HARMONi-3 Phase 3 Clinical Trial

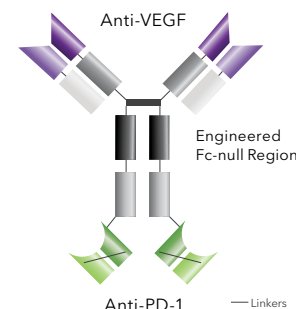First-Line Metastatic Squamous and Non-Squamous NSCLC / NCT05899608[1]

HARMONi-3

Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Lung Cancer Clinical Development in North America and Europe.*

Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule.
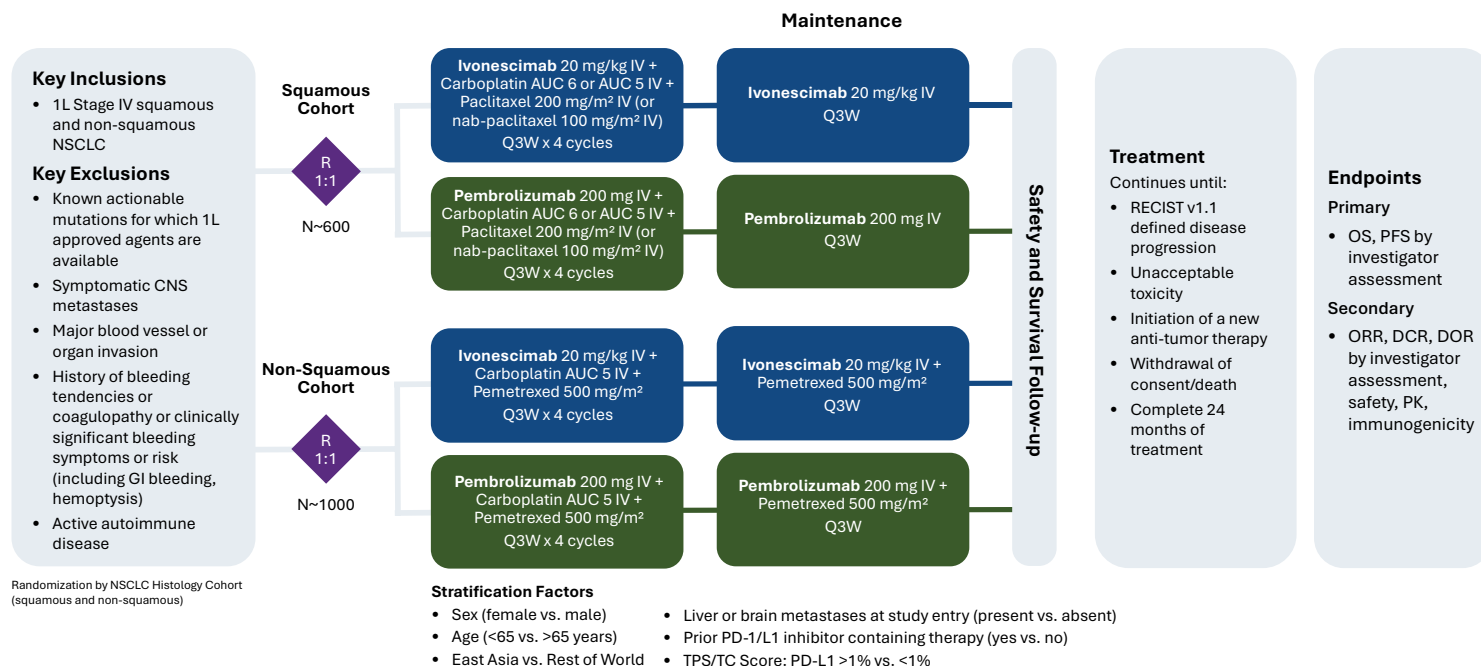
Ivonescimab Blocks Both PD-1 & VEGF Cooperatively

Globally 2,800+ patients have been treated with ivonescimab across Summit and Akeso clinical trials.[5] Summit is actively recruiting approximately 1,600 patients worldwide for the HARMONi-3 study.

Anti-VEGF

Engineered Fc-null Region

Anti-PD-1 — Linkers

HARMONi-3 TRIAL DESIGN

Maintenance

Key Inclusions
- 1L Stage IV squamous and non-squamous NSCLC

Key Exclusions
- Known actionable mutations for which 1L approved agents are available
- Symptomatic CNS metastases
- Major blood vessel or organ invasion
- History of bleeding tendencies or coagulopathy or clinically significant bleeding symptoms or risk (including GI bleeding, hemoptysis)
- Active autoimmune disease

Randomization by NSCLC Histology Cohort (squamous and non-squamous)

Squamous Cohort

R 1:1

N~600

Ivonescimab 20 mg/kg IV + Carboplatin AUC 6 or AUC 5 IV + Paclitaxel 200 mg/m² IV (or nab-paclitaxel 100 mg/m² IV) Q3W x 4 cycles

