Harbour BioMed: Advancing Global Biotherapeutics Innovation

Dr. Jingsong Wang

Founder, Chairman and CEO
Harbour BioMed

HBM HOLDINGS-B

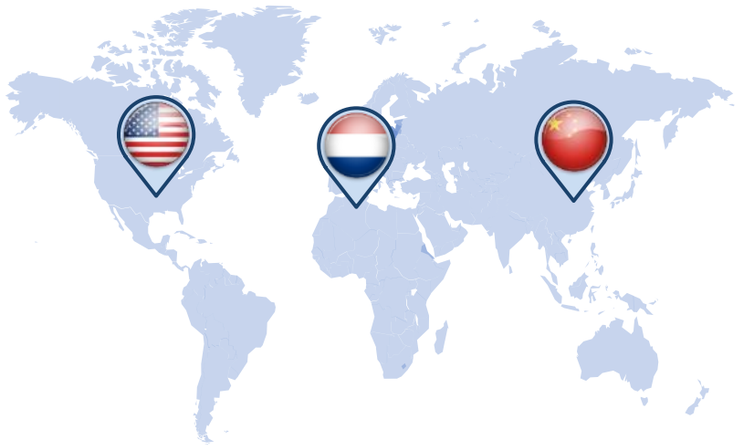
02142.HK

www.harbourbiomed.com

Harbour BioMed Rapidly Progressing Toward a Global Leading Biopharmaceutical Company

A Global Biotherapeutics Company Focusing on Breakthrough Medicines

USA Netherlands China



Therapeutic Focus:

- Immunology
- Immuno-Oncology

2016-2017
- Established in 2016
- Transformed into a clinical stage company in 2017

2018-2019
- 3 INDs in 2018
- Tanfanercept entered Ph2 in 2018
- HBM4003 entered Ph1 in 2019

2020
- Successfully listed in HKEX
- Batoclimab entered Ph2 for first wave indications

2021
- Batoclimab & Tanfanercept entered Ph3
- HBM4003 in multiple Ph1/2 globally
- 2 new assets apply for INDs globally

The Capital Group · BlackRock · 高瓴资本 Hillhouse Capital · HBM Healthcare Investments · GIC · Hudson Bay Capital · OrbiMed Healthcare Fund Management · Octagon Capital Advisors · 中国人寿 China Life · CDH Investments 鼎晖投资 · Legend Capital 君联资本 · 尚颀投资 ADVAN·TECH · Atlas Venture

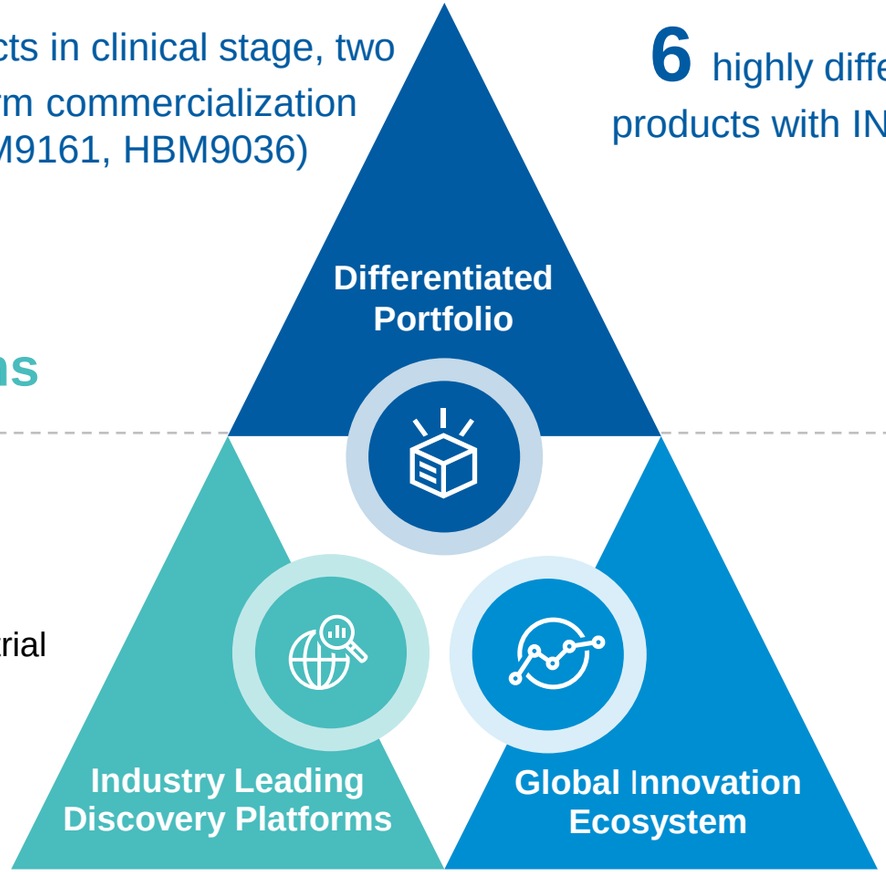
HARBOUR BIOMED

Leading Next Gen Biotherapeutics Innovation to Address Unmet Medical Needs in Global Market

Next Gen Therapeutics

4 products in clinical stage, two near-term commercialization (HBM9161, HBM9036)

6 highly differentiated products with INDs by 2022

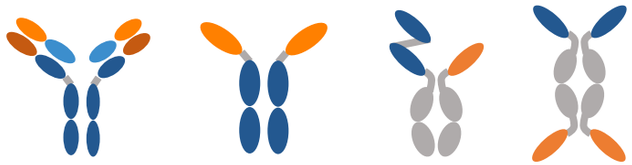


Industry Leading Platforms

Worldwide patent protection

45+ industry and academic partners

9 innovative therapeutics entered clinical trial



Pfizer abbvie Lilly VIR THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Dana-Farber Cancer Institute

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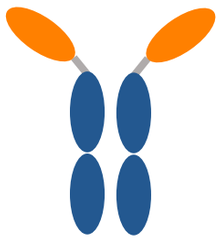
Build a Highly Differentiated Portfolio Leveraging Industry Leading Fully Human Technology Platforms

- **Worldwide patent protection**
- Validated by **45+** industry and academic partners
- **9** projects in clinical stage
- **>200** internal and external projects leveraging HBM platforms

Fully human classical antibody H2L2

Fully human heavy chain HCAb



Fully human bispecifics HBICE

Advantages of HBM Fully Human Antibody Platforms

Fully human classical antibody H2L2

1. Efficient and reliable (no need for humanization, high affinity)
2. Excellent druggability (immunity in mice, evolution by natural selection)
3. Great safety (low immunogenicity)

Fully human heavy chain antibody HCAb

1. Scarcity (the only fully human transgenic mice heavy chain antibody platform in the world)
2. Flexibility (widely used)
3. Good penetrability (small size, easy to penetrate tumor and tissue)

Fully human bispecific antibody HBICE

1. Unique and proven bispecific antibody mechanism

HARBOUR BIOMED

Internationally Renowned Scientific Advisory Board

FRANK GROSVELD
PhD

- Co-founder and CSO of Harbour Antibodies, inventor of Harbour Mice®
- Professor and former Head of the Department of Cell Biology and the Department of Clinical Genetics at the Erasmus University Medical Center
- Fellow of the Royal Society and a member of the Royal Netherlands Academy of Arts and Sciences

ROBERT KAMEN
PhD

- Venture Partner at Third Rock Ventures
- Co-founder and former chairman of BioAssets
- Former director of Neon Therapeutics and Harbour Antibodies
- Former president and unit head of Abbott Bioresearch Centre, Former SVP at Genetics Institute, Inc.
- Ph.D. in biochemistry and molecular biology from Harvard University

KENNETH MURPHY
MD, PhD

- Member of the National Academy of Sciences
- Eugene Opie First Centennial Professor of Pathology & Immunology, Washington University School of Medicine in St. Louis
- Ph.D. in pharmacology and M.D. from Hopkins University School of Medicine

JON WIGGINTON
MD

- Chief Medical Officer, Cullinan Oncology; Advisos of MPM Capital
- Former Chief Medical Officer and SVP of Clinical Development at MacroGenics, Inc.
- Former Therapeutic Area Head of Immuno-Oncology, Early Clinical Research at BMS
- Former President of the Society for Immunotherapy of Cancer

ROBERT KRAMER
PhD

- CSO of Portage Biotech Inc.
- Former VP and Head of Discovery for Oncology Therapeutics at Janssen Research & Development, LLC
- Former VP Drug Discovery and Research for Bristol-Myers Squibb (BMS)
- Ph.D. in pharmacology from the University of Vermont

PETER MOESTA
PhD

- Former executive roles at Bristol-Myers Squibb
- Oversaw the development, production and worldwide launch of important medicines, such as Humira, Yervoy and Opdivo

ZHIGANG TIAN
MD, PhD

- Academician of the Chinese Academy of Engineering
- Professor of the University of Science and Technology of China
- Council member of International Union of Immunological Societies
- Council member of Federation of Immunological Societies of Asia-Oceania

Robust Pipeline Combining Advanced Clinical Programs and Next-Gen Biotherapeutics Addressing Highly Unmet Needs

Project	Target	Indication	Commercial Rights	Status
● Batoclimab HBM9161	FcRn	MG	Greater China	Breakthrough Therapy Designation; Ph 3 ongoing
		NMOSD		Ph 1b/2 ongoing
		ITP		Ph 2/3 ongoing
		GO		Ph 2/3 ongoing
		CIDP		IND approval by NMPA
		PV		IND application accepted by NMPA
● Tanfanercept HBM9036	TNFα	Dry Eye Disease	Greater China	Ph 3 ongoing
● HBM9022	SARS-COV-2	COVID-19	Global License to AbbVie	
● HBM9378	TSLP	Asthma	Global	
● HBM4003	CTLA-4	Solid Tumors [a]	Global	Ph 1b/2 ongoing
		Solid Tumors [b]		Combo with PD-1 Ph 1 ongoing
		Solid Tumors [c]		Combo with PD-1 Ph 1 ongoing
● HBM7008	B7H4×4-1BB	Solid Tumors	Global	
● HBM1022	CCR8	Solid Tumors	Global	
● HBM1020	B7H7	Solid Tumors	Global	
● HBM7020	BCMA×CD3	Multiple Myeloma	Ex-Greater China[1]	
● HBM1007	CD73	Solid Tumors	Global	

Discovery | Pre-Clinical | IND | Phase I | Phase II | Phase III | BLA

1. Greater China rights out-licensed to Hualan Genetics

a. Melanoma, HCC, RCC and Other Advanced Solid Tumors
b. Melanoma, HCC, NEN and Other Advanced Solid Tumors
c. NSCLC and Other Advanced Solid Tumors

HBM | Partner | ★ Registrational Clinical Trial | ● In-license Program | ● Program from Harbour Discovery Platforms

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Building World-class CMC & Manufacturing Capacity & Enhanced Commercial Strategy

CMC & GMP Manufacturing Capability

CMC Process Development

- **In-house CMC**
  - Cell line / Cell culture /Purification /Formulation / Analytical development
- **15-20 projects**
  - IND/BLA filling / CDMO Management / Process development, Process characterization, Process validation

Pilot Plant, Ready by 2022

Commercialization Strategy

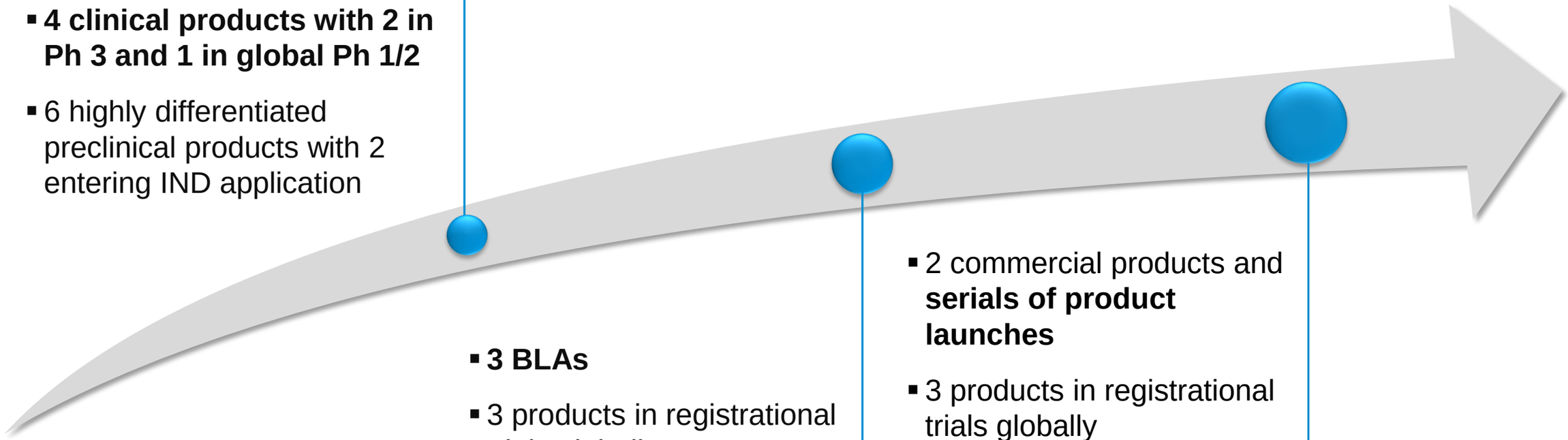
Stage 1: Focus on Immunology
Stage 2: Oncology 2025 -

Commercial Launch Readiness in Full Swing

Rapid Progress for Key Assets Towards Bringing Innovative Therapeutics to Patients Around the World

2021

- **4 clinical products with 2 in Ph 3 and 1 in global Ph 1/2**
- 6 highly differentiated preclinical products with 2 entering IND application



2022

- **3 BLAs**
- 3 products in registrational trials globally
- Multiple next gen therapeutics entering INDs

2023 & Beyond

- 2 commercial products and **serials of product launches**
- 3 products in registrational trials globally
- Multiple next gen therapeutics in global clinical trials

Harbour BioMed Advancing Global Biotherapeutics Innovation

Next Gen Therapeutics

- Biology-driven
- Unmet medical needs driven
- Industry leading technologies to provide sustainable innovation engine
- Highly differentiated portfolio with FIC/BIC next gen therapeutics

- Global Innovation Centers
- Collaboration with leading global biopharmaceutical companies and top-notch academies to advance next gen therapeutics
- Development and commercialization of HBM products globally

Global Innovation

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THANK YOU

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Unleash Powerful Technology for HBM's Sustained Innovation

Dr. Yiping Rong
Head of Research, Harbour BioMed

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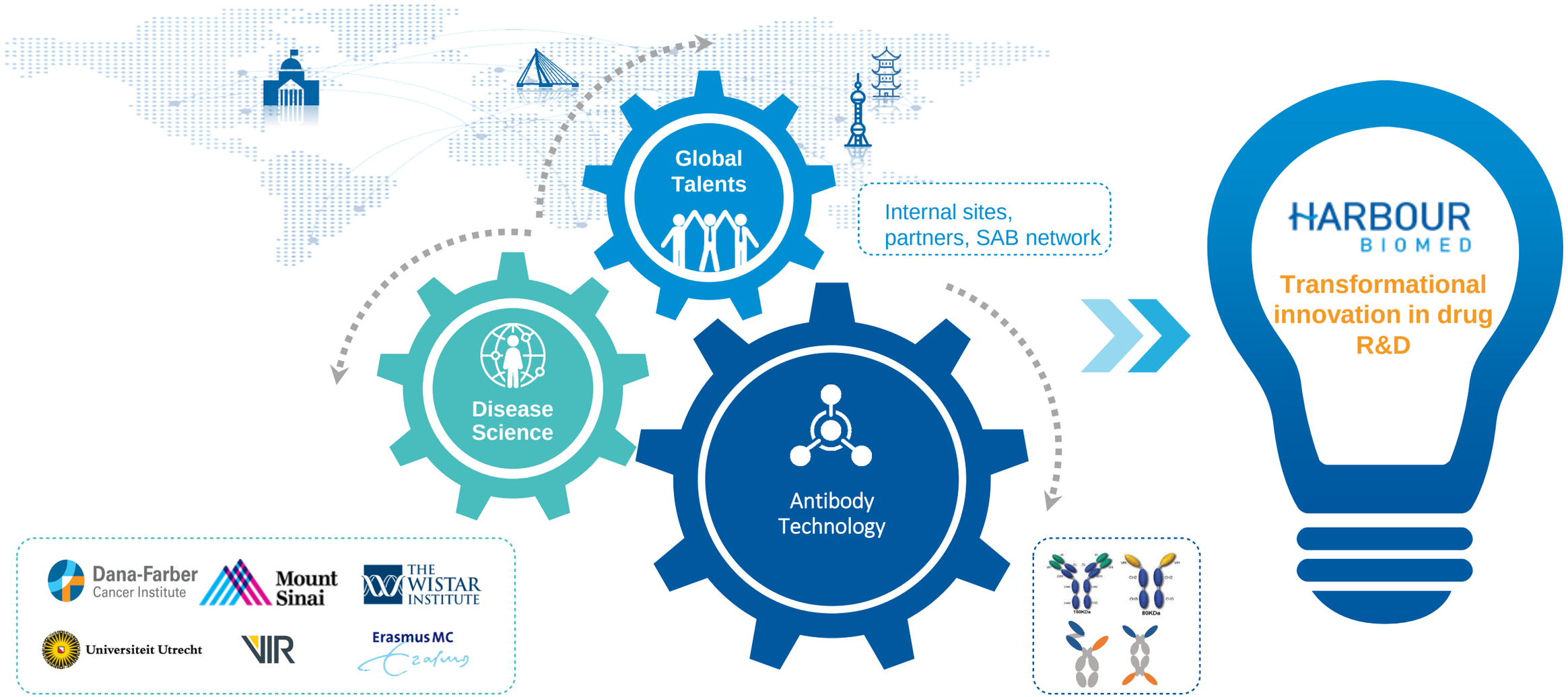
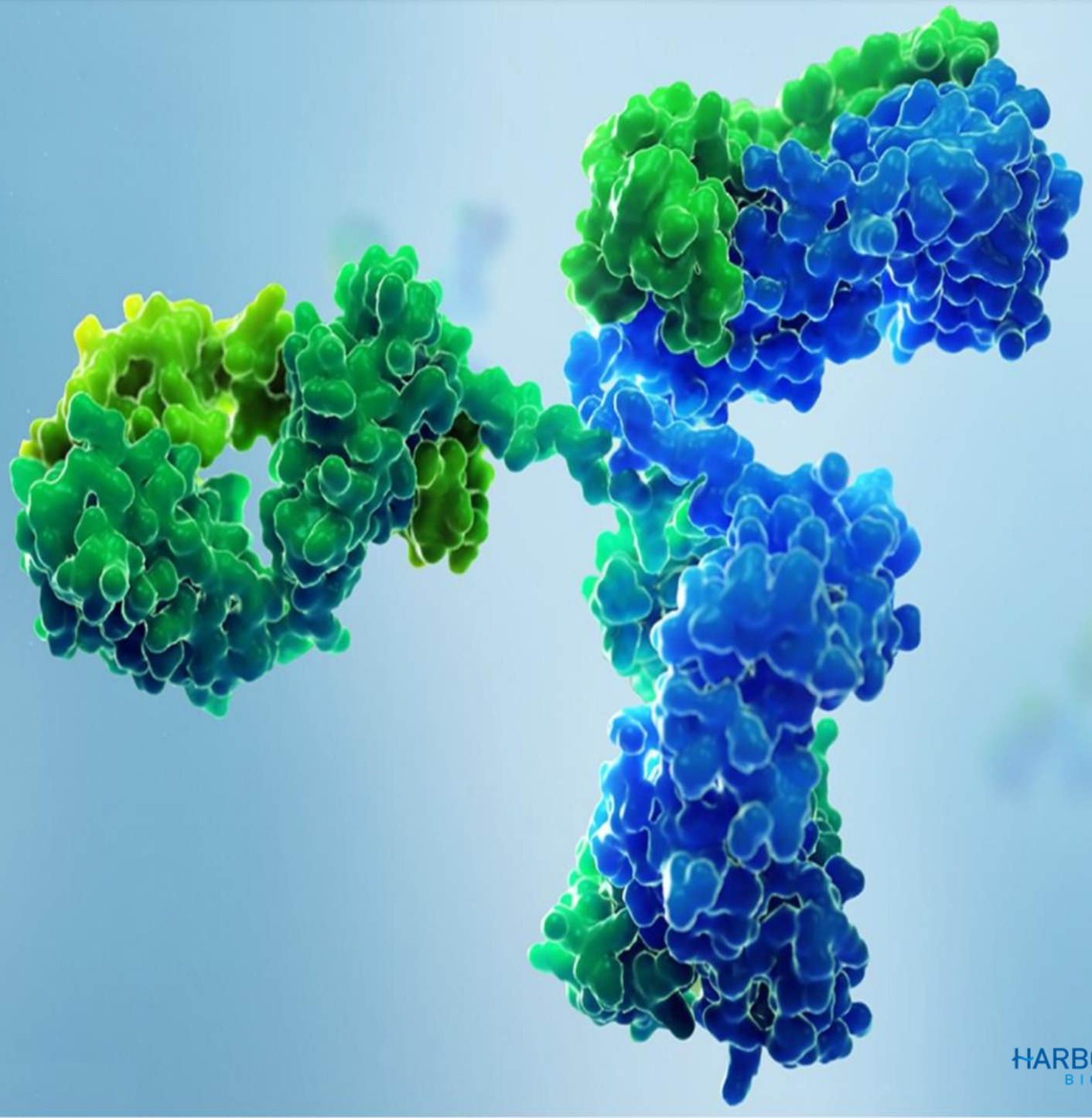
Drive Transformational Innovation with Three Pillars in HBM R&D



HBM’s Antibody Discovery Platform is the Engine of Portfolio Innovation



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Cutting Edge Fully Human Antibody Platforms Enable Sustained Invention of Novel Molecules

H2L2 – Full IgG Antibody Discovery Platform

HBM1020

A fully human antibody against B7 family target for the treatment of solid tumors

HBM9378

A fully human antibody against TSLP for severe asthma

Robust and highly efficient, global IP and clinically validated

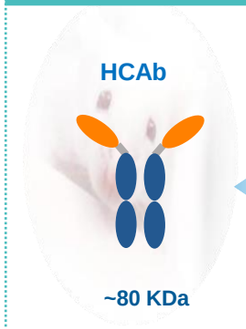
Ligand / MT

$ 178 M
Platform only

SANOFI / kymab

$1.1 B
Platform + 1 Ph2 + 1 Ph1

HCAb – Next-Generation Heavy-Chain-Only Antibody



HBICE®

A Unique, HCAb-Based Platform For Immune Cell Engagers

HBM4003

A next generation anti-CTLA4 antibody

Unique fully human HCAb, versatile for broad applications

SANOFI / Ablynx

$ 4.8 B
Nanobody + 1 BLA + 1 Ph2

AMGEN / Teneobio

$2.5 B
Platform + 1 Ph1

HBICE® – HCAb-Based Bispecific Platform for Immune Cell Engagers

HBM7020

A BCMAxCD3 bispecific antibody

HBM7008

A B7H4×4-1BB bispecific antibody

Self-developed, unique geometric flexibility, promising bispecific biology

Lilly / Merus

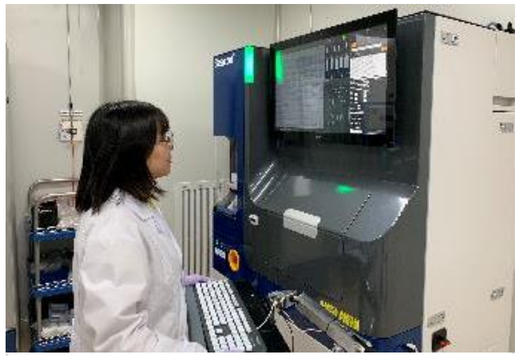
$ 1.6 B
3 BsAb slots based on Biclonics platform

abbvie / Genmab

$ 3.2 B
3 BsAb ADC slots based on Duobody platform

Integrated Technology Platforms Ensure Efficient Discovering Next-Gen Fully Human Antibody Therapeutics

Immunization	Hybridoma	HCAb& Bispecific Ab	Single Cell Technology
Molecule Biology	Protein Science	Phage Display	Yeast Display
Analytical Science	Bioinformatics	Cell Line Engineering	Antibody Engineering



Single B Cell cloning – Beacon Optofluidic System for High-throughput Antibody Screening

Transgenic fully human antibody mice

- No need for humanization, affinity maturation
- H2L2 and HCAb with knock-out or inducible immunization techniques

Single B cell cloning (Beacon System)

- Accelerated antibody discovery process and increased productivity
- Deep mining of rare clones

Display and antibody engineering to support bispecific molecule design

Antibody generation with Single B Cell cloning method (Beacon) in ~4 months*

Animal Immunization 1-2 months → SBC 1 -2 weeks → SC Sequence (1-2 weeks) → Recombinant Antibody (4-5 weeks) → Lead Characterization 1-2 weeks

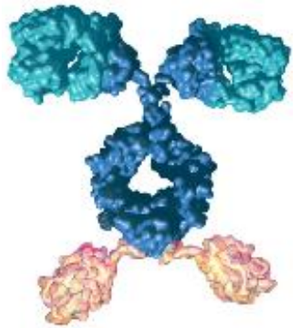
**Traditional hybridoma method need 7-9 months with additional 3-6 months of humanization*

Advancing HBM Core Technologies for Next-Gen Therapeutics Beyond Harbour Mice

Delivery Technology

mRNA technology for immunogen or drug delivery to tackle difficult targets

Protein Engineering

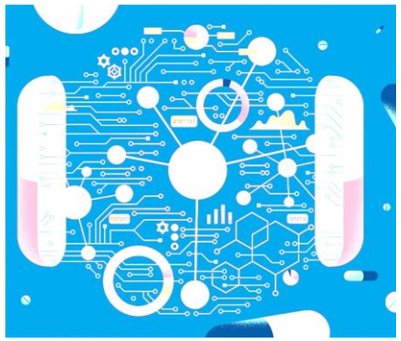


Combine human antibody platforms and **protein engineering** to generate multifunctional molecules

Conjugation Technology

Novel **conjugation technology** for bringing new modalities against solid tumors

Artificial Intelligence



Artificial Intelligence for accelerating drug discovery and translation research

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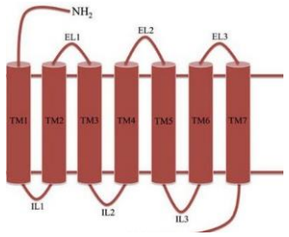
Advancing HBM Core Technologies for Next-Gen Therapeutics

Using mRNA Technology to Tackle Challenging Targets for Ab Generation

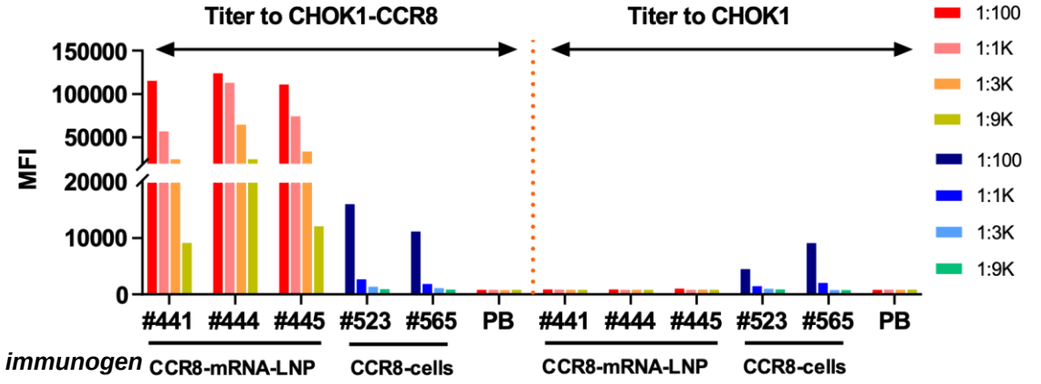
Good immunogen is key to generate GPCR antibodies



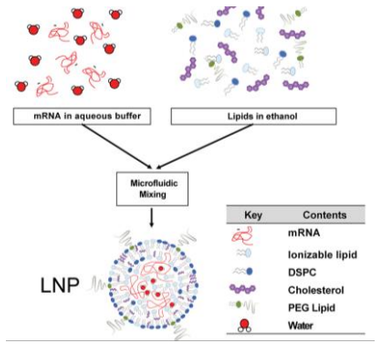
7TM GPCR

Immunogen	issues
Proteins	Generally not available
Cells	Low target expression, raise non-specific immune response
DNA	Low immune response
mRNA	Technical difficulty ?

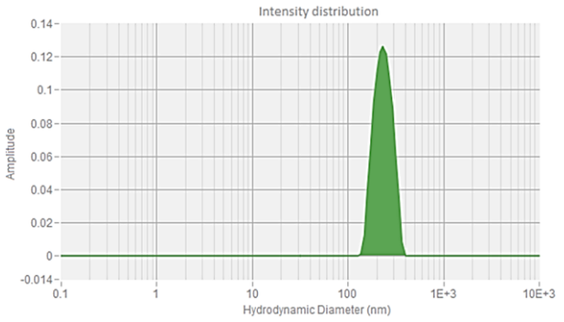
CCR8-mRNA-LNP raised stronger and specific immune responses than CCR8 cells



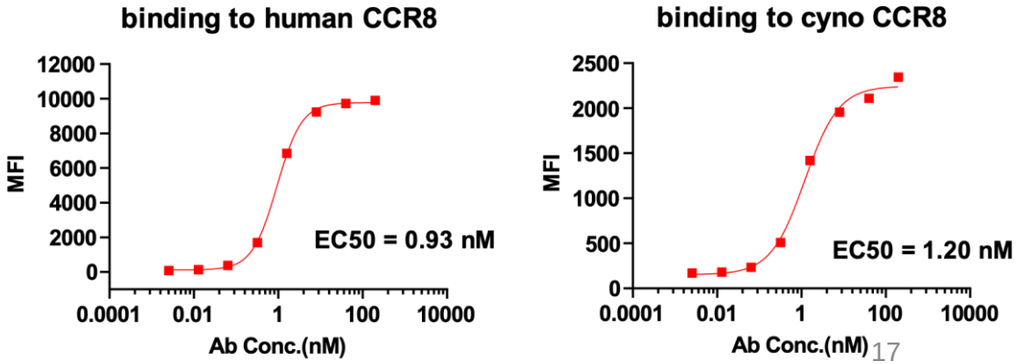
Tailored and efficient mRNA-lipid nanoparticles (LNP)



CCR8-mRNA-LNP had homogeneous size distribution and > 80% encapsulation efficiency



Identified candidate with cross-reactivity to cyno CCR8



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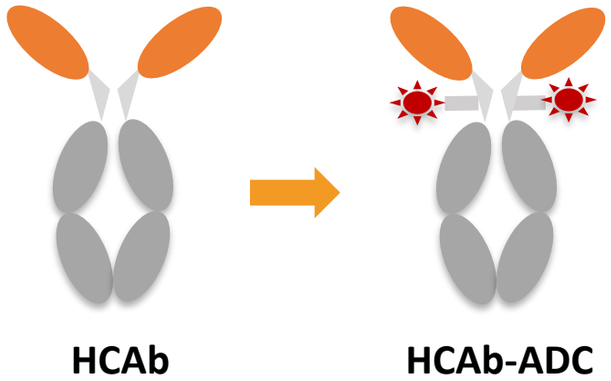
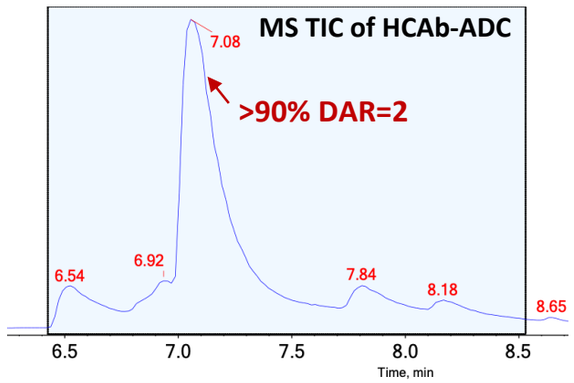
Advancing HBM Core Technologies for Next-Gen Therapeutics

HBM Proprietary Fully Human HCAb Site-Specific ADC is the New Class ADC Platform

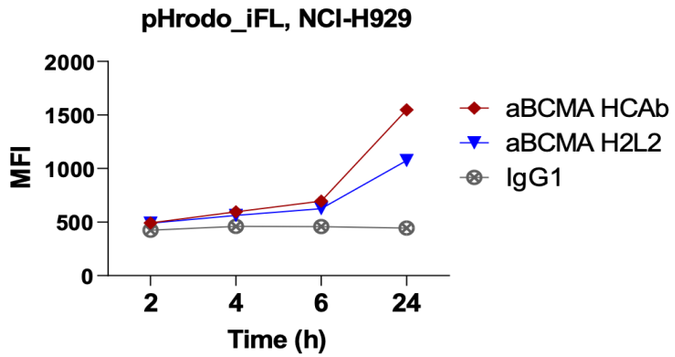


Smaller size (~ 85 KDa)	✓ better tissue penetration
Access special epitope	✓ better target internalization
Site-specific conjugation	✓ High homogeneous product
Fully human antibody sequences	✓ No additional tags ✓ No non-natural amino acids ✓ No changes on glycosylation patterns
Simple conjugation	✓ Good manufacturability
Flexibility	✓ Expand to other modalities e.g. bsAb

