福可苏
伊基奥仑赛注射液

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Fully Human CAR-T Therapy:
A Breakthrough in MRD Efficacy

全力以福 未来可苏

XLMA20230705-1 Expired Date: 2023-09-30

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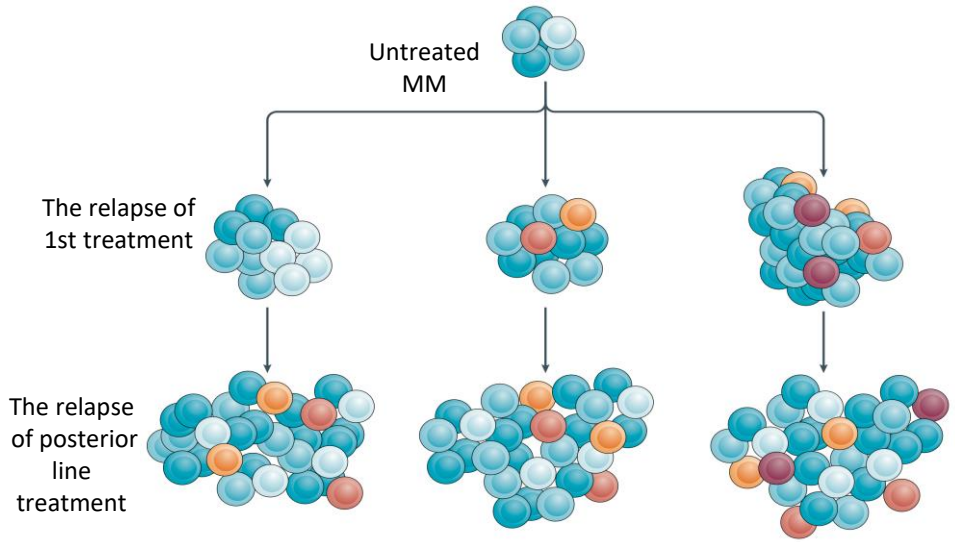
Contents

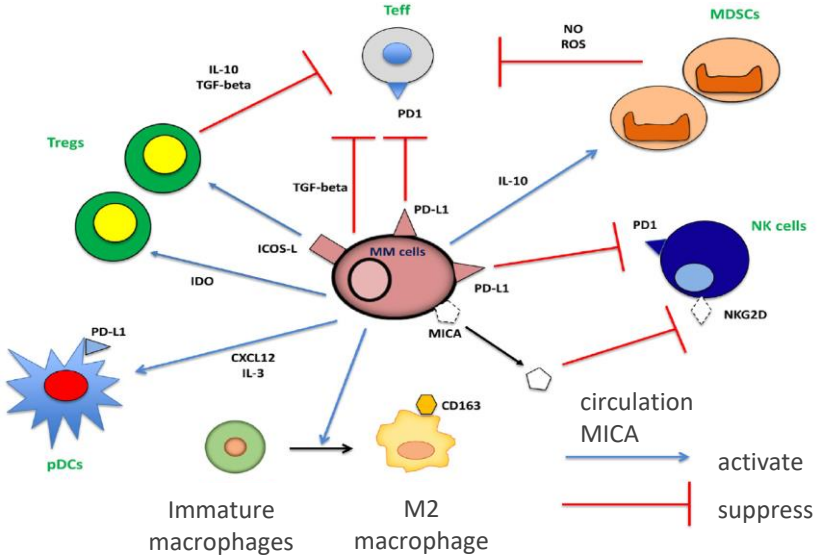
The Clonal Evolution of MM Cells and The Interaction between MM Cells and Immune Microenvironment Make MM Are Hard to Cure

Multiple myeloma (MM) is marked by a complex clonal heterogeneity; the processes of clonal evolution and proliferation are key drivers of tumor progression, underpinning the challenges in treatment resistance and the propensity for disease recurrence.



MM includes different subclones, which can acquire new mutations over time and with the effect of treatment, and subclones that acquire new mutations may develop resistance to MM treatment. Patients with MM usually have shorter PFS when treated at the posterior line[1]

MM cells interact with the surrounding immune microenvironment to induce host immune tolerance, enabling MM cells to escape immune surveillance, promote disease progression, treatment resistance and disease recurrence[2,3]



The interaction between MM cells and the immune microenvironment leads to the reduction of antigen presentation, the dysfunction of immune effector cells, and the increase of immunosuppressive cells, which makes MM cells escape from immune surveillance[2]

1. Mikkilineni L, Kochenderfer JN. Nat Rev Clin Oncol. 2021 Feb;18(2)：71-84.
2. Kawano Y, et al. Curr Cancer Drug Targets. 2017;17(9)806-818.
3. Luptakova K, Avigan D. Clin Adv Hematol Oncol. 2015 Nov;13(11)：767-75.

