combination with anlotinib vs pembrolizumab in the 1L

Strengths

- Anlotinib is already an approved drug in China
- Well-designed phase 3 study with positive primary endpoint of PFS
- Manageable safety profile; AEs consistent with VEGF inhibition

Limitations

- Impact on OS to be determined
- No predictive biomarker for the combination
- Comparator arm is not a SOC for all PD-L1 levels
- Study conducted in China only

Ahn M-J et al. J Clin Oncol. 2025 Jan 20;43(3):260-272

Inmunoterapia en enfermedad avanzada.

Abstract: 8515

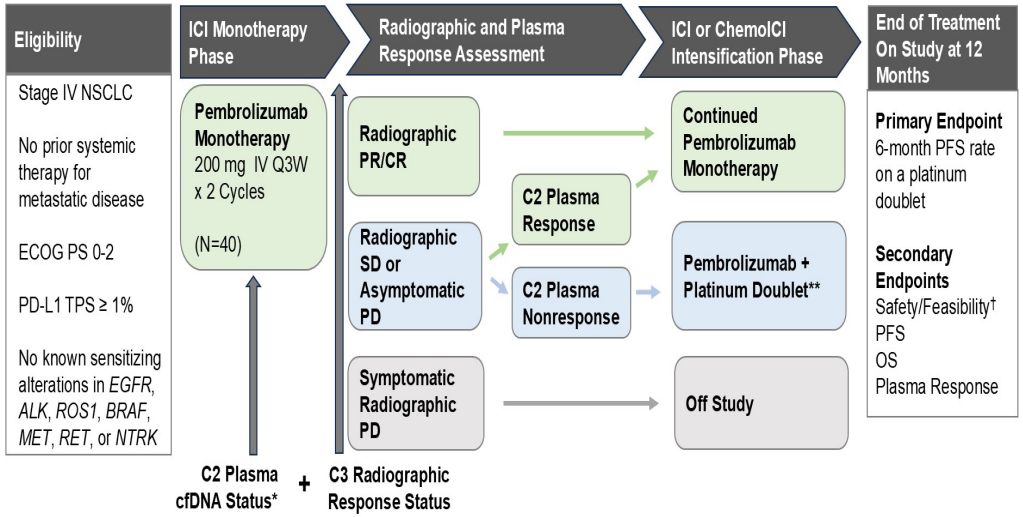
2025 ASCO ANNUAL MEETING

Plasma-guided adaptive first-line chemoimmunotherapy for non-small cell lung cancer (NSCLC)

Julia K. Rotow, Grace Heavey, Mizuki Nishino, Shail Maingi, Christopher S. Lathan, Umit Tapan, Alexandra S. Bailey, Zihan Wei, Emanuele Mazzola, Diandra Ocot, Geoffrey R. Oxnard, David A. Barbie, Pasi A. Jänne, Cloud P. Paweletz, Michael L. Cheng

Julia Rotow, MD
Clinical Director, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute
Assistant Professor, Harvard Medical School

Plasma response-guided adaptive treatment of advanced NSCLC receiving first-line pembrolizumab



*Plasma Response defined as ≥50% reduction in plasma ctDNA max AF for patients with high shed [≥0.5% max AF] at baseline or continued low shed [<0.5% max AF] for patients with low shed at baseline, as measured by amplicon-based plasma NGS

**NSQ: Carboplatin AUC 5 + Pemetrexed 500 mg/m2 Q3W x 4 cycles followed by Pemetrexed 500 mg/m2 Q3W; SQ: Carboplatin AUC 6 + Paclitaxel 200 mg/m2 Q3W x 4 cycles, with concurrent pembrolizumab 200 mg IV Q3W to end of study treatment

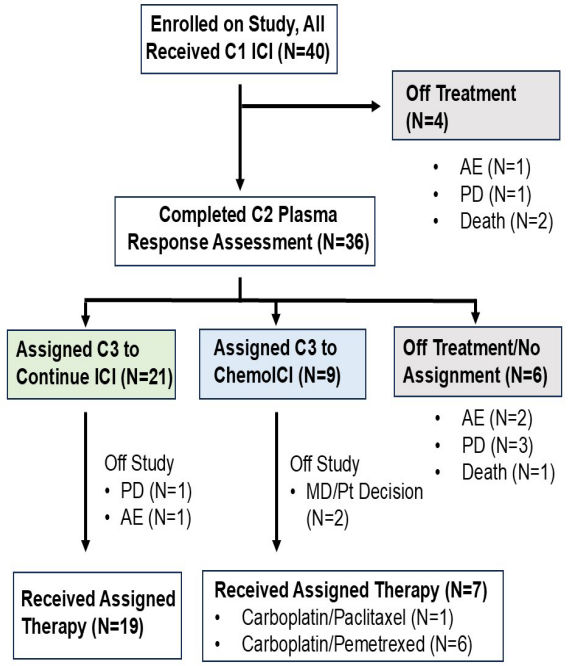
†Feasibility defined as completion of the integrated plasma response and C3 imaging assessment, with one-sided upper 90% binomial confidence interval >82.5%

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Julia Rotow, MD
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Inmunoterapia en enfermedad avanzada.