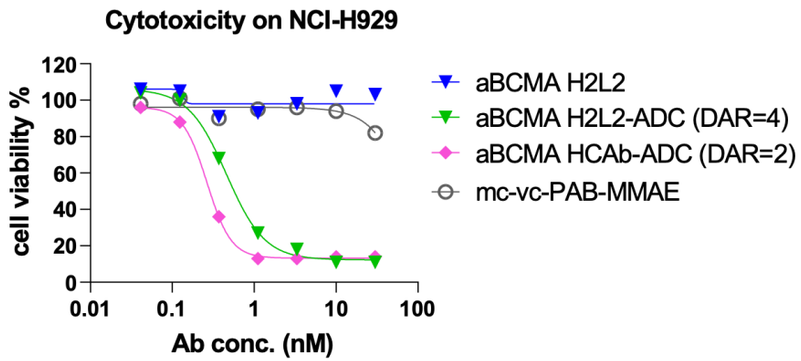
Homogeneous Product



Improved Internalization



Enhanced Cytotoxicity



HBM Innovative R&D Strategy is Powered by Unique Technology Platform

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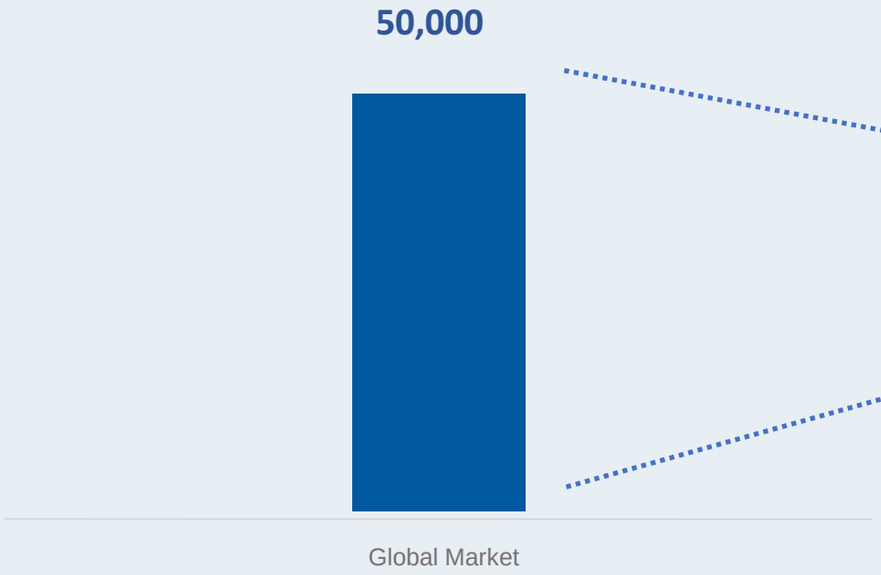
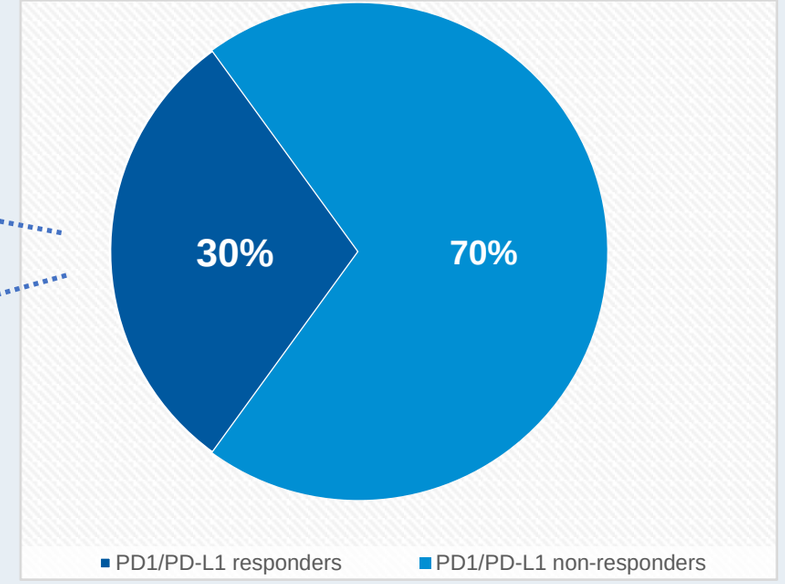
Current IO Therapy – Only 20-30% Patients Respond to PD1/PDL1 Therapies

- Huge PD1/PD-L1 market
- A large number of indications: lung cancer, liver cancer, gastric cancer, esophageal cancer, melanoma, lymphoma, urothelial cancer, breast cancer, nasopharyngeal cancer, colorectal cancer, cervical cancer, etc.
- **70-80% of patients are resistant or have no response for PD1/PD-L1 -- huge market potential**

Expected PD1/L1 Market Size in 2025 (unit: USD Mil)



Most Patients Are Resistant or Not Responded to PD1/PDL1 Treatment



Data source: Frost & Sullivan, Southwest Securities

Note: Compiled data of PD1/PDL1 development and marketed drugs

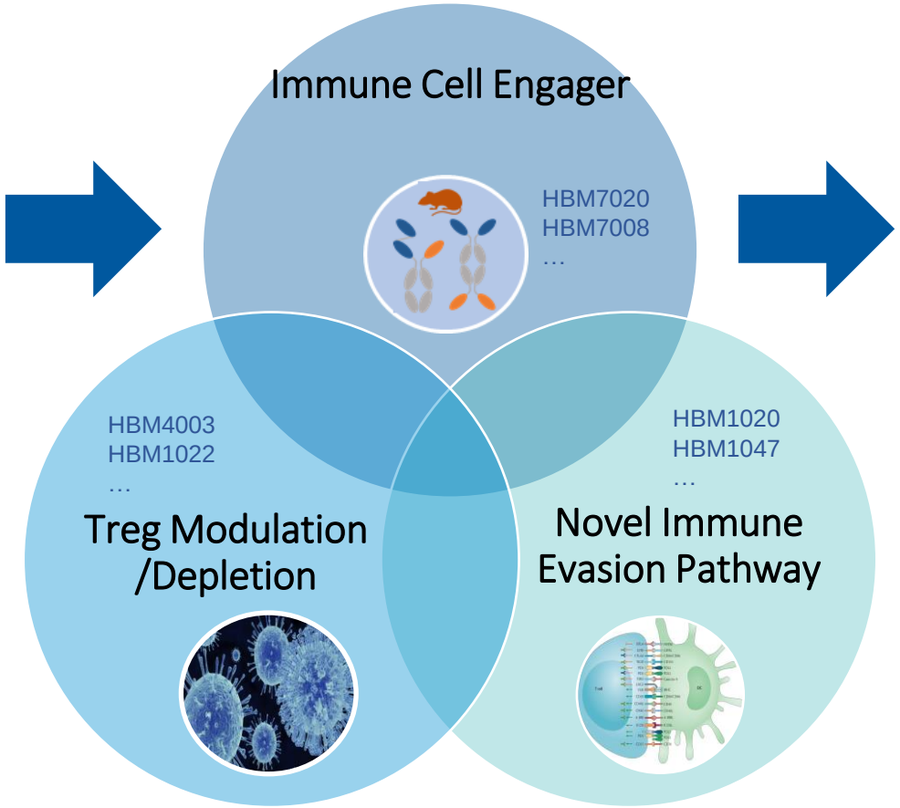
HARBOUR BIOMED

HBM Provides Innovative Solutions for Next-Gen Immuno-Oncology Therapy

The Major Causes of Current IO Limitation

1. No enough immune cells in tumor microenvironment (TME)
2. Suppressive immune cells in TME (Tregs, MDSC, CAF etc.)
3. Complementary immune evasion pathways besides PD1/PD-L1

HBM Next-Gen IO Therapy Strategy



Scientific Strategy is Warranted by Cutting-edge Technologies

1. Increase T/NK cell infiltration /proliferation via immune cell engager (HBICE, SBC, Fc engineering)
2. Depletion of regulatory T cells (eADCC, Afucosylation, HCAb)
3. Innovative targets and pathways of the B7 family (H2L2, HBICE, mRNA/DNA immunization, ADC)

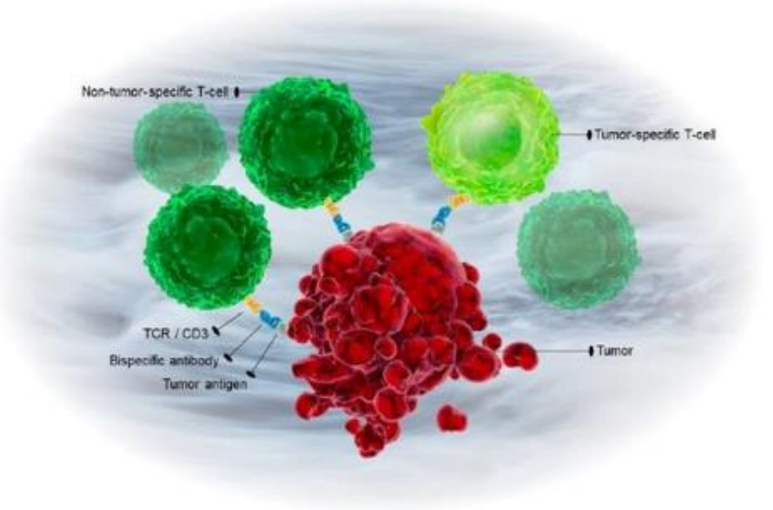
Goal: Breakthrough Efficacy with Improved Safety Profile

HARBOUR BIOMED

Solution 1:

Immune Cell Engager (HBICE®) is One of the Exciting Solutions to Turn Cold Tumor to Hot Tumor

HBICE®	Target validation	Lead generation	candidate selection	Pre-clinical	IND
HBM7020	Multiple myeloma				
HBM7008	Ovary cancer, TNBC, Lung cancers				
Undisclosed	Multiple solid tumors				
Undisclosed	Gastric cancer, pancreatic cancer				



HBICE® Expands Immune Cell Engagers Beyond CD3 TCE

Tumor-associated Antigens For Specific Targeting

A panel of TAA antibodies on various of tumors

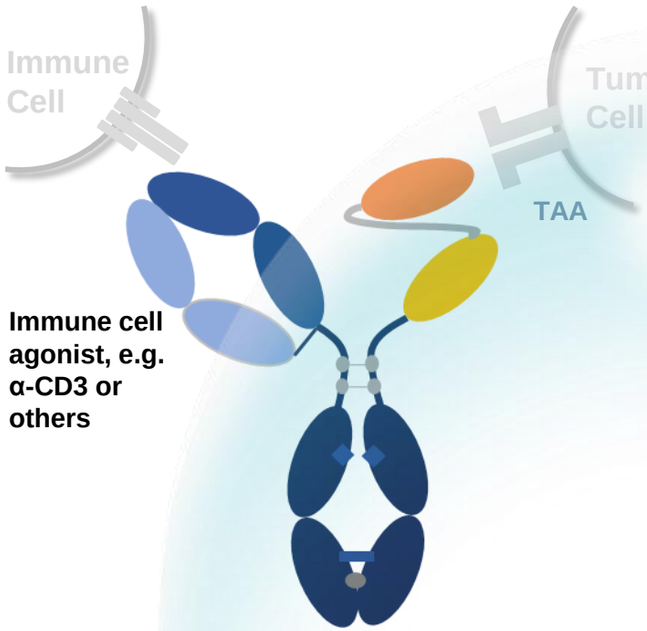
Agonistic Modules For Immune Cell Activation

A panel of immune cell (T, NK, DC, Mϕ) activation or co-stimulatory engagers

Immune Cell Engager

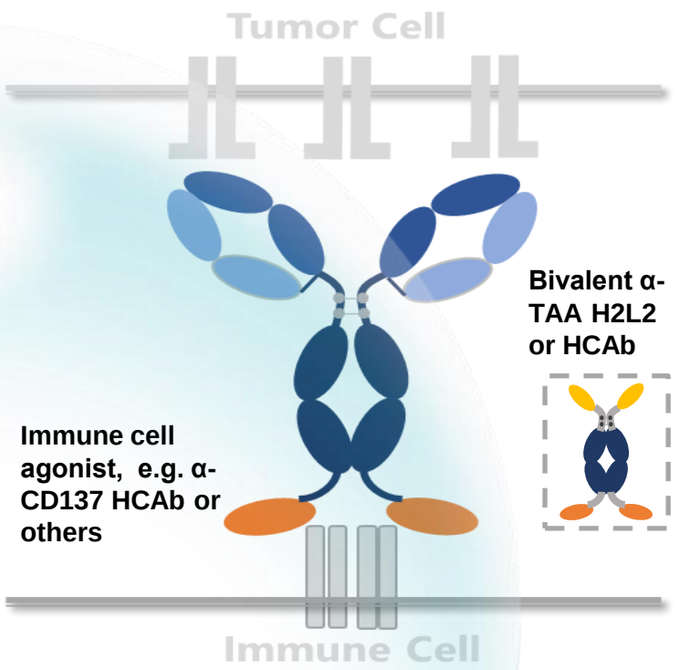
Deliver tumor-killing effects unachievable by combination therapies only in TME

Asymmetric '2+1' HBICE (A-HBICE)



CD3 mediated cytotoxic T engaging and directly kill tumor cells with CRS

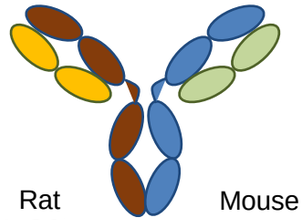
'2+2' symmetric HBICE (S-HBICE)



4-1BB mediated tumor dependent T cell activation including memory T without CRS

HBM is at the Forefront of New Generation of T-Cell Engager Bispecific Antibodies

FcyR engaging

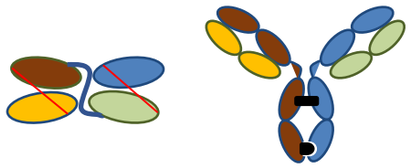


Catumaxumab

FcyR-silenced

Short half life

Extended half-life



Blinatumomab

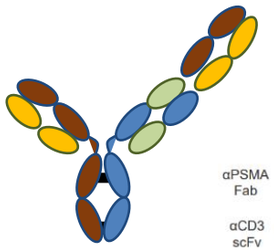
AMGEN

MacroGenics

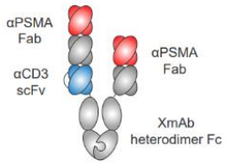
Genmab

...

Optimized aCD3, 2+1 format



RG7802



2+1 PSMA x CD3

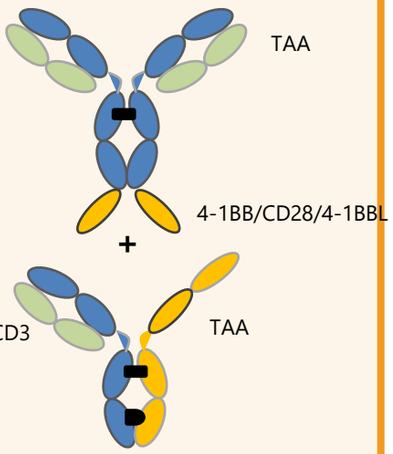
Roche

xencor

abbvie

Teneobio

Trispecific or 2nd signal bispecific combination



Roche

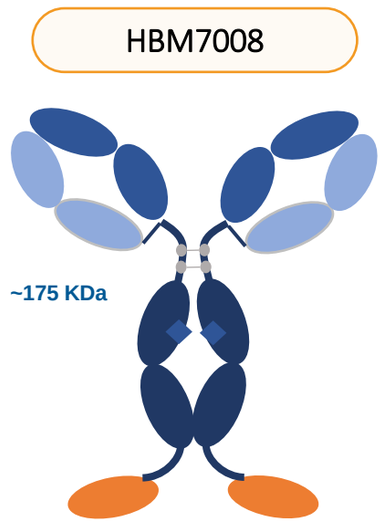
SANOFI

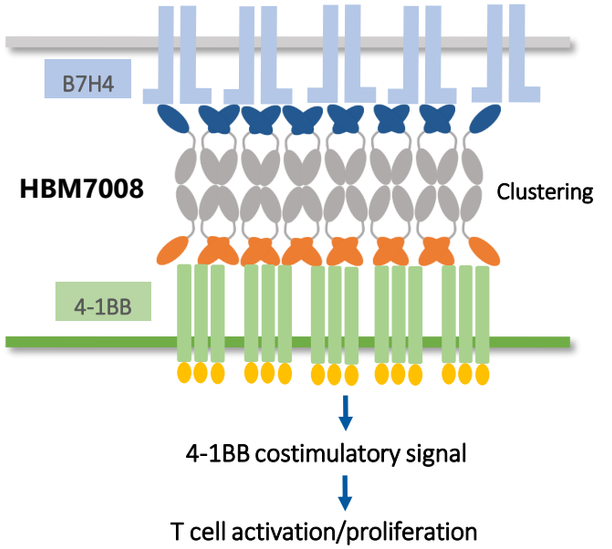
HARBOUR BIOMED

HBM7008: First-in-Class Bispecific Antibody from the HBICE® Platform

Highlights:

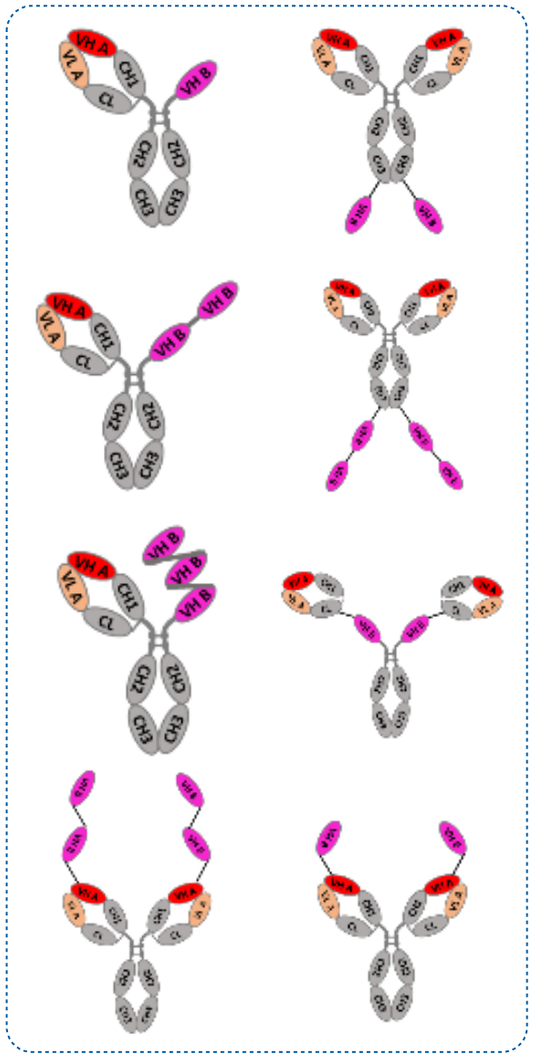
1) MoA: Crosslinking dependent 4-1BB activation is stringently mediated by B7H4 binding
2) Molecule: Based on HBICE® platform to optimize the geometry for 4-1BB clustering, T/Tumor cell dual binding
3) Druggability: Fully human sequences from Harbour mice undergone natural in-vivo selection. Symmetrical format with excellent biophysical properties
4) Indications: Mutual exclusively expressed with PD-L1, potential for PD1/PD-L1 therapy refractory patients, particularly in multiple gynecological cancers





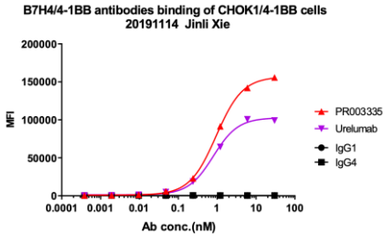
HARBOUR BIOMED

HBICE® Platform Provides the Best Geometry Design for the MoA of HBM7008

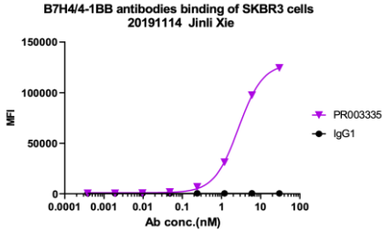


Format Engineering

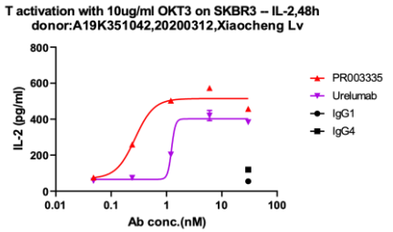
4-1BB Binding



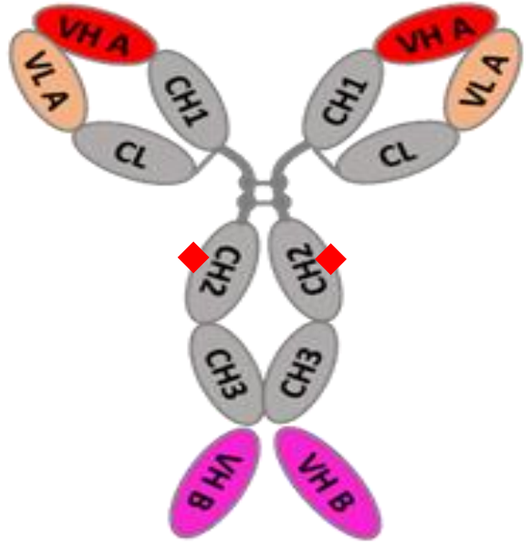
B7H4 Binding



T Activation



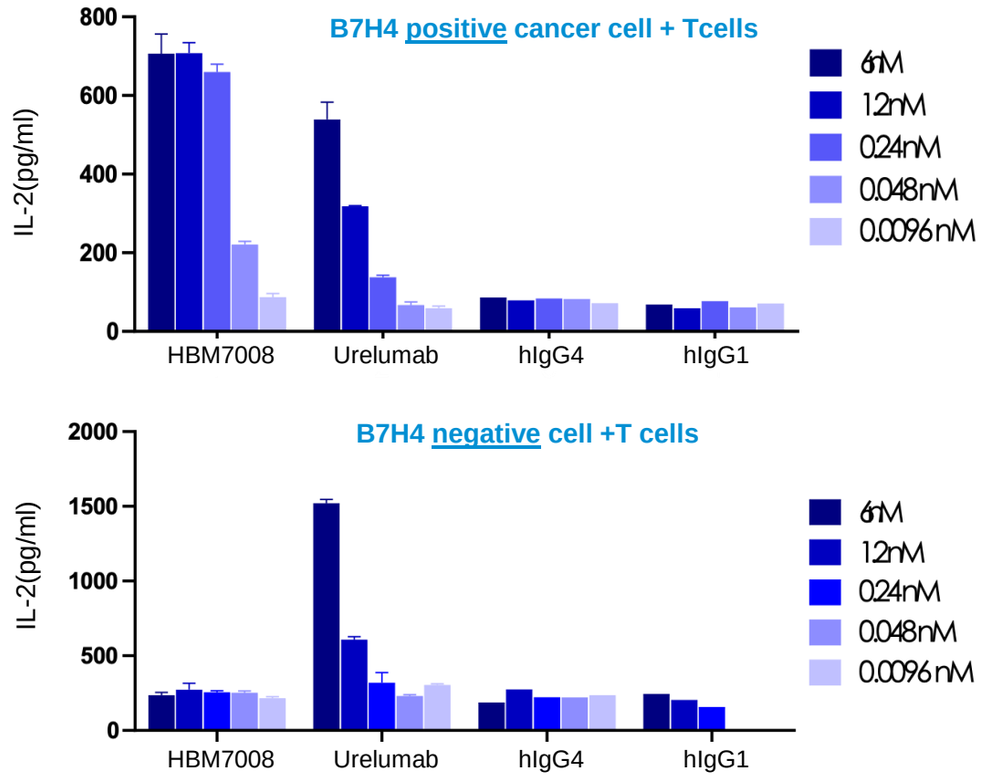
Linker/ Sequence Engineering



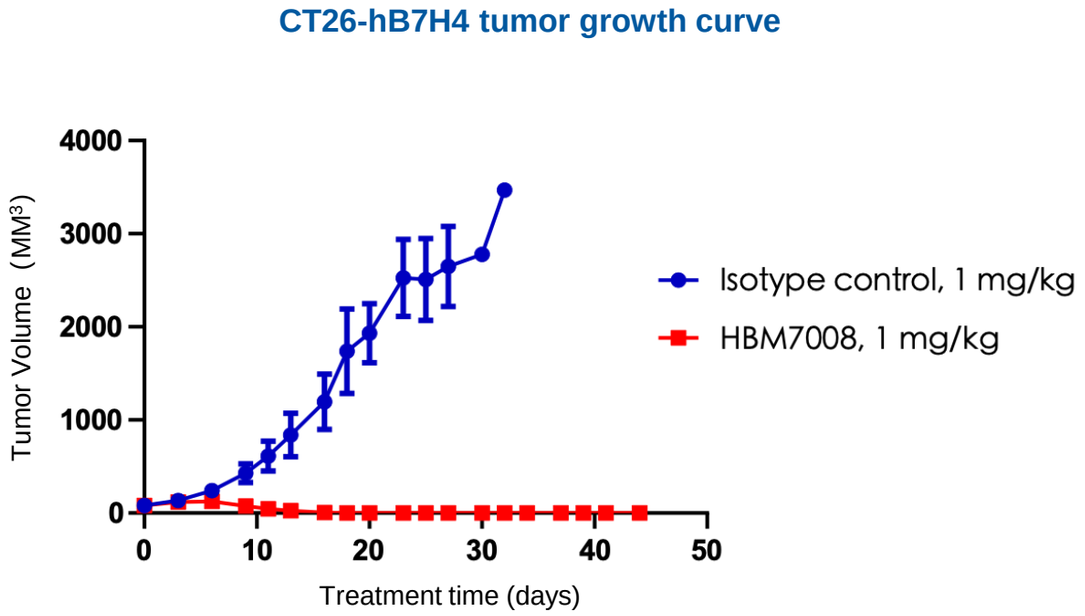
HBM7008: First-in-Class Bispecific Antibody from the HBICE® Platform

Encouraging monkey DRF and Tox data also suggest its excellent PK and safety profile

B7H4 dependent 4-1BB activation and T cell stimulation



HBM7008 completely leads tumor regression in B7H4 positive syngeneic model

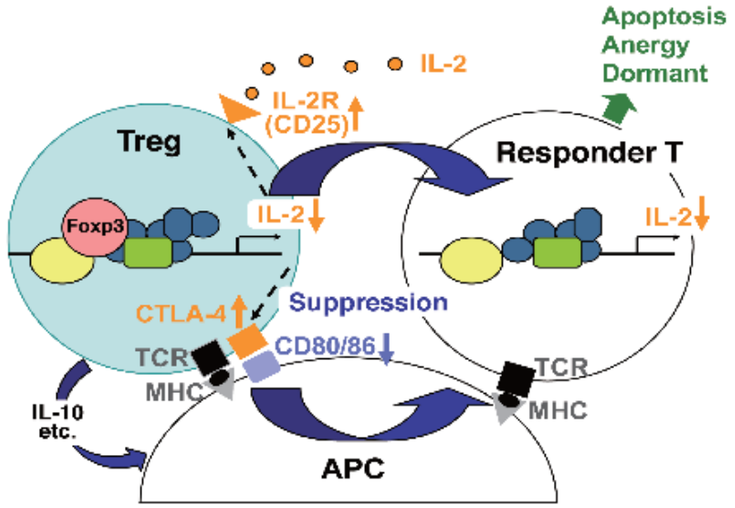


HARBOUR BIOMED

Solution 2:

Unique Treg Depletion Mechanism – *Leading Treg Based Next-Gen Antibody Therapeutics*

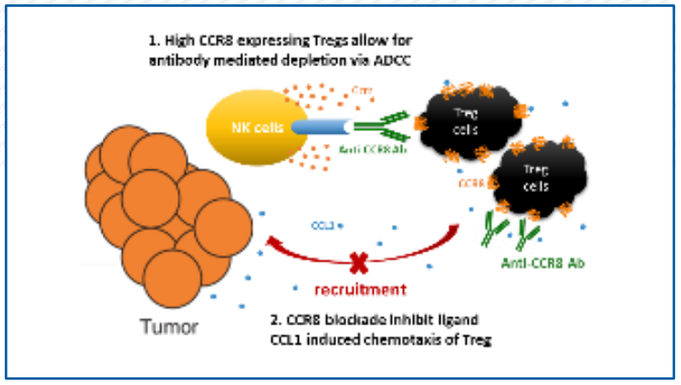
Two main mechanisms of immune tolerance: T cell receptor-mediated immune exhaustion; **Regulatory T cell-mediated** immune surveillance

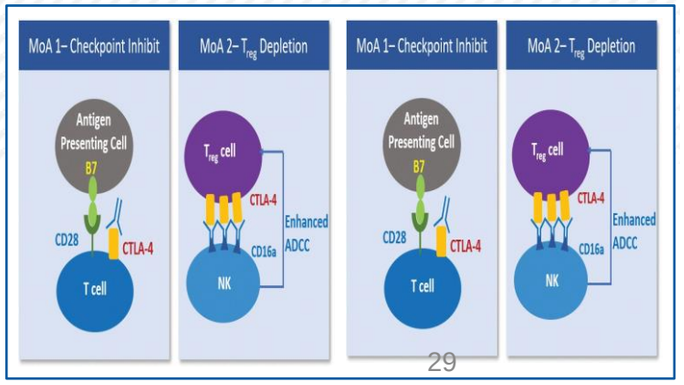


Projects	Target validation	Lead generation	Candidate Selection	Pre-clinical	IND	Ph1	Ph2
HBM4003 (CTLA4)							
HBM1022 (CCR8)							
Undisclosed							

Unique Treg Depletion Mechanism to Develop Next-Gen Antibody Therapeutics

	HBM1022 (CCR8)	HBM4003 (CTLA-4)
Highlights	• Potently antagonizes CCL1-CCR8 signaling and depletes CCR8-expressing cells • **First reported functional antibody that cross-reacts with human & cyno** • **The only CCR8 antibody shown anti-tumor efficacy in animal models instead of using surrogate antibody**	• Enhanced ADCC strategy to deplete CTLA4+ Treg cells in tumor • **The world's first fully human heavy chain antibody to enter the clinical study** • Developing monotherapy and combo clinical research
Indication	Solid Tumors	Solid Tumors
Development Stage	IND in 2022	Monotherapy Ph1b/2 Combo therapy Ph1





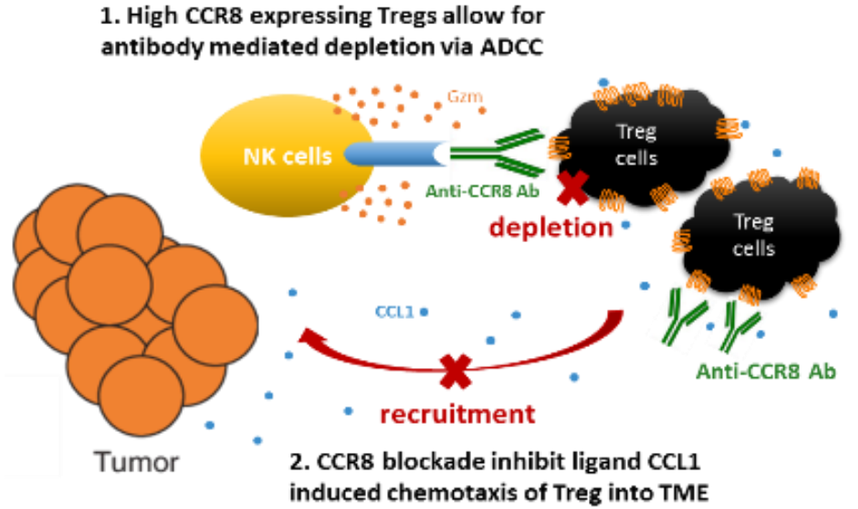
HARBOUR BIOMED

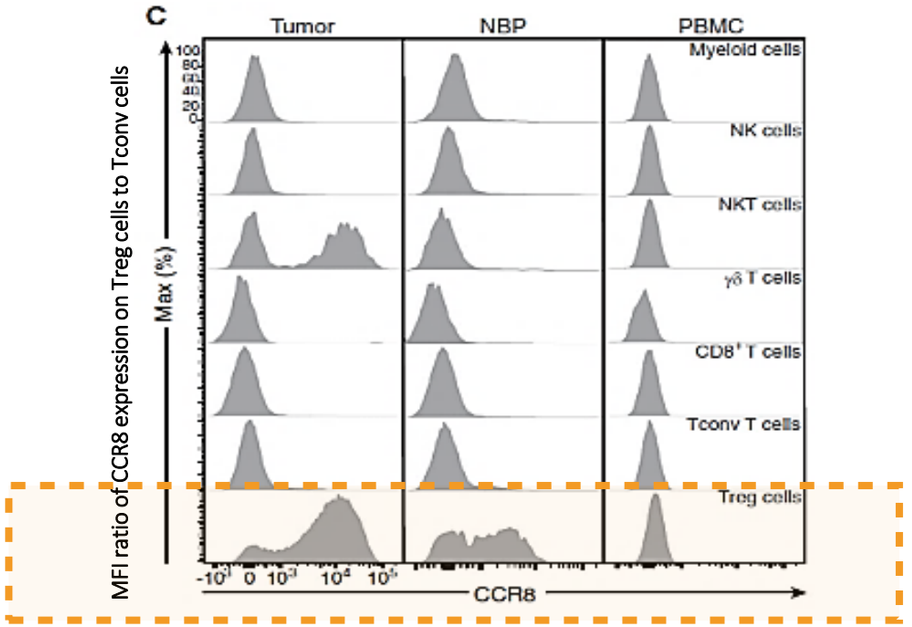
HBM1022: CCR8 is a Novel Target Expressed on Tumor Infiltrated Treg Cells

HBM1022 Highlights:

1. Potent tumor resident T_{reg} depletion activity
2. Potent inhibition of CCL1-induced signaling pathway / *in vivo* anti-tumor efficacy
3. Comparable human/cyno binding affinity
4. Significant potential for breast cancer, colon cancer, and multiple solid tumors and hematological malignancies

Mechanism of Action



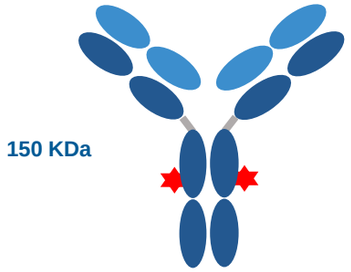


Breast cancer, Analysis of over 70 individual patients
Immunity 2016, 45:1122–1134

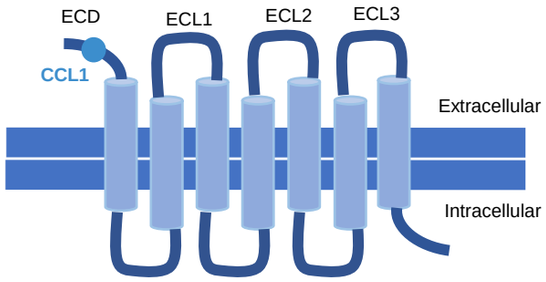
HARBOUR BIOMED

HBM1022: A Unique CCR8 Antibody Shows Treg Cell Depletion and Anti-Tumor Efficacy in Pre-clinical Models

HBM1022

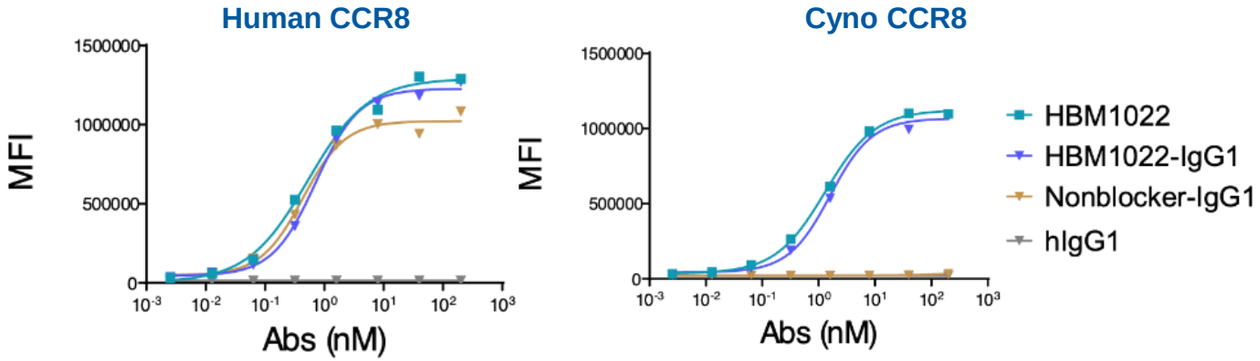


Target CCR8



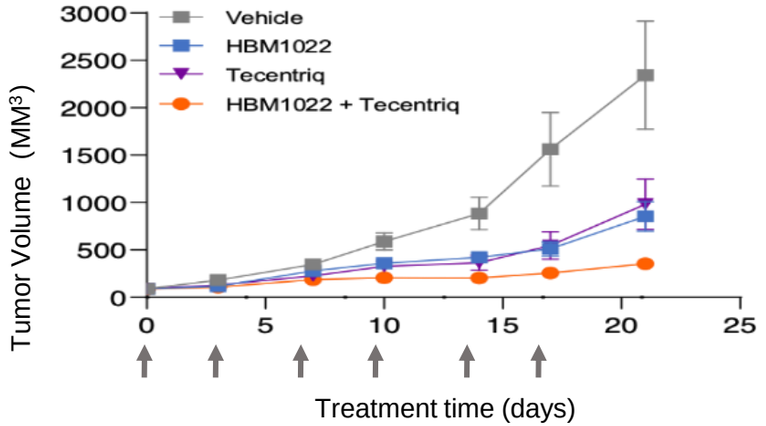
HBM1022 preclinical study was presented on the 16th PEGS Boston Summit in August 2020