Ivonescimab 20 mg/kg IV Q3W

Pembrolizumab 200 mg IV + Carboplatin AUC 6 or AUC 5 IV + Paclitaxel 200 mg/m² IV (or nab-paclitaxel 100 mg/m² IV) Q3W x 4 cycles

Pembrolizumab 200 mg IV Q3W

Non-Squamous Cohort

R 1:1

N~1000

Ivonescimab 20 mg/kg IV + Carboplatin AUC 5 IV + Pemetrexed 500 mg/m² Q3W x 4 cycles

Ivonescimab 20 mg/kg IV + Pemetrexed 500 mg/m² Q3W

Pembrolizumab 200 mg IV + Carboplatin AUC 5 IV + Pemetrexed 500 mg/m² Q3W x 4 cycles

Pembrolizumab 200 mg IV + Pemetrexed 500 mg/m² Q3W

Safety and Survival Follow-up

Treatment

Continues until:
- RECIST v1.1 defined disease progression
- Unacceptable toxicity
- Initiation of a new anti-tumor therapy
- Withdrawal of consent/death
- Complete 24 months of treatment

Endpoints

Primary
- OS, PFS by investigator assessment

Secondary
- ORR, DCR, DOR by investigator assessment, safety, PK, immunogenicity

Stratification Factors
- Sex (female vs. male)
- Age (<65 vs. >65 years)
- East Asia vs. Rest of World
- Liver or brain metastases at study entry (present vs. absent)
- Prior PD-1/L1 inhibitor containing therapy (yes vs. no)
- TPS/TC Score: PD-L1 >1% vs. <1%

KEY ELIGIBILITY CRITERIA

- Metastatic (Stage IV) NSCLC
- Histologically or cytologically confirmed squamous or non-squamous NSCLC
- Must have TPS or TC with PD-L1 expression prior to randomization
- No prior systemic treatment for metastatic NSCLC
- No histologic or cytopathologic evidence of the presence of small cell lung carcinoma
- No known actionable genomic alterations in EGFR, ALK, ROS1, BRAF V600E or genes for which first-line approved therapies are available

- No radiographic evidence of major blood vessel encasement with narrowing of the vessel or intratumor lung cavitation or necrosis that the investigator determines will pose a significantly increased risk of bleeding
- No symptomatic CNS metastases, CNS metastases with hemorrhagic features, or CNS metastases ≥1.5cm
- No history of bleeding tendencies or coagulopathy and/or clinically significant bleeding symptoms or risk within 4 weeks (including GI bleeding, hemoptysis)

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

*There are no known PD-1-based bispecific antibodies approved by the U.S. Food and Drug Administration ("FDA") or the European Medicines Agency ("EMA").

Abbreviations: 1L=first-line; ALK=anaplastic lymphoma kinase; CNS=central nervous system; DCR=disease control rate; DOR=duration of response; EGFR=epidermal growth factor receptor; GI=gastrointestinal; NSCLC=non-small cell lung cancer; ORR=overall response rate; OS=overall survival; PD-1=programmed cell death protein 1; PD-L1=programmed death-ligand 1; PFS=progression-free survival; PK=pharmacokinetics; Q3W=every 3 weeks; R=randomization; RECIST=Response Evaluation Criteria in Solid Tumors; TC=tumor cell; TME=tumor microenvironment; TPS=tumor proportion score; VEGF=vascular endothelial growth factor.

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Cooperative Binding Offers Potential to Drive Synergistic Activity[6-8]
Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule
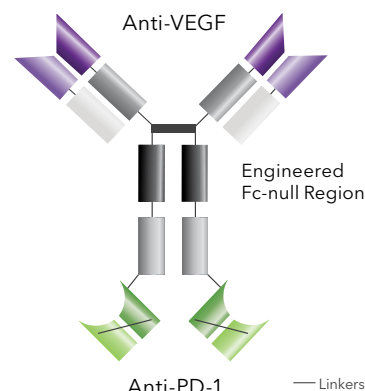
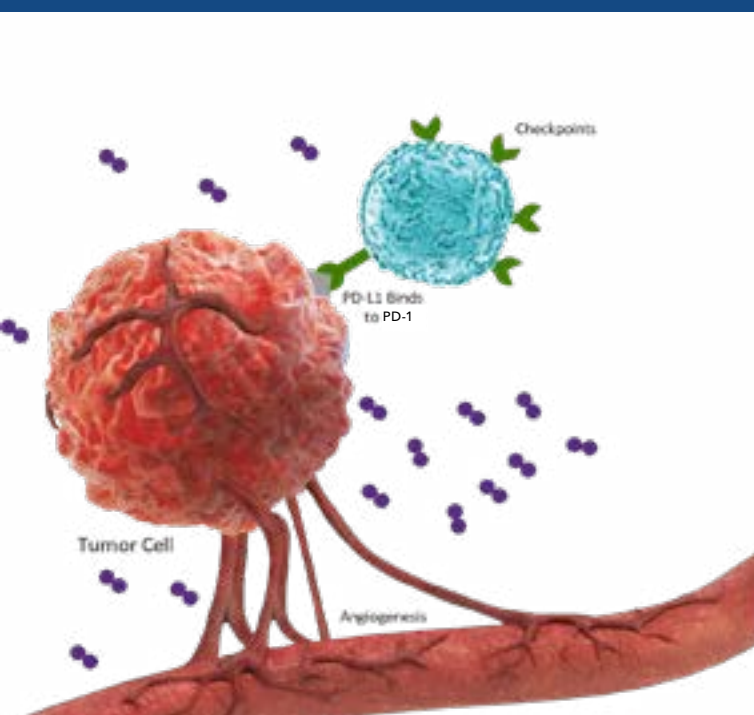## Dual Blocking of PD-1 & VEGF[8]