Patients with Residual Disease Still Face the Difficulty of Relapse after They Achieved CR

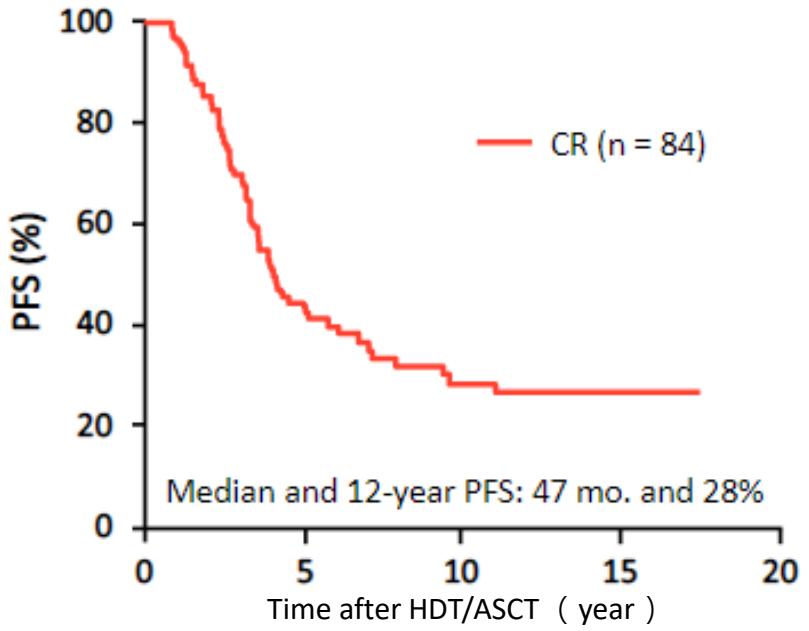
The advent of novel combination drug therapies has notably enhanced the treatment response for multiple myeloma, with over 60% of patients now achieving complete remission (CR).[1,2]

Despite achieving complete remission, the majority of patients are still confronted with the likelihood of disease relapse, signaling the persistence of residual disease within the body[1,3,4]

Higher sensitive measurements of residual tumor cells are needed to better predict , with the goal of tailoring therapy and improving outcomes[1,4,5,8]

Even when patients reach a complete remission (CR), the eventuality of disease relapse remains an inescapable reality.

Patients who chieve CR after HDT/ASCT， mPFS 47 months[6]



Despite the depth of remission achieving CR, approximately 40% of CR patients will have a relapse, and 20% will die within 4 years after the initiation of treatment[7]

1. KUMAR S, et al. Lancet Oncol, 2016, 17 (8)：e328-e346.
2. Faith E Davies. Hematology Am Soc Hematol Educ Program (2017) 2017 (1)：205-211.
3. J Clin Oncol. 2013 Jul 10;31(20)：2523-6.
4. Munshi NC, et al. JAMA Oncol. 2017 Jan 1;3(1)：28-35.
5. 侯健. 中华医学杂志,2022,102(36)：2819-2822.
6. Martinez-lopez J, et al. Blood. 2011 Jul 21;118(3):529-34.
7. Paiva B, et al. Blood. 2015 May 14;125(20):3059-68.
8. Ho M, Kourelis T. Hematology Am Soc Hematol Educ Program. 2022 Dec 9;2022(1)：356-362.

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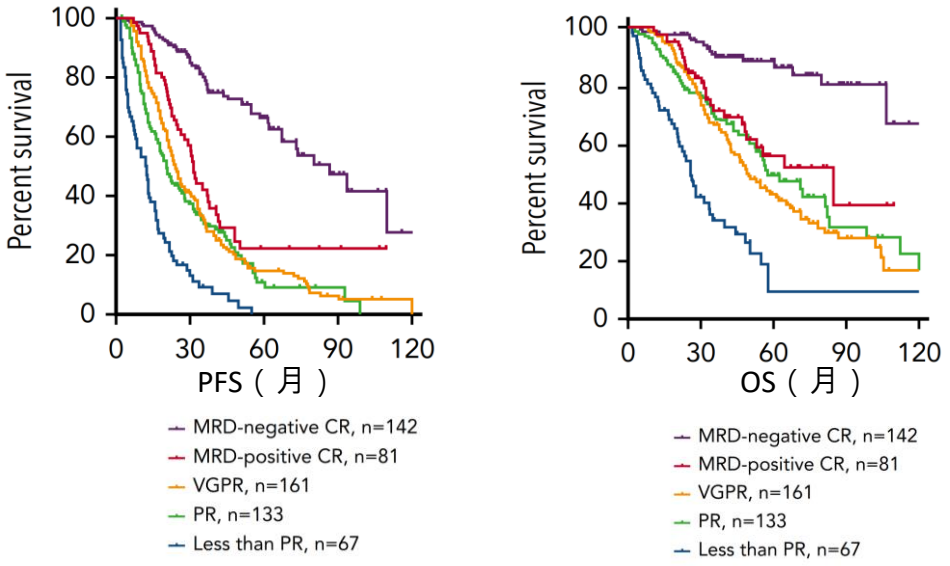
MRD Negativity is The Prerequisite for Long-term Survival (Functional Cure) of MM