High On-cell Affinity to Human/Cyno CCR8



On-cell affinity	KD (pM)
Human CCR8	21.3

Mono and Combo Efficacy in Syngeneic Knock-in Mouse Model



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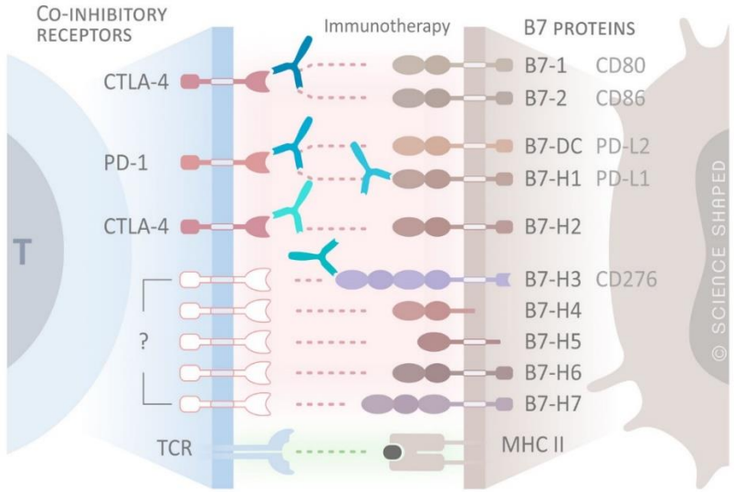
Solution 3:

Focus on Novel Immune Escape Pathway *Develop First-in-Class Targets in B7 Family*

The most important tumor immunomodulatory family, Targets of current immuno-oncology drugs are all from this family



Projects	Target validation	Lead generation	Candidate Selection	Pre-clinical	IND
HBM7008 (B7H4x4-1BB)	→	→	→	→	
HBM1020 (B7H7)	→	→	→		
Undisclosed	→	→			

HBM1020: First-in-Class Fully Human mAb Against a Novel B7 Family Target

Highlights:

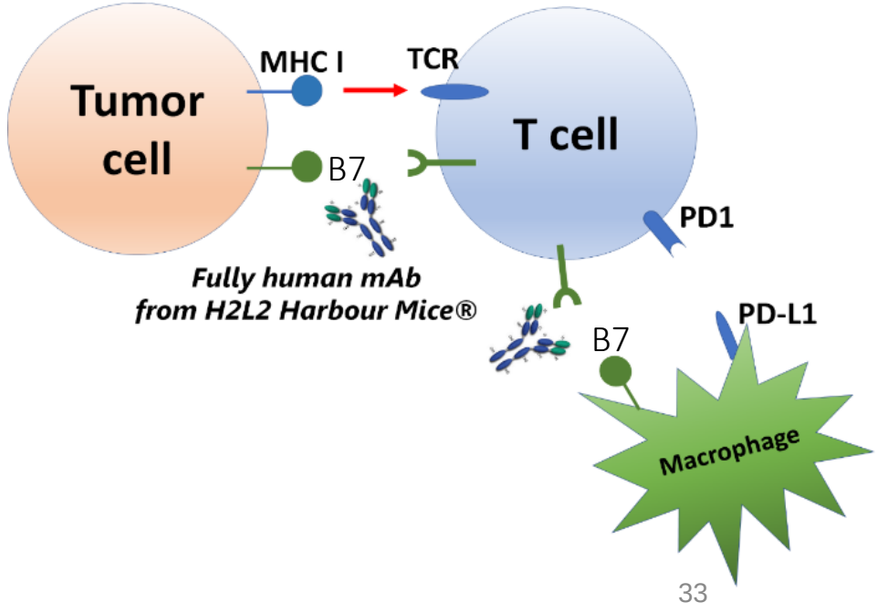
1) First-in-class target potentially serves as an alternative immune escape pathway
2) Potent receptor blocking, T cell activation activity and excellent in vivo efficacy in humanized tumor models
3) Huge potential to treat PD-L1 negative or anti-PD1/PD-L1 refractory cancer patients

H2L2

IND in 2022

HARBOUR BIOMED

HBM1020



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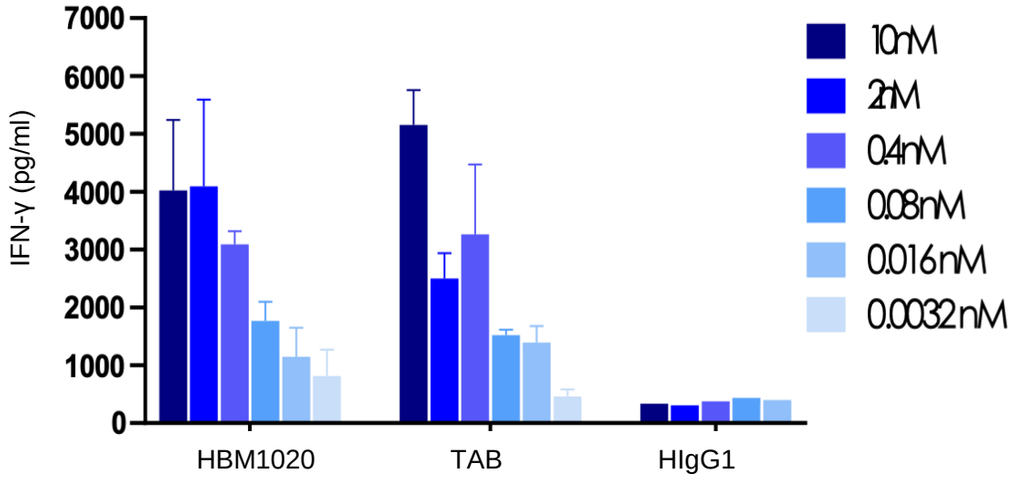
HBM1020: First-in-Class Antibody Shows Promising Anti-Tumor Preclinical Efficacy in Multiple Cancer Types

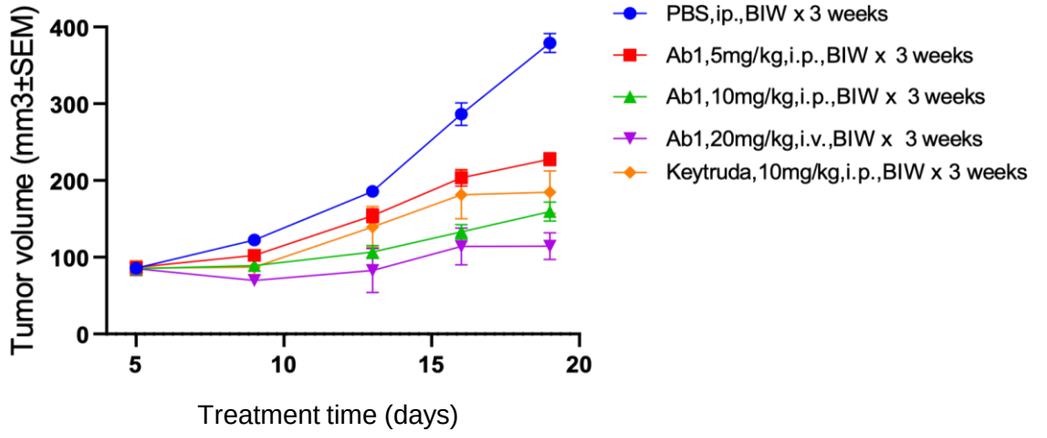
Lead Antibody Shows Strong T Cell Activation

T cell activation test



Lead Antibody Shows Strong Tumor Growth Inhibition

Breast Cancer Human PBMC Mouse Model



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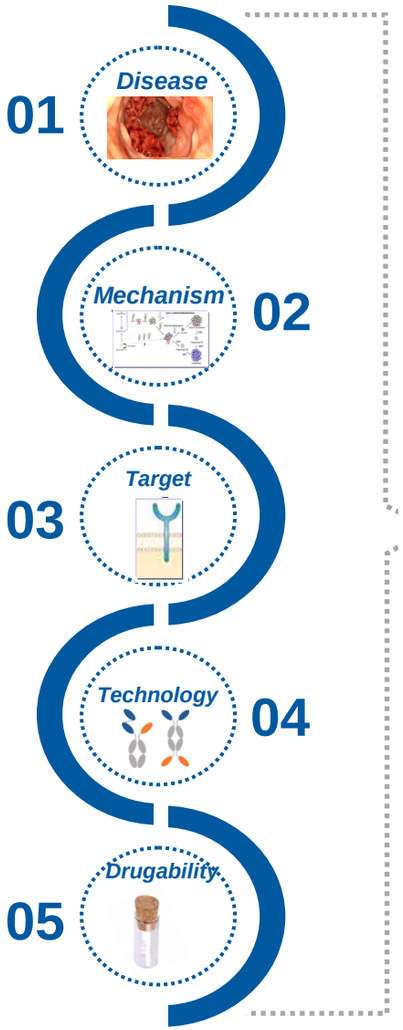
HBM Continuously Drives Innovative Portfolio and Leads the Next-Gen Therapeutics



ICE: Immune cell engager
Treg: Regulatory T modulation/depletion
IEP: Novel immune escape pathway

	2021	2022	2023
Ph3		Treg	Treg, ICE
Ph2	Treg	ICE	Treg, ICE, IEP
Ph1	ICE	Treg, ICE, IEP	Treg, ICE, IEP
Preclinical	Treg, ICE, IEP	Treg, ICE, IEP	Treg / MDSC, ICE, IEP

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THANK YOU

HBM HOLDINGS-B

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Breakthrough IO Therapy for Unmet Medical Needs

Treg Depletion – A Novel Mechanism Unlocking Therapeutic Potential

Prof. Shun Lu
Director of Clinical Medicine Department
Shanghai Chest Hospital

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www.harbourbiomed.com

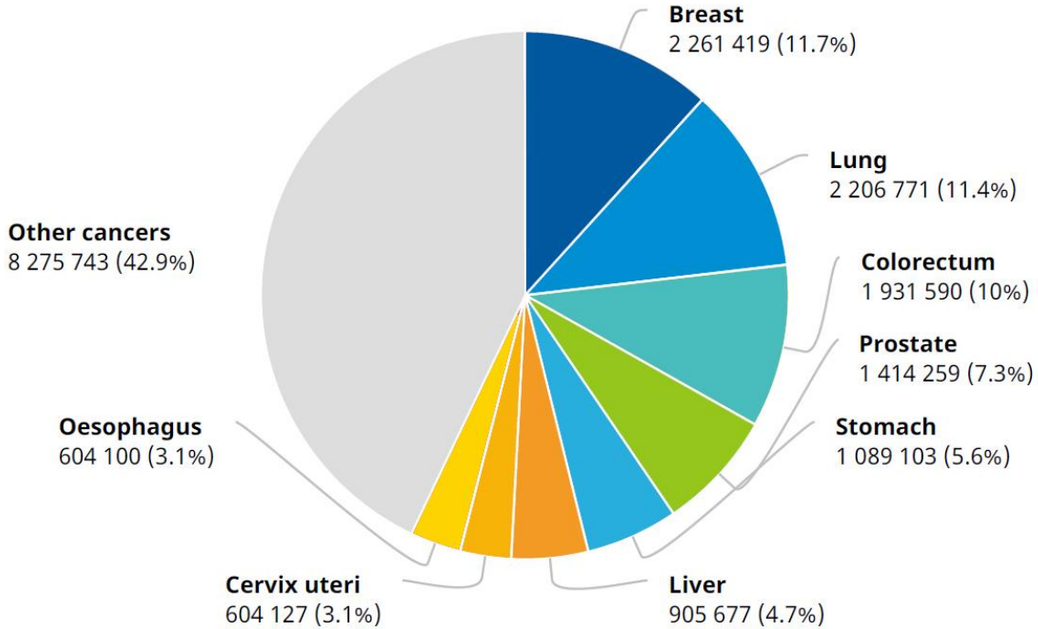
DISCLOSURE

- Received research support from AstraZeneca, Hutchison, BMS, Heng Rui, Beigene and Roche, Hansoh, Lilly Suzhou Pharmaceutical Co.Ltd
- Received speaker fees from Astra Zeneca, Roche, Hansoh, Hengrui Therapeutics
- An advisor and consultant of Astra Zeneca, Pfizer , BoehringerIngelheim, Hutchison MediPharma, ZaiLab, GenomiCare , Yuhan Corporation, Menarini, InventisBio Co. Ltd., and Roche.

HARBOUR BIOMED

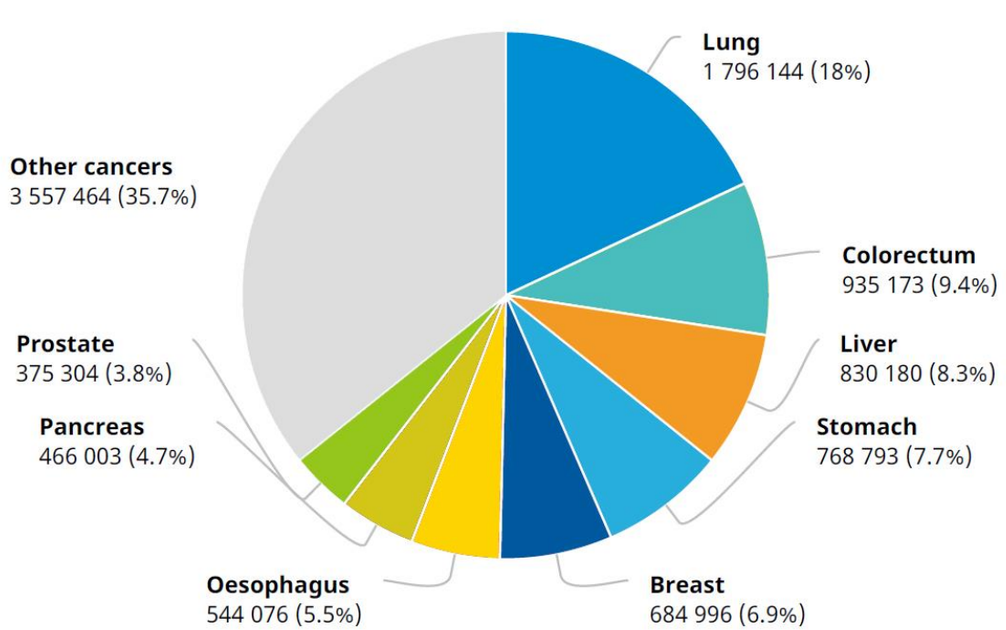
Cancer Is A Major Public Health Problem and the Second Leading Cause of Death Worldwide

Number of new cases in 2020, both sexes, all ages



Total: 19 292 789 cases

Number of deaths in 2020, both sexes, all ages

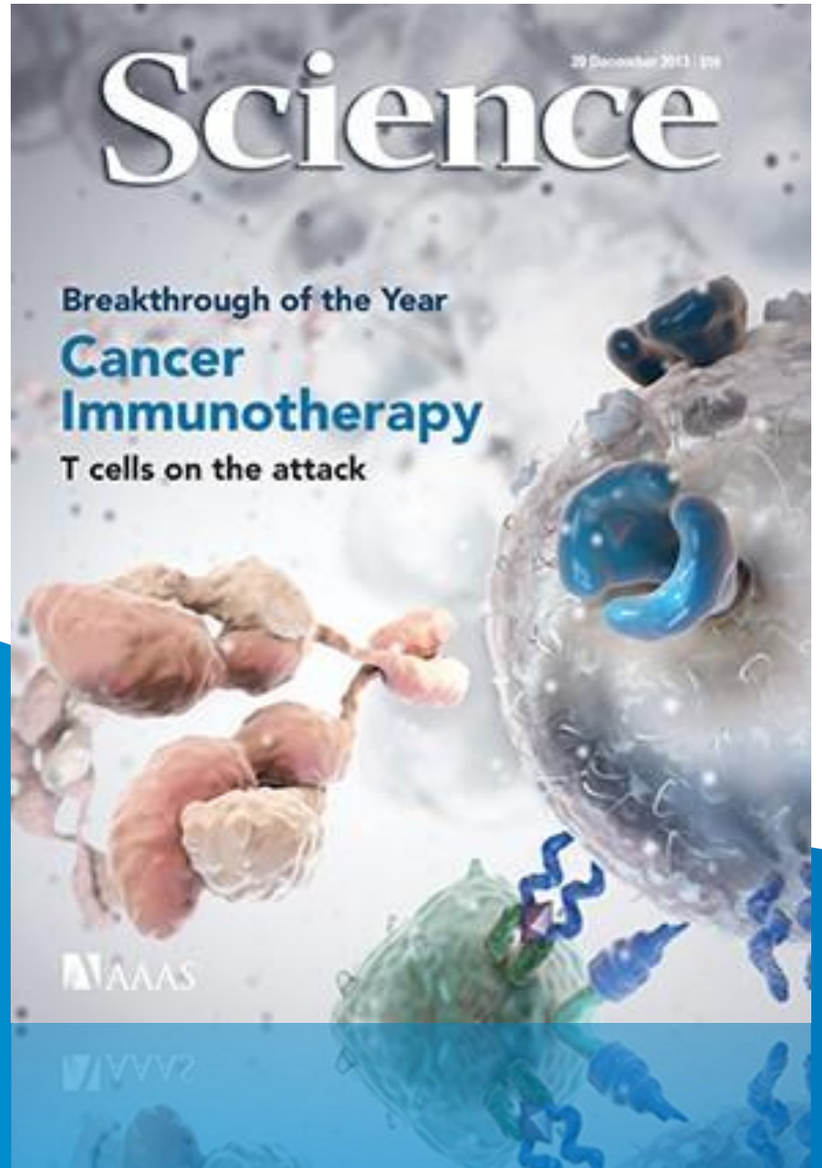


Total: 9 958 133 deaths

- Lung cancer is the most frequent cause of cancer-related deaths worldwide.
- Much progress has been made in research, cancer screening, and personalized therapy (precision medicine) in recent years. However, most patients with advanced cancer will ultimately progress which remains a great unmet medical need.

Hirsh et al. Lancet. 2017 Jan 21;389(10066):299-311.

Cancer Immunotherapy –
2013 Science “Breakthrough of the Year” and 2014 Special Nature Edition



Cancer Immunotherapy –
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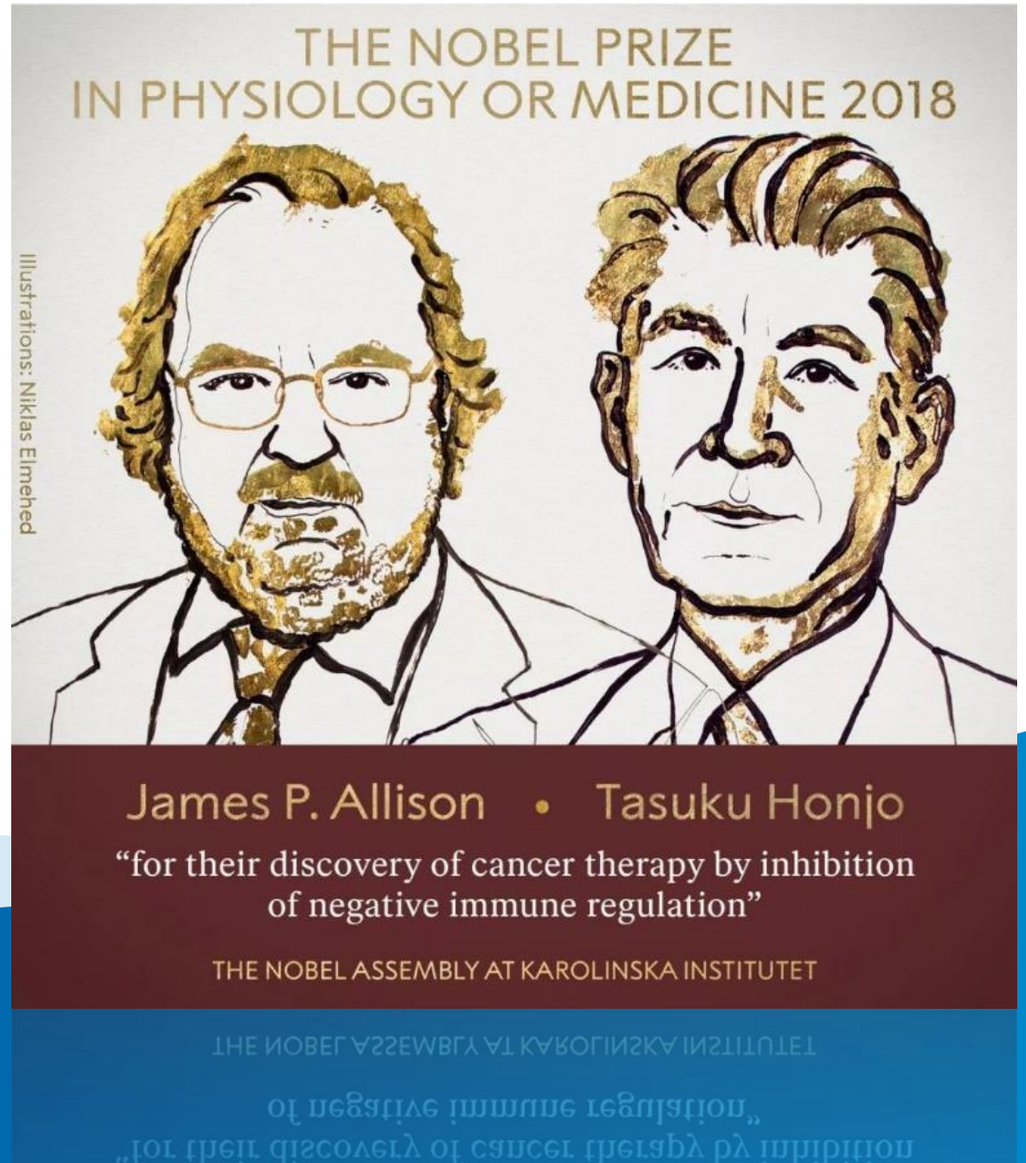
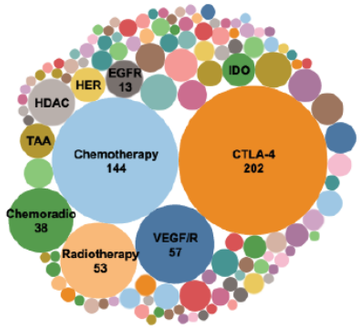


Immune Combination Regimens Are in Full Swing, And the Exploration of New Combinations and New Targets Is the Key to Overcome IO Resistance

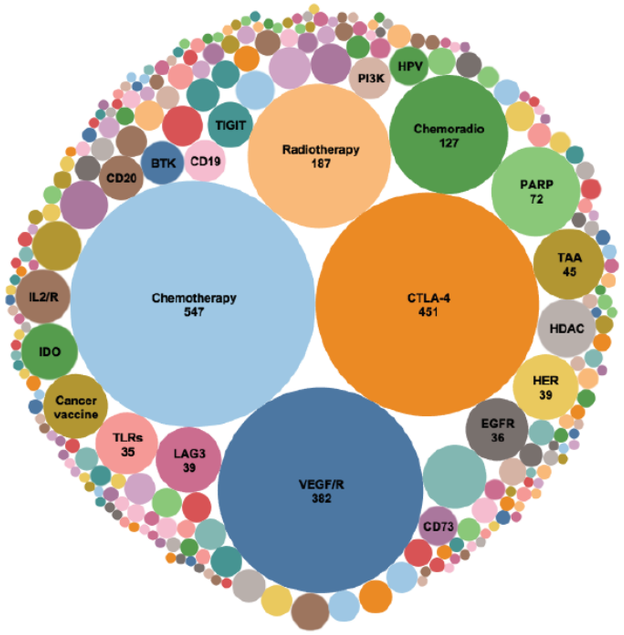
- 3-fold increase in number of combination trials in 2020 compared to 2017 [1]
- Added 129 targets from 124 target groups [1]

- Chemotherapy, CTLA-4 and VEGF/R are most common partners in combination with anti- PD-(L)1 [2]

857 IO combination trials in 2017

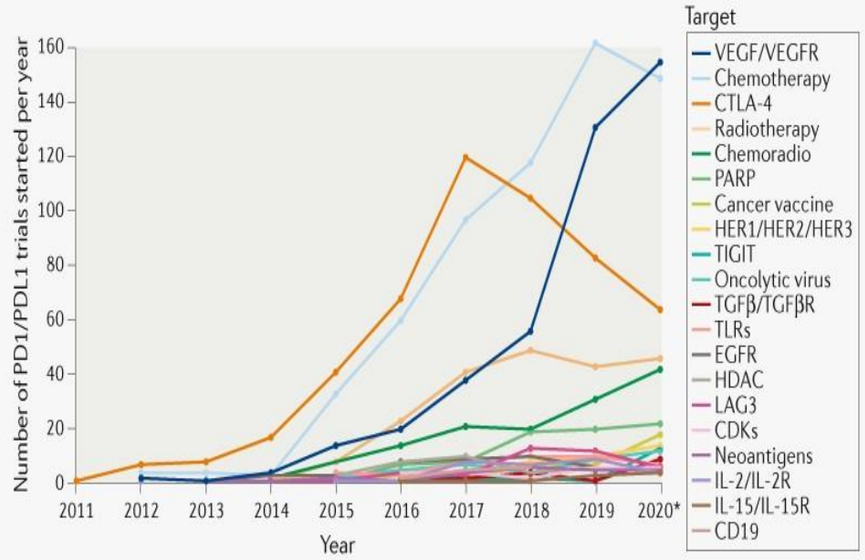


2900 IO combination trials in 2020



* Data 2020 till the first three quarters

Main targets combined with anti-PD-1/L1



* Data 2020 till the first three quarters

Nature Reviews | Drug Discovery

1. https://www.cancerresearch.org/scientists/immuno-oncology-landscape/pd-1-pd-l1-landscape
2. Upadhaya S, et al. Combinations take centre stage in PD1/PDL1 inhibitor clinical trials. Nature Reviews Drug Discovery (November 2020)

The Combination of CTLA-4 Antibody and PD-1 Antibody Has Synergistic Effect – Traditional View

Anti-CTLA-4

Main organs acted in:

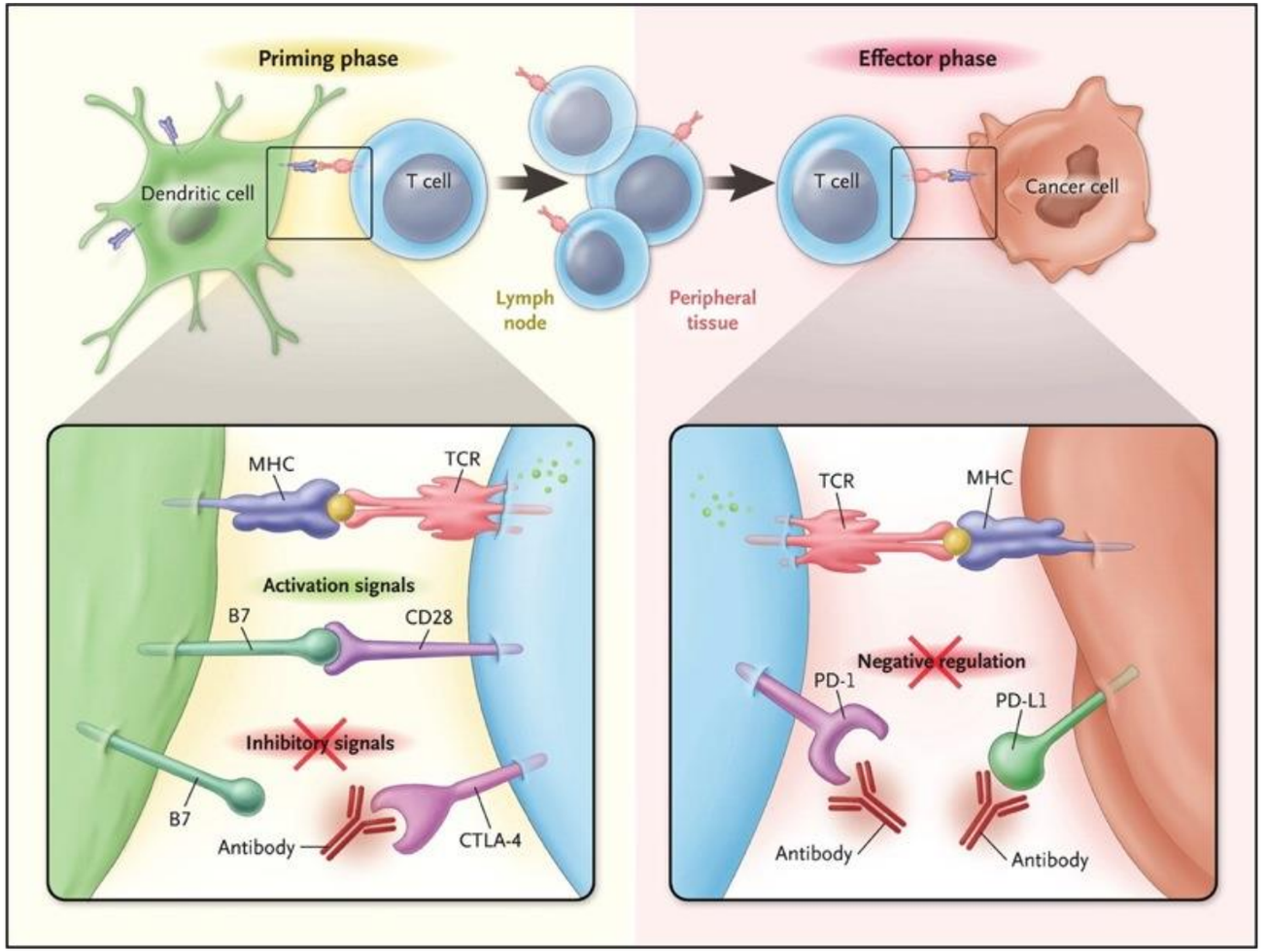
- Lymph nodes, spleen and tumor tissue

The main phase of being affected:

- The priming phase of T cells activation

Main mechanism:

- Block the interaction between CTLA-4 and its ligand CD80/86, and relieve the inhibition of CTLA-4 on T cell activation
- Kills and inhibits Treg cells



Anti-PD-1

Main organs acted in:

- Tumor tissue

The main phase of being affected:

- The effector phase of activated T cells

Main mechanism:

- Block the interaction between PD-1 and its ligand PD-L1, and relieve the inhibition of PD-1 on activated T cells

Antoni Ribas, NEJM epub June 2012

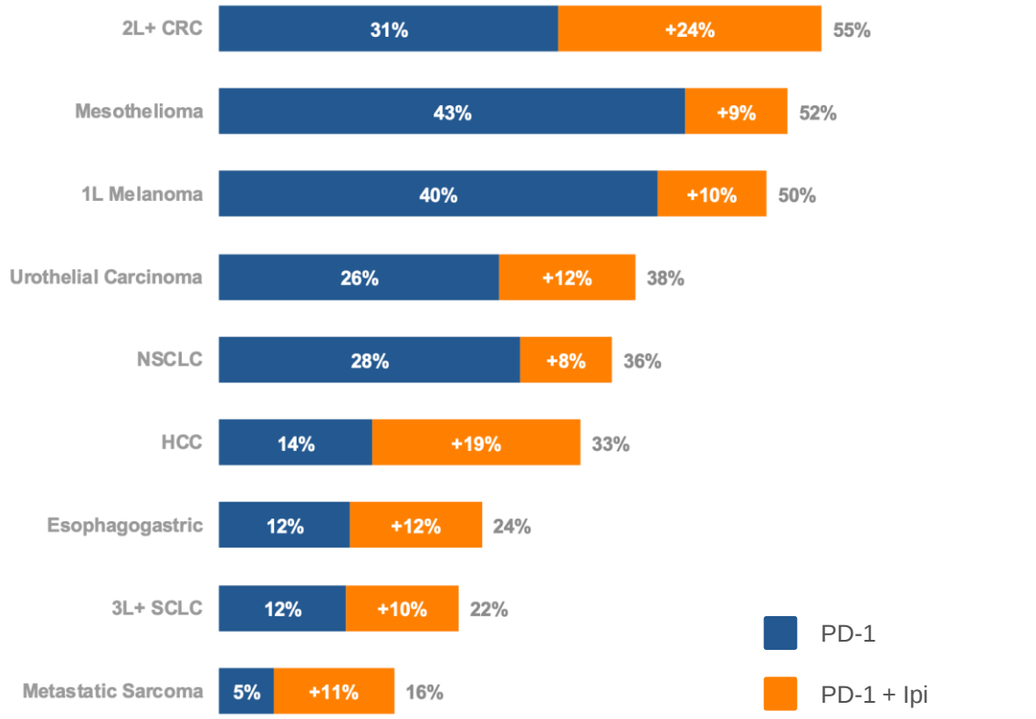
Anti-CTLA-4 Treatment Improves anti-PD-1 Responses and Durability in Multiple Tumor Types

Anti-CTLA-4 Enhances anti-PD-1 Durability

	Trial Name	Median PFS (Months) PD-1		+Ipi	Median OS (Months) PD-1		+Ipi
1L Melanoma	Checkmate-067	6.9	→	11.5	36.9	→	>60 (NR)
NSCLC (PD-L1 ≥1%)	Checkmate-227	4.2	→	5.1	15.7	→	17.1
Metastatic Sarcoma	Alliance A091401	1.7	→	4.1	10.7	→	14.3

Combination Has Demonstrated Stronger Anti-tumor Response

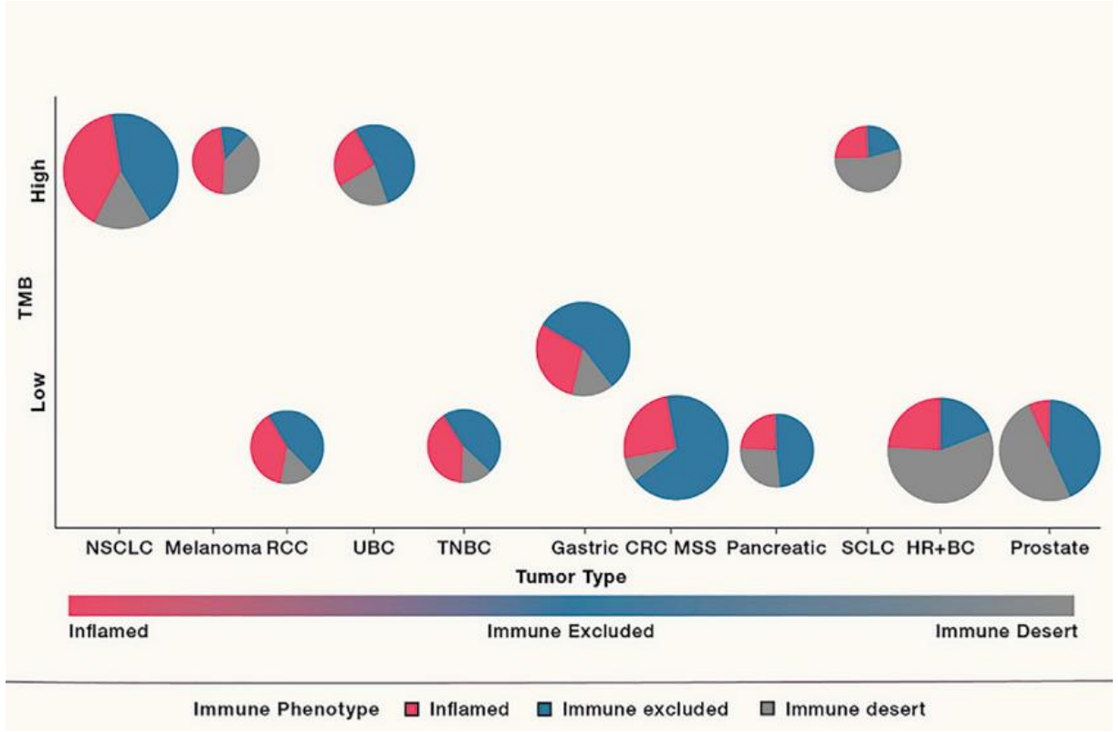
Anti-CTLA-4 Enhances anti-PD-1 Durability

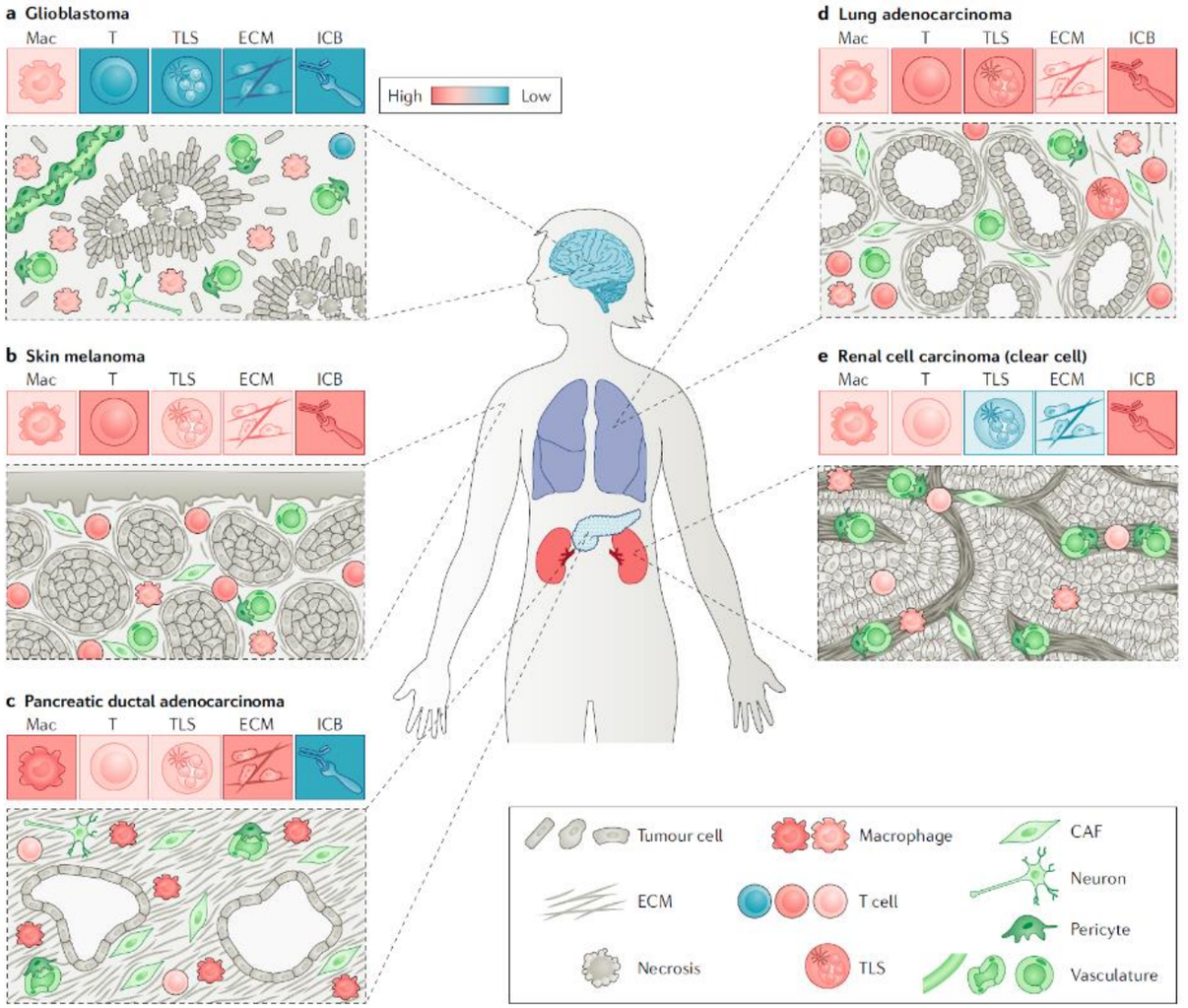


2-3x Improvement in Certain Tumors

Source: NCBI, NEJM, PubMed, the Journal of Experimental & Clinical Cancer and other publicly clinical information.
Note: Reflects clinical data from various Nivolumab (PD-1) and Nivolumab + Ipilimumab (PD-1 + CTLA-4) trials; NR denotes median not reached.
(1) Objective Response Rate: 2L+ CRC, Urothelial Carcinoma, NSCLC, Esophagogastric, 3L+ SCLC; Overall Response Rate: 1L Melanoma, Metastatic Sarcoma, HCC; Disease Control Rate: Mesothelioma.