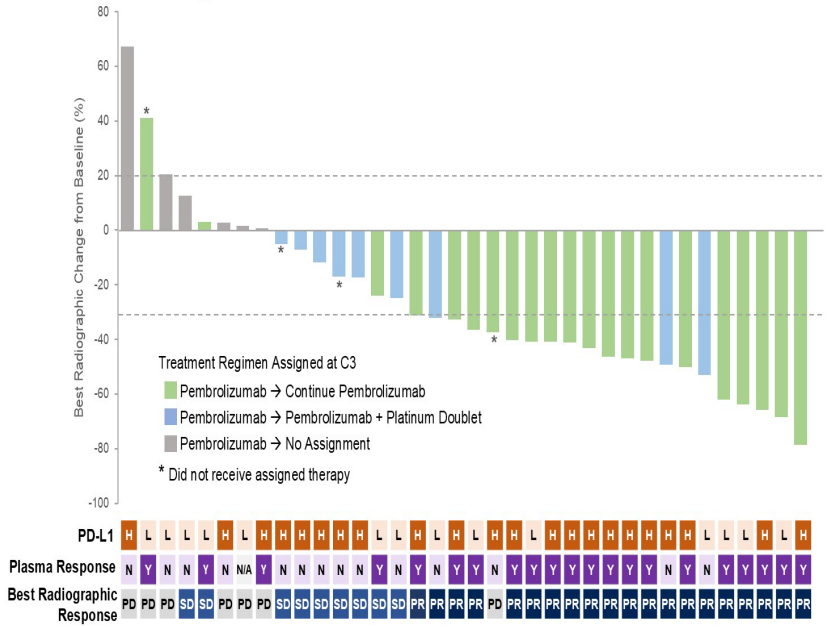
Abstract: 8515

Treatment Allocation at Cycle Three



n (%)	Assigned ICI Monotherapy (N=21)	Assigned ChemoICI (N=9)	Off Rx Prior to Assignment (N = 10)
Age (mean)	68.4	69.8	72.2
Gender			
Male	11 (52.4%)	5 (55.6%)	6 (60.0%)
Female	10 (47.6%)	4 (44.4%)	4 (40.0%)
ECOG PS			
0	7 (33.3%)	2 (22.2%)	3 (30%)
1	14 (66.7%)	6 (66.7%)	6 (60%)
2	0 (0)	1 (11.1%)	1 (10%)
Histology			
NSQ	15 (71.4%)	7 (77.8%)	8 (80.0%)
SQ	6 (28.6%)	1 (11.1%)	2 (20.0%)
Adenosqua.	0 (0 %)	1 (11.1%)	0 (0%)
Tobacco			
Current	5 (23.8%)	3 (33.3%)	0 (0%)
Former	15 (71.4%)	5 (55.6%)	10 (100%)
Never	1 (4.8%)	1 (11.1%)	0 (0%)
PD-L1			
1-49%	8 (38.1%)	3 (33.3%)	4 (40.0%)
≥50%	13 (61.9%)	6 (66.7%)	6 (60.0%)
CNS+	4 (19.0%)	5 (55.6%)	1 (10.0%)

Best Response to Treatment



Best Response, All Patients

	All Patients (N = 40)
PR	20 (50%)
SD	9 (22.5%)
PD	7 (17.5%)
UE	4 (10%)

Best Response by C2 Plasma Response

	Plasma Response	
	No (N=15)	Yes (N=21)
PR	3 (21%)	17 (81%)
SD	7 (50%)	2 (9.5%)
PD	4 (29%)	2 (9.5%)
UE	1 (6.7%)	0

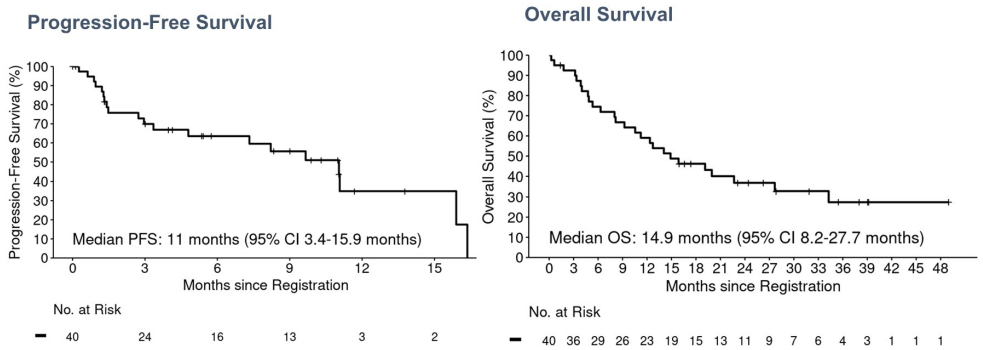
P=0.001†

†Fisher exact test; UE, unevaluable
Four subjects not shown due to lack of at least one radiographic response assessment

Inmunoterapia en enfermedad avanzada.

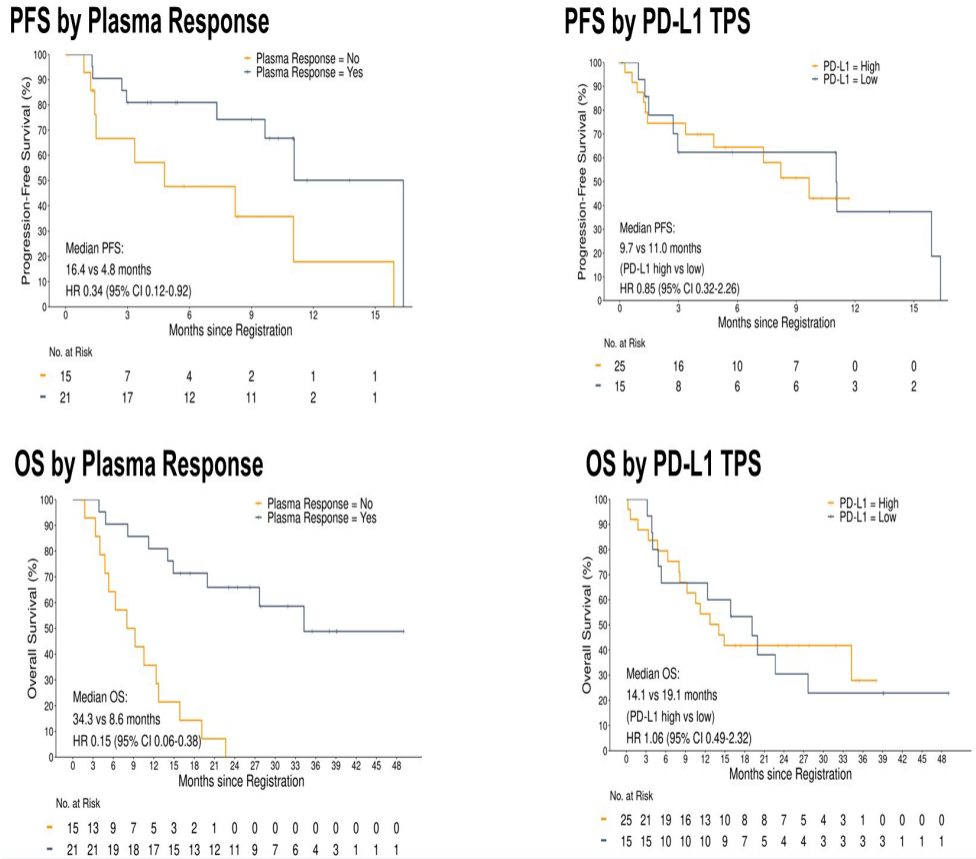
Abstract: 8515

Survival Outcomes to an Adaptive Treatment Strategy



Survival outcomes were calculated for all enrolled patients from date of registration to date of progression or death inclusive of pembrolizumab monotherapy and, if indicated per protocol, adaptive pembrolizumab plus platinum doublet

Survival by PD-L1 TPS and by Plasma Response



Key Conclusions

Plasma-guided intensification from first-line pembrolizumab monotherapy to platinum doublet/pembrolizumab is feasible in metastatic NSCLC

A plasma-guided strategy resulted in a median PFS of 11.0 months with fewer patients receiving first-line platinum doublet chemotherapy than would be predicted by PD-L1 TPS

As a dynamic biomarker, ctDNA kinetics are an important emerging tool to guide clinical decision making in NSCLC. Further validation within a randomized study is needed to clarify implications for clinical practice

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Julia Rotow, MD
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Inmunoterapia en enfermedad avanzada.

