HARMONi Phase 3 Clinical Trial

Patients With EGFR+ NSCLC Who Have Progressed After 3rd Generation EGFR-TKI (osimertinib) / NCT06396065[1]

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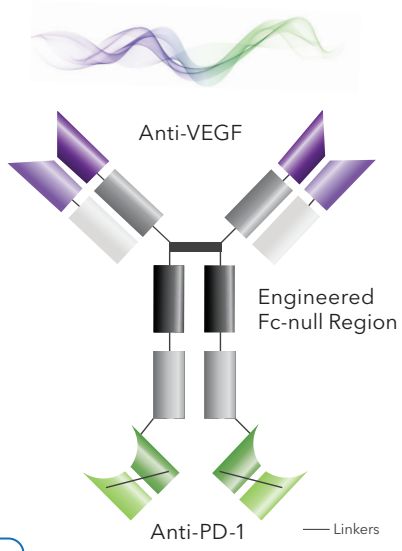
Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Clinical Development in the U.S. and EU.*

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



Ivonescimab simultaneously engages both PD-1 & VEGF

Globally 2,300+ patients have been treated with ivonescimab across Summit and Akeso Inc. clinical trials[5].

HARMONi PHASE 3 STUDY DESIGN

Locally advanced or metastatic non-squamous NSCLC:

- → Positive sensitive EGFR mutation
- → Progressed on 1st/2nd generation EGFR-TKI with negative T790, or on 3rd generation EGFR-TKI
- → ECOG = 0 or 1
- → Regardless of PD-L1 expression

(N~420)

1:1

Group A
Ivonescimab 20 mg/kg Q3W
+Pemetrexed 500 mg/m² Q3W
+Carboplatin AUC 5 Q3W
4 cycles (3 weeks/cycle)

Group A
Ivonescimab 20 mg/kg Q3W
+Pemetrexed 500 mg/m² Q3W
Maintenance Period

Group B
Placebo Q3W
+Pemetrexed 500 mg/m² Q3W
+Carboplatin AUC 5 Q3W
4 cycles (3 weeks/cycle)

Group B
Placebo Q3W
+Pemetrexed 500 mg/m² Q3W
Maintenance Period

Treatment Until

- → Intolerable toxicity
- → No clinical benefit (Investigator assessment)
- → Initiation of a new anti-tumor therapy
- → Complete 24 months of treatment

Safety and Survival Follow up

Primary Endpoints: OS, PFS assessed by irRC
Secondary Endpoints: ORR by irRC, DoR, safety and tolerability

KEY ELIGIBILITY CRITERIA

- Expected survival ≥3 months
- Locally advanced (Stage IIIB/IIIC) or metastatic (Stage IV) non-squamous NSCLC that has progressed on 3rd generation EGFR-TKI (e.g., osimertinib)
- At least 1 measurable noncerebral per RECIST v1.1 lesion
- Adequate organ and hematologic function
- Prior treatment with one non-EGFR therapy is allowed (i.e amivantamab, REQORSA, etc,). Prior treatment with immune checkpoint inhibitors, anti-angiogenic therapy and chemotherapy (including ADCs) remain exclusionary
- Tumor does not surround important blood vessels or invade the surrounding vital organs and blood vessels. Lesions with necrosis or cavitation applies only to pulmonary parenchymal lesions (ie, not lymph nodes etc)
- No symptomatic metastases of the central nervous system
- No history of esophageal gastric varices, severe ulcers or wounds that do not heal
- No history of severe bleeding tendencies or coagulopathy, or hemoptysis within last 4 weeks

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: ADC=antibody-drug conjugates; DoR=duration of response; ECOG=eastern cooperative oncology group; EGFR=Epidermal growth factor receptor; IRRC= independent radiographic review committee; NSCLC=non-small cell lung cancer; PD-1=programmed cell death protein 1; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; TKI=tyrosine kinase inhibitor; Q3W=every 3 weeks; TME=tumor microenvironment; VEGF=vascular endothelial growth factor.

