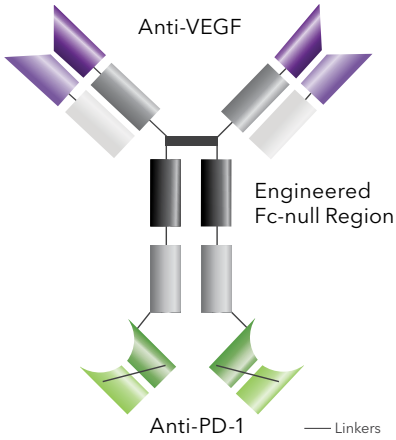
HARMONi-3 Phase 3 Clinical Trial

First Line Metastatic Squamous NSCLC / NCT05899608[1]

HARMONi-3

Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Clinical Development in the U.S. and EU.*

Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule.



Ivonescimab simultaneously blocks both PD-1 & VEGF

Globally 1,600+ patients have been treated with ivonescimab across Summit and Akeso clinical trials. Summit is actively recruiting approximately 400 patients worldwide for the HARMONi-3 study.

HARMONi-3 PHASE 3 STUDY DESIGN

Key Inclusion Criteria:

- → Untreated metastatic squamous (Stage IV) NSCLC
- → ECOG 0 or 1
- → No symptomatic CNS metastases or CNS metastasis ≥1.5 cm
- → No known actionable genomic alterations in EGFR, ALK, ROS1 or genes for which first-line approved therapies are available

(N~400)

1:1

Group A
Ivonescimab + carboplatin + paclitaxel (or nab-paclitaxel) Q3W
4 cycles: (3 weeks/cycle)

Group B
Pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel) Q3W
4 cycles: (3 weeks/cycle)

Group A
Ivonescimab Q3W
(maintenance up to 24 mo)

Group B
Pembrolizumab Q3W
(maintenance up to 24 mo)

Treatment Until

- → Intolerable toxicity
- → No clinical benefit
- → Initiation of a new anti-tumor therapy
- → 24 months of treatment

Primary Endpoint: OS
Secondary Endpoint: PFS by Inv, ORR, safety, PK

Safety and Survival Follow up

KEY ELIGIBILITY CRITERIA

- Metastatic (Stage IV) NSCLC
- Histologically or cytologically confirmed squamous NSCLC
- Patients must have Tumor Proportion Score (TPS) with PD-L1 expression percentage
- No prior systemic treatment for metastatic NSCLC. No histologic or cytopathologic evidence of the presence of small cell lung carcinoma, or non-squamous NSCLC histology
- No known actionable genomic alterations in EGFR, ALK, ROS1 or genes for which first-line approved therapies are available
- No radiologically documented evidence of major blood vessel invasion or organ invasion
  Note: Encasement by cancer with narrowing of the vessel, or intratumor cavitation are eligible
- No symptomatic CNS metastases or CNS metastasis ≥1.5 cm
- 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 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").

Ivonescimab: Designed to Potentially Improve the Balance of Anti-tumor Activity & Safety[5,6]

Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule

Cooperative Binding

Potential to drive synergistic anti-tumor activity[5-7]

Simultaneous blocking of PD-1 & VEGF[5-7]

Increased Avidity in the Tumor Microenvironment (TME)

VEGF increases affinity to **PD-1 by >18X**[7]

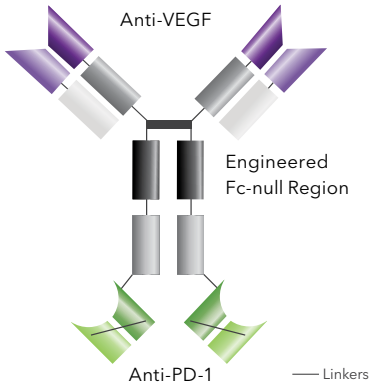
PD-1 increases affinity to **VEGF by >4X**[7]

(in vitro)