Abstract: 8516

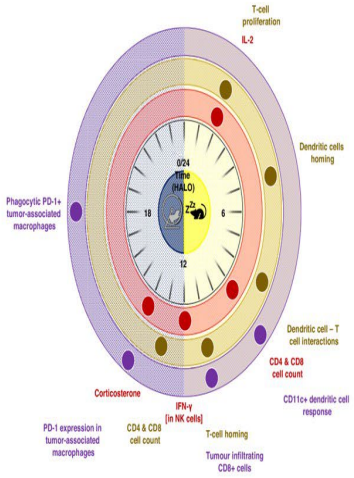
2025 ASCO ANNUAL MEETING

Randomized trial of Time-of-Day immunochemotherapy on Survival in Non-Small Cell Lung Cancer

Zhe Huang[1,2*], Liang Zeng[1*], Zhaohui Ruan[1*], Qun Zeng[3*], Huan Yan[1], Wenjuan Jiang[1], Yi Xiong[1], Chunhua Zhou[1], Haiyan Yang[1], Li Liu[1], Jiacheng Dai[1], Nachuan Zou[1], Shidong Xu[1,2], Ya Wang[1], Zhan Wang[1], Jun Deng[4], Xue Chen[4], Jing Wang[5], Hua Xiang[5], Xiaomei Li[6], Boris Duchemann[6,7], Guoqiang Chen[8,9], Christoph Scheiermann[3,11,12,13†], Francis Lévi[6,10†], Nong Yang[14†], Yongchang Zhang[1,2,4,15†]

Presenter: Yongchang Zhang, MD, PhD, Hunan Cancer Hospital, zhangyongchang@csu.edu.cn

Background



- Circadian rhythms is known to impact on sleep, disease and therapy.
- Pre-clinical studies have shown the association of circadian rhythms and immune cell function and distribution, thus may impact on efficacy of immunotherapy[1].
- Over 20 retrospective studies, and it's meta-analysis, have demonstrated improvement in the efficacy of ICIs given at early rather than late time of day[2-3]
- This is the first prospective randomized phase III study comparing early (before 15:00hr) with late (after 15:00hr) Time of Day (ToD) infusion of chemo-immunotherapy in patients with advanced NSCLC

[1] Cermakian et al, *JCI Insight*. 2020
[2] Huang Z et al, *eBioMedicine*. 2025 (our group)
[3] Zachary et al, *Lancet Oncology*. 2021

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Yongchang Zhang MD, zhangyongchang@csu.edu.cn
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Inmunoterapia en enfermedad avanzada.

Abstract: 8516

Study design

A Phase 3, randomized, open-label study (Clinicaltrials.gov: NCT05549037)

Key eligibility criteria

- Stage IIIC-IV NSCLC
- More than 18 years old
- Driver gene negative
- PS 0-1
- ≥1 measurable lesion (RECIST 1.1)
- Clinical stable brain metastasis

N=210, R 1:1

Early ToD group

Standard chemotherapy* in combination with standard ICI** with first 4 cycles starting and completed before 15:00hr

Late ToD group

Standard chemotherapy* in combination with standard ICI** with first 4 cycles starting after 15:00hr

Endpoints

Primary endpoint:
- PFS by BIRC

Secondary endpoint:
- OS
- ORR by BIRC
- Whole blood lymphocyte subset analysis***

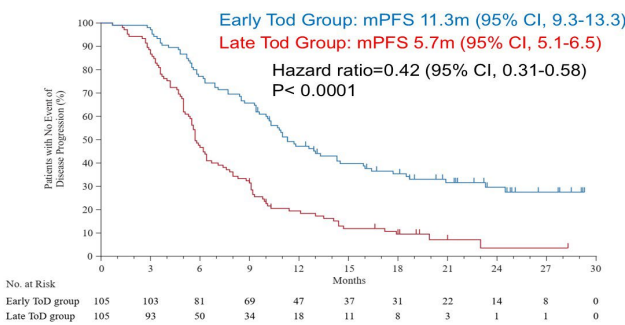
Stratification factor: None

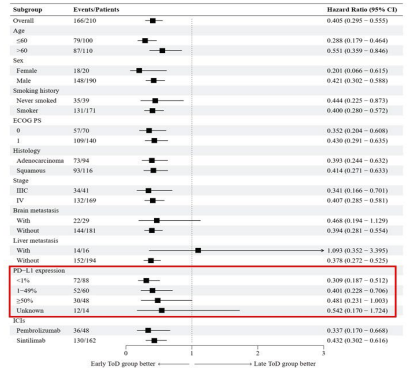
*(for details of chemotherapy: carboplatin (AUC of 5 mg/ml/min) and nab-paclitaxel (200 mg/m²), pemetrexed (500 mg/m²)
**(details of ICI: 200 mg of pembrolizumab or sintilimab)
***T cells (CD3⁺), CD4⁺ T cells (CD3⁺, CD4⁺), CD8⁺ T cells (CD3⁺, CD8⁺), B cells (CD3⁻, CD20⁺), and NK cells (CD16⁺, CD56⁺)