Scientific Rationales of Immunotherapy in NSCLC





High rates of somatic mutations and high proportion of patients with immune-inflamed contexture in NSCLC contribute to increased sensitivity to immunotherapy.

Hegde and Chen. Immunity. 2020;14;52(1):17-35.
Salmon et al. Nat Rev Cancer. 2019;19(4):215-227.

Immunotherapy has Comprehensively Changed the Treatment Landscape for Advanced Lung Cancer, but There Are Still Many Unknowns to be Explored

Radiotherapy

Radiotherapy+ IO

- PACIFIC
- KN799

Immunotherapy

- **Ipilimumab + nivolumab**
- **Tremelimumab + durvalumab**
- **Enhanced T-cell stimulation (vaccine) Novel agents (i.e. ea.ant - NK-R, immune checkpoint inhibitor)**

- CheckMate 227
- MYSTIC
- KEYNOTE 598

Targeted therapies

Combination with targeted therapies, e.g. VEGF, EGFRTKI

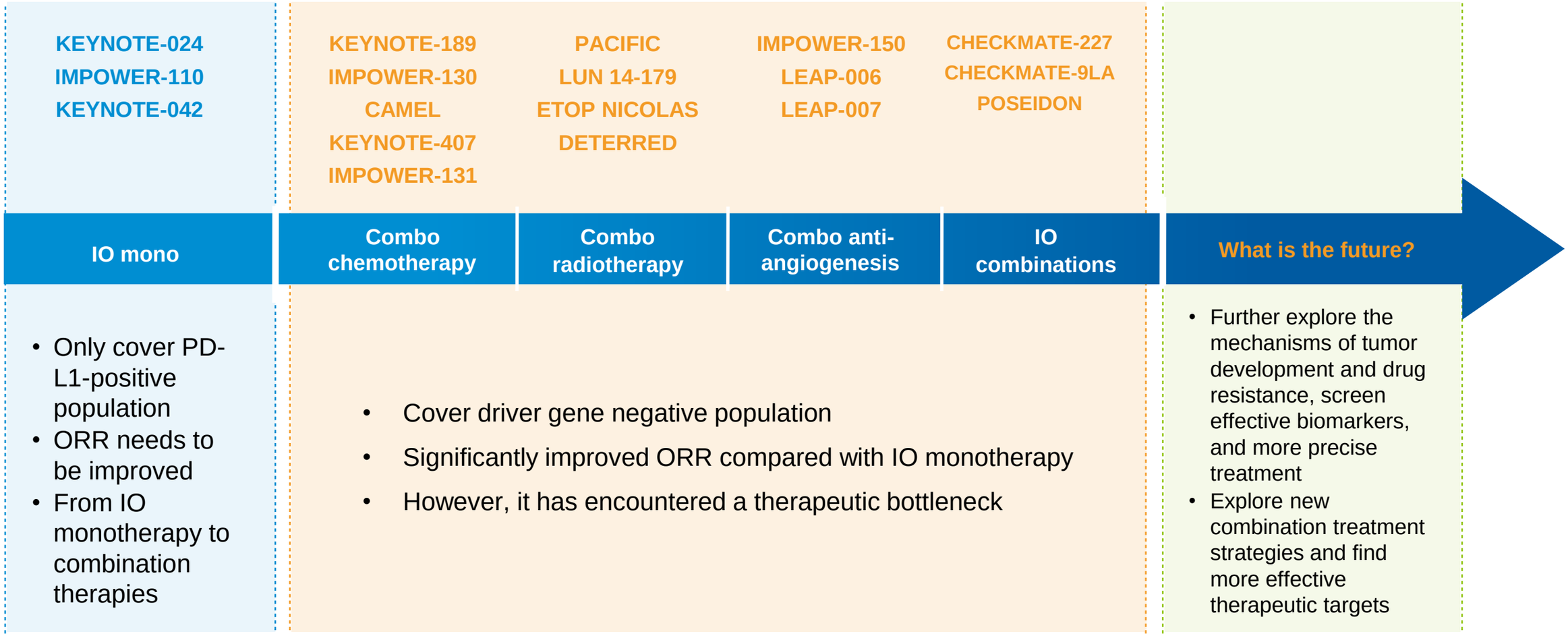
- IMPOWER-150
- ORIENT-31

Chemotherapy

Use the immunomodulatory effects of chemotherapy

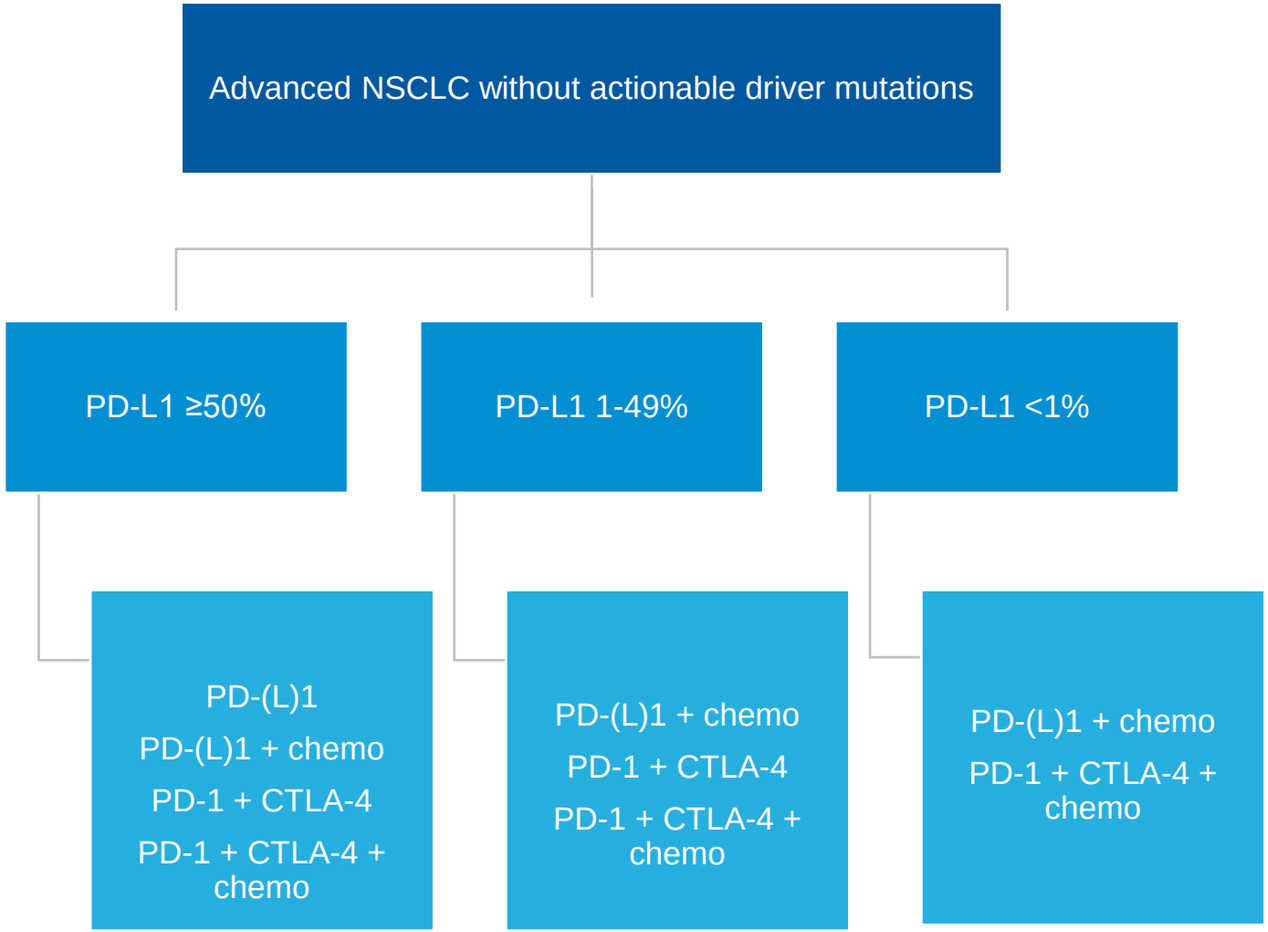
- KEYNOTE-021G
- KEYNOTE-189
- KEYNOTE-407
- IMPOWER-131
- IMPOWER-132
- CHCKMATE 227

Immunotherapy for Metastatic NSCLC: Monotherapy? Combinations? What Is the Future?



At present, the approved indications of pembrolizumab for lung cancer in mainland China are: ① PD-L1 TPS ≥ 1% for first-line treatment of EGFR, ALK-negative locally advanced or metastatic NSCLC; ② combo pemetrexed/platinum for first-line treatment of EGFR, ALK-negative metastatic non-squamous NSCLC; ③ combo carboplatin and paclitaxel for first-line treatment of metastatic NSCLC patients. Nivolumab has been indicated for second-line treatment of advanced NSCLC in mainland China. Atezolizumab in Combination with Carboplatin and Etoposide for the First-Line Treatment of Extended Staged Small Cell Lung Cancer. Durvalumab in Mainland China for the treatment of Stage III unresectable NSCLC that has not progressed after concurrent chemoradiotherapy.

Paradigm 2021 – First Line Treatments for NSLCL without Actionable Driver Mutations



Anti-PD-1 monotherapy:

Pembrolizumab, Atezolizumab, Cemiplimab

ICI + chemo:

- Pembrolizumab + carboplatin + pemetrexed (nsq)
- Atezolizumab + carboplatin + paclitaxel + bevacizumab (nsq)
- Atezolizumab + carboplatin + nab-paclitaxel (nsq)
- Pembrolizumab + carboplatin + paclitaxel or nab-paclitaxel (sq)
- Nivolumab + ipilimumab + 2 cycles of chemotherapy (nsq/sq)

ICI combination:

Nivolumab + ipilimumab

The Efficacy of anti-PD-(L)1 Monotherapies as First Line Treatment for NSCLC

Study name	KEYNOTE-024[1]	CheckMate-026[2]	KEYNOTE-042[3]		IMPOWER 110[4]	MYSTIC[5]	PEARL[6]
Study drug	Pembrolizumab	Nivolumab	Pembrolizumab		Atezolizumab	Durvalumab	Durvalumab
Target population	PD-L1 ≥ 50% advanced NSCLC	PD-L1 ≥ 1% advanced NSCLC	PD-L1 ≥ 1% advanced NSCLC		PD-L1-selected advanced NSCLC	Advanced NSCLC	Advanced NSCLC
Patients enrolled	305	423	1247	262	572	1118	440
Main results	PFS: 10.3 vs 6.0m 2-yOS: 51.7% vs 34.2%	PFS (PD-L1 ≥ 5%): 4.2 vs 5.9 m, study failed to meet primary endpoint	OS: 16.4 vs 12.1m 2yOS: 39% vs 28%	OS: 20.0 vs 13.7m 2yOS: 45% vs 30%	TC3/IC3:20.2 vs 13.1m 1-yOS: 60.9% vs 50.6%	OS (TC ≥ 25%): 16.3 vs 12.9m Study fails to meet primary endpoint	PFS, OS (PD-L1 ≥ 25%)
HR (95% CI) P value	0.5 (0.37-0.68) P = 0.001	1.15 (0.91 – 1.45) P = 0.2511	0.82 (0.71-0.93) P = 0.0018	0.65 (0.45-0.94) P = 0.0003	0.59 (0.4-0.89) P = 0.0106	0.76 (0.56-1.02) P = 0.036	/

1. Martin Reck et al. 2019 WCLC
2. N Engl J Med. 2017 Jun 22; 376 (25): 2415-2426
3. Tony S K Mok, et al. 2019
4. Spigel et al. IMpower110 Interim OS Analysis. 2019 ESMO
5. 2018 ESMO-ASIA.
6. https://www.clinicaltrials.gov/ct2/show/NCT03003962?term=Durvalumab&cond=NSCLC&draw=3&rank=13

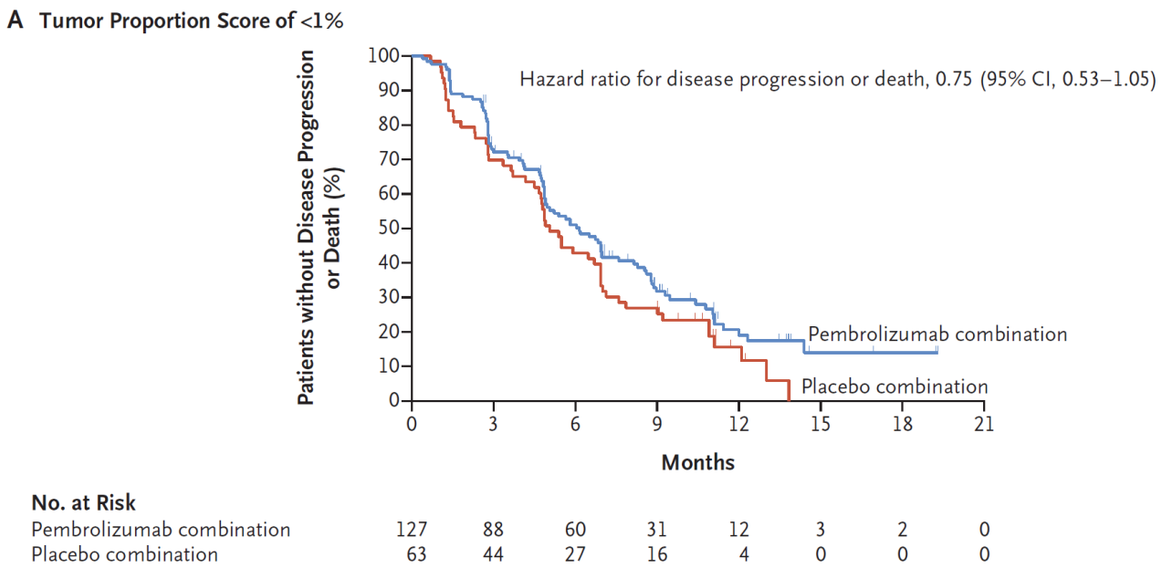
The Efficacy of anti-PD-(L)1 + Chemotherapy as First Line Treatment for NSCLC

Key Parameter	Pembro + Pemetrexed + Platinum (KN-189) [1, 2, 3]	Pembro + Carbo + Abraxane or Paclitaxel (KN-407) [4, 5, 6]	Nivo + Ipi (CM-227 Part 1) [7, 8, 9]	Nivo + Ipi + 2 cycles Platinum + Paclitaxel (sq) or Pemetrexed (non-sq) (CM-9LA) [10]
Population	Non-sq NSCLC Whole population N = 616	Sq NSCLC Whole population N = 559	Sq + non-sq NSCLC Whole population N = 1166	Sq + non-sq NSCLC Whole population N = 719
Primary endpoint	OS, PFS, intragroup crossover allowed	OS, PFS, intragroup crossover allowed	PFS in high TMB, OS in PD-L1 ≥ 1% Intragroup crossover not allowed	OS, intragroup crossover not allowed
ORR	**48.3% pembro + chemotherapy** Vs. 19.9% chemotherapy	**62.6% pembro + chemotherapy** Vs. 38.4% chemotherapy	**33.1% nivo-ipi** Vs. 27.8% chemotherapy	**38% nivo-ipi-chemotherapy** Vs. 25% chemotherapy
PFS	**9.0 mos pembro + chemotherapy** Vs. 4.9 mos chemotherapy (HR = 0.49)	**8.0 mos pembro + chemotherapy** Vs. 5.1 mos chemotherapy **(HR = 0.57)**	**5.1 mos nivo-ipi** Vs. 5.5 mos chemotherapy **(HR = 0.79)**	**6.7 mos nivo-ipi-chemotherapy** Vs. 5.0 mos chemotherapy
OS	**22.0 mos pembro + chemotherapy** Vs. 10.6 mos chemotherapy **(HR = 0.56)**	**17.1 mos pembro + chemotherapy** Vs. 11.6 mos chemotherapy **(HR = 0.71)**	**17.1 mos nivo-ipi** Vs. 13.9 mos chemotherapy **(HR = 0.73)**	**15.6 mos nivo-ipi-chemotherapy** Vs. 10.9 mos chemotherapy **(HR = 0.66)** **(HR = 0.69 at IA)**
Survival rate	**70.0% vs. 48.1% 12-month OS** **45.7% vs. 27.3% 24-month OS**	**73% vs. 50% 12-month OS**	**64% vs. 54% 12-month OS** **40% vs. 30% 24-month OS**	**63% vs. 47% 12-month OS**
Duration of Response	**12.4 mos pembro + chemotherapy** Vs. 7.1 mos chemotherapy	**8.8 mos pembro + chemotherapy** Vs. 4.9 mos chemotherapy	**19.6 mos nivo-ipi** Vs. 5.8 mos chemotherapy	**11.3 mos nivo-ipi-chemotherapy** Vs. 5.6 mos chemotherapy
Grade 3-4 (5) (Treatment related) AEs	**72.1% pembro + chemotherapy** Vs. 66.8% chemotherapy (Entire Population, All Causes)	**74% pembro + chemotherapy** Vs. 70% chemotherapy (Entire Population, All Causes)	**32.8% nivo-ipi** Vs. 36.0% chemotherapy (Treatment-related)	**47% nivo-ipi-chemotherapy** Vs. 38% chemotherapy (Treatment-related)
Discontinuation Rate	**33.6% pembro + chemotherapy** Vs. 16.3% chemotherapy (Entire Population, All Causes)	**27% pembro + chemotherapy** Vs. 13% chemotherapy (Entire Population, All Causes)	**18.1% nivo-ipi** Vs. 9.1% chemo (Treatment-related)	**19% nivo-ipi-chemotherapy vs. 7% chemotherapy** (Treatment-related)

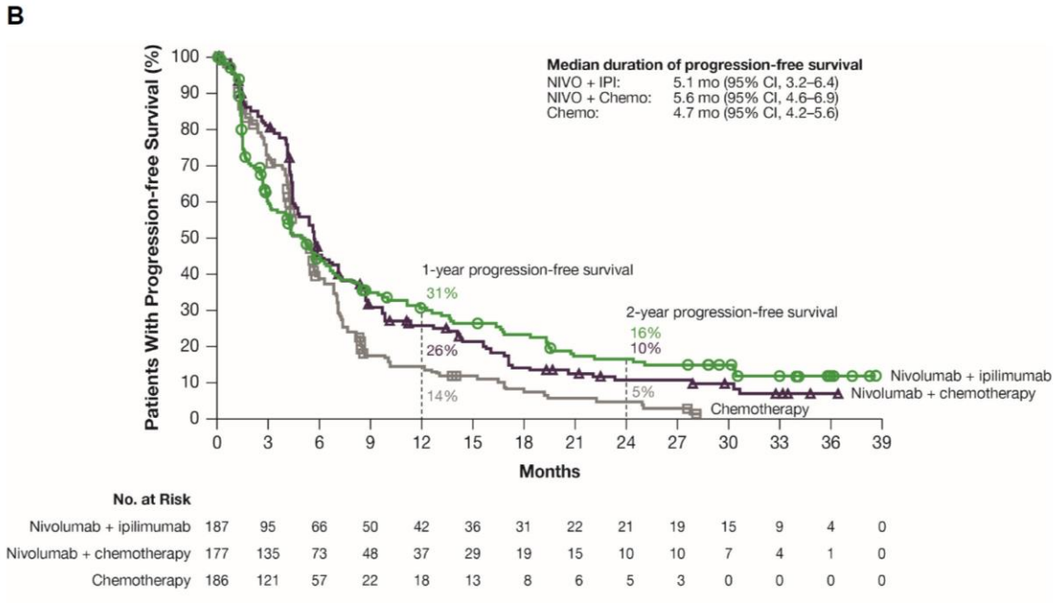
1), Ghandi L, et al. NEJM. 16 April 2018. 2), Gadgeel S, et al. Presented at ASCO 2019. Abstract 9013. 3) Rodriguez-Abreu D. Presented at ASCO 2020. Abstract 9582. 4), Paz-Ares L, et al. Presented at ASCO 2018. Abstract 105. 5), Paz-Ares, et al. N Engl J Med 2018; 379:2040-2051. 6), Paz-Ares L, et al. Presented at ESMO 2019. Abstract LBA82. 7), Peters S, et al. Presented at ESMO 2019. Abstract LBA4. 8), Hellman M, et al. NEJM. 28 Sept 2019. 9), Ramalingam S, et al. Presented at ASCO 2020. Abstract 9500. 10), Reck M, et al. Presented at ASCO 2020. Abstract 9501.

The Efficacy of PD-1 + Chemotherapy Is limited in PD-L1 Negative Patients, While Addition of First Generation CTLA-4 Antibody Only Brings Moderate Excess Benefit

Keynote-189 study: Pembrolizumab + chemotherapy for non-sq NSCLC, PFS in PD-L1 <1% subgroup



CheckMate 227 study: Nivo + ipi, Nivo + chemotherapy and chemotherapy for NSCLC, PFS in PD-L1 <1% subgroup

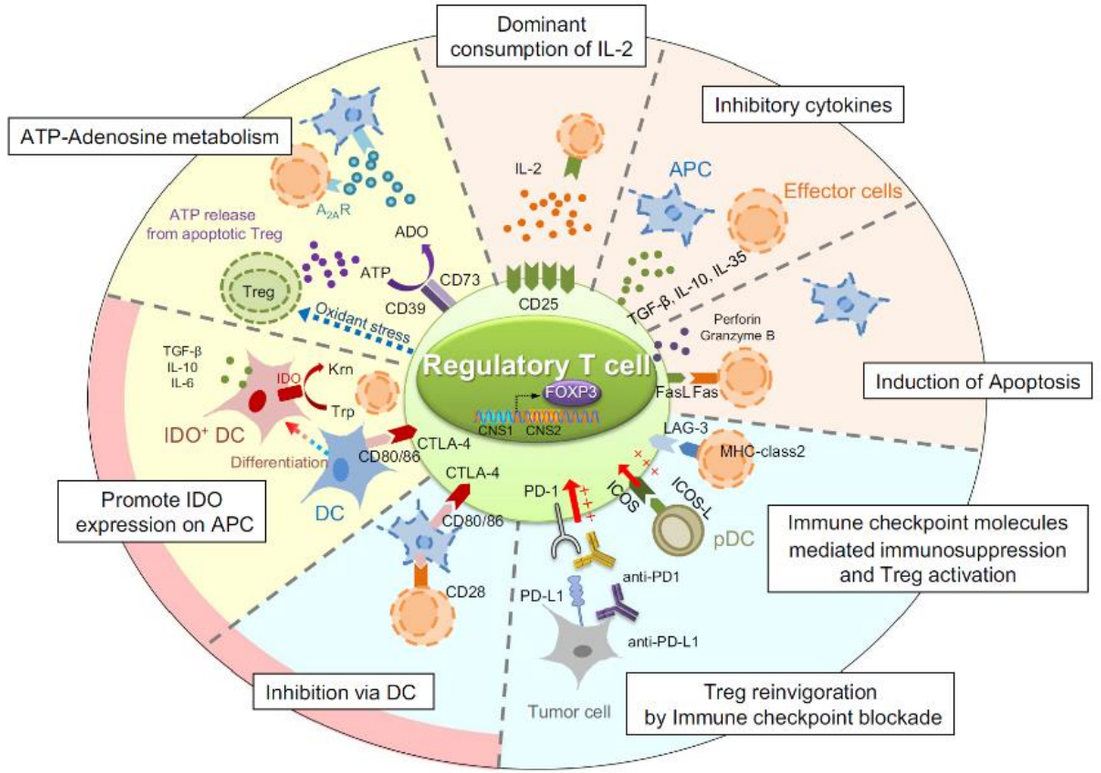


- The benefit of PFS by PD-1 + chemotherapy in subgroup of PD-L1 <1% was limited and not as high as subgroup of PD-L1 >1%.
- Combination of first generation anti-CTLA-4 antibody with anti-PD-1 only brings moderate excess benefit over PD-1 + chemotherapy in this population.
- There remains high unmet medical needs for NSCLC patients in the immunotherapy era, especially in patients who have negative PD-L1 expression.

Gandhi et al. N Engl J Med 2018;378:2078-92.
Hellmann et al. N Engl J Med . 2019 Nov 21;381(21):2020-2031.

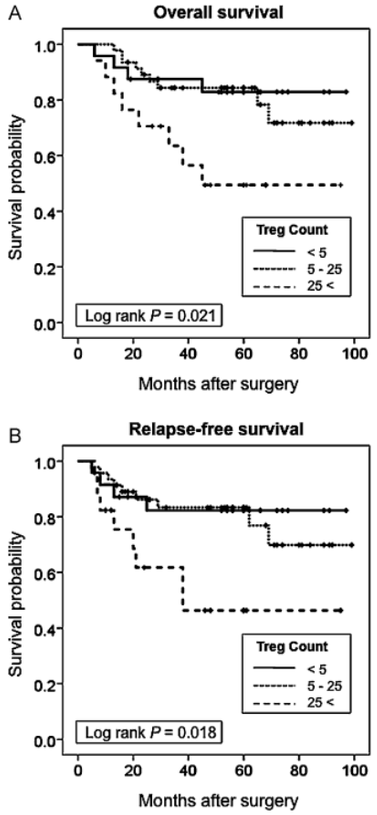
Treg Is the Main Suppressor of Anti-Tumor Immunity and Is Associated with Poor Prognosis

Tregs suppress anti-tumor immunity via various mechanisms

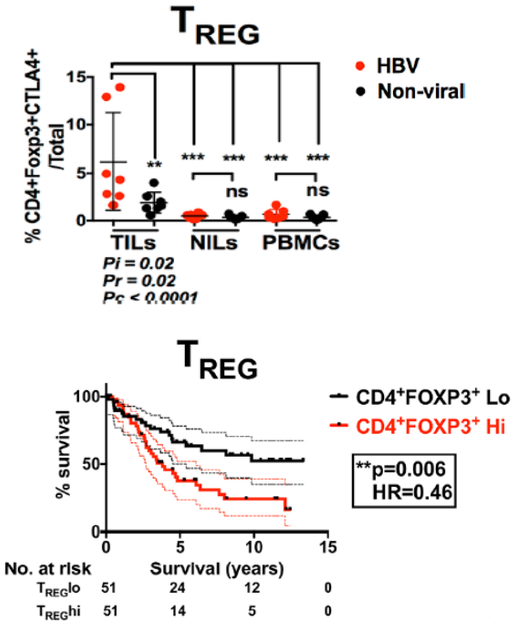


High infiltration of Tregs in tumors is associated with a poor prognosis in various types of cancers

NSCLC



HBV-related HCC

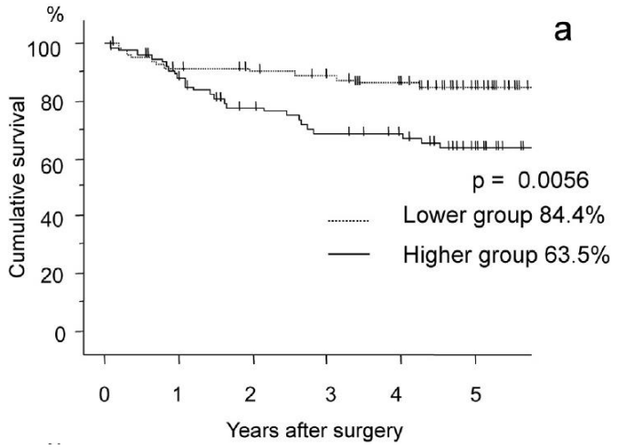


TILs: HBV Tumor-infiltrating leukocytes
NILs: Non-tumor-infiltrating leukocytes
PBMCs: Peripheral blood mononuclear cells

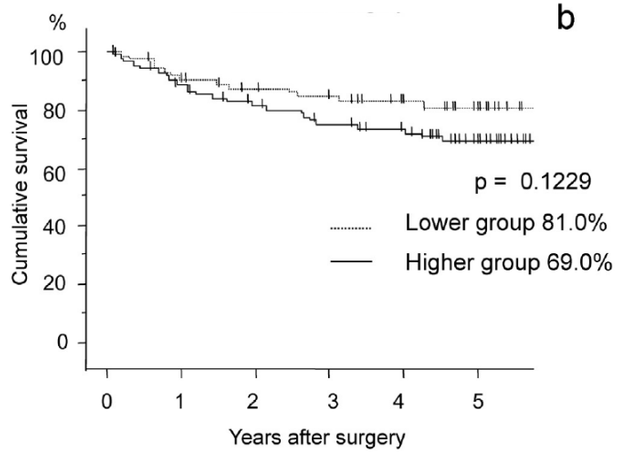
Ohue and Nishikawa, Cancer Science. 2019;110:2080–2089.
Tao et al. Lung Cancer . 2012 Jan;75(1):95-101.
Lim et al. Gut. 2019 May;68(5):916-927.