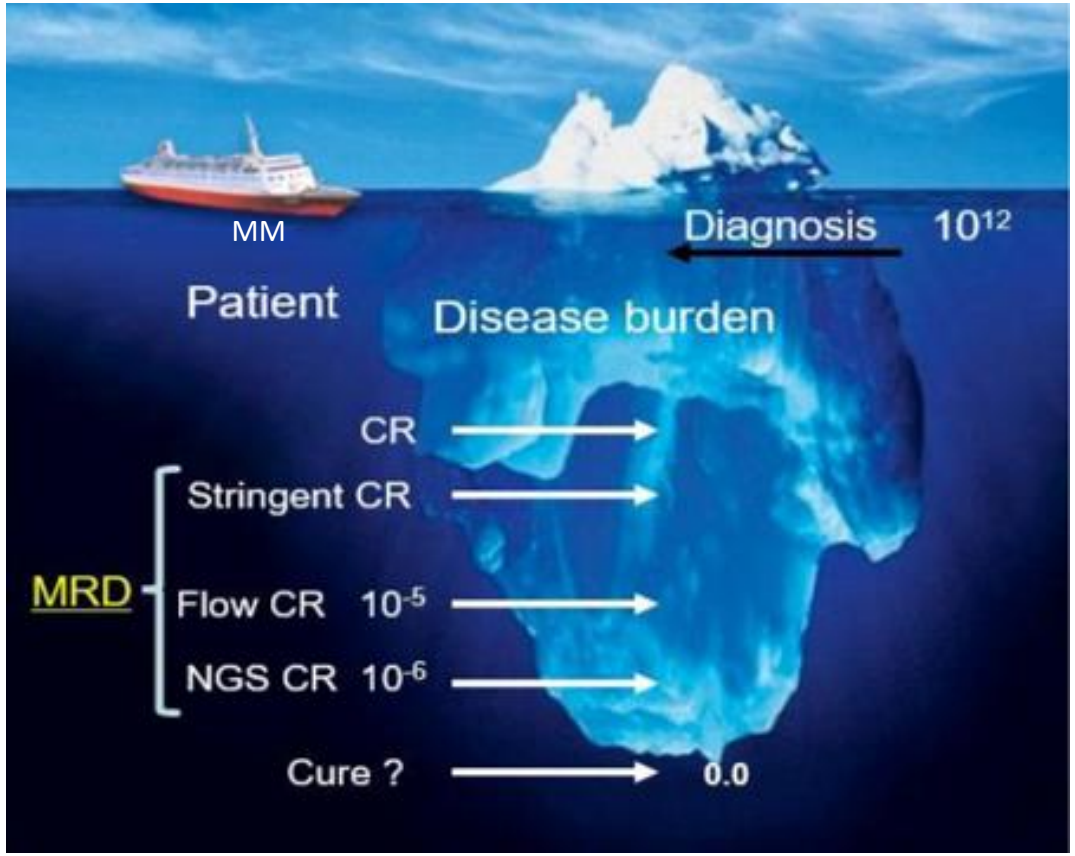
MRD has better prognostic value than CR[1]

- Patients who attain complete remission with MRD negativity experience superior progression-free survival (PFS) and overall survival (OS) compared to those who remain MRD positive.



In a prospective, nonrandomized clinical trial (BDH 2008/02) involving 626 patients with newly diagnosed multiple myeloma, the correlation between response kinetics and patient outcomes was evaluated. Participants received treatment regimens based on either immunomodulatory drugs or proteasome inhibitors.

Achieving MRD negativity is associated with long-term disease control, which is often referred to as a functional cure[2-4]



1. Yuting Yan, et al. Blood Adv. 2019 Oct 8;3(19)：2895-2904.
2. Mailankody S, et al. Nat Rev Clin Oncol. 2015 May;12(5):286-95.
3. Paiva B, et al. Blood. 2015 May 14;125(20):3059-68.
4. Yanamandra U, Kumar SK. Leuk Lymphoma. 2018 Aug;59(8):1772-1784.