Cooperative Binding Offers Potential to Drive Synergistic Activity[6-8]

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

Increased Avidity in TME[8*]

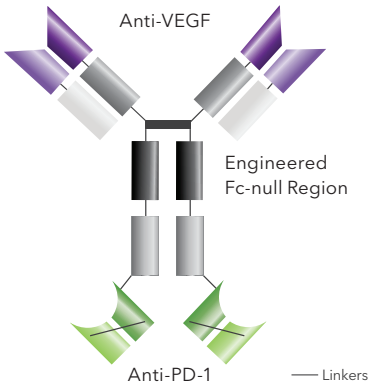
Enhanced Activity of T Cells[8*]

VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T Cells

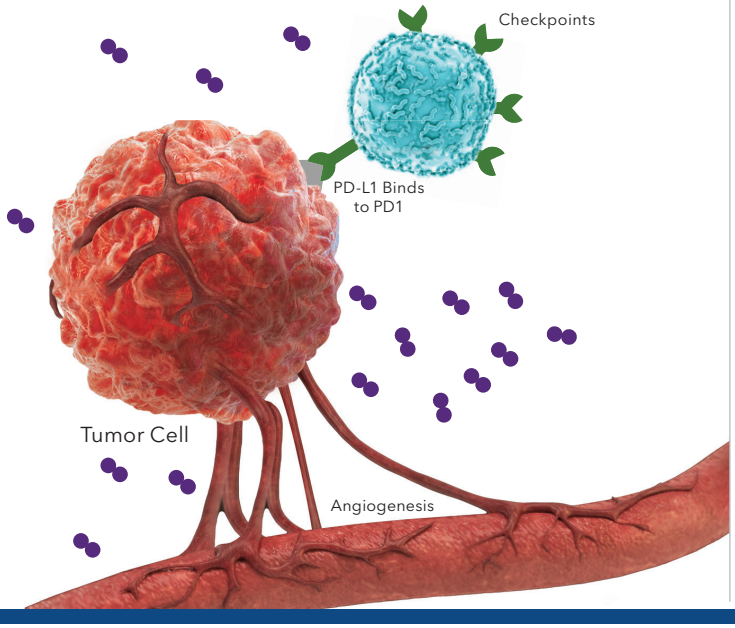
T½ ~10 days[9] and Fc-null region[8]

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

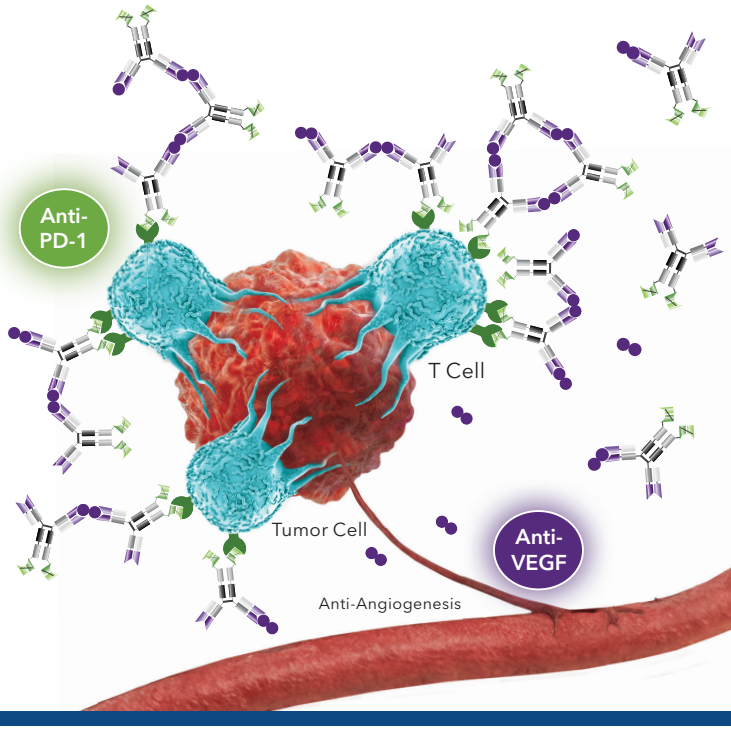
**in vitro*



Tumor Microenvironment



Tumor Microenvironment with Ivonescimab Cooperative Binding



Images for illustrative purposes only.

VEGF Dimer PD-1 Receptor in T Cell

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For more information contact medinfo@smmttx.com

1. Phase III Study of AK112 for NSCLC Patients. ClinicalTrials.gov identifier: NCT06396065. https://clinicaltrials.gov/study/NCT06396065. (Accessed 2025, May 12).; 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. Data on File 38. Summit Therapeutics Inc.; 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.; 9. Data on File 39. Summit Therapeutics Inc.

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