PRESENTED BY: Yongchang Zhang MD, zhangyongchang@csu.edu.cn

Results: PFS

Statistically significant improvement in PFS comparing early with late ToD group



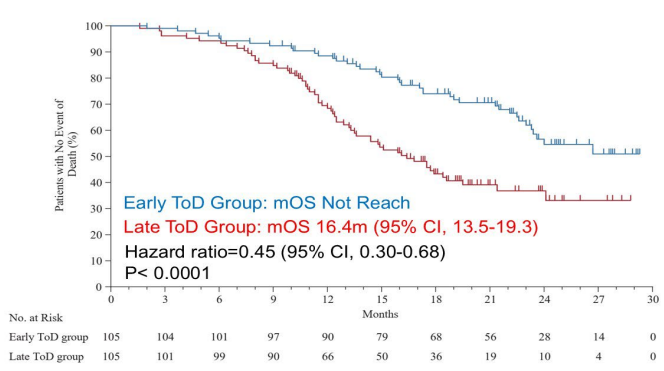


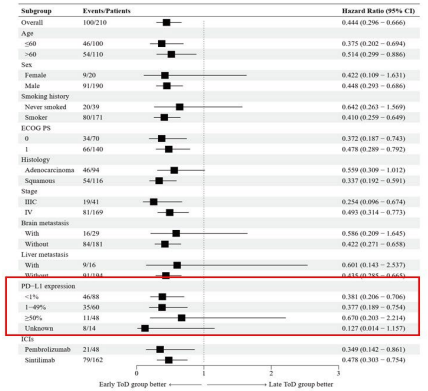
Median follow-up time: 23.2 months.

PRESENTED BY: Yongchang Zhang MD, zhangyongchang@csu.edu.cn

Results: OS

Statistically significant improvement in OS comparing early with late ToD group





Median follow-up time: 23.2 months.

PRESENTED BY: Yongchang Zhang MD, zhangyongchang@csu.edu.cn

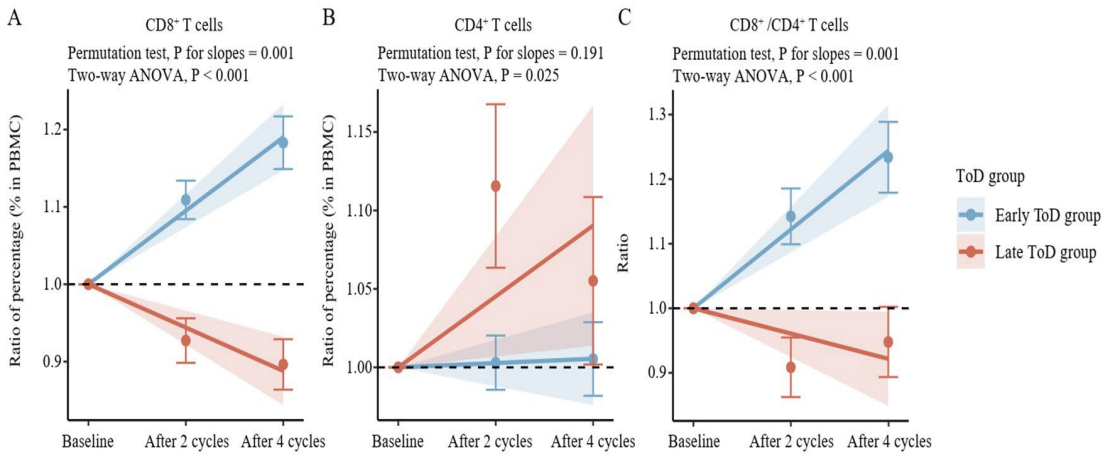
Inmunoterapia en enfermedad avanzada.

Abstract: 8516

GECP lung cancer research

Results: Circulating T cells

Increase of circulating CD8+ T cells in the early ToD group versus decrease in the late ToD group.



Conclusions

- This is the first prospective randomized phase III study demonstrating infusion of immunochemotherapy at early ToD (before 15:00) improves PFS and OS in patients with advanced NSCLC irrespective of PDL1 status.
- Significant difference in CD8⁺ T cell dynamics in peripheral blood comparing early with late ToD groups.
- Given the potential impact of circadian rhythms on immunotherapy, it is recommendable to document and/or stratify the infusion ToD in future clinical studies on immunotherapy

PRESENTED BY: Yongchang Zhang MD, zhangyongchang@csu.edu.cn

Inmunoterapia en enfermedad avanzada.

Abstract: 8514

2025 ASCO ANNUAL MEETING

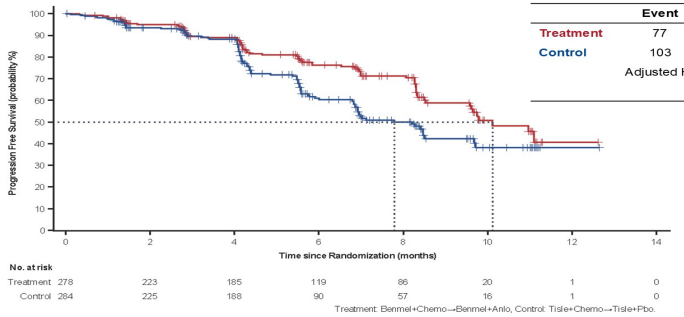
Phase 3 study of benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib for the first-line treatment of locally advanced or metastatic squamous non-small cell lung cancer (sq-NSCLC)

Yuankai Shi[1], Longhua Sun[2], Runxiang Yang[3], Dingzhi Huang[4], Yongzhong Luo[5], Haichuan Su[6], Qiang Liu[7], Peng Zhang[8], XingYa Li[9], Xiangjiao Meng[10], Yu Yao[11], Lingfeng Min[12], Yan Wang[13], Lei Yang[14], Conghua Xie[15], Junquan Yang[16], Jianhua Shi[17], Zhi Xu[18], Hongbo Wu[19], Honghai Wang[20]

[1]Department of Medical Oncology, Beijing Key Laboratory of Key Technologies for Early Clinical Trial Evaluation of Innovative Drugs for Major Diseases, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; [2]Department of Respiratory Medicine, The First Affiliated Hospital of Nanchang University, Nanchang, China; [3]Second Internal Medicine, Yunnan Cancer Hospital (Third Affiliated Hospital of Kunming Medical University), Kunming, China; [4]Department of Pulmonary Medical Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [5]Department of Pulmonary Medical Oncology, Hunan Cancer Hospital, Changsha, China; [6]Department of Oncology, The Second Affiliated Hospital of PLA Air Force Military Medical University, Xi'an, China; [7]Department of Oncology, China Shenyang The Tenth People's Hospital, China Shenyang Chest Hospital, Shenyang, China; [8]Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Shanghai, China; [9]Department of Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [10]Department of Radiation Oncology, Shandong Provincial Tumour Hospital, Jinan, China; [11]Department of Oncology, The First Affiliated Hospital of Xi'an Jiao Tong University, Xi'an, China; [12]Department of Respiratory Medicine and Critical Care Medicine, Northern Jiangsu People's Hospital Affiliated to Yangzhou University, Yangzhou, China; [13]Respiratory Ward Two, Affiliated Cancer Hospital of Harbin Medical University, Harbin, China; [14]Department of Respiratory Oncology, Gansu Provincial Cancer Hospital, Lanzhou, China; [15]Department of Radiation and Chemotherapy for Lung Oncology, Zhongnan Hospital of Wuhan University, Wuhan, China; [16]Department of Chemistry, Tangshan People's Hospital, Tangshan, China; [17]Second Internal Medicine, Linyi Cancer Hospital, Linyi, China; [18]Department of Respiratory Medicine, Second Affiliated Hospital of Third Military Medical University (Army Medical University), Chongqing, China; [19]Department of Oncology, Henan Cancer Hospital, Zhengzhou, China; [20]Department of Oncology, Anyang Tumor Hospital, Anyang, China