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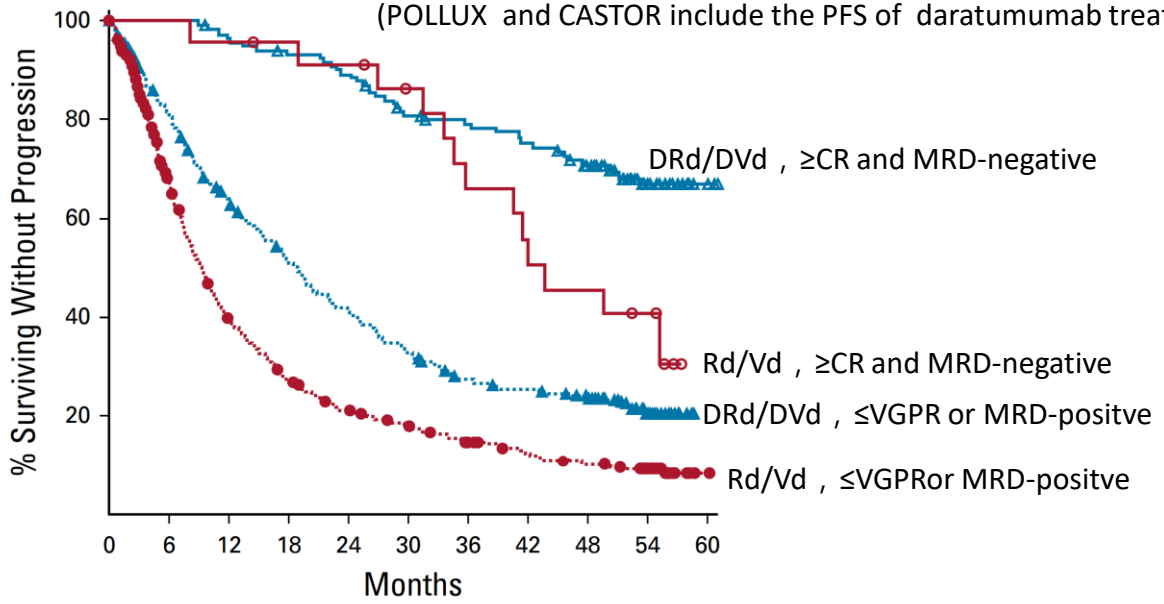
Attaining MRD negativity can enhance the survival outcomes for patients with relapsed and refractory multiple myeloma

- Patients with relapsed or refractory multiple myeloma (R/R MM) generally have a bleak prognosis, positioning them as an ideal cohort for adopting MRD status as a treatment endpoint and a potential surrogate for overall survival (OS)[1]
- The primary cause of relapse in multiple myeloma is the persistence of minimal residual disease (MRD). Patients with relapsed or refractory multiple myeloma (R/R MM) face greater challenges in achieving MRD negativity. However, it has been observed that those who do attain MRD-negative status may experience improved survival outcomes.[2,3]

The patients with RRMM who achieved MRD negativity predict better outcomes after the different treatments[4]

(POLLUX and CASTOR include the PFS of daratumumab treatment and control groups)



Groups	HR (95% CI)	*P*
D-Rd/D-Vd ≥ CR and MRD-negative *v* Rd/Vd ≥ CR and MRD-negative	0.51 (0.27 to 0.96)	.0358
D-Rd/D-Vd ≥ CR and MRD-negative *v* D-Rd/D-Vd ≤ VGPR or MRD-positive	0.23 (0.17 to 0.32)	< .0001
D-Rd/D-Vd ≥ CR and MRD-negative *v* Rd/Vd ≤ VGPR or MRD-positive	0.14 (0.10 to 0.19)	< .0001

Proportion of patients with sustained MRD-negative for ≥12 months：

- POLLUX： DRd 16.1%，Rd 1.4%，p<0.0001；CASTOR：DVd 6.8%，Vd 0%，p<0.0001

1. Paiva B, et al. Blood. 2015 May 14;125(20)3059-68
2. Kostopoulos IV, et al. Front Oncol. 2020 May 27;10：860.
3. Diamond BT, et al. Blood Rev. 2021 Mar;46：100732.
4. Hervé Avet-Loiseau, et al. J Clin Oncol. 2021 Apr 1;39(10)：1139-1149.

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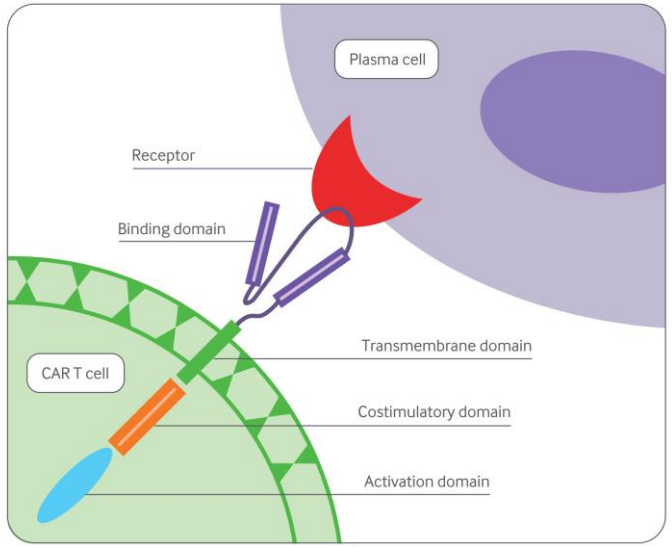
Contents