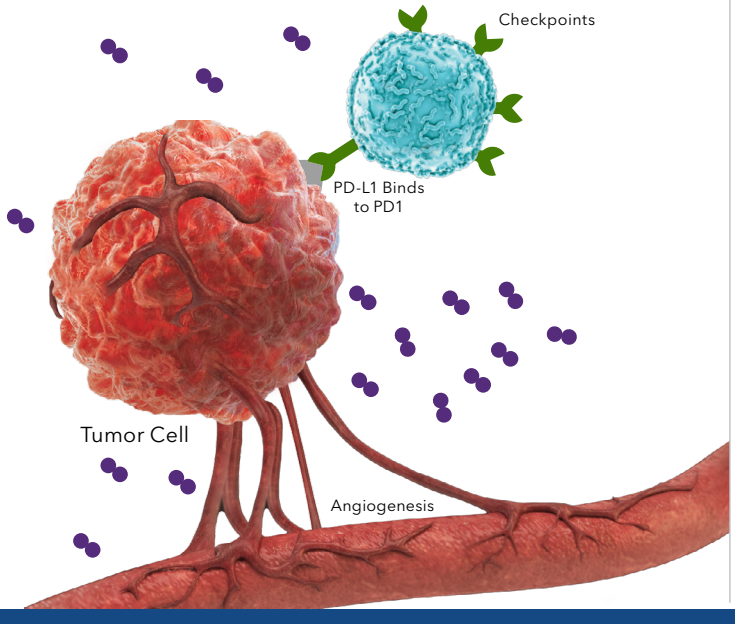
Enhanced Activity of T Cells

VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T cells[7]

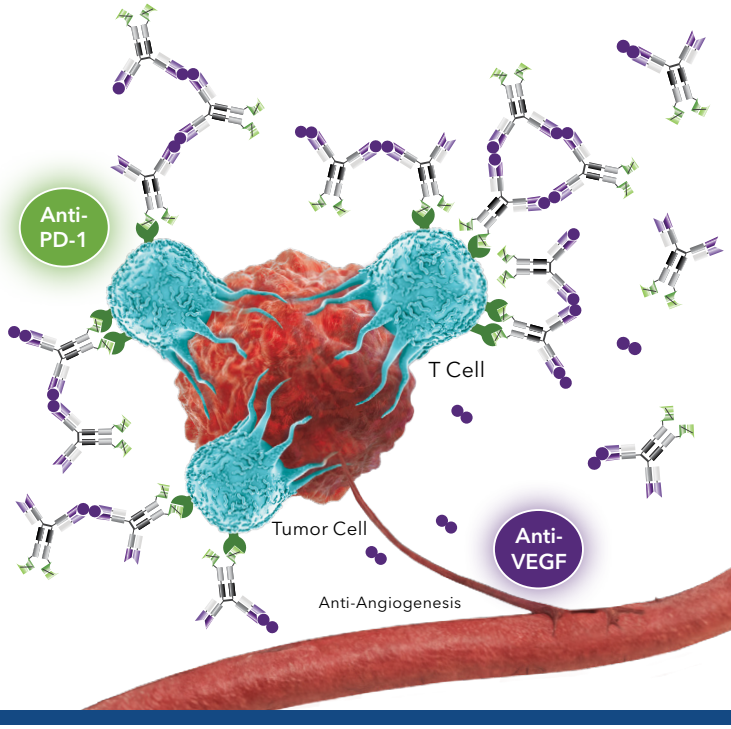
(in vitro)



Tumor Microenvironment



Tumor Microenvironment with Ivonescimab Cooperative Binding



Images for illustrative purposes only.

VEGF Dimer PD-1 Receptor in T Cell

For more information contact medinfo@smmttx.com

1. Clinical Study of Ivonescimab for First-line Treatment of Metastatic Squamous NSCLC Patients. ClinicalTrials.gov identifier: NCT05899608. *https://clinicaltrials.gov/study/NCT05899608*. (Accessed 2024, May 14).; **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.** Zhao Y, et al. *eClinicalMedicine*.2023; 3(62): 102106.;**6.** Wang L, et al. *J Thorac Oncol*. 2024 Mar;19(3):465-475.; **7.** Zhong T, et al. AACR-NCI-EORTC International Conference 2023.Poster #B123,Abstract #35333,

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SMMTTX.com
medinfo@smmttx.com

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