Yuankai Shi, Cancer Hospital, Chinese Academy of Medical Sciences

PFS (per RECIST version 1.1 by IRC, ITT), Interim Analysis



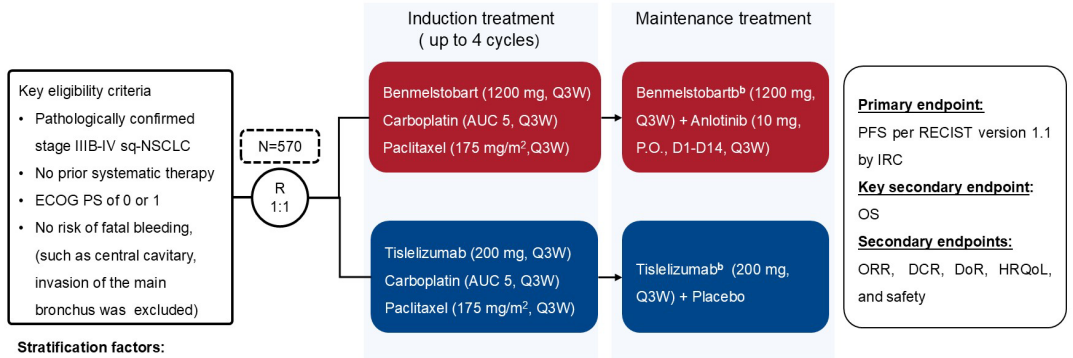
	Event	Censor (%)	Median (95 CI%)
Treatment	77	201 (72.30)	10.12 (8.54-NE)
Control	103	181 (63.73)	7.79 (6.87-9.69)
Adjusted Hazard Ratio 0.64 (98.35% CI 0.45-0.93)			
Stratified Log-rank P=0.0038			

a: Superiority boundary α=0.0165; Data cutoff date for this interim analysis: March 1, 2024. Median follow-up of PFS: 6.97 months (95%CI: 5.78, 7.62) vs. 6.87 months (95%CI: 5.62, 7.29).

Abbreviation: PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; IRC, Independent Review Committee; ITT, intent to treatment; NE, not estimated.

Study Design

TQB2450-III-12 is multicenter, randomized, double-blind, parallel-controlled phase III study



Stratification factors:
- **PD-L1 TPSa: < 1% vs. 1-49% vs. >=50%**
- **Sites of metastases: <=3 vs. > 3**
- **ECOG PS: 0 vs. 1**

a: Assessed at a central laboratory using PD-L1 IHC E1L3N (AmoyDx PD-L1 assay); b: up to 2 years;

Data cutoff date for this interim analysis: March 1, 2024. ClinicalTrials. Gov: NCT05718167

Abbreviation: sq, squamous; NSCLC, non-small cell lung cancer; ECOG, Eastern Cooperative Oncology Group, PS, Performance Status; PD-L1, programmed death ligand 1; TPS, , tumor proportion score; AUC, area under the curve; PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; IRC, Independent Review Committee; OS, overall survival; ORR, objective response rate; DCR, disease control rate; DoR, duration of response; HRQoL, health related quality of life.

Conclusions

- Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib demonstrated a significantly improvement in PFS compared with tislelizumab plus chemotherapy for locally advanced or metastatic sq-NSCLC.
  - Median PFS: 10.12 (95% CI: 8.54, NE) vs. 7.79 (95% CI: 6.87, 9.69) months, HR 0.64 (98.35% CI: 0.45, 0.93), P=0.0038.
  - PFS benefit favored benmelstobart in combination with anlotinib group in almost all subgroups.
- Improvements in ORR, DCR, and a more durable tumor response were observed.
- OS was not matured at this interim analysis.
- Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib showed a manageable safety profile.

Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib might be a new first-line treatment option for sq-NSCLC.

Abbreviation: PFS, progression free survival; sq, squamous; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; NE, not estimated; ORR, objective response rate; DCR, disease control rate; OS, overall survival

Inmunoterapia en enfermedad avanzada.

Poster Bd#135b: HARMONi-3

A Randomized Phase 3 Study of Ivonescimab Plus Chemotherapy Versus Pembrolizumab Plus Chemotherapy for the First-line Treatment of Metastatic Non-small Cell Lung Cancer: HARMONi-3

TPS8664

Jianjun Zhang,[1] Jun Cai,[2] Hui Wang,[3] Yan Yu,[4] Joaquim Bosch-Barrera,[5] Maria Reyes Bernabé Caro,[6] Zoran Andric,[7] Firas Badin,[8] Yusuke Okuma,[9] Paul Paik,[10] Jarushka Naidoo,[11] Haralabos Kalofonos,[12] Bo Wang,[13] Robert Jotte,[14] Nathan Pennell,[15] Jonathan Riess,[16] Deborah Doroshow,[17] Makoto Nishio,[18] Jorge Alatorre-Alexander,[19] Shun Lu[20]