The Treatment of MM Has Entered the Time of Immunotherapy

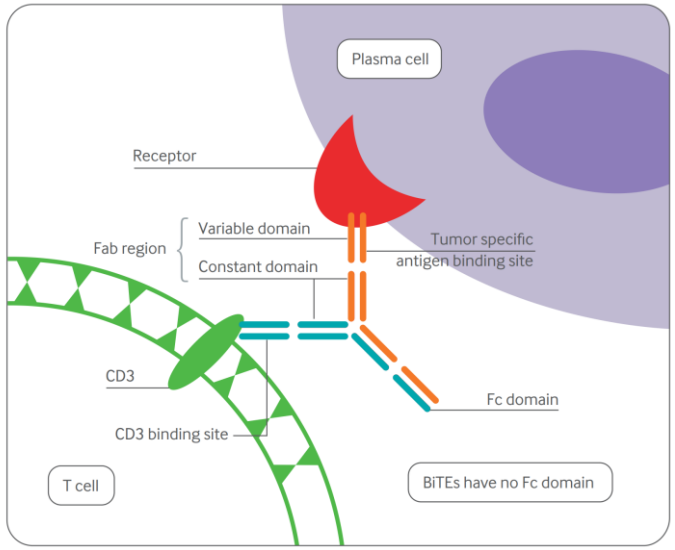
Emerging Immunotherapies[1]

CAR-T



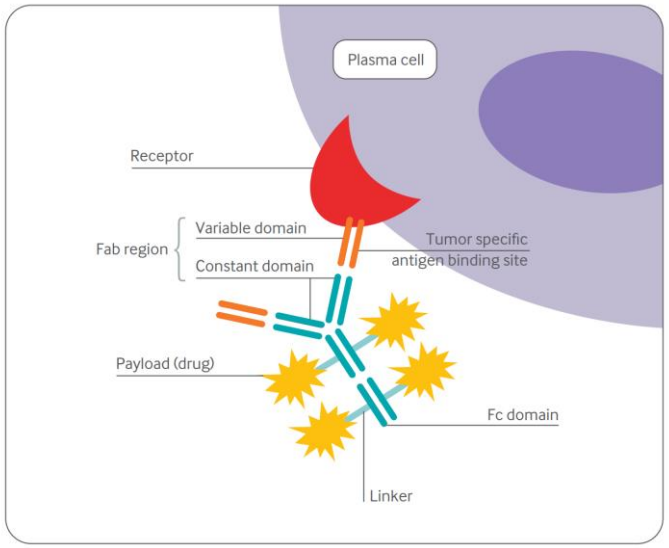
Binding of the specific antigen on tumor cells triggers CAR-T cell activation, leading to their proliferation, cytokine secretion, and targeted tumor cell destruction.

BsAb



Bispecific antibodies simultaneously engage CD3 on cytotoxic T cells and a tumor-associated antigen, thereby directing T cell-mediated cytotoxicity towards the targeted cancer cells.

ADC



Antibody-drug conjugates (ADCs) consist of a monoclonal antibody specific to cancer cells, a stable linker, and a potent cytotoxic agent (payload). This design harnesses the precise targeting capability of antibodies with the cell-killing power of chemotherapy agents, enabling selective destruction of cancer cells.

1. Urvi A Shah, Sham Mailankody. BMJ 2020;370：m3176.
2. Song EZ, Milone MC. Annu Rev Pharmacol Toxicol. 2021 Jan 6;61：805-829.
3. Choi T, Kang Y. Pharmacol Ther. 2022 Apr;232：108007.
4. Yang J, et al. Cancer Lett. 2023 Jan 28;553：215949.

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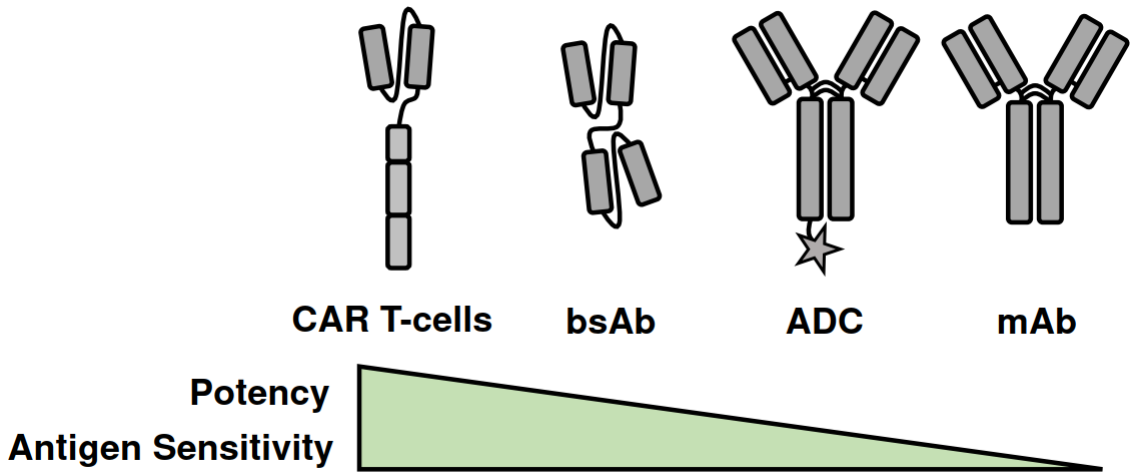
The Rapid Development of Emerging Immunotherapy Has Brought Great Hope to The Treatment of MM

Antitumor efficacy and antigen sensitivity of different immunotherapies[1]



BsAb

It relies on the patient's own T cells, with theoretical concerns about dysfunction of the patient's own T cells[2]

ADC

Target antigen, antibody, payload, linker, and coupling mode can affect the efficacy and safety of ADCs. After infusion, part of ADCs is separated into naked antibody and payload in the systemic circulation, which affects the delivery of payload to tumor cells[3]

CAR-T

Genetic modification of T cells transforms them from having moderate immune capabilities into highly specific and cytotoxic entities. These engineered T cells can then proliferate and persist in the body, enhancing immune surveillance and exerting a potent and durable antitumor effect.