High Infiltration of Tregs in Tumors and Regional Lymph Nodes but not in Peripheral Blood Is Associated with A Significant Poor Prognosis in NSCLC

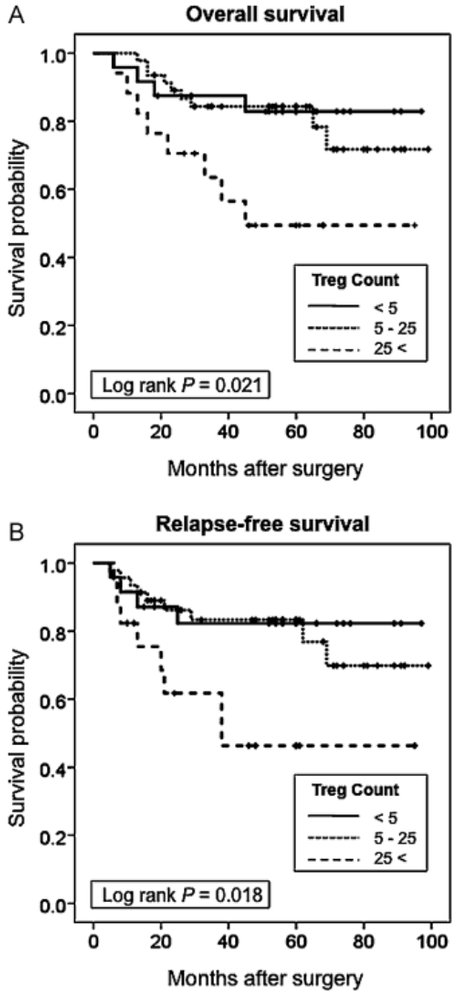
Regional lymph nodes



Peripheral blood



Resected tumor



Resected tumor

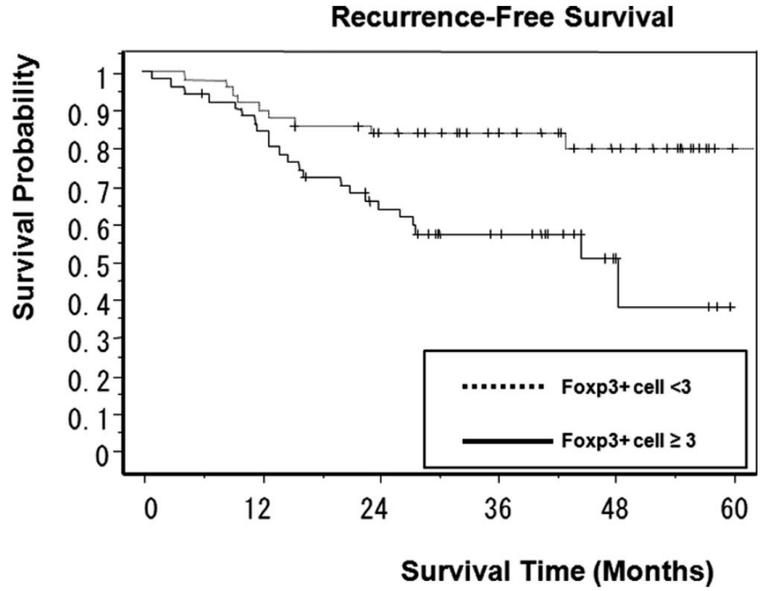
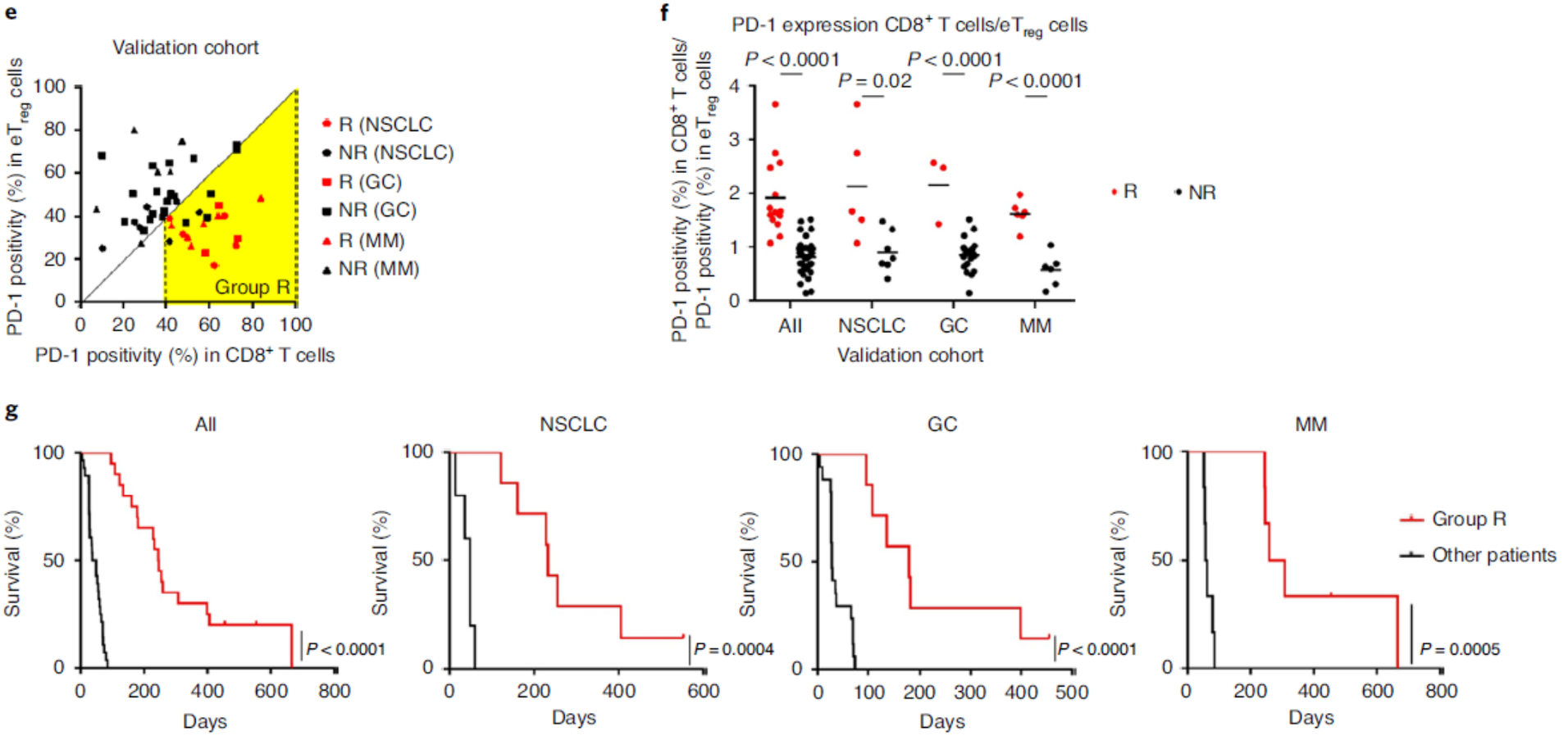


FIGURE 4. Kaplan-Meier recurrence-free survival curve according to Foxp3 expression, log-rank $p = 0.004$.

Hanagiri et al. Lung Cancer. 2013; 81(3), 475-479.
Shimizu et al. J Thorac Oncol. 2010;5(5):585-90.
Tao et al. Lung Cancer . 2012 Jan;75(1):95-101.

Ratio of PD-1 Positivity (%) in CD8+ T cells to PD-1 Positivity (%) in eTreg Cells Predicts Responses to PD-1 Blockade Therapies

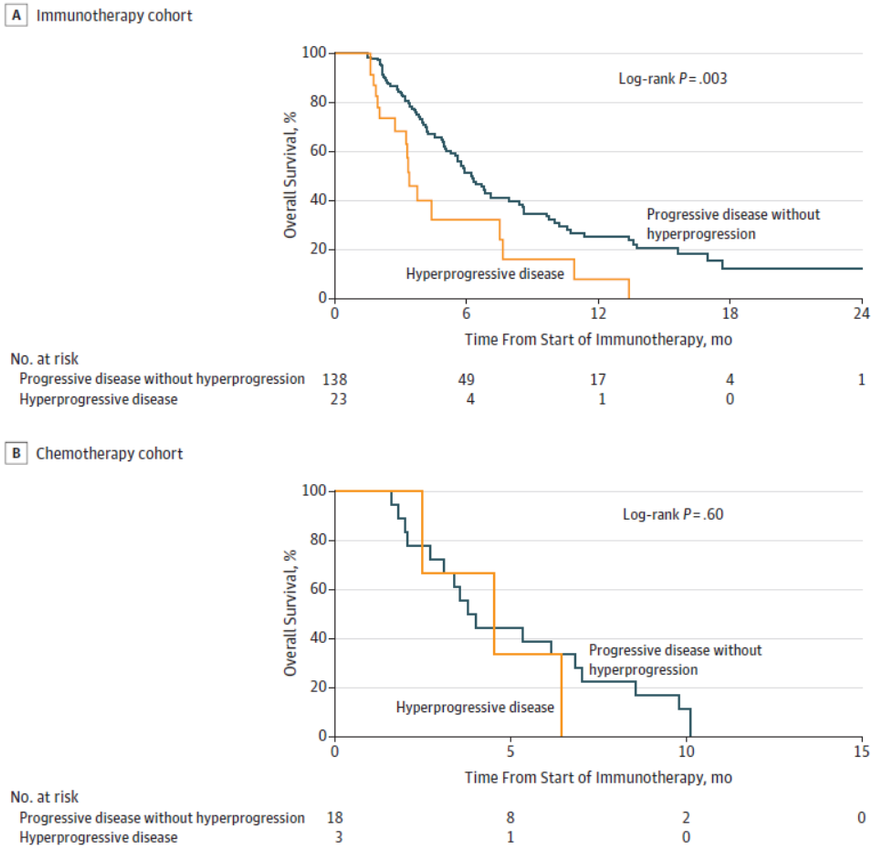
Group R (PD-1 positivity in CD8+TILs ≥40% and PD-1 expression ratio of CD8+ T cells to eTreg cells in TILs ≥1) had significant better PFS compared with other patients



Kamagai et al. Nat Immunol . 2020 Nov;21(11):1346-1358..

Dark Side of Anti-PD-1 Treatment: Hyperprogression

Around 10% of patients treated with anti-PD-1 had hyperprogression and dismal prognosis

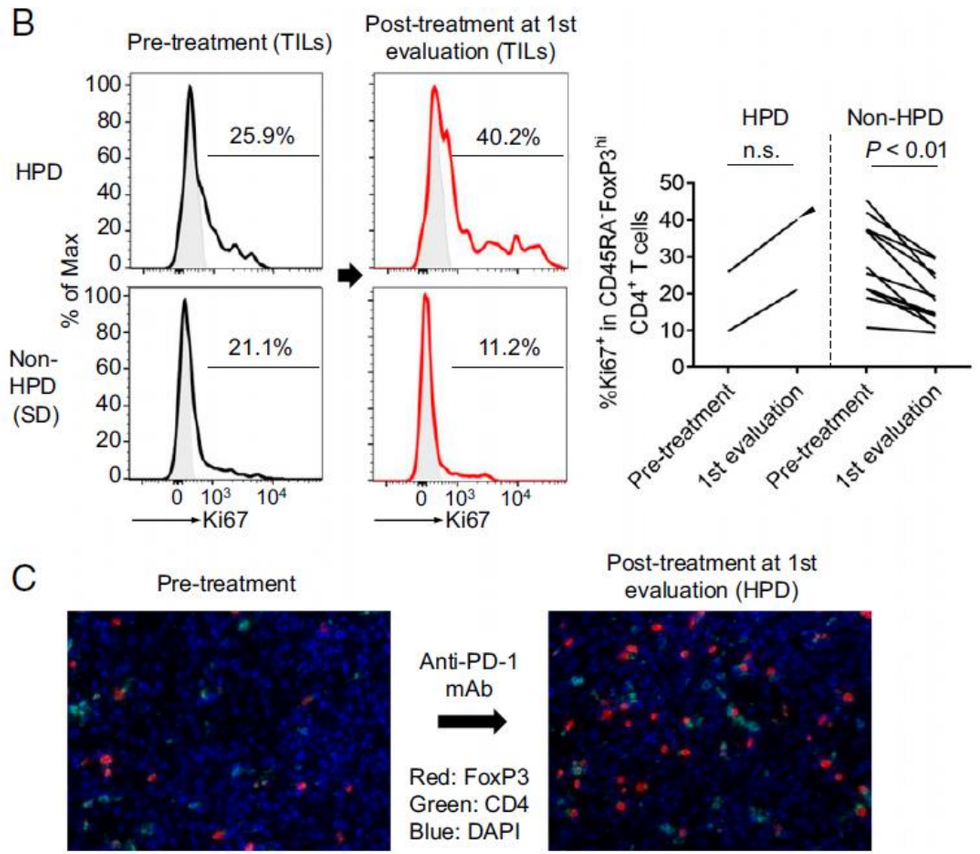


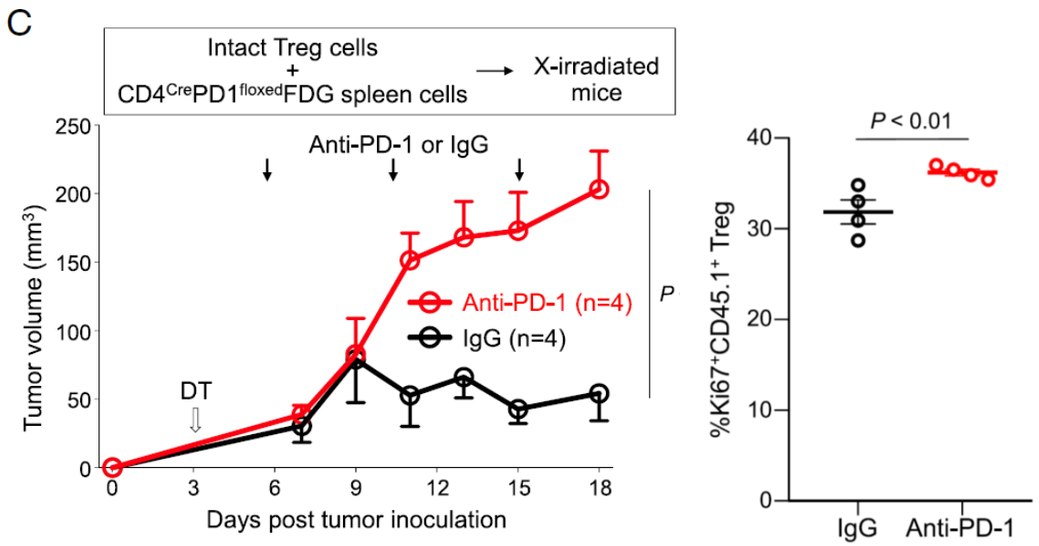
- Hyperprogressive disease (HPD) was defined as disease progression at the first evaluation with ΔTGR exceeding 50%.
- Among 406 advanced NSCLC patients treated with PD-(L)1 inhibitors, 56 (13.8%) were classified as having HPD.
- Patients experiencing HPD within the first 6 weeks of PD-(L)1 inhibitor treatment had significantly lower OS compared with patients with progressive disease (median OS, 3.4 months [95%CI, 2.8-7.5 months] vs 6.2 months [95%CI, 5.3-7.9 months]; hazard ratio, 2.18 [95%CI, 1.29-3.69]; P = .003).
- Among 59 eligible patients treated with chemotherapy, 3 (5.1%) were classified as having HPD.

Ferarra et al. JAMA Oncol . 2018 Nov 1;4(11):1543-1552.

PD-1+ Tregs Amplified by PD-1 Blockade Promote Hyperprogression of Cancer

Depletion of Treg may help to treat and prevent hyperprogression during an-PD-1 treatment



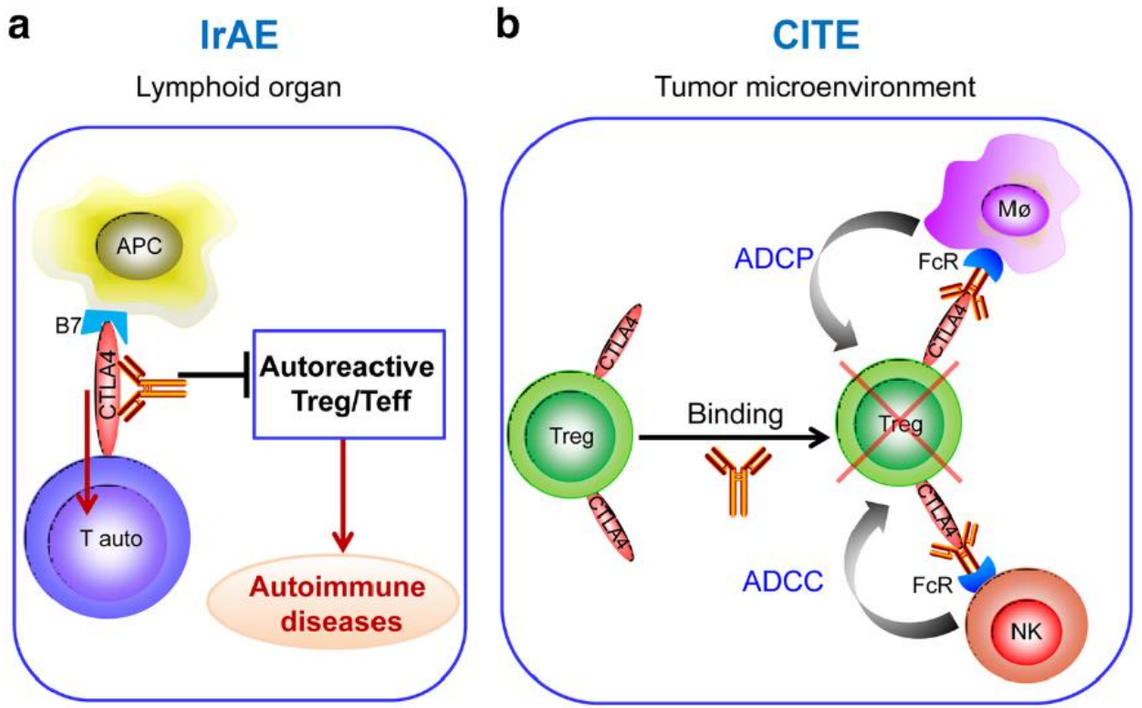


- (Left) Comparison of GC tissue samples before and after anti–PD-1 therapy revealed that the treatment markedly increased tumor-infiltrating proliferative (Ki67+) eTreg cells in HPD patients.
- (Up) in mice, antibody-mediated blockade of PD-1 in Treg cells increased their proliferation and suppression of antitumor immune responses.

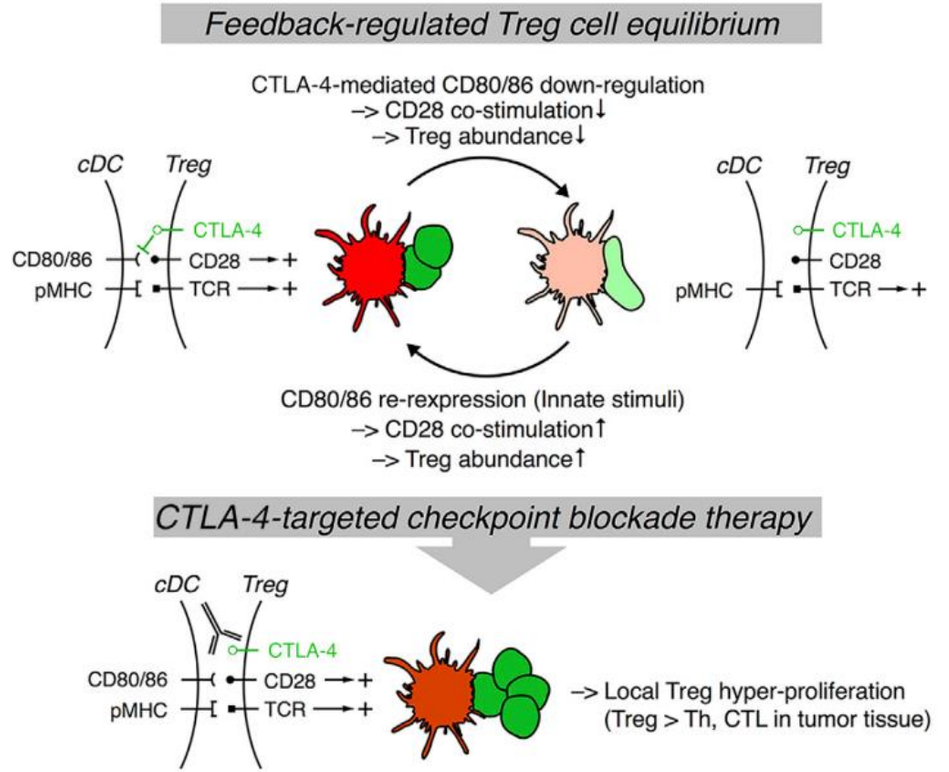
Kamada et al. PNAS. 2019 May 14;116(20):9999-10008.

Anti-tumor Activity Is Mainly Achieved by Intratumoral Treg Depletion, While CTLA-4 Blockade Might Cause IrAEs and even Treg Hyper-proliferation

IrAE is caused by inhibiting the conversion of autoreactive T cells into Tregs, while cancer immuno-therapeutic effect is achieved by intratumoral Treg depletion



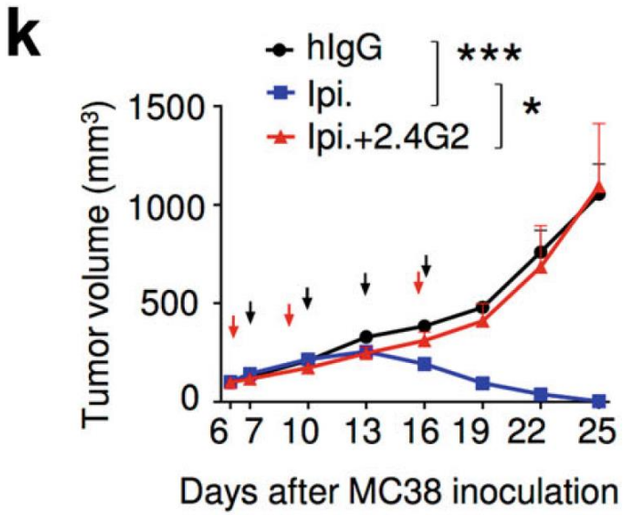
CTLA-4 blockade disrupts the CTLA-4 dependent feedback loop and causes the CD28-mediated expansion of tumor-associated Treg cells

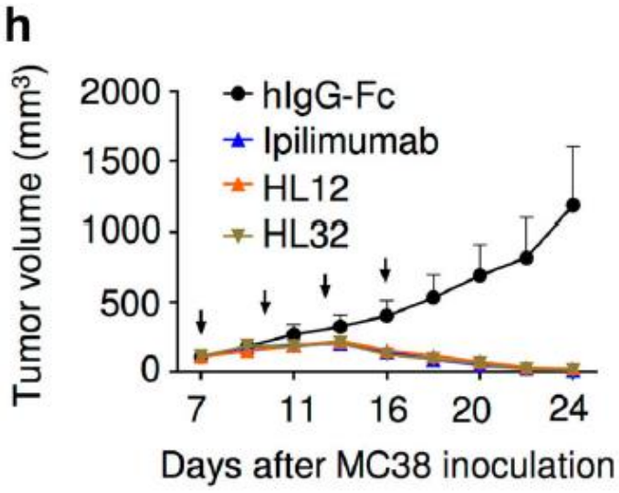


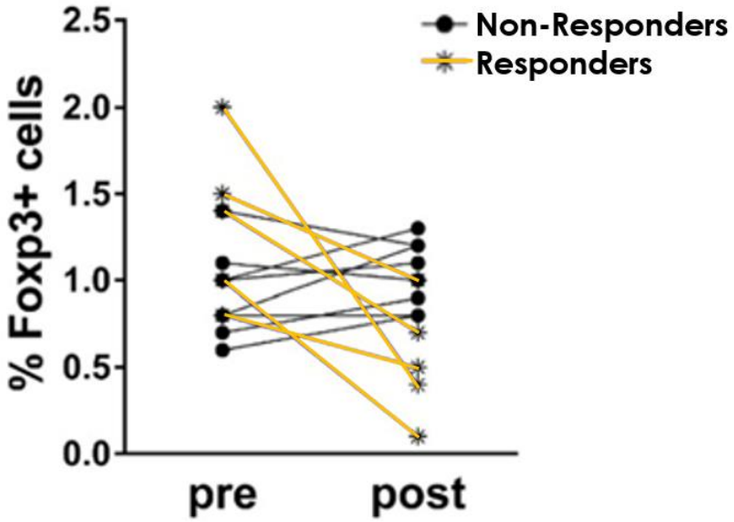
Du et al. Cell Research 2018, 28:1–17.
Marangoni et al. Cell 2021, 184, 3998–4015.

Anti-Tumor Activity of CTLA-4 Antibody Is Dependent on Intratumoral Treg Depletion, While Not Necessarily Dependent on CTLA-4 Blockade

Depletion of intratumoral Tregs is associated with efficacy in both animal models and patients treated with anti-CTLA-4 antibody







- In mouse model, Anti-FcR mAb administration abrogated the therapeutic effect of Ipilimumab.

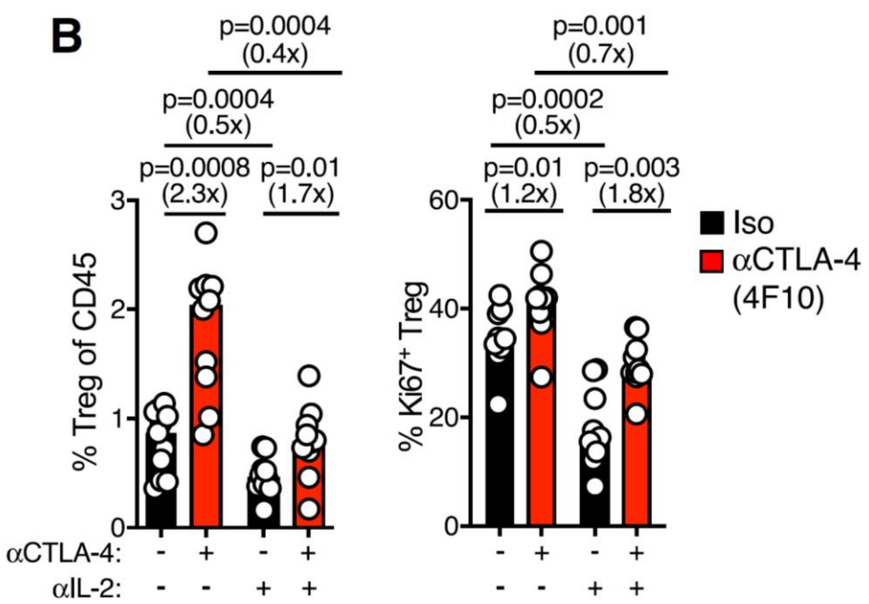
- In mouse model, anti-CTLA-4 mAb HL12 and HL32 that lost blocking activities remain effective in local Treg depletion and tumor rejection.

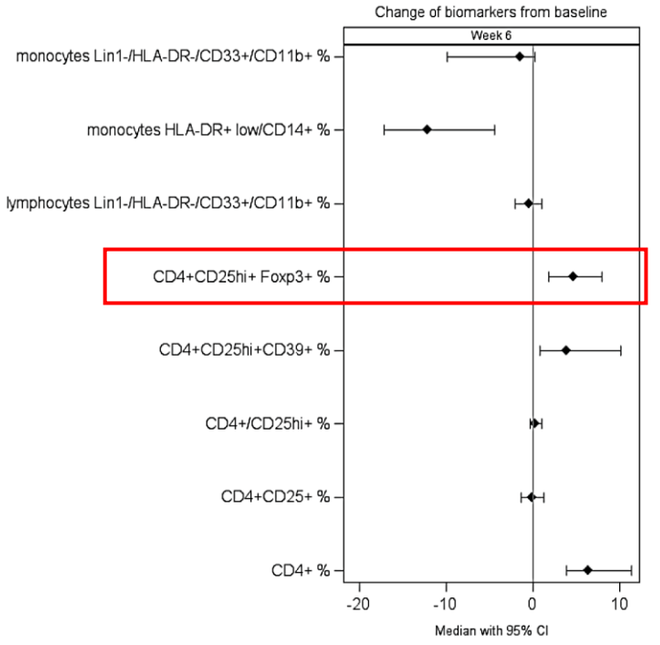
- Patients who responded to ipilimumab had decreased intratumoral Tregs post treatment.

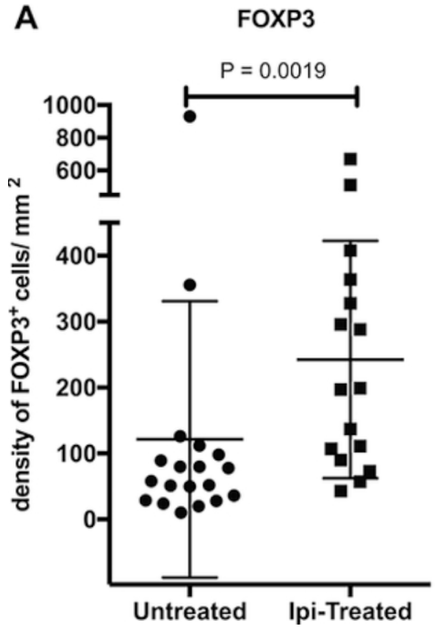
Du et al, Cell Research (2018) 28:1–17.
Romano et l. PNAS . 2015 May 12;112(19):6140-5.

CTLA-4 Blockade Enhances Proliferation of Tregs and Limits the Anti-Tumor Activity

CTLA-4 blockade enhanced proliferation of Tregs which was showed in animal model as well as peripheral blood and tumor samples of patients







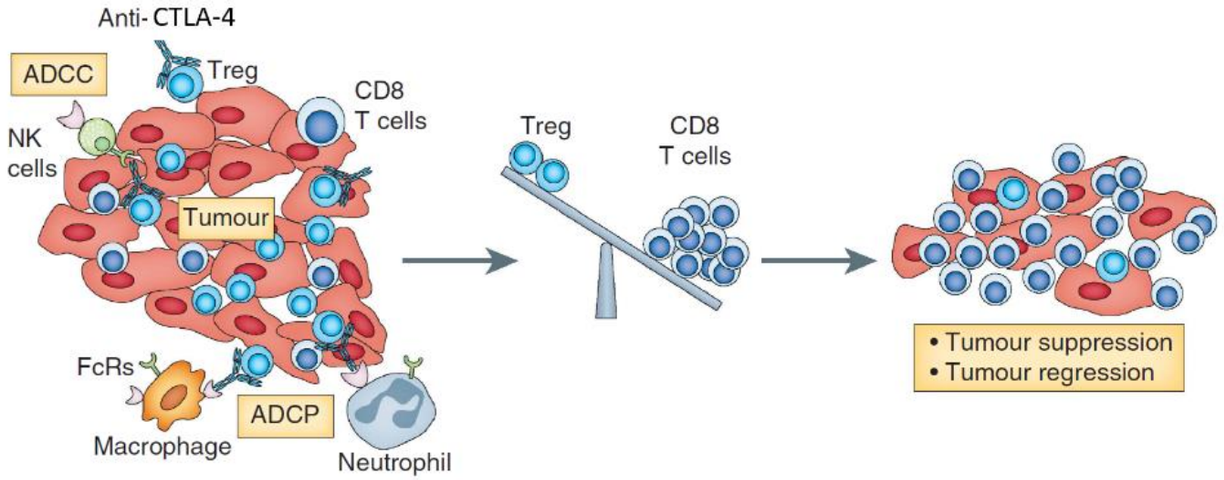
- In mouse model, blockade of CTLA-4 enhances intratumoral Treg proliferation, while simultaneously blockade of IL-2 could inhibit this effect.

- Treg level in peripheral blood increased at Week 6 following treatment with ipilimumab.

- Higher Treg level was found in the tumor of patients treated with ipilimumab compared to untreated patients.

Marangoni et al. Cell 2021, 184, 3998–4015.
Tarhini et al. PLoS One . 2014 Feb 3;9(2):e87705.
Sharma et al. Clin Cancer Res. 2019 Feb 15; 25(4): 1233–1238.

Summary: Develop Treg Targeted Treatment to Expand the Therapeutic Potential of IO



- Treg is the main suppressor of anti-tumor immunity, high infiltration of Tregs in tumors is associated with poor prognosis
- Hyperprogression and dismal prognosis associated with anti-PD- treatment, might be caused by amplification of PD-1+ Tregs in tumor
- Anti-tumor activity of CTLA-4 antibody is mainly dependent on intratumoral Treg depletion

Next generation anti-CTLA-4 antibody with enhanced Treg depletion might overcome the resistance to immunotherapy and expand the therapeutic potential

The image was modified from: Smyth et al. Immunology & Cell Biology. 2014: 92(60).473-474.

HARBOUR BIOMED

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HBM4003 Leading the Way of Next Gen IO therapy

Clinical Validation of Treg Depletion Mechanism

Dr. Xiaoxiang Chen
Chief Development Officer, Harbour BioMed

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www.harbourbiomed.com

HBM4003: Next Generation Anti-CTLA-4 With Encouraging Efficacy and Safety Profile

HBM4003 is a **next generation anti-CTLA-4** fully human Heavy-Chain-Only Antibody (HCAb) with enhanced ADCC for **T_{reg} depletion** and unique PK resulting **reduced drug exposure**

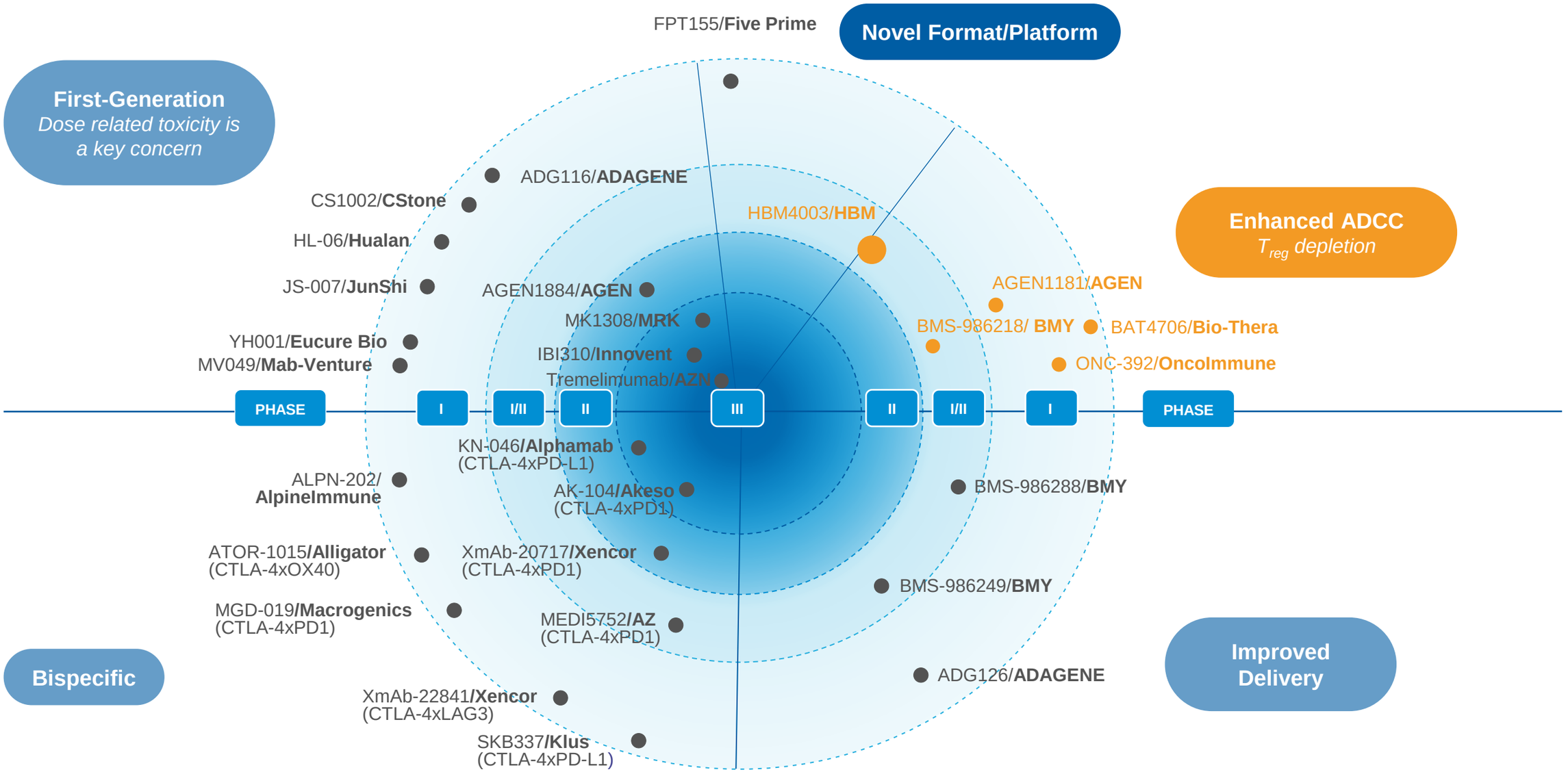
HBM4003 demonstrated **potent tumor growth inhibition** and prolonged survival in mouse tumor models and a **favorable safety profile** compared to Ipilimumab

Preliminary clinical data from mono dose escalation trial **validated MOA and PK/PD profile** and demonstrated **encouraging efficacy and tolerability**

The 1st clinical abstract has been presented at annual ESMO Congress in September 2021

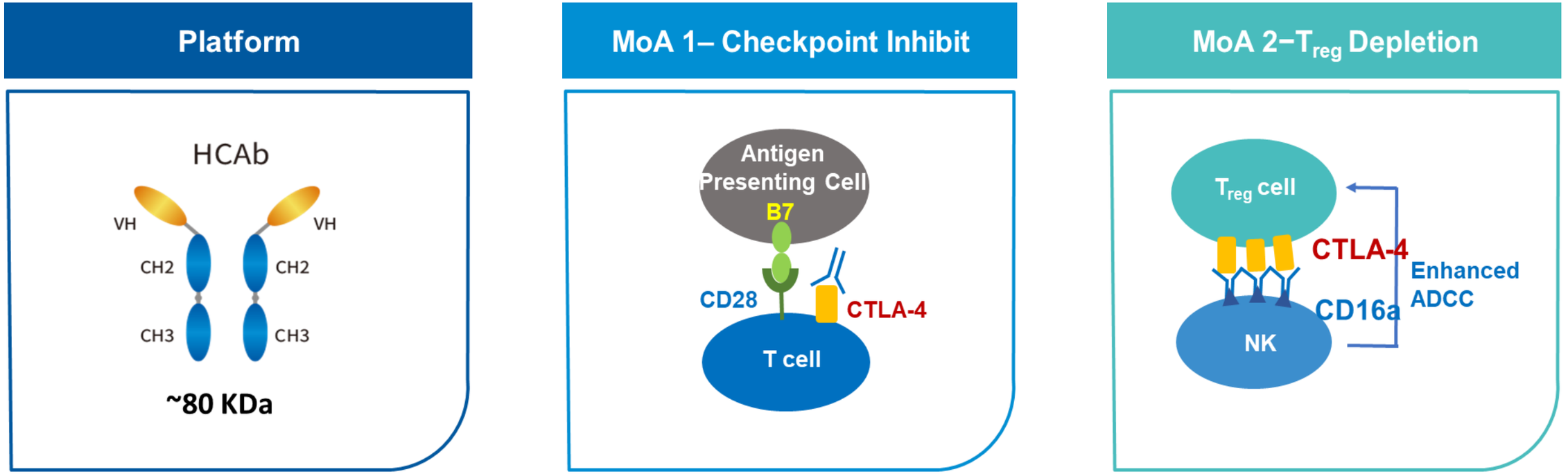
Ph2 trials have been kicked off globally for both mono and combo therapy, covering various solid tumors including melanoma, HCC, RCC, NEN and NSCLC

HBM4003: Leading Development of Next Gen Anti-CTLA-4 Therapeutics with Novel MoA to Improve Efficacy and Safety



Source: Company websites, filings and other publicly available information.