Increased Avidity in TME
VEGF-A efficiently enhances the binding affinity to PD-1 by several fold[8] *(in vitro)*
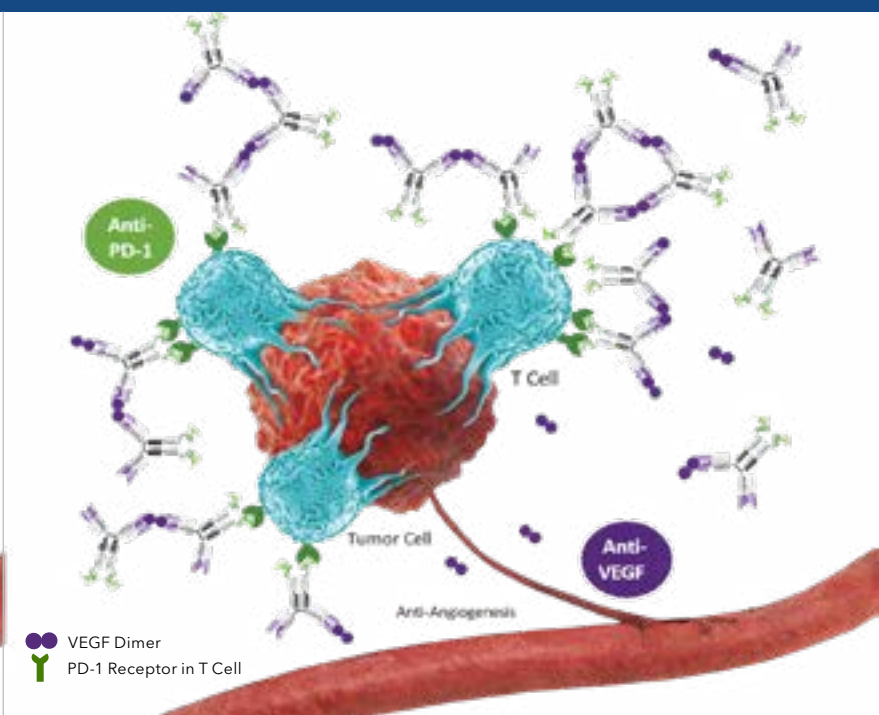
Enhanced Activity of T Cells
VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T cells[8] *(in vitro)*

Anti-VEGF

Engineered Fc-null Region

Anti-PD-1 — Linkers

Tumor Microenvironment	Tumor Microenvironment with Ivonescimab Cooperative Binding

Checkpoints

PD-L1 Binds to PD-1

Tumor Cell

Angiogenesis

Anti-PD-1

T Cell

Anti-VEGF

Tumor Cell

Anti-Angiogenesis

VEGF Dimer
PD-1 Receptor in T Cell

Images for illustrative purposes only

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For more information contact medinfo@smmttx.com

HARMONi-3

Summit therapeutics

Intended for Clinical Site Staff Use Only

1. Clinical Study of Ivonescimab for First-line Treatment of Metastatic NSCLC Patients. ClinicalTrials.gov identifier: NCT05899608. https://clinicaltrials.gov/study/NCT05899608. Updated March 21, 2025 (Accessed May 20, 2025); 2. Manegold C, et al. J Thorac Oncol 2017;12(2):194-207.; 3. Pardoll, D. Nat Rev Cancer 2012;12(4):252-64.; 4. Tamura R, et al. Med Oncol 2020;37(1):2.; 5. Summit Press Release (August 11, 2025); 6. Zhao Y. et al., eClinicalMedicine. 2023; 3(62): 102106.; 7. Wang L, et al. J Thorac Oncol. 2024 Mar;19(3):465-475; 8. Zhong T, et al. iScience. 2024;28(3):111722.;