CAR-T cells have demonstrated an exceptional overall response rate (ORR) and a high rate of MRD negativity in patients with relapsed or refractor multiple myeloma (RRMM), establishing it as one of the most efficacious treatment modalities for this condition.

1. Rasche L, et al. Blood. 2020 Nov 26;136(22)：2491-2497.
2. Choi T, Kang Y. Pharmacol Ther. 2022 Apr;232：108007.
3. Fu Z, et al. Signal Transduct Target Ther. 2022 Mar 22;7(1)：93.
4. Rohit Reddy S, et al. Cureus. 2021 Feb 25;13(2)：e13552.
5. Hosen N. Immunol Med. 2021 Jun;44(2)：69-73.
6. Huang R, et al. J Hematol Oncol. 2020 Jul 2;13(1)：86.
7. Davila ML, et al. Int J Hematol. 2014 Apr;99(4)：361-71.
8. Yang J, et al. Cancer Lett. 2023 Jan 28;553：215949.
9. 王莹, 徐开林. 临床内科杂志,2022,39(9)：589-593.
10. Martin T, et al. J Clin Oncol. 2023 Feb 20;41(6)：1265-1274.
11. 2022ASH. Poster 3311.
12. Mi JQ, et al. J Clin Oncol. 2023 Feb 20;41(6)：1275-1284.

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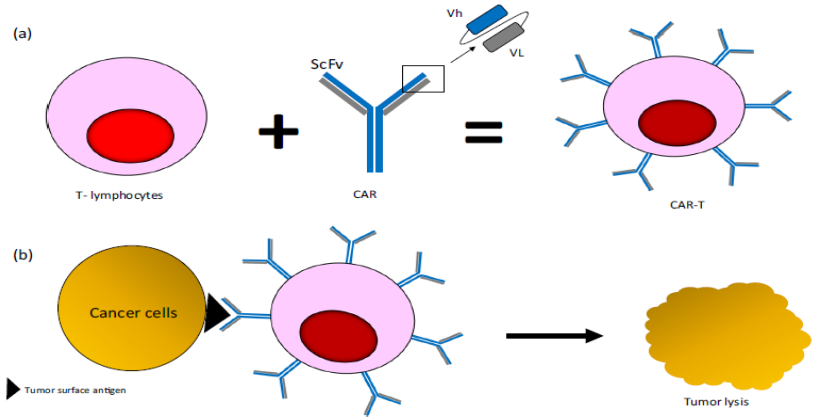
MOA of targeting BCMA CAR-T Cell Therapy

BCMA-targeted CAR-T therapy represents a novel and potent approach for the treatment of relapsed or refractory multiple myeloma (RRMM). This therapy is designed to specifically recognize and eliminate MM cells that express the B cell maturation antigen (BCMA). Clinical trials have repeatedly demonstrated the significant clinical benefits of this targeted therapeutic strategy.

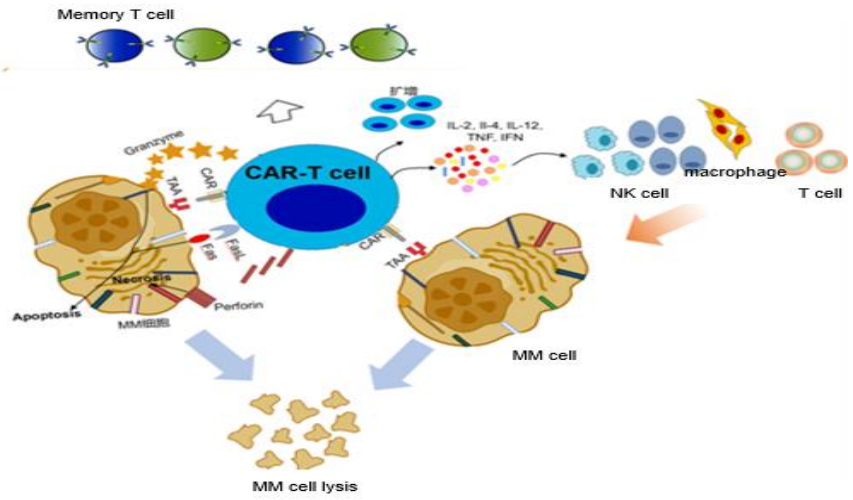
Basic principles of CAR-T therapy

- T cells have been genetically modified to express chimeric antigen receptors, which consist of monoclonal antibodies targeting specific antigen （BCMA）. The ScFV region specifically recognizes antigen（BCMA）related to the surface of tumor cells and initiates a cascade of cytotoxic signals, thereby killing tumors. cell