Unique Design With Dual Mechanism of Action – Checkpoint Inhibition and Treg Depletion



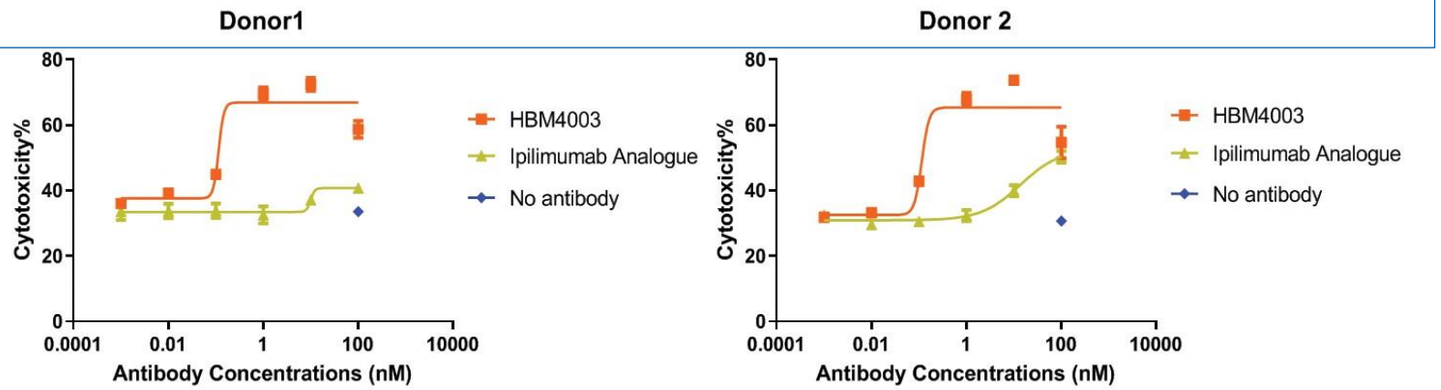
- **HBM4003 dual mechanism of action inhibits negative signaling from the interaction of CTLA-4 and the co-stimulatory molecule B7, and depletes immune suppressive regulatory T cells (T_{reg}) through enhanced ADCC**
- HBM4003 demonstrated near dose-proportional pharmacokinetics (PK), extended pharmacodynamic (PD) effect, and low immunogenicity

Preclinical Evidence – Superior TIL T_{reg} Depletion Activity

100x More Potent Than Ipilimumab Analogue

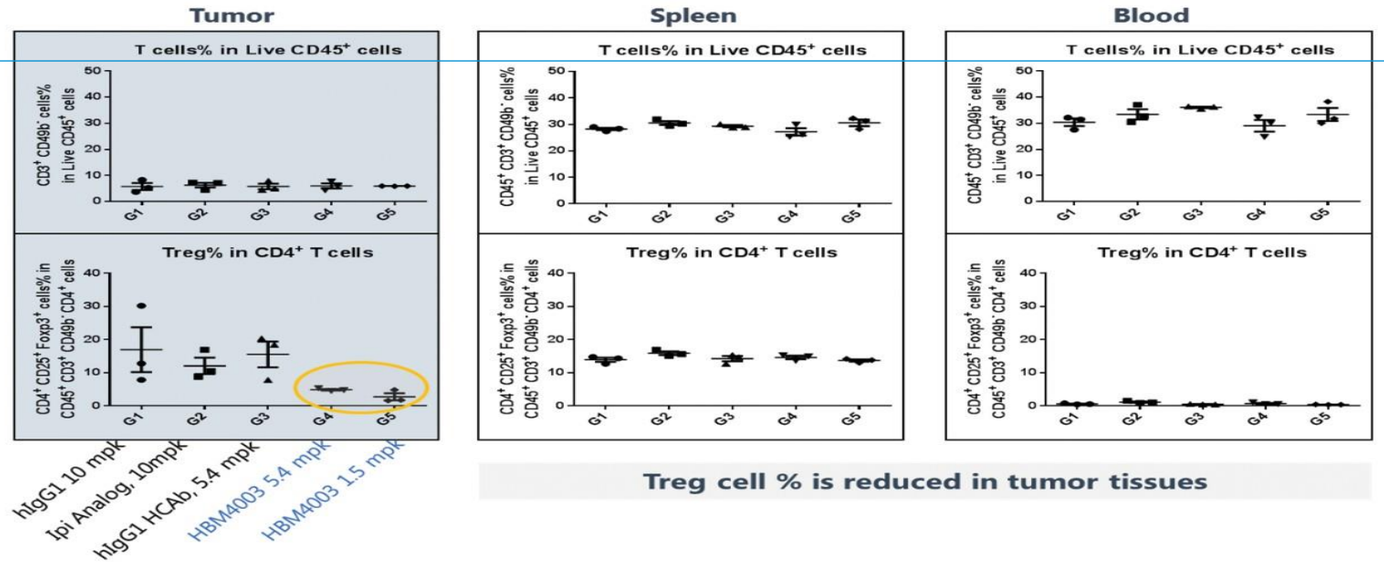
Superior T_{reg} Depletion Activity in Comparison to Ipilimumab Analogue as Measured in Vitro via ADCC Killing Assay

- T_{reg} depletion by HBM4003 in primary human PBMCs in in vitro ADCC assay



Led to Substantial Depletion of TIL T_{regs} in MC38 Bearing hCTLA-4 KI Mice

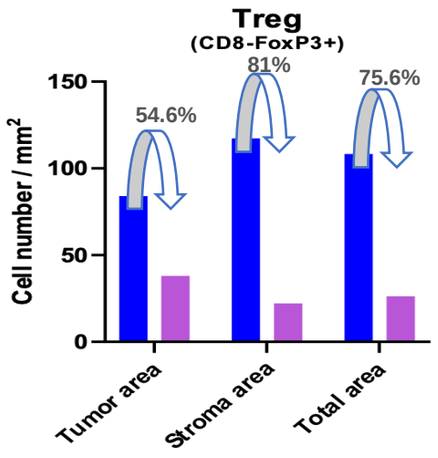
- In vivo T_{reg} (%) in tumor, spleen, and blood in MC38-bearing hCTLA-4 KI mice (3 mice per group)
- Samples were collected 24hrs post 2nd dosing and analyzed by FACS

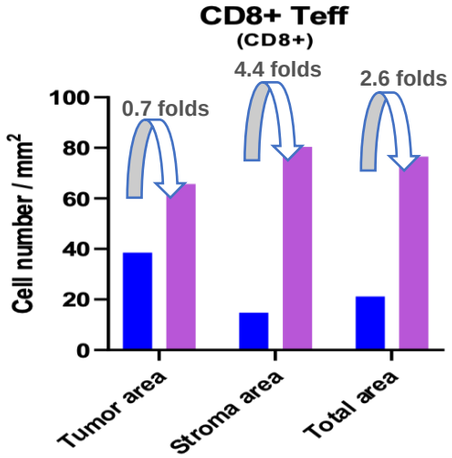


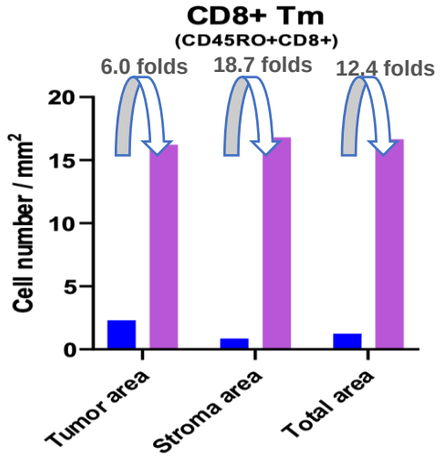
Treg cell % is reduced in tumor tissues

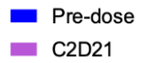
Translation Medicine Evidence – Selective Intratumor T_{reg} Depletion and CD8+ Stimulation

Tumor Biopsy



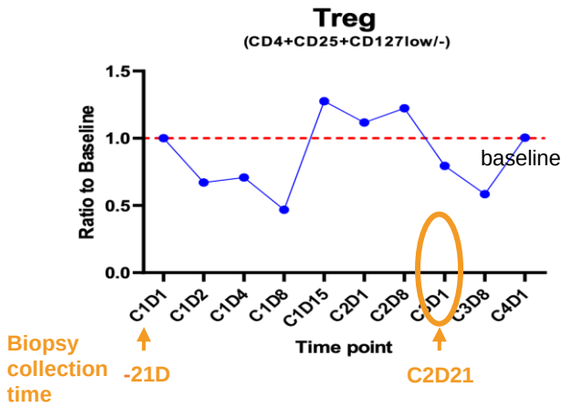


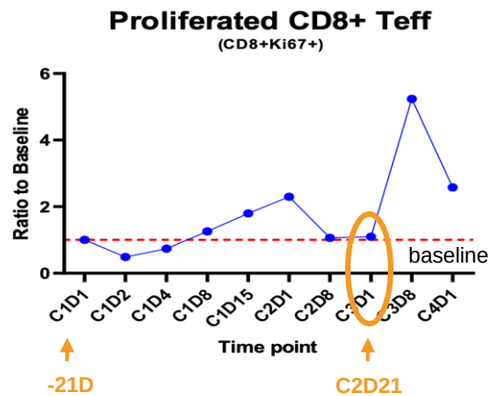




- Subject 89301, 48y, Male, Chromophobe RCC, HBM4003 0.45mg/kg Q3W
- 6w tumor assessment: SD

Peripheral Blood



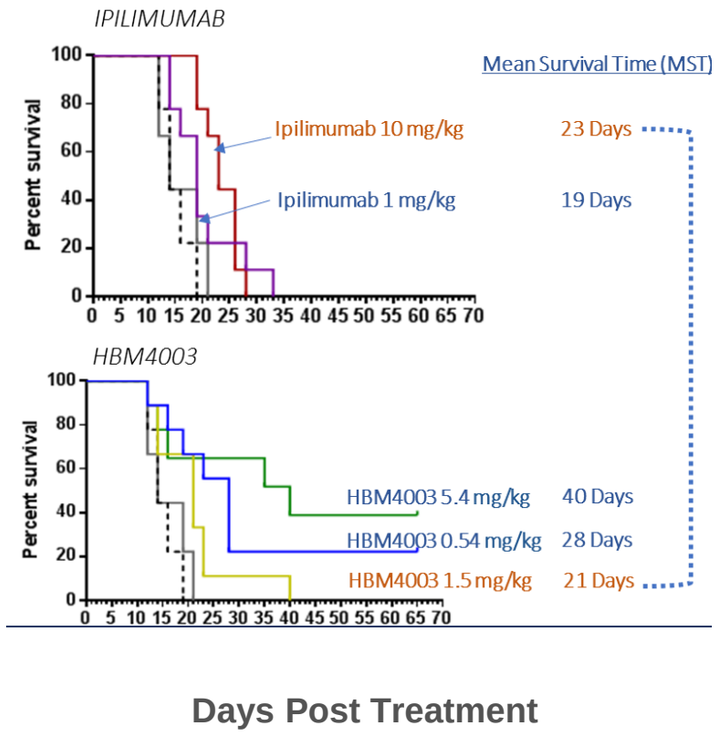


Validation of Preclinical Data

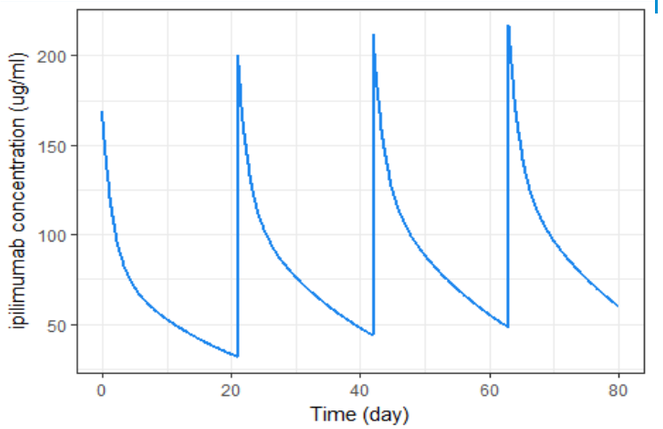
Dual Mechanism Makes HBM4003 More Efficient with Optimized Therapeutic Profile

Preclinical Data: Comparable Mean Survival Time At 1/6 Of Dose Compared to Ipilimumab, and Predicted Human Exposure Is Much Lower (~1/35 of AUC)

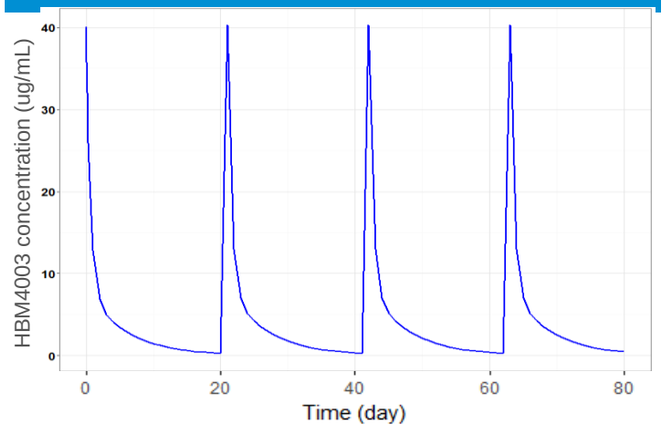
Survival Prolongation (Mean Survival Time)



Ipilimumab (10mg/kg q3w)



HBM4003 (1.5mg/kg q3w)

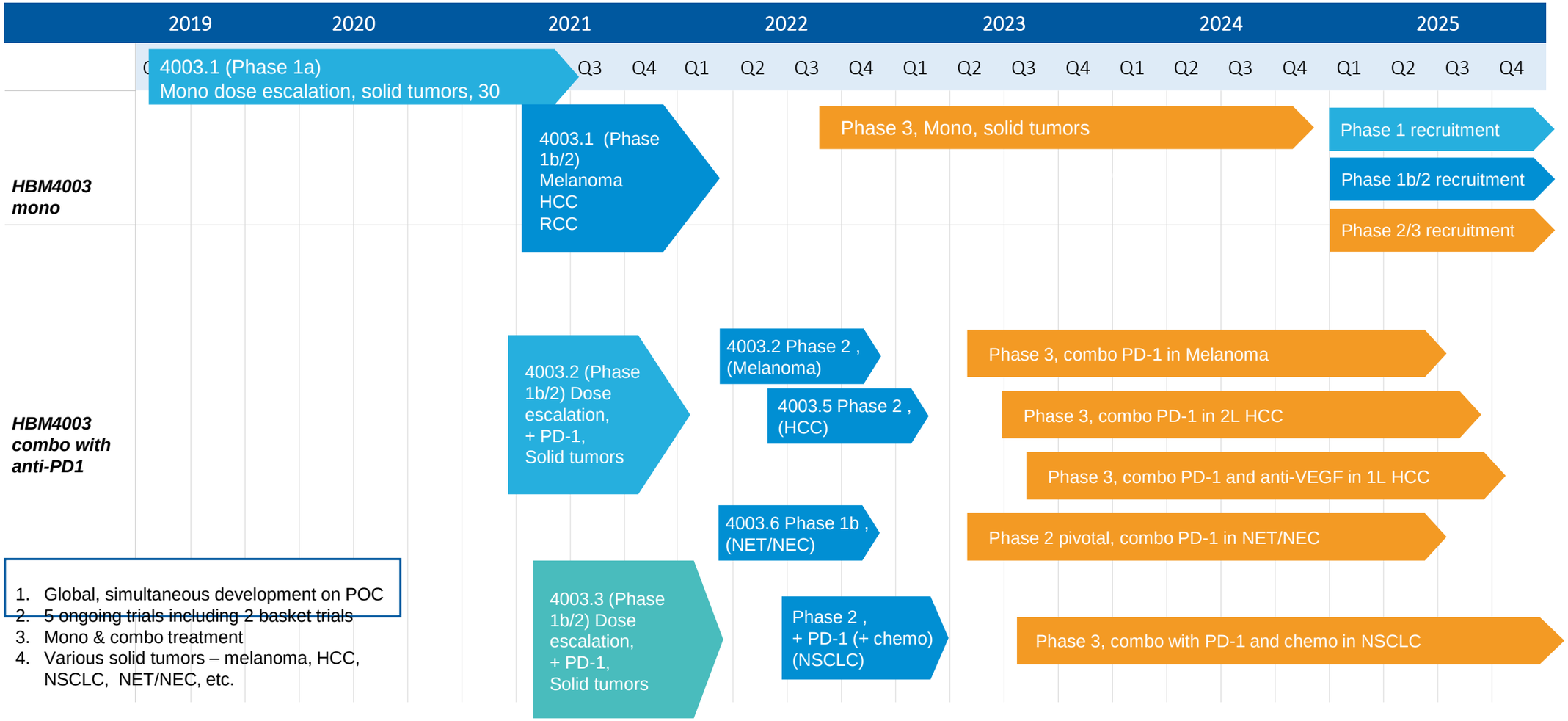


Simulated PK Exposure at Steady State

$AUC_{(0\text{-}tau)}$ µg*day/ml	Cmax µg/ml	Cmin µg/ml
1942.7	744.9	576.3

$AUC_{(0\text{-}tau)}$ µg*day/ml	Cmax µg/ml	Cmin µg/ml
54.27	40.26	2.50

Global Development Roadmap for HBM4003 Aiming to Unlock Potential of Broad Tumor Setting



Mono Therapy: Study 4003.1 Overall Design Outline

Includes Two Parts: Part 1 Abstract Read Out at 2021 ESMO Congress

Part 1

Dose Escalation in Previously Treated (Including Anti-PD-1 Therapy) Advanced Solid Tumors

- **Primary endpoint:**
  - Proportional of patients with DLT

0.6mg/kg Q3W

0.45mg/kg Q3W

0.3mg/kg QW

HBM4003 IV QW or Q3W

RP2D

Part 2

Dose Expansion

- **Primary endpoint:**
  - ORR
- **Secondary endpoints:**
  - DOR, DCR, DDC, maximum tumor shrinkage

Melanoma, HCC, RCC…

HBM4003 IV Q3W

Note: ClinicalTrials.gov identifier: NCT04135261. Data cutoff 12 April 2021.

4003.1 – Key Patient Features and Demographics

Heavily Pre-treated including PD-1, Diversified Cancer Types Mixed with Rare, Cold Tumors

- 20 patients with advanced solid tumors (no melanoma patients), at 4 Australian sites
- **Heavily pre-treated population**
  - ✓ **13 out of 20 patients (65%) having received 2 or more prior regimens**
  - ✓ **8 out of 20 patients (40%) were treated previously with immune checkpoint inhibitor**
  - ✓ The average age of subjects is 62.5 (SD=11.5)
- None of the patients studied had melanoma

	0.3mg/kg QW (N=7)	0.45mg/kg Q3W (N=7)	0.6mg/kg Q3W (N=6)	Total (N=20)
Age, mean (SD)	67.6 (8.3)	62.3 (10.2)	56.8 (15.0)	62.5 (11.5)
ECOG PS, n(%)				
0	3 (42.9)	3 (42.9)	3 (50.0)	9 (45.0)
1	**4 (57.1)**	**4 (57.1)**	**3 (50.0)**	**11 (55.0)**
N of Previous Treatment Lines, n(%)				
0	2 (28.6)	0	0	2 (10.0)
1	2 (28.6)	2 (28.6)	1 (16.7)	5 (25.0)
2 or more	**3 (42.8)**	**5 (71.4)**	**5 (83.3)**	**13 (65.0)**
Previous PD-1/PD-L1 Therapies, n(%)	2 (28.6)	3 (42.9)	3 (50.0)	8 (40.0)

Tumor Type	Safety Assessment (n)	Post-Treatment Data for Anti-tumor Assessment (n)
Endometrial Carcinoma	1	1
PRCC	1	1
ccRCC	4	3
Prostate Cancer	2	2
HCC	1	1
Penile Cancer	1	
Testicular Cancer	1	
Esophagus Cancer	2	1
Colorectal Cancer	1	1
Breast Cancer	2	2
Bladder Cancer	1	1
HNSCC	1	1
NSCLC	1	
Mesothelial Cancer	1	1
TOTAL	**20**	**15**

4003.1 – HBM4003 Was Well Tolerated

- **No toxicity was reported related to lung, kidney, heart or endocrine system**
- **No TRAE was > Grade 3**
  - Grade 3 TRAEs included diarrhea, and 1 case of abnormal liver function test who has HCC. All were manageable and reversible
- **The most common TRAE of any grade was diarrhea/enterocolitis, manageable & reversible with SOC**
- **Maximum tolerated dose (MTD) was not achieved**
  - No dose limiting toxicity (DLT) was observed in any Q3W dose level
- **No treatment-related serious adverse event (TRSAE) was reported at 0.45mg/kg Q3W**

Preferred Term	0.3mg/kg QW (N=7)		0.45mg/kg Q3W (N=7)		0.6mg/kg Q3W (N=6)		Total (N=20)	
	Any Grade	Grade 3	Any Grade	Grade 3	Any Grade	Grade 3	Any Grade	Grade 3
Any irAE	4 (57.1)	1 (14.3)	2 (28.6)	1 (14.3)	5 (83.3)	3 (50.0)	11 (55.0)	5 (25.0)
Enterocolitis	2 (28.6)	0 (0.0)	1 (14.3)	0 (0.0)	3 (50.0)	0 (0.0)	6 (30.0)	1 (5.0)
Diarrhea	1 (14.3)	1 (14.3)	0 (0.0)	0 (0.0)	3 (50.0)	3 (50.0)	4 (20.0)	4 (20.0)
Rash	3 (42.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (15.0)	0 (0.0)
Abnormal hepatic function(1)	0 (0.0)	0 (0.0)	1 (14.3)	1 (14.3)	0 (0.0)	0 (0.0)	1 (5.0)	1 (5.0)
Immune-mediated hepatitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (5.0)	0 (0.0)

Source: Publicly available posters HBM4003 data presented at ESMO 2021 Congress.
Note: Enterocolitis includes colitis and immune-mediated enterocolitis; rash includes rash and rash maculo-popular.
(1) As measured by elevated blood bilirubin and transaminases levels, and abnormal liver function test scores.

Recommended Phase 2 (RP2D) Dose

4003.1 – Differentiated Safety Profile Indicated From Preliminary Data

Even with limited number of patients, encouraging HBM4003 safety profile especially given the extent of pre-treatment in patients

- More severe baseline conditions: more prior treatments (including PD-(L)1), higher ECOG, broad range of solid tumors mixed with cold tumors vs ≥ 2 line melanoma for Ipilimumab
- irAE & TRAE focused on diarrhea vs broad involvement with vital organs

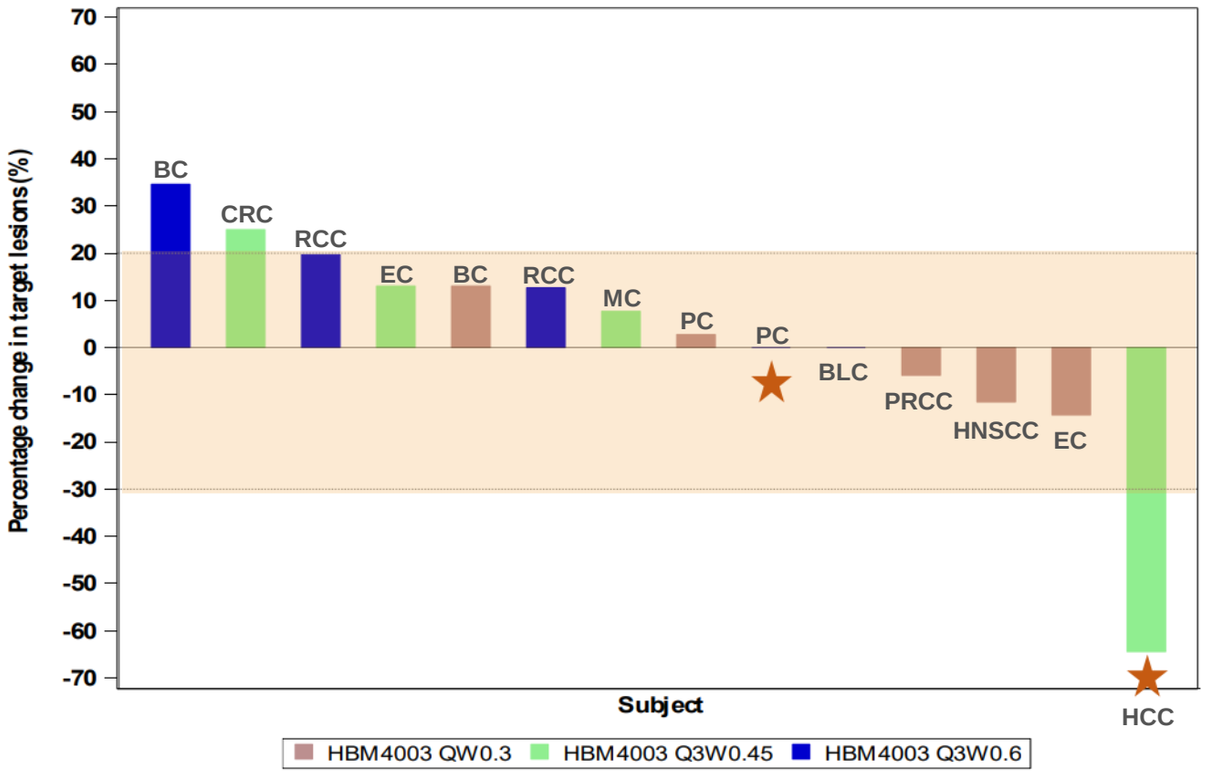
	HBM4003 Overall, n(%)	HBM4003 0.45mg/kg Q3W, n(%)	Ipilimumab 3mg/kg Q3W, n(%)
Total No. Patients	20 (pooled)	7	137/131 (AE)
Tumor Types	Solid tumors	Solid tumors	Melanoma
Prior Treatment Lines	**≥2: 13 (65.0)** **Prior PD-(L)1 Therapy: 8 (40.0)**	**≥2: 5 (71.4)** **Prior PD-(L)1 Therapy: 3 (42.9)**	**≥1: 137 (100)**
ECOG	**0: 9 (45.0)** **1: 11 (55.0)**	**0: 3 (42.9)** **1: 4 (57.1)**	**0: 72 (52.6)** **1: 64 (46.7)** **2: 1 (0.7)**
TRAE	20 (76.9)	4 (57.1)	105 (80.2)
irAE	**Total: 11 (55.0)** Enterocolitis: 6 (30.0) Diarrhea: 4 (20.0) Rash: 3 (15.0) Abnormal hepatic function(1): 1 (5.0) Immune-mediated hepatitis: 1 (5.0)	**Total: 2 (28.6)** Enterocolitis: 1 (14.3) Abnormal hepatic function(1): 1 (14.3)	**Total: 80 (61.1)** Dermatologic: 57 (43.5) Diarrhea: 36(27.5) Colitis: 10 (7.6) Endocrine: 10 (7.6) Abnormal hepatic function(1): 5 (3.8) Other: 6 (4.6)
Gr ≥3 irAE	**Total: 5 (25.0) (No irAEs > G3)** Enterocolitis: 1 (5.0) Diarrhea: 4 (20.0) Abnormal hepatic function(1): 1 (5.0)	**Total: 1 (14.3) (No irAE>G3)** Abnormal hepatic function(1): 1 (14.3)	**Total: 19 (14.5)** Diarrhea: 6 (4.6) Colitis: 7 (5.3) Dermatologic: 2 (1.5) Endocrine: 5 (3.8) Other: 3 (2.3)

Note: TRAE: treatment related adverse event; irAE: immune related adverse event. Ipilimumab data from Hodi FS, et al. N Engl J Med. 2010.
(1) As measured by elevated blood bilirubin and transaminases levels, and abnormal liver function test scores.

4003.1 – Encouraging Preliminary Efficacy Been Observed with HBM4003 Monotherapy

FIH with Dose Escalation, Heavily Pre-treated (including PD-1), Broad Range of Solid Tumors

Maximum Percent Change in Sum of



Best Overall Response, n (%)

	0.3mg/kg QW (n=7)	0.45mg/kg Q3W (n=7)	0.6mg/kg Q3W (n=6)
CR	0 (0.0)	0 (0.0)	0 (0.0)
PR	0 (0.0)	1 (14.3)	0 (0.0)
SD	5 (71.4)	0 (0.0)	4 (66.7)
PD	1 (14.3)	3 (42.9)	1 (16.7)

Tumor Shrinkage Reported for 3 SD Patients (0.3mg/kg QW)

Note: FIH = first in human; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; Breast cancer (BC), colorectal cancer (CRC), clear cell renal cell carcinoma (RCC), esophagus cancer (EC), mesothelial cancer (MC), prostate cancer (PC), bladder cancer (BLC), papillary renal cell carcinoma (PCRC), head and neck squamous cell carcinoma (HNSCC), hepatocellular carcinoma (HCC).

4003.1 – Preliminary Monotherapy Efficacy Data Show Potential in Multiple Solid Tumors

Effect Could Be Attributed to HBM4003's Dual MOA vs. Ipilimumab Which Showed Efficacy Primarily in Melanoma

HBM4003 Monotherapy

- **2 Clinical Responses**
  - 1 patient with **HCC** who was pre-treated with Sorafenib, Lenvatinib and anti-PD-1 had confirmed partial response (PR)
  - 1 patient with **CRPC** had PSA response for > 71 weeks with SD in RECIST assessment
- **Study did not include melanoma patients**
- **9 patients had stable disease (SD 60%)**
  - 15 patients had at least 1 post-treatment tumor assessment
  - Tumor shrinkage was reported in 3 patients

Ipilimumab Monotherapy

- **Most Clinical Responses in solid tumors are in melanoma**
- All clinical responses in solid tumors were dosed at 3 or 10mg/kg
- With >1000 patients, 4 clinical responses were reported across all solid tumors outside of melanoma

Note: Efficacy is assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. An independent imaging reading group was hired to review CT scan and RECIST assessment for responders.

4003.1 – HCC Patient pre-treated with PD-1 mAb: Confirmed PR in Target Lesion

Patient profile

- 64-year-old man, Asian, HBV infected
- Prior treatments: sorafenib, lenvatinib and anti-PD-1
- HBM4003, 0.45 mg/kg Q3W

Strong and durable efficacy observed

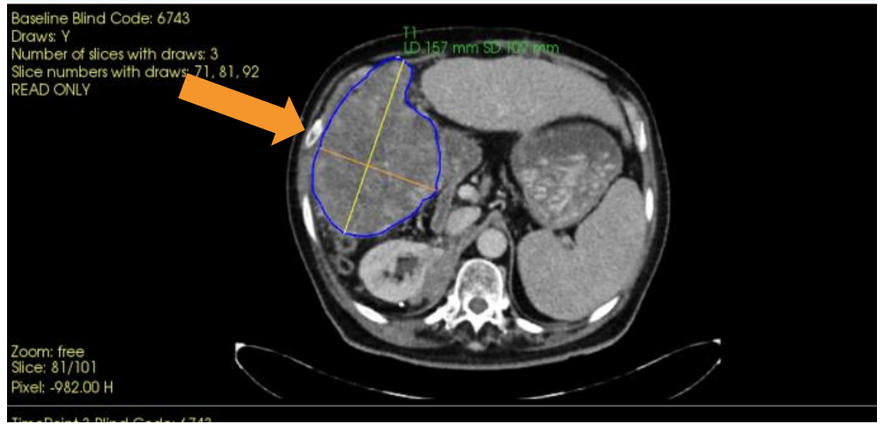
- Tumor reduction reached 64.4% at week 22 and continued to remain as 64.4% at week 40 for target lesions, response of non-target lesions was CR at week 22

	Location	Baseline	6 W	11 W	16 W	22W	28 W	34W	40 w
Non Target Lesions	Lung , LN, Left Liver	NA	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	CR	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD
Target Lesions (mm)	Right Superior Liver, Right Kidney	225	175	115	105	80	80	80	80
	Change From Baseline	N/A	22.2%	48.9%	53.3%	64.4%	64.4%	64.4%	64.4%
AFP u/L		170	5	5	9	6	7	10	ND
Overall Response		NA	SD	PR	PR	PR	PR	PR	PR

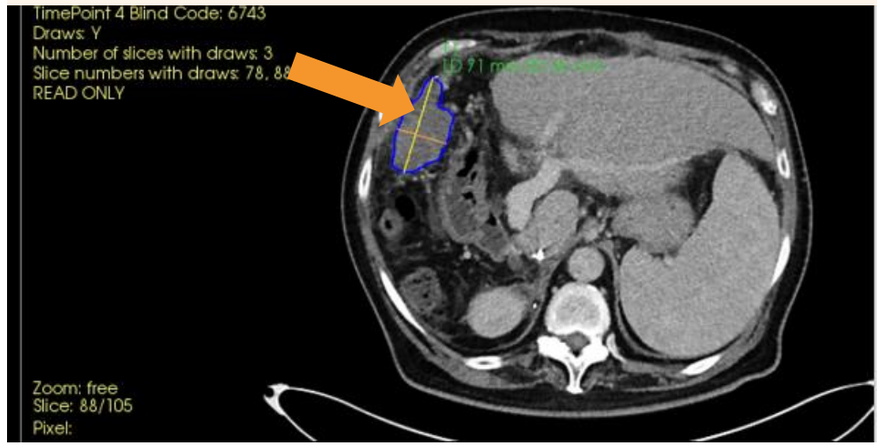
Note: HCC = hepatocellular carcinoma; PR = partial response. The target lesion was measured at the longest diameter.