1. MD Anderson Cancer Center, Houston, TX, USA. 2. The First Affiliated Hospital of Yangtze University, Hubei, China. 3. Hunan Cancer Hospital, Changsha, Hunan, China. 4. Harbin Medical University Cancer Hospital, Heilongjiang, China. 5. Catalan Institute of Oncology Girona, Josep Trueta University Hospital, Girona, Spain. 6. Virgen del Rocio University Hospital, Sevilla, Spain. 7. University Hospital Medical Center Bezanijska kosa, Belgrade, Serbia. 8. Baptist Health Lexington, Lexington, KY, USA. 9. National Cancer Center Hospital, Tokyo, Japan. 10. Memorial Sloan Kettering Cancer Center, New York, NY, USA. 11. Beaumont Hospital, Dublin, Ireland. 12. Patras Medical School, Olympion Hospital, Patras, Greece. 13. Willamette Valley Cancer Institute and Research Center/Sarah Cannon Research Institute, Eugene, OR, USA. 14. Rocky Mountain Cancer Centers, Lone Tree - Sky Ridge Medical Center, Lone Tree, CO, USA. 15. Cleveland Clinic, Cleveland, OH, USA. 16. UC Davis Comprehensive Cancer Center, Sacramento, CA, USA. 17. Icahn School of Medicine at Mount Sinai, New York, NY, USA. 18. Cancer Institute Hospital of JFCR, Tokyo, Japan. 19. Health Pharma Professional Research, Mexico City, Mexico. 20. Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China

BACKGROUND

- A combination of platinum-based chemotherapy plus programmed cell death protein 1 (PD-1) and programmed cell death ligand 1 (PD-L1) is the most common treatment approach for patients with newly diagnosed Stage IV non-small cell lung cancer (NSCLC) regardless of tumor PD-L1 status[1]
- Ivonescimab is a first-in-class investigational bispecific antibody against PD-1 and vascular endothelial growth factor (VEGF; Figure 1)[2,3]
  - > By blocking both PD-1 and VEGF in the tumor microenvironment, ivonescimab has the potential to drive synergistic anti-tumor activity through higher binding affinity and increased activity of T cells
  - > In vitro studies have shown that the presence of VEGF increases PD-1 binding strength by more than 10-fold
- In Phase 3 studies, ivonescimab has yielded promising clinical outcomes in patients with advanced/metastatic NSCLC[4-6]
  - > In HARMONi-A, patients with relapsed advanced/metastatic epidermal growth factor receptor (EGFR)-mutated NSCLC (excluding patients with T790M variant) treated with ivonescimab plus chemotherapy had a median progression-free survival (mPFS) of 7.1 months (vs 4.8 months for the placebo plus chemotherapy group) and an overall response rate (ORR) of 50.6% (vs 35.4%)
  - > In HARMONi-2, patients with PD-L1–positive advanced NSCLC treated with ivonescimab experienced a longer mPFS compared with those treated with pembrolizumab (11.1 months vs 5.8 months, respectively)
    - The PFS benefit of ivonescimab was consistent across patients with PD-L1 tumor proportion scores of 1%-49% (hazard ratio [HR] 0.54) and >50% (HR 0.48)
  - > In the Phase 3 trial, HARMONi-6, patients with squamous NSCLC treated first-line (1L) with ivonescimab plus chemotherapy achieved superior PFS vs patients treated with tislelizumab (anti-PD-1) plus chemotherapy regardless of PD-L1 status making it the first known regimen to achieve clinically meaningful benefit over an anti-PD-(L)1 antibody-chemotherapy combination
- HARMONi-3 is the first global study to investigate the efficacy and safety of ivonescimab plus chemotherapy in patients with metastatic (Stage IV) NSCLC with no prior systemic treatment history[7]

Figure 1. Ivonescimab PD-1/VEGF Bispecific Antibody. Anti-PD-1 scFv attaches to the C-terminus of each anti-VEGF-A antibody heavy chain. Ivonescimab has a heterotetrameric structure consisting of 2 heavy chains of the IgG1 subclass and 2 light chains of the kappa subclass, which are covalently linked through disulfide bonds.[2]

KEY ELIGIBILITY CRITERIA[3,7]

Key Inclusion Criteria

- ≥18 years of age at time of enrollment
- ECOG Performance Status score of 0 or 1
- Metastatic (Stage IV) NSCLC with histologically or cytologically confirmed squamous or non-squamous NSCLC
- Tumor proportion score for PD-L1 expression, irrespective of the PD-L1 expression, prior to randomization
- ≥1 measurable noncerebral lesion according to RECIST v1.1
- No prior systemic treatment for metastatic NSCLC[a]

Key Exclusion Criteria

- Histologic or cytopathologic evidence of the presence of small cell lung carcinoma
- Known actionable genomic alterations (EGFR, ALK, ROS1, and BRAF V600E) for which 1L approved therapies are available
- Has received any prior therapy for NSCLC in the metastatic setting
- Radiologically documented evidence of major blood vessel invasion or tumor invading organs or there is a risk of esophagotracheal or esophagopleural fistula in the opinion of the investigator
- Symptomatic central nervous system (CNS) metastases or CNS metastasis ≥1.5 cm
- History of bleeding tendencies or coagulopathy and/or clinically significant bleeding symptoms or risk within 4 weeks (including gastrointestinal bleeding, hemoptysis)

[a] Patients receiving adjuvant or neoadjuvant chemotherapy or curative-intent chemoradiotherapy with or without PD-(L)1 inhibitors are eligible if the adjuvant/neoadjuvant therapy was completed at least 6 months prior to the development of metastatic disease.

TRIAL ENDPOINTS[3,7]

Primary Endpoints

- Overall survival
- PFS as assessed by investigator based on RECIST v1.1[b]

Secondary Endpoints

- ORR,[b] disease control rate, and duration of response as assessed by investigator based on RECIST v1.1
- Safety assessment: incidence and severity of adverse events and clinically significant abnormal laboratory test results
- Pharmacokinetics: ivonescimab serum drug concentration profiles
- Immunogenicity: number of patients with detectable anti-ivonescimab antibody at baseline and post treatment

[b] Images will be collected for blind review by the IRRC as a sensitivity analysis.

TRIAL DESIGN[3,7]

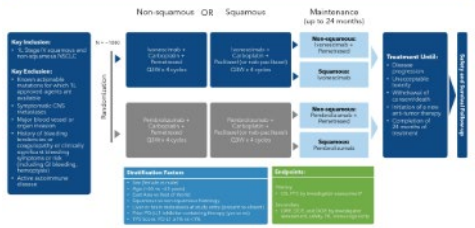


Figure 2. HARMONi-3 Trial Design. HARMONi-3 is a global, randomized, double-blind, phase 3 study to compare the efficacy and safety of ivonescimab or pembrolizumab, combined with platinum-doublet chemotherapy in patients with metastatic NSCLC without activating mutations who have not previously received systemic therapy for metastatic disease. Approximately 1080 patients will be randomized (1:1) to receive 4 cycles of ivonescimab (20 mg/kg) or pembrolizumab (200 mg) combined with platinum doublet chemotherapy as an IV injection Q3W followed by ivonescimab or pembrolizumab +/- pemetrexed maintenance therapy Q3W as determined by histology.