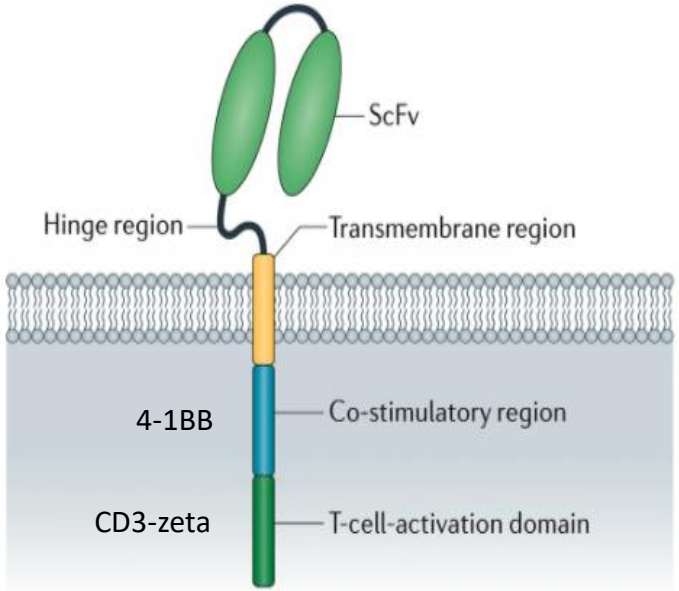
CAR-T therapy treatment mechanism

- CAR-T can overcome immune evasion , quickly eliminate myeloma cells, reshape immune function, transform to memory T cell and continuously improve the tumor microenvironment



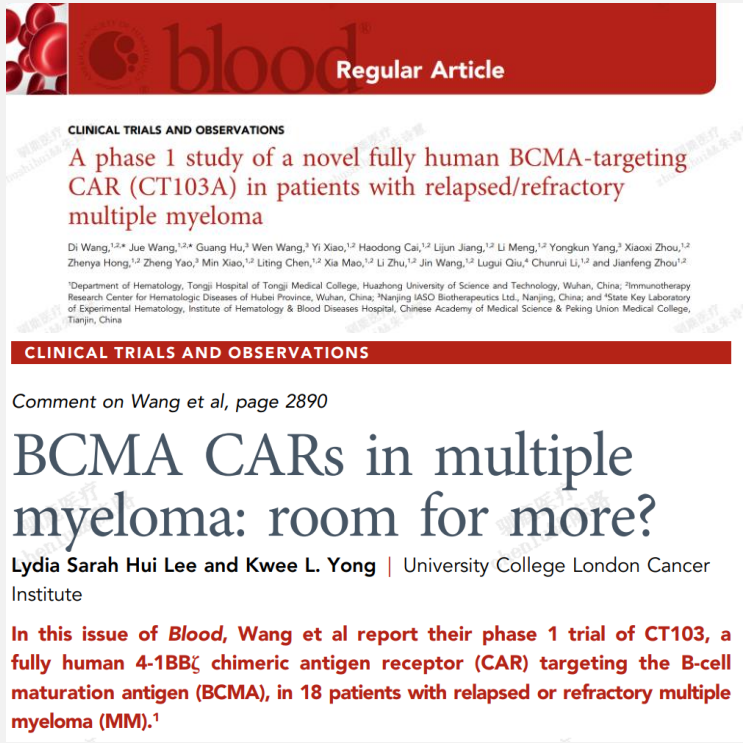
1. Hosen N. Immunol Med. 2021 Jun;44(2)：69-73.
2. Mohamed-Reda Benmebarek, et al. Int J Mol Sci. 2019 Mar; 20(6)：1283.

FUCASO® A Revolutionary Treatment For RRMM



Eque-cel- received breakthrough therapy designation from the NMPA in Feb 2021

- An autologous CAR-T targeting BCMA
- Produced with a 3rd gen Lentiviral vector carrying a 2nd gen CAR
- Low immunogenic scFv derived from fully human antibody.
- Outstanding efficacy and durable response with favorable safety profile
- Significant expansion and long term persistence of CAR-T cells in vivo.
- Effective in patients relapsed post other targeting BCMA CAR-T



blood Regular Article

CLINICAL TRIALS AND OBSERVATIONS

A phase 1 study of a novel fully human BCMA-targeting CAR (CT103A) in patients with relapsed/refractory multiple myeloma

Di Wang,[1,2,*] Jue Wang,[1,2,*] Guang Hu,[3] Wen Wang,[3] Yi Xiao,[1,2] Haodong Cai,[1,2] Lijun Jiang,[1,2] Li Meng,[1,2] Yongkun Yang,[3] Xiaoxi Zhou,[1,2] Zhenya Hong,[1,2] Zheng Yao,[3] Min Xiao,[1,2] Liting Chen,[1,2] Xia Mao,[1,2] Li Zhu,[1,2] Jin Wang,[1,2] Lugui Qiu,[4] Chunrui Li,[1,2] and Jianfeng Zhou[1,2]

[1]Department of Hematology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [2]Immunotherapy Research Center for Hematologic Diseases of Hubei Province, Wuhan, China; [3]Nanjing IASO Biotherapeutics Ltd., Nanjing, China; and [4]State Key Laboratory of Experimental Hematology, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Tianjin, China

CLINICAL TRIALS AND OBSERVATIONS

Comment on Wang et al, page 2890

BCMA CARs in multiple myeloma: room for more?