Target Lesion

Baseline



16 Week



4003.1 – CRPC Patient: Durable SD by RECIST 1.1 associated with PSA Response

Patient profile

- 80-year-old man, HBM4003 0.6 mg/kg Q3W
- Prior treatments: docetaxel, cabazitaxel and bicalutamide

PSA response

- More than 50% reduction in PSA level from baseline at 6 week

Extended clinical benefits

- The PSA response continues until week 71
- The SD of adrenal and axillary lymph node by RECIST 1.1 also last until week 35, no CT scan has been done since then but the patient stay well without any anti-tumor treatment

	May 2020	Jun 2020	July 2020	Dec 2020	Jan 2021	Apr 2021	Sep 2021
	Baseline	**5 W ★**	**10 W**	**30w**	**35W**	**45 W**	**71 W**
PSA (ng/ml)	240	92 PSA response	89 PSA response	89 PSA response	74 PSA response	58 PSA response	77 PSA response
Sum of Diameter of TLs(mm)	45	45	45	-	-	-	-
Overall Response	NA	SD	SD	-	SD	-	-

Note: CRPC = castration-resistant prostate cancer; SD: stable disease; PSA: prostate-specific antigen; TLs: Target lesions

★Treatment Cessation

4003.1 Conclusion: Preliminary Data Demonstrate Encouraging Activity across a Broad Range of Tumors with Improved Tolerability for HBM4003 vs Ipilimumab

HBM4003 is the next generation anti-CTLA-4 fully human HCAb with enhanced ADCC for T_{reg} depletion and the first HCAb under clinical development

Novel MOA

- Selective intratumor Treg depletion been validated by both pre-clinical and clinical evidence

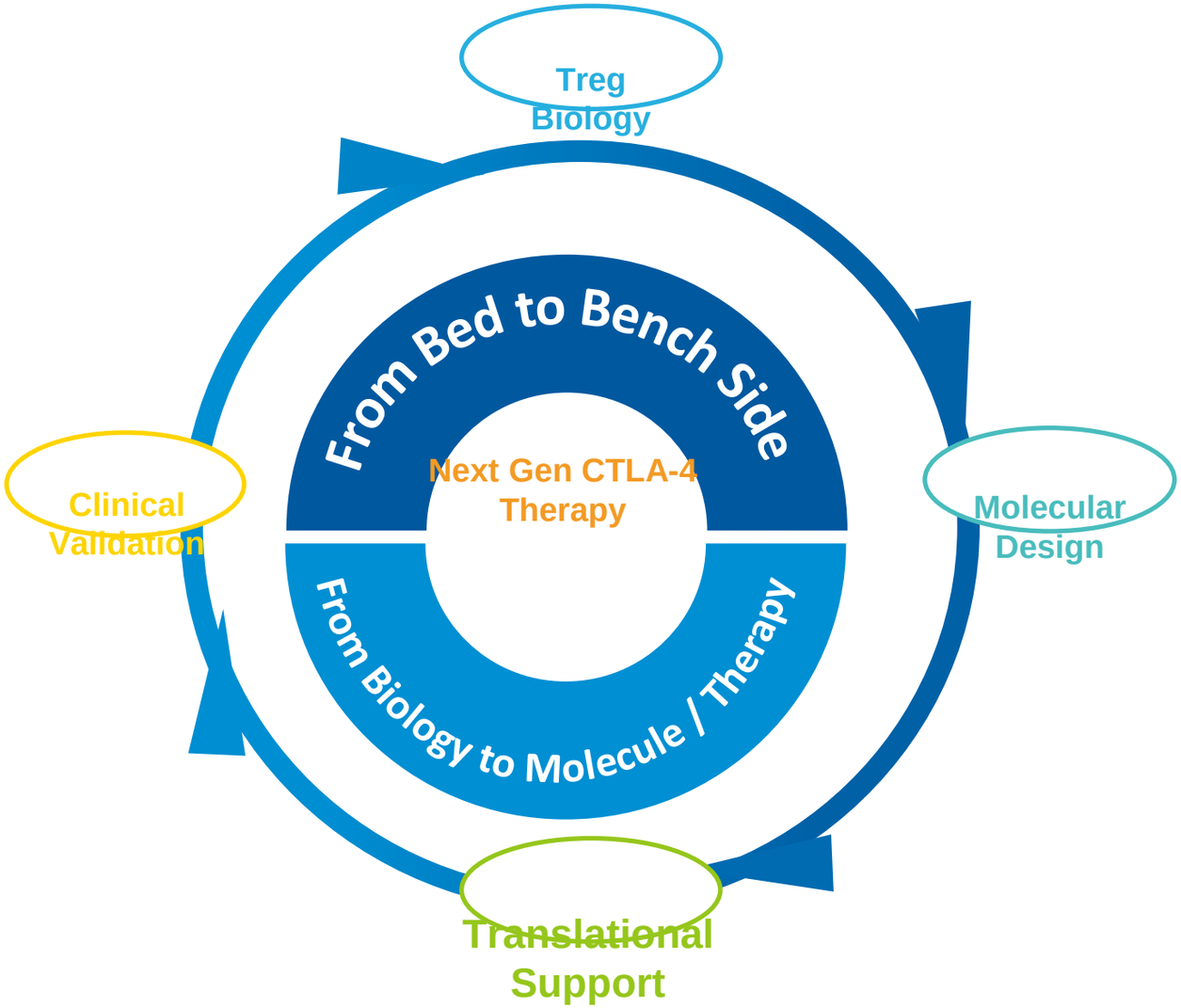
Well Tolerated

- The most common TRAE of any grade was diarrhea/enterocolitis
- No toxicity was reported related to lung, kidney, heart or endocrine system
- No TRAE was > Grade 3
- Maximum tolerated dose (MTD) was not achieved

Encouraging Efficacy

- 9 (out of 15) patients achieved SD with heavily pre-treated tumors
- 2 clinical response- 1 patient pre-treated by all SOCs (including PD-1) was confirmed as PR, 1 patient had PSA response with SD by RECIST

HBM4003 Outlook
The First Full Evidence Chain to Demonstrate Next Gen Treg MoA Therapeutics



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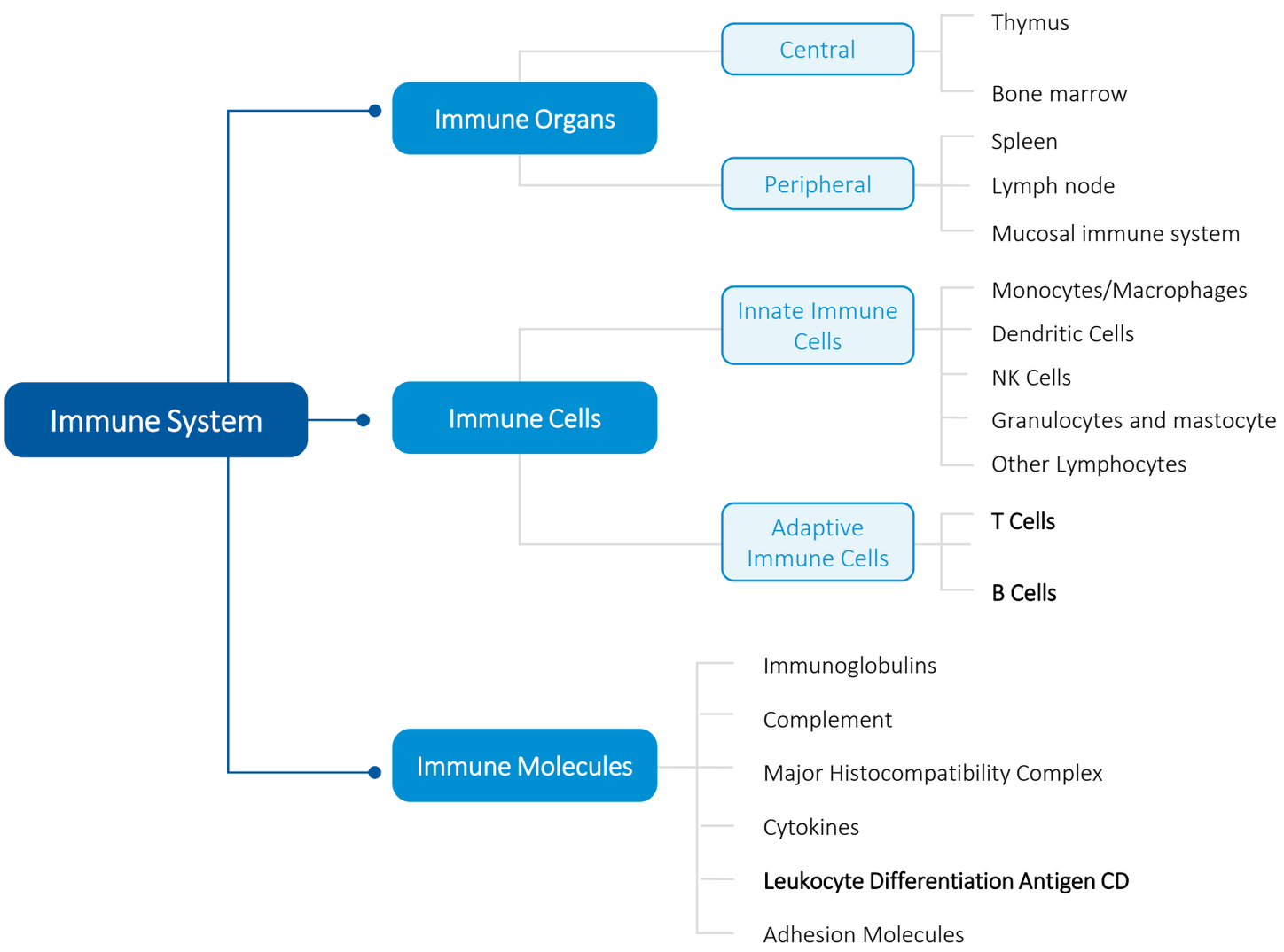
Batoclimab:
A Breakthrough Therapy for Autoimmune Diseases

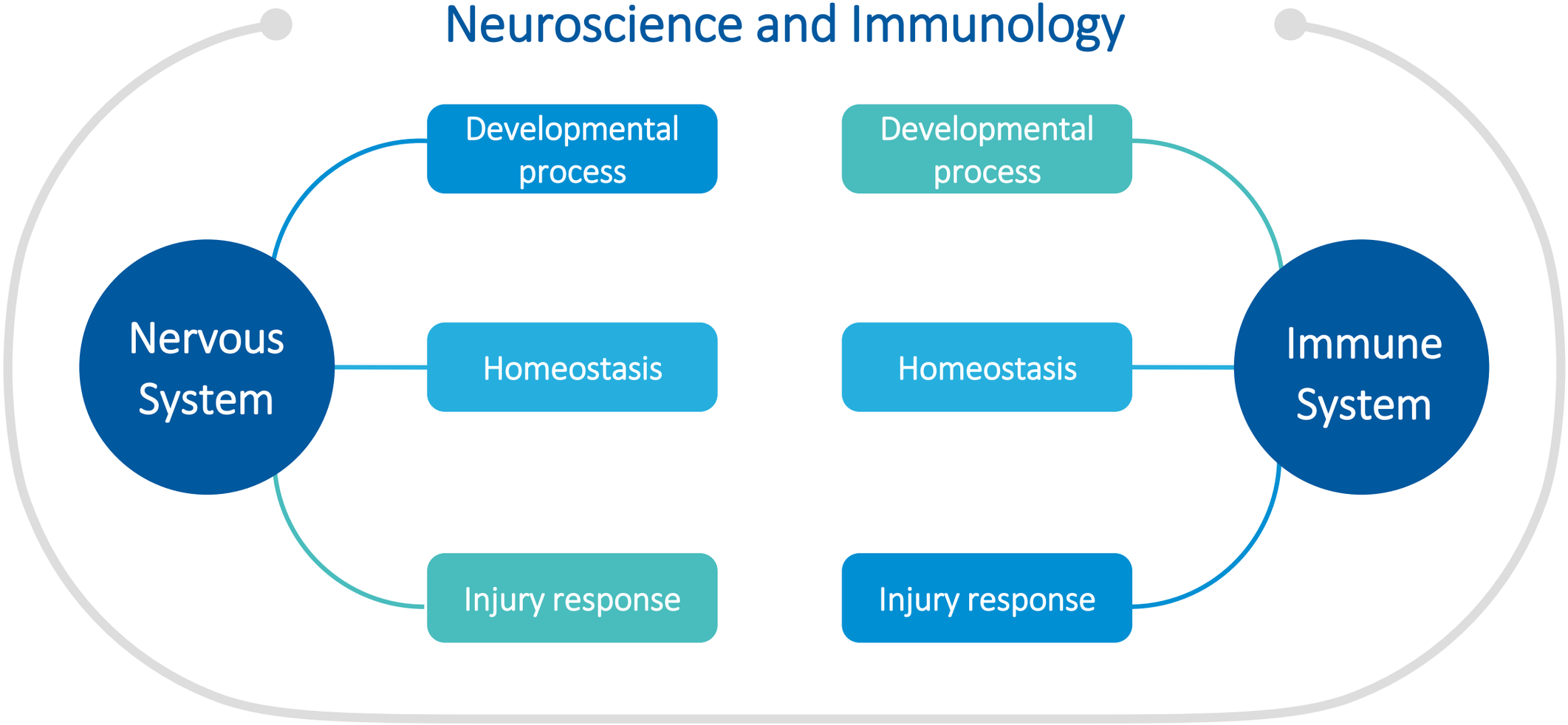
Prof. Chongbo Zhao
Professor of Neurology
Huashan Hospital of Fudan University

Immune System and Autoimmune Diseases

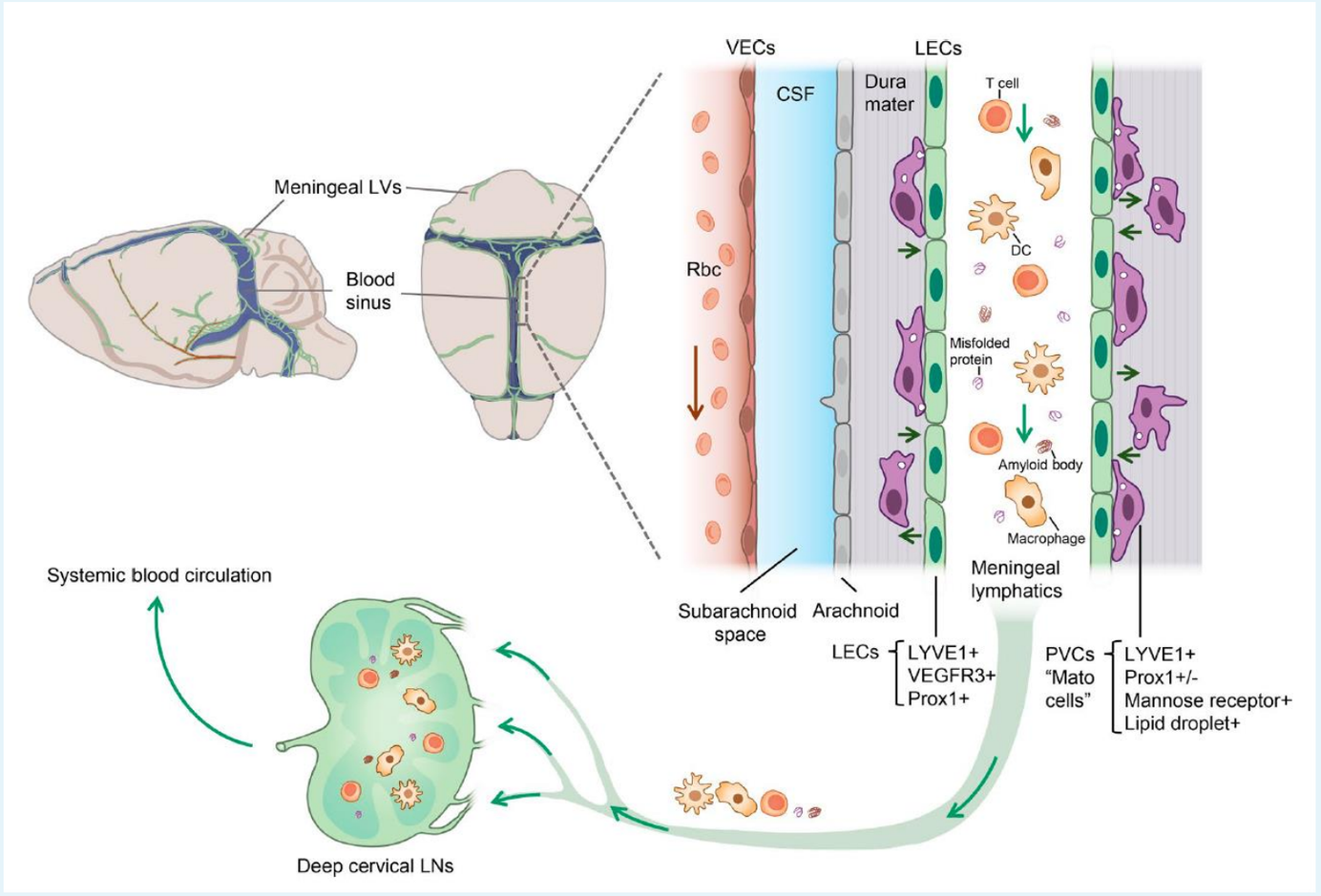


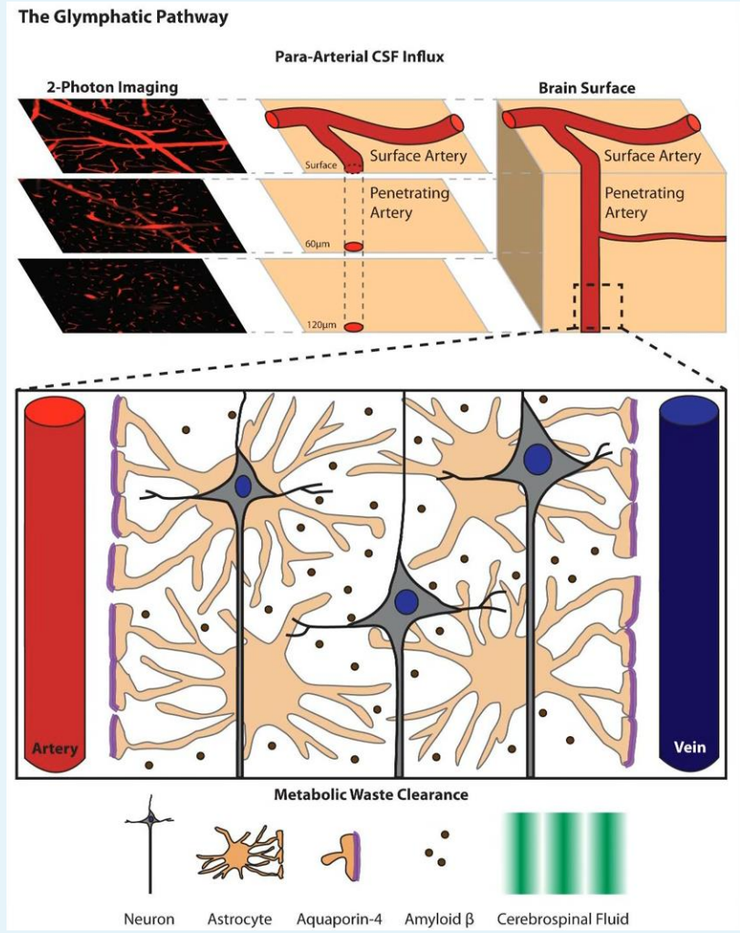
- About 4.5% of the population has autoimmune diseases
- > 80 autoimmune diseases
- > 30 of these neuroimmunological disorders
- The nervous system can be secondarily affected due to a variety of autoimmune diseases (SLE, Sicca syndrome, etc.)

Neuroimmunology Evolution



CNS: Not An Immunoprivilaged Site Anymore

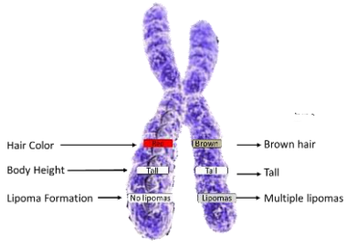




J Exp Med. 2018 Jan 2;215(1):35-49.

Common Features of Neuroimmune Disorders

Gene susceptibility

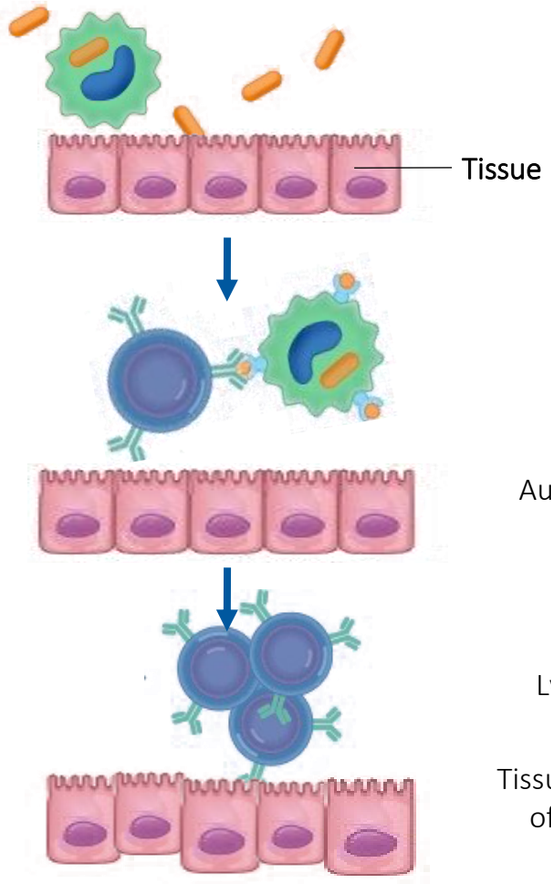


Susceptibility Gene

Loss of autoimmunity regulation

Lymphocytes that responds to autoantigens

Environmental stimulation



Infection tissue damage inflammation

Tissue antigen presenting cell activation

Autoreactive lymphocytes enter tissues

Autoreactive T/B Lymphocyte Activation

Tissue damage: Development of autoimmune diseases

Intrinsic factors

- Gene susceptibility
  - HLA polymorphisms
  - SNPs enriched in major immune pathways
  - Genetic susceptibility of the X chromosome ? Female ↑

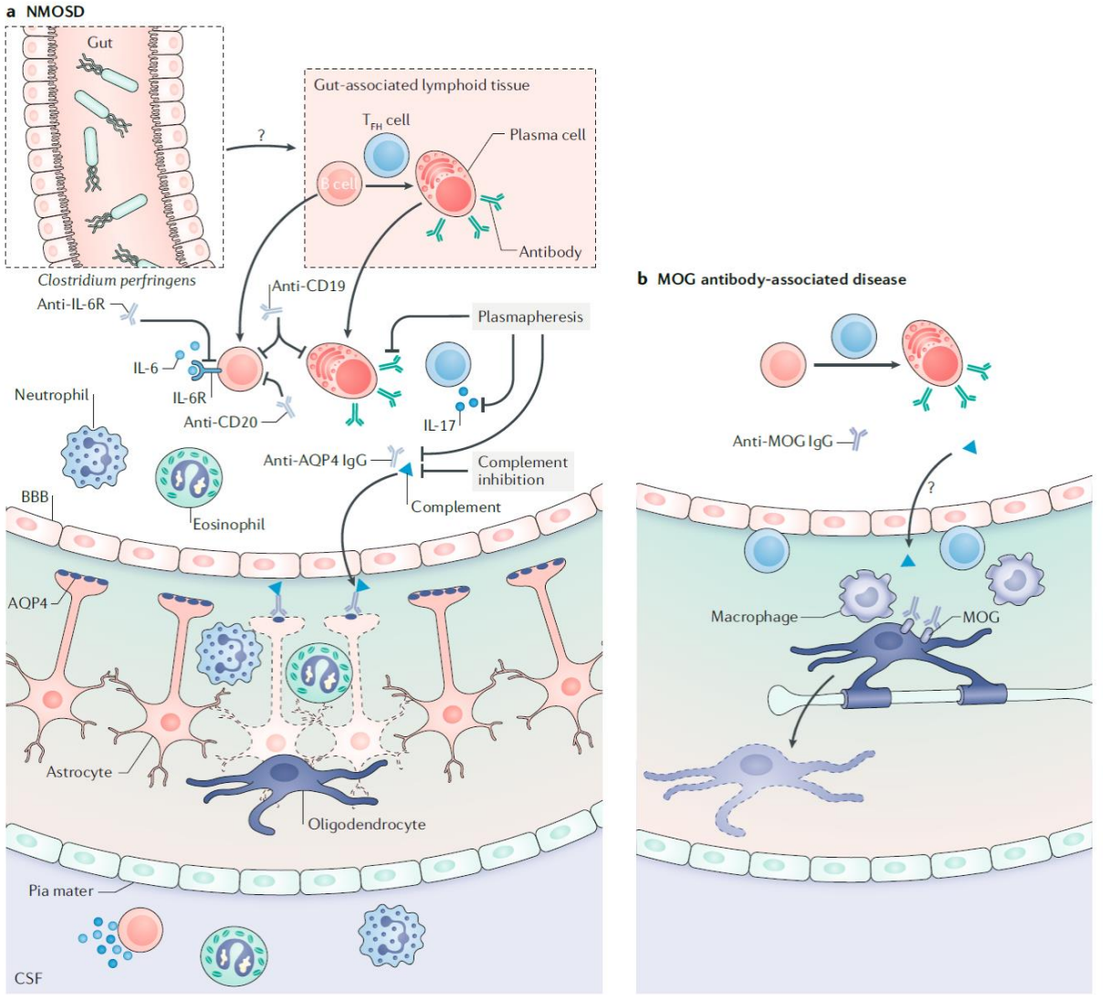
Extrinsic/Predisposing Factors

- Pathogen infection
  - EBV、CMV、C. *jejuni*, etc
- Gut bacteria
  - GDP-L-fucose synthase
- Tumor
  - Ectopic antigen
- Vitamin D

Molecular mimicry
Epitope spreading

Neuro Immune Disease – Central Inflammatory Demyelination

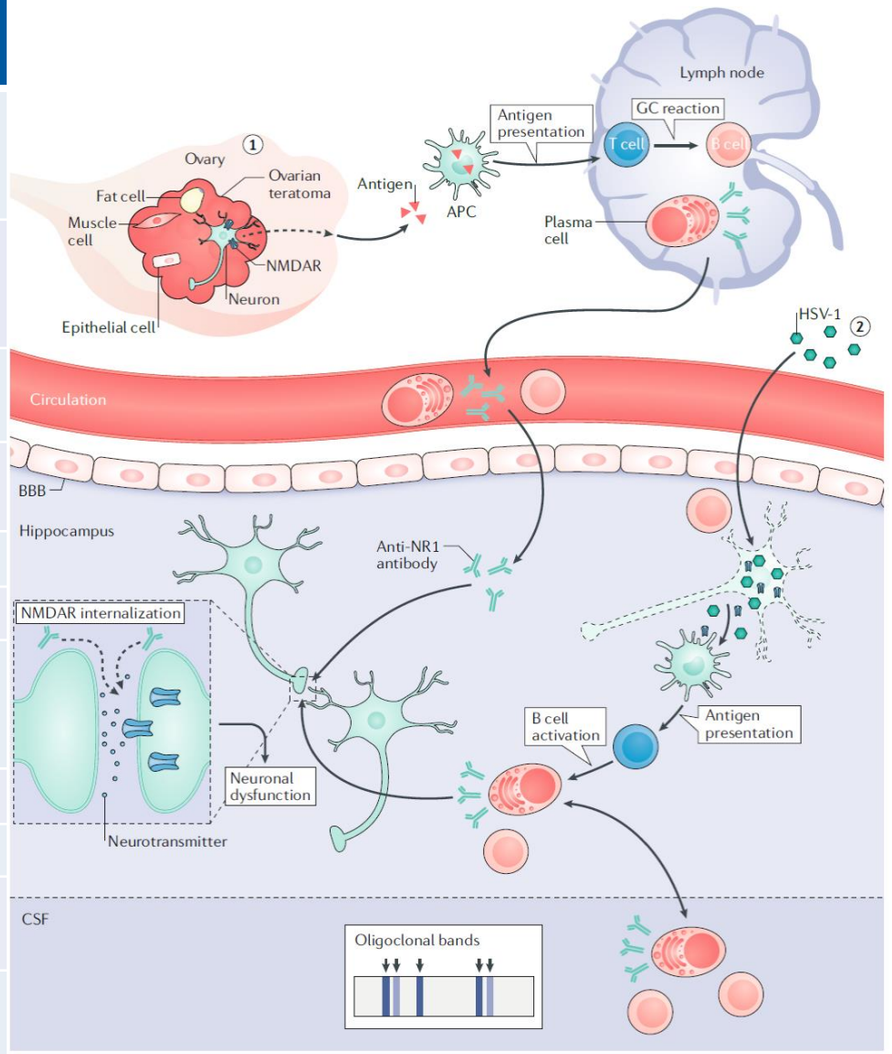
Disease/Target Antigen	Pathogenic autoantibody	Hallmark autoantibody	Clinical characteristics
MS	None	None	Relapsing-remitting; neurological signs and symptoms
NMOSD	**AQP4**	AQP4	Optic neuritis; transverse myelitis; area postrema syndrome
ADEM		~40% MOG	Acute encephalopathy; neurological symptoms and signs; optic neuritis; myelitis
MOG-AD	MOG	MOG	Recurrent optic neuritis; papilledema; myelitis; cranial nerve involvement
GFAP		GFAP	Subacute and chronic meningitis; encephalitis; myelitis; papilledema



Front Neurol. 2021 Apr 14;12:664664.
Nat Rev Neurosci. 2019 Dec;20(12):728-745.

Neuro Immune Disease – Auto Immune Encephalitis

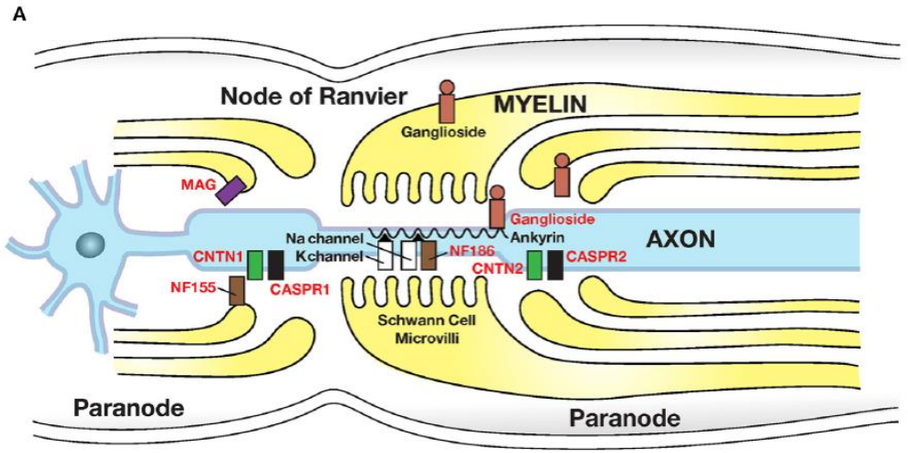
Pathogenic antibody	Clinical main phenotype	Tumor correlation
NMDAR IgG1	Pan-encephalitis; autonomic dysfunction; extrapyramidal symptoms	~60%, ovarian teratoma
LGI1 IgG1, IgG4	limbic encephalitis; dysmyotonia of face, shoulder and arm; hyponatremia	5 – 10%, thymoma
AMPAR	limbic encephalitis	> 50%, cell lung cancer, thymoma, breast cancer
GABABR	limbic encephalitis; cerebellar ataxia	> 50%, small cell lung cancer
GABAAR	Intractable epilepsy	~30%, thymoma
GlyR	PERM; brain stem encephalitis	
CASPR2 IgG1, IgG4	limbic encephalitis; Autonomic dysfunction; Neuromyotonia; Insomnia	20%, thymoma
MGluR1	Cerebellar ataxia; ageusia	~10%, Hodgkin lymphoma
MGluR5	Encephalitis; epilepsy	< 10%, lymphoma
IgLON5 IgG4	Sleep disorder; extrapyramidal symptoms	
DPPX IgG1, IgG4	Diarrhea; encephalitis; epilepsy; PERM; cerebellar ataxia	< 10%, lymphoma



Front Neurol. 2021 Apr 14;12:664664.
Nat Rev Neurosci. 2019 Dec;20(12):728-745.

Neuro Immune Disease – Peripheral Neuropathy

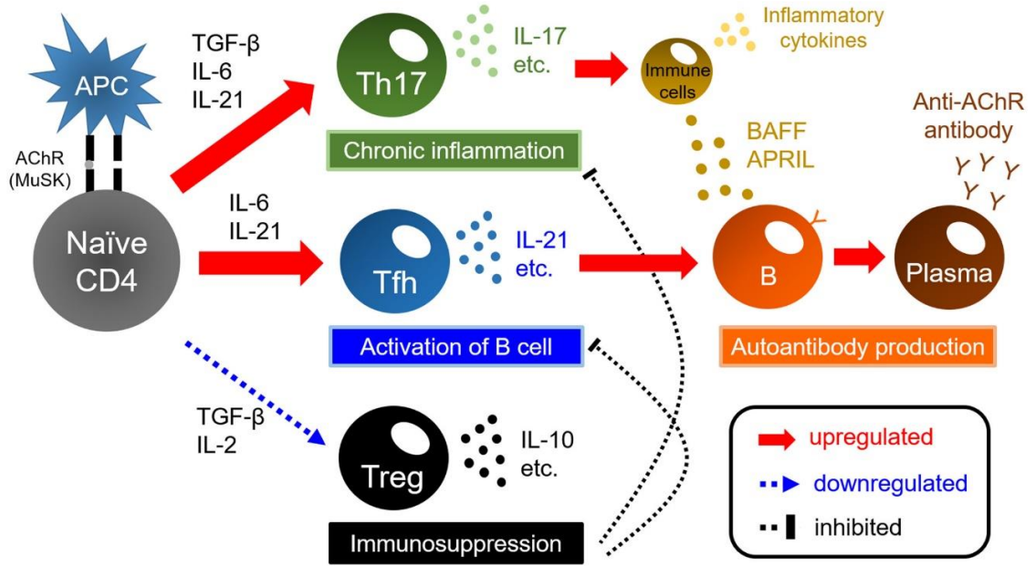
Disease	Target antigen	Autoantibody	Clinical characteristics
AIDP	Unknown	None	Acute peripheral neuropathy
AMAN	GM1, GD1a	GM1, GD1a	Motor axonal neuropathy
AMSAN	GalNAcGD1a, GM1, GD1a	GalNAcGD1a, GM1, GD1a	Sensorimotor axonal neuropathy
Miller-Fisher	GQ1b, GT1a	GQ1b, GT1a	Ophthalmoplegia; Ataxia; Loss of tendon reflexes
CIDP	Mostly unknown	Unknown	Chronic sensorimotor neuropathy
	NF155	NF155	Tremor; deep sensory ataxia
	NF186/140	NF186/140	Progressive disease course
	CNTN1	CNTN1	Deep sensory ataxia; glomerulonephritis
	Caspr1	Caspr1	Severe sensorimotor neuropathy; pain
MMN	GM1	GM1	Chronic progressive asymmetric motor neuropathy; motor block
MAG-PN	MAG	MAG	Deep sensory ataxia; distal muscle weakness
CANOMAD	GD3, GD1b, GT1b, GQ1b	IgM, cold agglutinin	Deep sensory ataxia; ophthalmoplegia

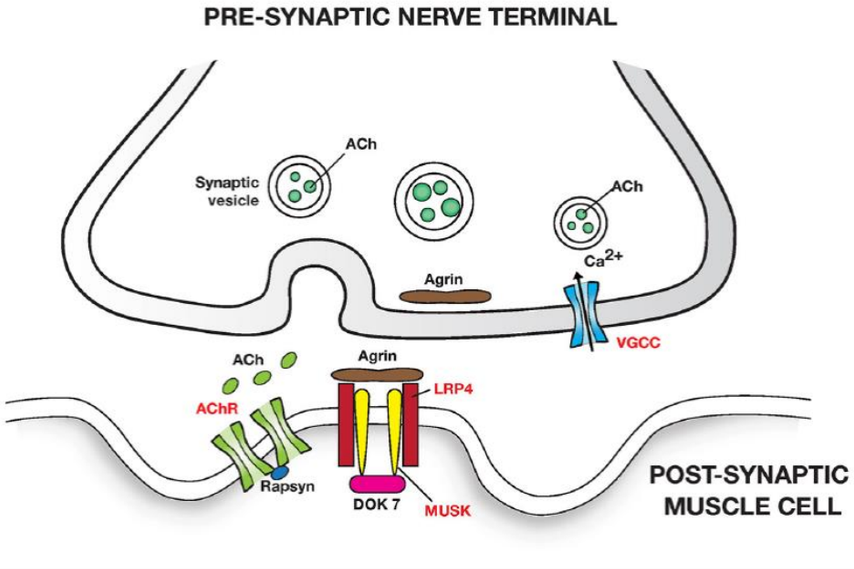


Front Neurol. 2021 Apr 14;12:664664.