[a] PFS sensitivity analysis will be performed based on IRRC's assessment.

1L, first line; CNS, central nervous system; DOR, disease control rate; DOR, duration of response; GI, gastrointestinal; IRRC, Independent Radiology Review Committee; N, intravenous; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, once every 3 weeks; TPS, tumor proportion score.

TRIAL STATUS[7]

- This study is expected to enroll participants at 174 locations across North America, Europe, and Asia (Figure 3)
- The latest information on this study can be found at ClinicalTrials.gov, reference number NCT05899608

Figure 3. HARMONi-3 Study Locations.

ACKNOWLEDGMENTS

The authors thank participants and their caregivers, the investigators, and all the site staff who have participated and who are participating in this study. This study is sponsored by Summit Therapeutics, Inc. Medical writing assistance was provided by Sandra Diedrick, PhD, at Ashfield Oncology and was funded by Summit Therapeutics.

REFERENCES

1. Hendriks LE et al. Ann Oncol. 2023;34(4):358-376. 2. Zhang T et al. Science. 2024;283(6):111722. 3. Summit Therapeutics, Inc. Data on File 29 December 2024. 4. HARMONi-A Study Investigators et al. JAMA. 2024;332(7):561-570. 5. Xiong A et al. Lancet. 2025;405(10481):839-849. 6. Significant superiority in PFS vs tislelizumab (PD-1 inhibitor)-plus-chemotherapy in 1L treatment of patients with squamous NSCLC in HARMONi-6 study conducted by Akeso in China. 2025. Available at: https://www.akeso.com/en/press-release/Significant-superiority-in-PFS-vs-tislelizumab-PD-1-inhibitor-plus-chemotherapy-in-1L-treatment-of-patients-with-squamous-NSCLC-in-HARMONi-6-study-conducted-by-Akeso-in-China.html. Accessed April 14, 2025. 7. ClinicalTrials.gov Identifier: NCT05899608. Accessed April 14, 2025. https://clinicaltrials.gov/study/NCT05899608