Neuro Immune Disease – Neuromuscular Junction Disease

Disease	Target antigen	Autoantibody	Clinical Characteristics
MG	AChR	AChR IgG1, IgG3	Fluctuating skeletal muscle weakness
	MuSK	MuSK IgG4	
	LRP4	LRP4 IgG1, IgG2	
LEMS	Presynaptic membrane VGCC	VGCC	Fluctuating skeletal muscle weakness; lower limb > > upper limb; autonomic dysfunction; tendon reflex facilitation phenomenon





Front Neurol. 2021 Apr 14;12:664664.
Clin Exp Immunol. 2021 Mar;203(3):366-374.

Clinical Practice and Unmet Medical Needs in Neuroimmune Diseases

First Generation:

Steroid/IVIg/PLEX/
Immunosuppressant chemicals

01

Second Generation:

Immunosuppressant
biologics
Anti-CD20 mAb

02

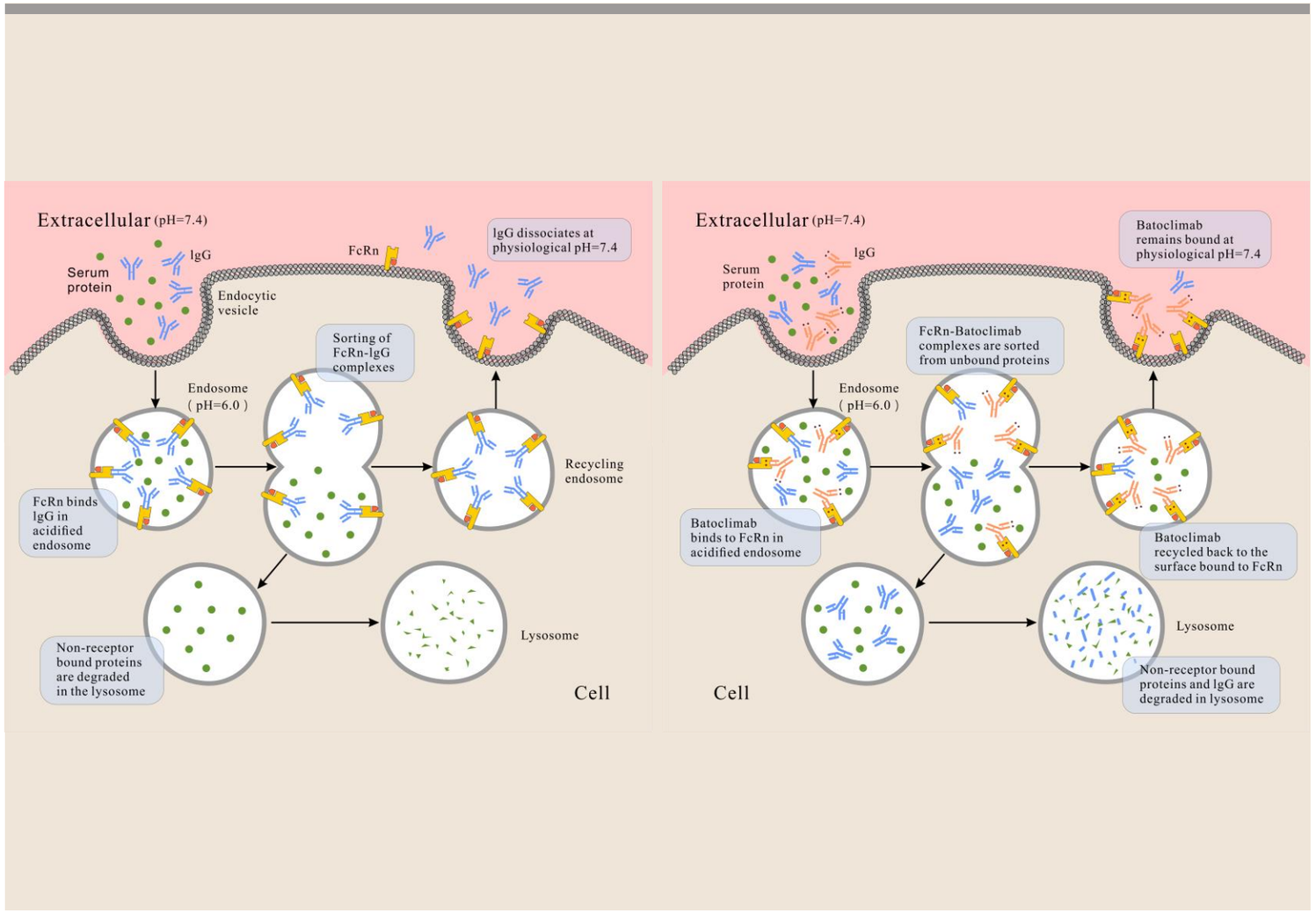
Next Generation:

FcRn antagonist

A more effective and differentiated treatment for autoimmune diseases

03

Batoclimab: A Breakthrough Therapy for IgG Mediated Autoimmune Diseases with a Portfolio-in-a-product Approach

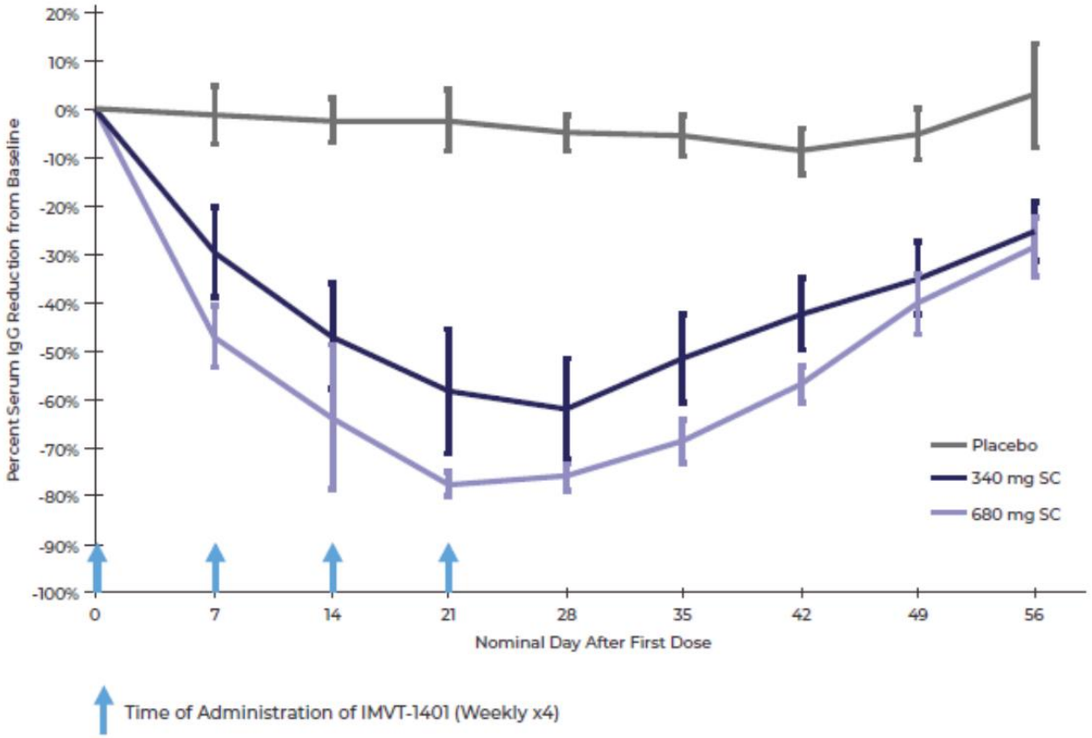


Competitive Advantages

Strong Efficacy	✓Potent & dose-dependent IgG reduction ✓Clinical POC established across indications
Safety	✓Full human IgG with low immunogenicity risk ✓Less likely to lead to inflammation with reduced effector function ✓Well tolerated, majority of AEs are mild and/or moderate
Convenient Treatment	✓Fixed-dose subcutaneous injection ✓Possible for patient self-administration ✓Improved patient compliance

Batoclimab – Ph1 Study Results* (PD: Serum IgG reduction)

Significant Reduces Serum IgG Following SC or IV, Results was Published on AAO 2019

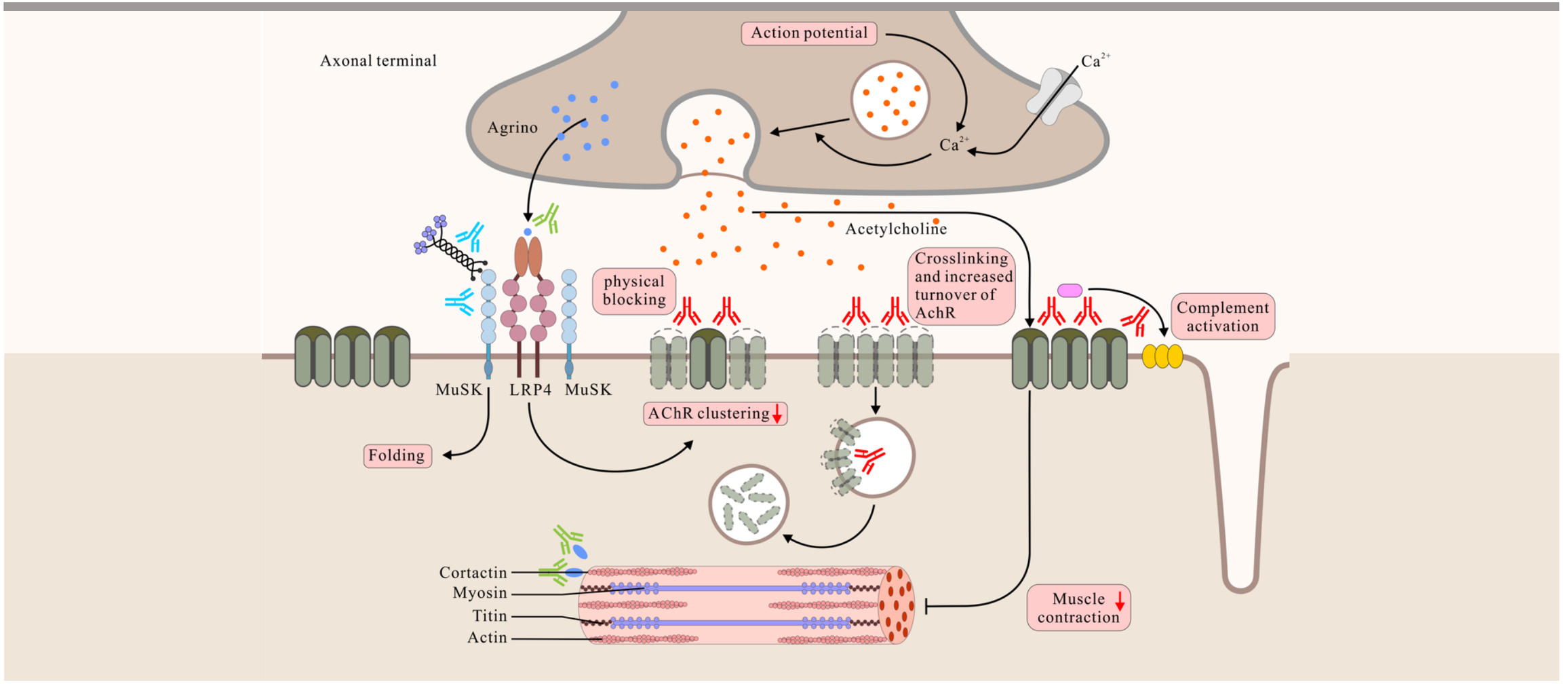


- Mean maximum IgG reduction of 78.4% from baseline at weekly SC dose of 680mg (4 doses), suggests HBM9161 is potential to be best in class product
- An average reduction in total IgG of 47% was observed following single SC dose of 765 mg
- Total IgG reduction increased with increasing doses, with a nadir at approximately 8-10 days after a single dose

*： Data cut off Dec 14, 2018

Nature Reviews
Getting Specific: Targeting Fc Receptor in Myasthenia Gravis

Myasthenia Gravis (MG) – a Prototypical Autoantibody Mediated Disease



Significant Unmet Medical Needs for Myasthenia Gravis

~200,000 people in China affected

85% MG patients progress to generalized MG

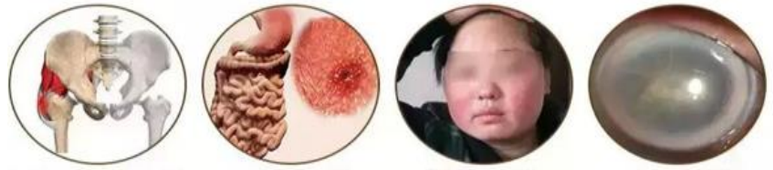
20% MG patients may experience a life-threatening crisis

Limited efficacy with available treatments - huge unmet medical needs

Batoclimab is granted by NMPA
"**Breakthrough Therapy Designation**" for MG

First-line steroids treatment:

serious adverse reactions to long-term use



Osteonecrosis of the femoral head | Gastric ulcer | Full moon face | Cataract

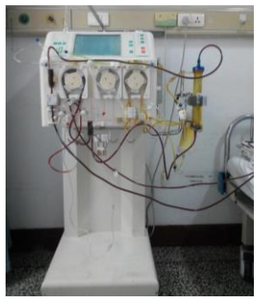
Immunosuppressants:

such as azathioprine, limited efficacy and slow onset

IVIg/PLEX：

Expensive;

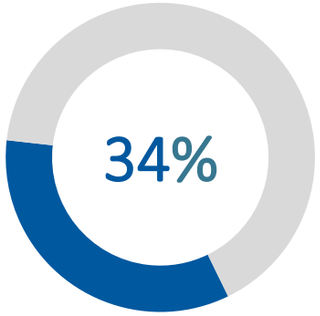
limited accessory



1. Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, Verschuuren JJGM. Myasthenia gravis. *Nat Rev Dis Primer*. 2019;5(1):30.
2. Fang W, Li Y, Mo R, et al. *Neurol Sci.* 2020 May;41(5):1211-1223.
3. Gilhus NE. Myasthenia Gravis. Longo DL, ed. *N Engl J Med*. 2016;375(26):2570-2581.
4. Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. *Lancet Neurol*. 2015;14(10):1023-1036.

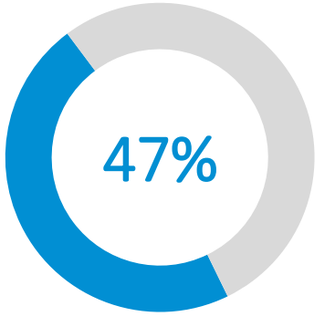
Poor Quality of Life of MG Patients Under Current Treatment

A snapshot of Chinese MG patients Quality of Life in a 2018 survey



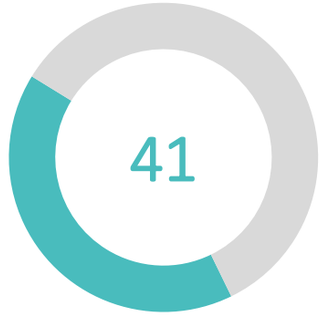
34% exacerbation

Patients experienced **exacerbation within 6 months**, living in fear



47% comorbidity

47.4% patients suffer from **at least one comorbid**

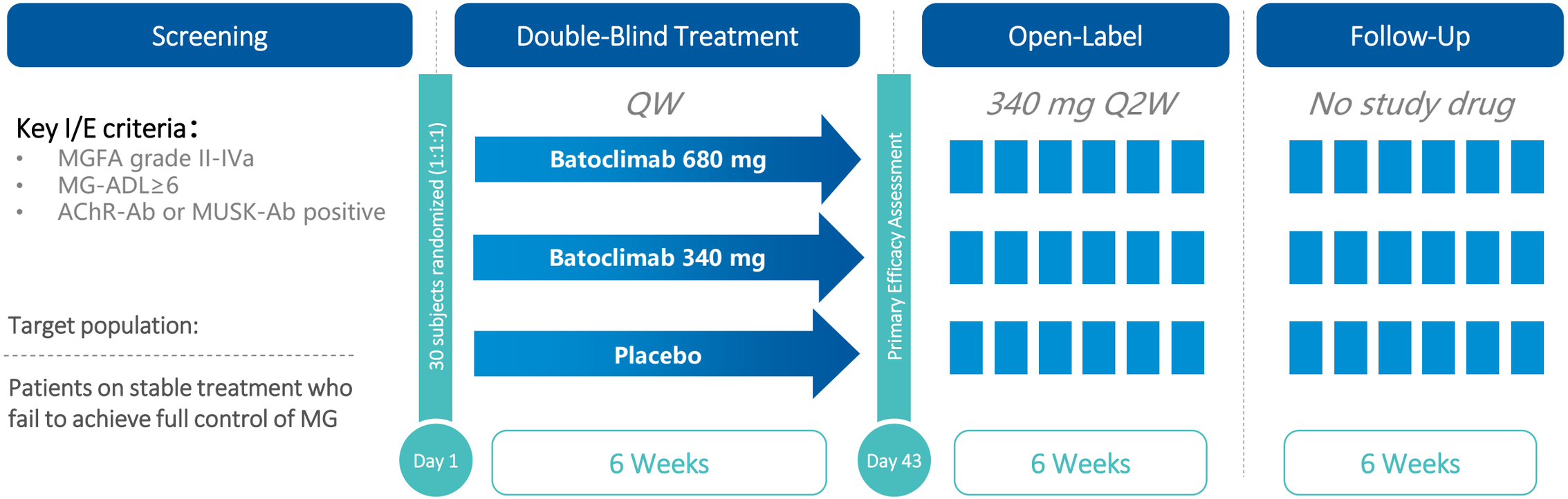


41 years old

Average age of surveyed patients are 41. 1 years old, the **prime time of life**

Gender differences in quality of life among patients with myasthenia gravis in China. *Health Qual Life Outcomes* . *2020 Sep 3;18(1):296. doi: 10.1186/s12955-020-01549-z.*

Batoclimab Phase 2 Study for the Treatment of gMG: Study Design



Efficacy endpoints：

- MG-ADL, QMG score improvement compared with baseline
- Primary time point: Day 43

Safety endpoint：

- Safety and tolerability

Clinical pharmacological endpoints:

- Change of anti-AChR IgG, total IgG and IgG subtypes compared with baseline
- Batoclimab PK
- Biomarkers （gene expression, serum inflammatory markers）

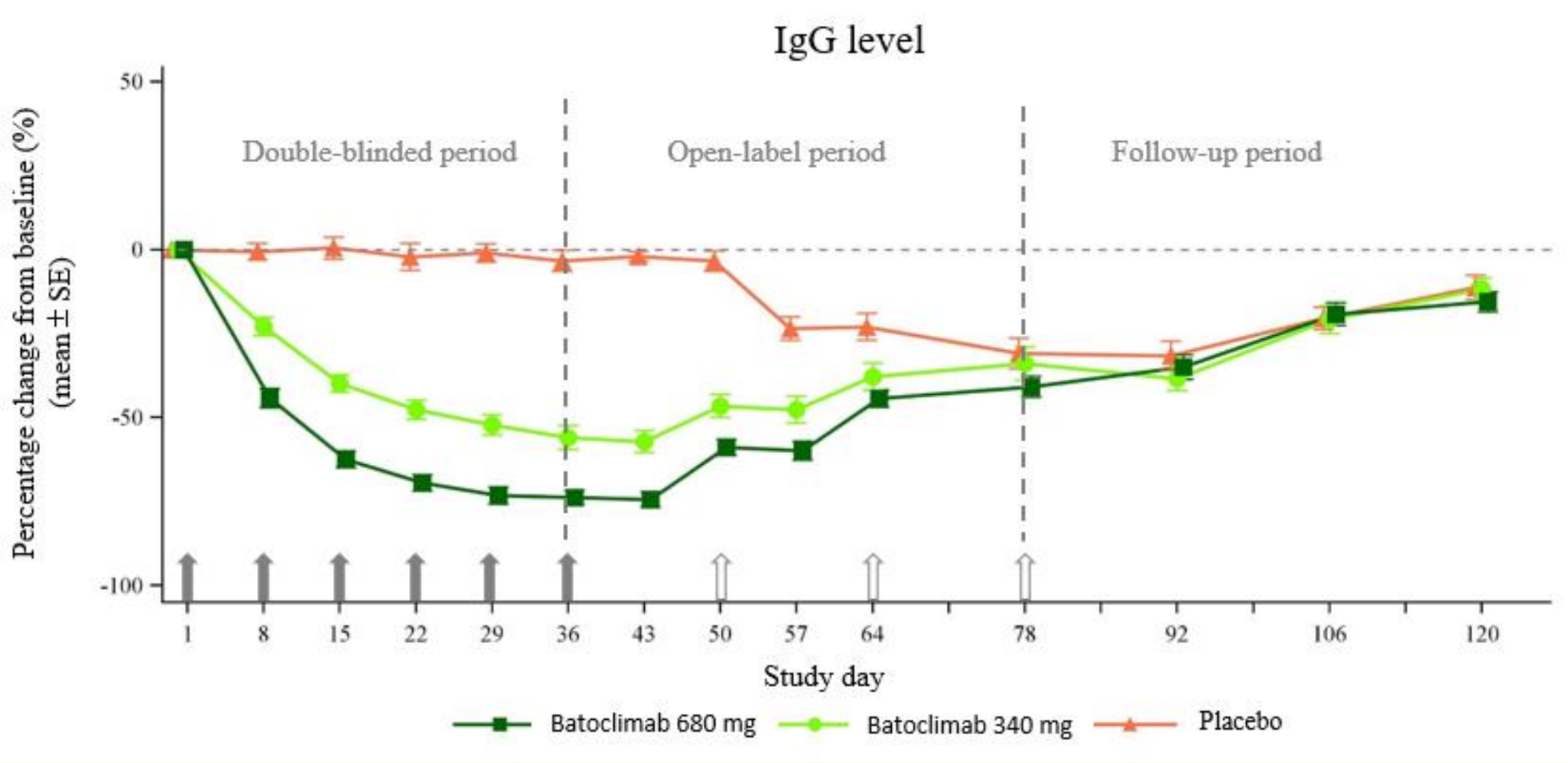
❖ Two interim data reviews are pre-specified when ~15 and all subjects completed efficacy endpoint assessment at the primary time point (Day 43), respectively.

❖ Because a few subjects are still in the open-label or follow-up period, this data release only includes data in the double-blind treatment period (up to Day 43).

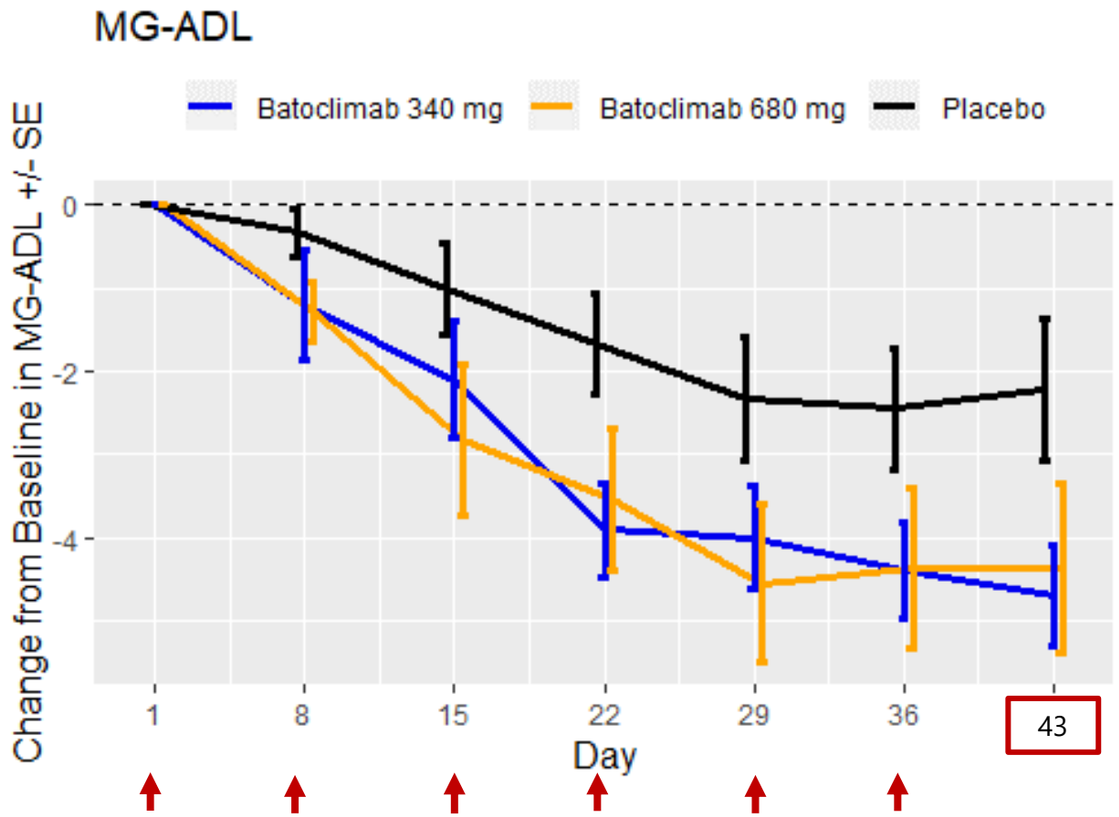
❖ Unblinded team has been set up to review and evaluate unblinded data, including albumin, ALP, IA package.

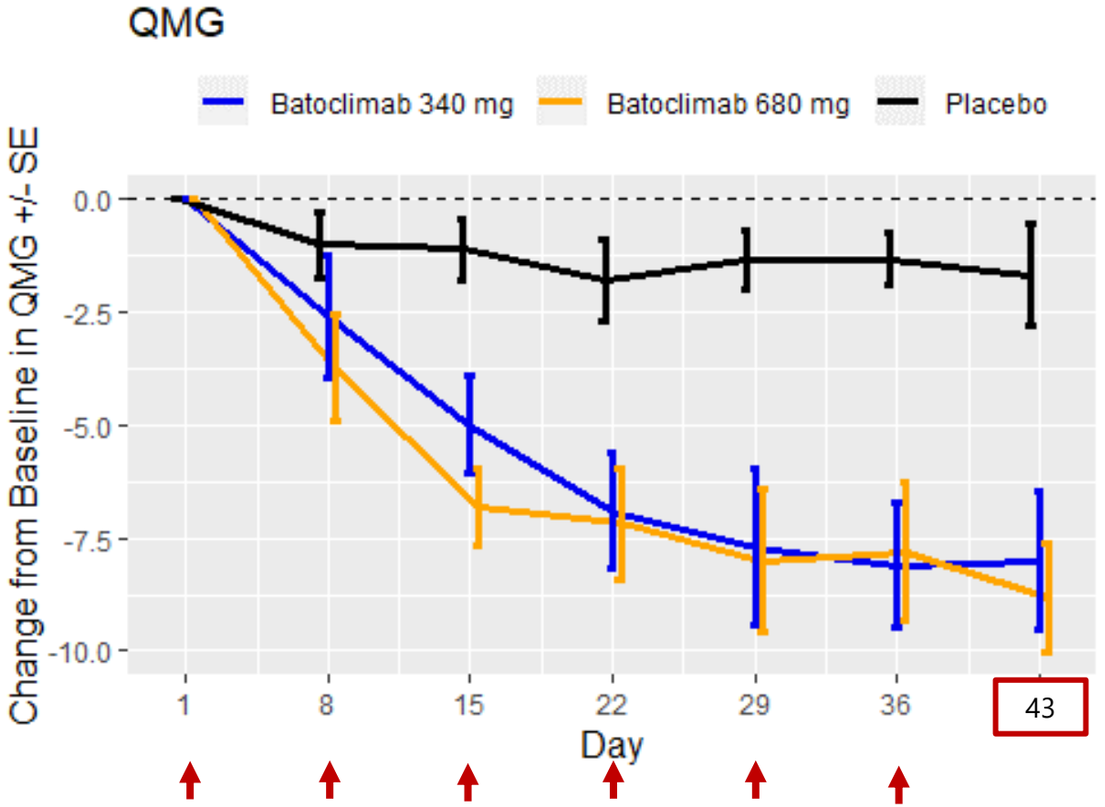
Rapid and Robust IgG Reduction

Available Evidence Suggests that Reduced Levels of Pathogenic IgG in Patients with MG are Associated with Clinical Benefit



Batoclimab gMG Ph2 Study
- Fast, Substantial, and Persistent Clinical Improvements



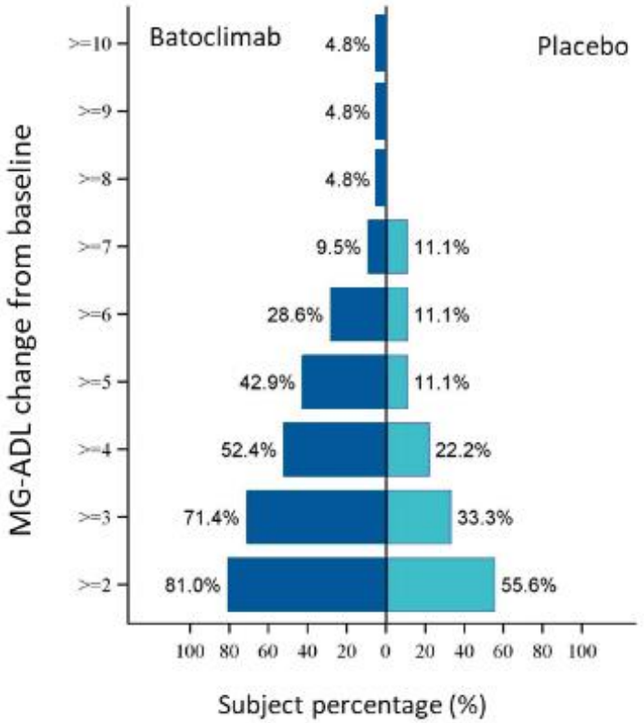


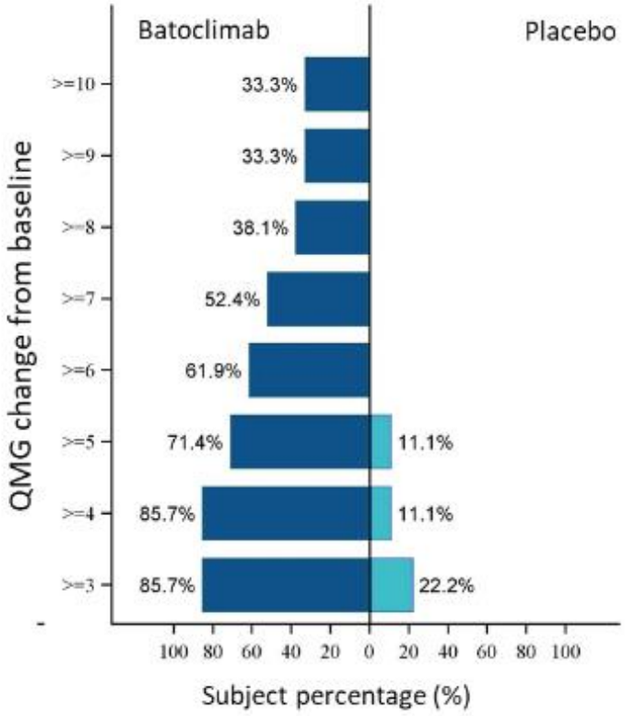
Drug administration

HARBOUR BIOMED

Durable Clinical Improvements vs Placebo

Durable Response





Proportion of subjects in the double-blind period who had improved MG-ADL score at different thresholds of 2 points or more and continued for at least 4 weeks from baseline

Proportion of subjects in the double-blind period who had improved QMG score at different thresholds of 3 points or more and continued for at least 4 weeks from baseline

Batoclimab: Exciting Results of Ph2 Study

- Fast, strong and sustained benefit; clinically meaningful and statistically significant
- Strong correlation between IgG level reduction and disease improvement; validating focus on IgG-mediated disorders
- International leading position and profound influence in the autoimmune neurological disorders area
- China's independent development: led by Chinese MG experts, focuses on Chinese clinical and Chinese MG patients, fully developed by China, earlier than the same class molecule development 2-3 years
- The first breakthrough therapy designated by CDE in the neuroimmune diseases area

Batoclimab: Global Publication

Highlights of HARMONI Study – Ph3

HARMONI MRCT Ongoing: 29 sites, 144 subjects

	Timeline
First SIV	14th Sep 2021
First patient Screening	15th Sep 2021
First patient randomization	25th Sep 2021
Interim analysis	July 2022
Last patient randomization	Aug 2022
LPLV	May 2023
Date base lock	Jul 2023




HUASHAN HOSPITAL FUDAN UNIVERSITY 華山醫院 1907

首都医科大学宣武医院 Xuanwu Hospital Capital Medical University 1958

XIANGYA SCHOOL OF MEDICINE 湘雅医院 1914

CHINESE ACADEMY OF MEDICAL SCIENCES PEKING UNION MEDICAL COLLEGE

TANGDU HOSPITAL 1939 第四军医大学 唐都医院

浙大一院 1947 THE FIRST AFFILIATED HOSPITAL, ZHEJIANG UNIVERSITY

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Batoclimab Position in Autoimmune Disease Therapy

Autoimmune disease

- Great complicated clinical manifestations
- Huge unmet medical needs due to limited treatment options and severe side effects

Next generation of promising therapy, targeting the root cause shared across various autoimmune diseases

Provides the first clinical study evidence of anti-FcRn therapy in Chinese patients

Compelling overall efficacy and safety profile

THANK YOU

HBM HOLDINGS-B

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