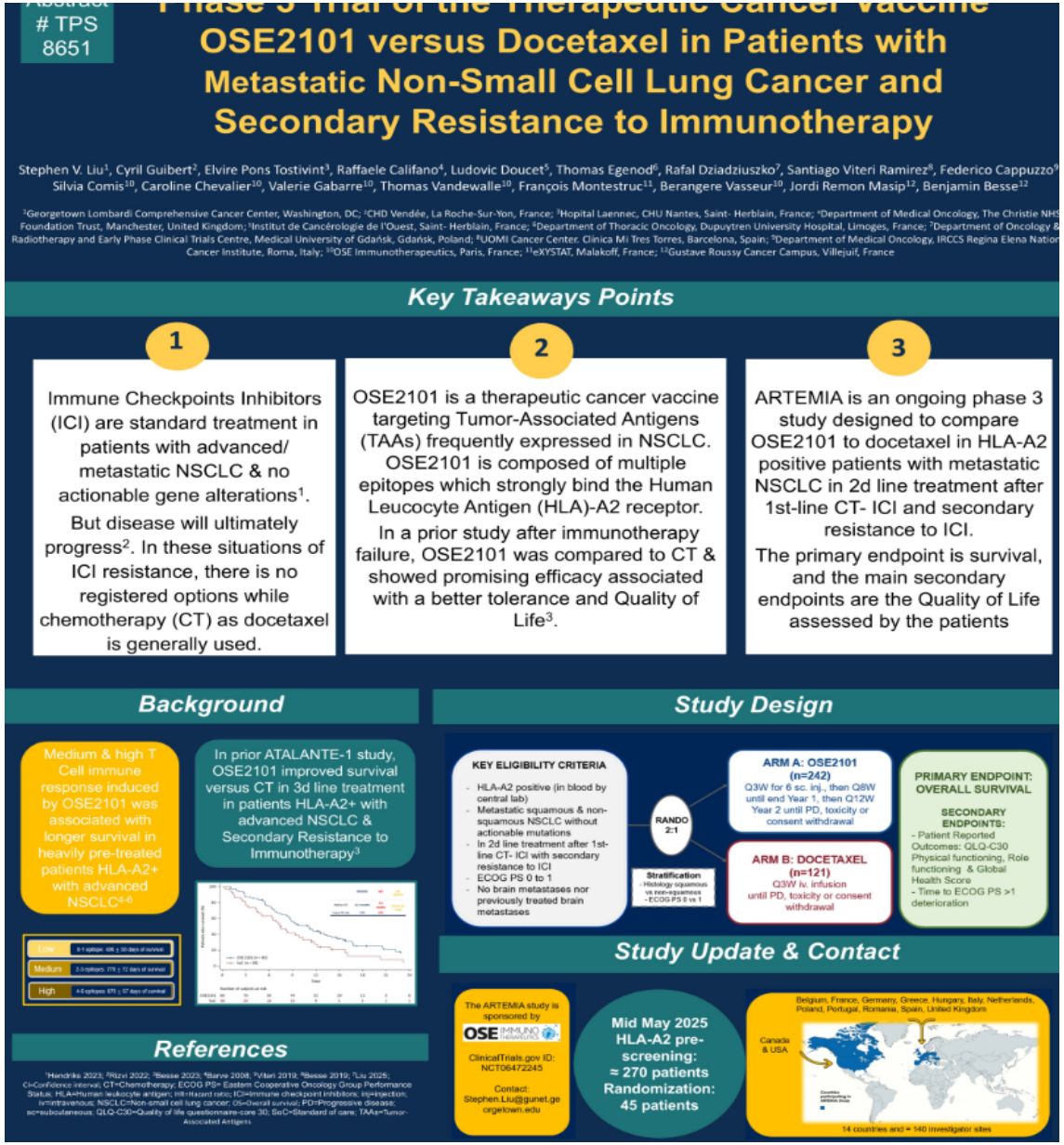
CONTACT INFORMATION

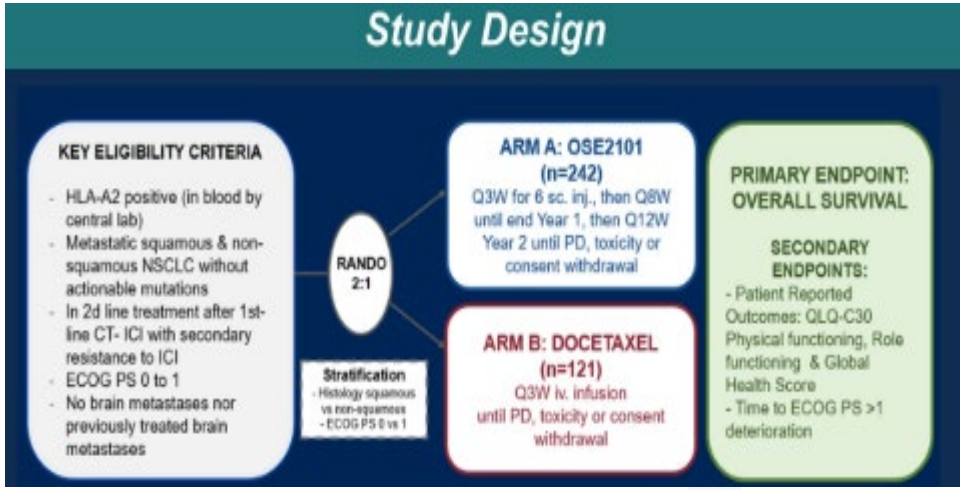
Please contact the presenting author Jianjun Zhang at jjzhang@medicalmedicon.org for questions or comments

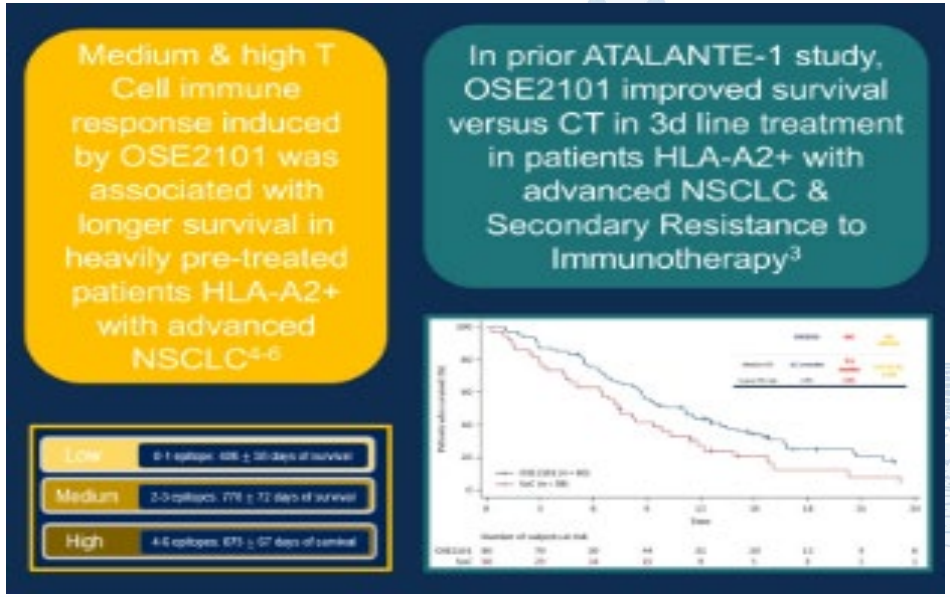
Presented at the American Society of Clinical Oncology (ASCO) 2025; May 30 - June 3, 2025; Chicago, IL

Inmunoterapia en enfermedad avanzada.

Poster: Bd#129a







Inmunoterapia en enfermedad avanzada.

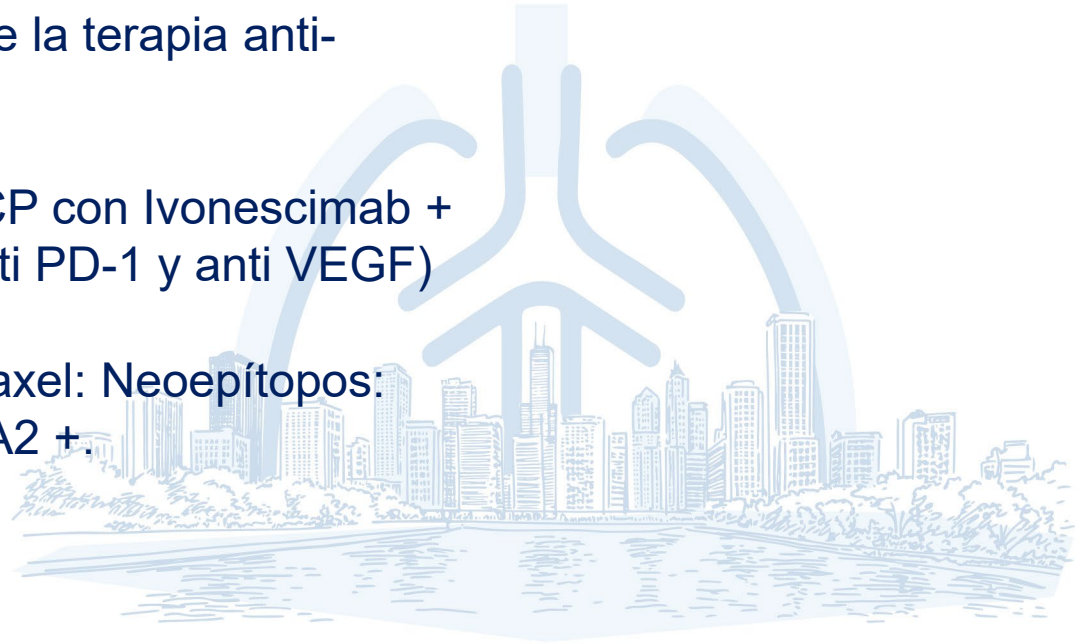
- El estado del ctDNA como guía para la escalada de tratamiento: estudio prometedor: precisa validación.

- Time-of-day: la hora de administración de la IO importa e impacta en supervivencia: LT- CD8+

- Ambos estudios asiáticos: plantean el uso de la terapia anti-angiogénica (Anlotinib).

- HARMONi-3: Estudio fase III: 1ª línea CPNCP con Ivonescimab + doblete basado en platino (bioespecífico: anti PD-1 y anti VEGF)

- ARTEMIA: OSE2101 (Tedopi) versus Docetaxel: Neoepítopos: objetivo mejorar la respuesta inmune, HLA-A2 +.



¡GRACIAS!