Lydia Sarah Hui Lee and Kwee L. Yong | University College London Cancer Institute

In this issue of *Blood*, Wang et al report their phase 1 trial of CT103, a fully human 4-1BBζ chimeric antigen receptor (CAR) targeting the B-cell maturation antigen (BCMA), in 18 patients with relapsed or refractory multiple myeloma (MM).[1]

1. Blood. 2021;137(21)：2890-2901.

FUCASO® Exhibits Superior Efficacy and Safety Profile

CAR-T therapy exhibits substantial efficacy in CAR-T naïve patients.

98.9% ORR

82.4% sCR/CR

85.5% 12m-PFS

in 91 heavily pre-treated R/R MM patients without prior CAR-T

First-in-class efficacy demonstrated in CAR-T pre-treated patients.

75% ORR (9/12)

42% achieved sCR (5/12)

>18 months sustained sCR in 4 patients

in 12 patients relapse relapse post prior anti-BMCA CAR-T therapy

All patients exhibit a favorable safety profile.

0% >Grade3 ICANS

1.0% >Grade3 CRS

in 103 heavily pre-treated R/R MM patients

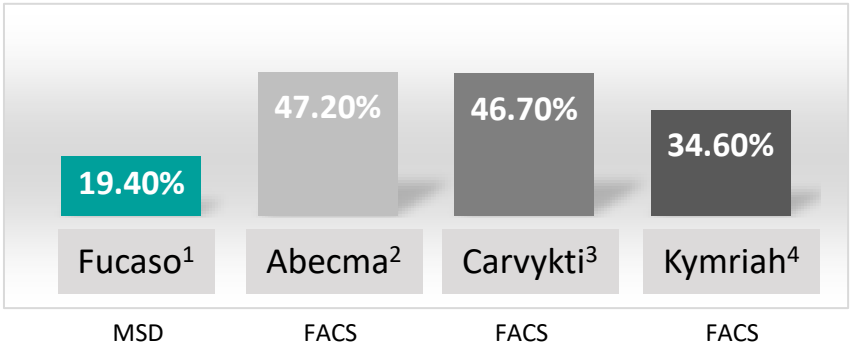
1. Data presented in 2023 IMS meeting, at the median follow-up of 18.07 months

FUCASO® Fully Human Design Results in Extraordinary Persistence

FUCASO® is the only CAR-T approved with scFv derived from **FULLY HUMAN ANTIBODY**

ADA level is much lower than other approved CAR-Ts

Immuno-genicity comparison



Median persistence time is 307.5 days, and it may increase with extended follow-up

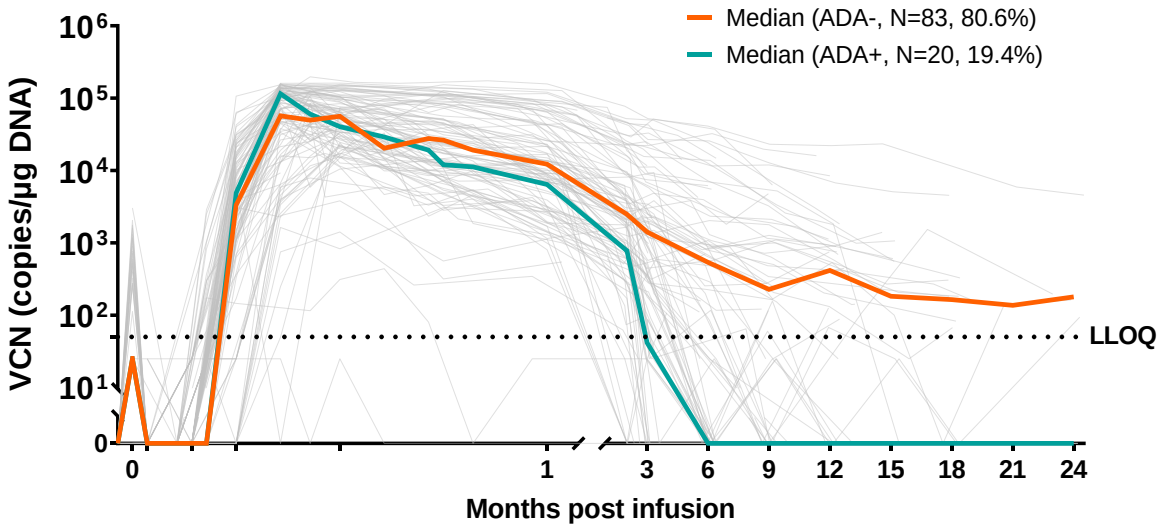
Percentage of subjects with CAR transgene ≥100 copies/μg DNA after cell reinfusion:

6 Month：57.8%

12 Month：50.0%

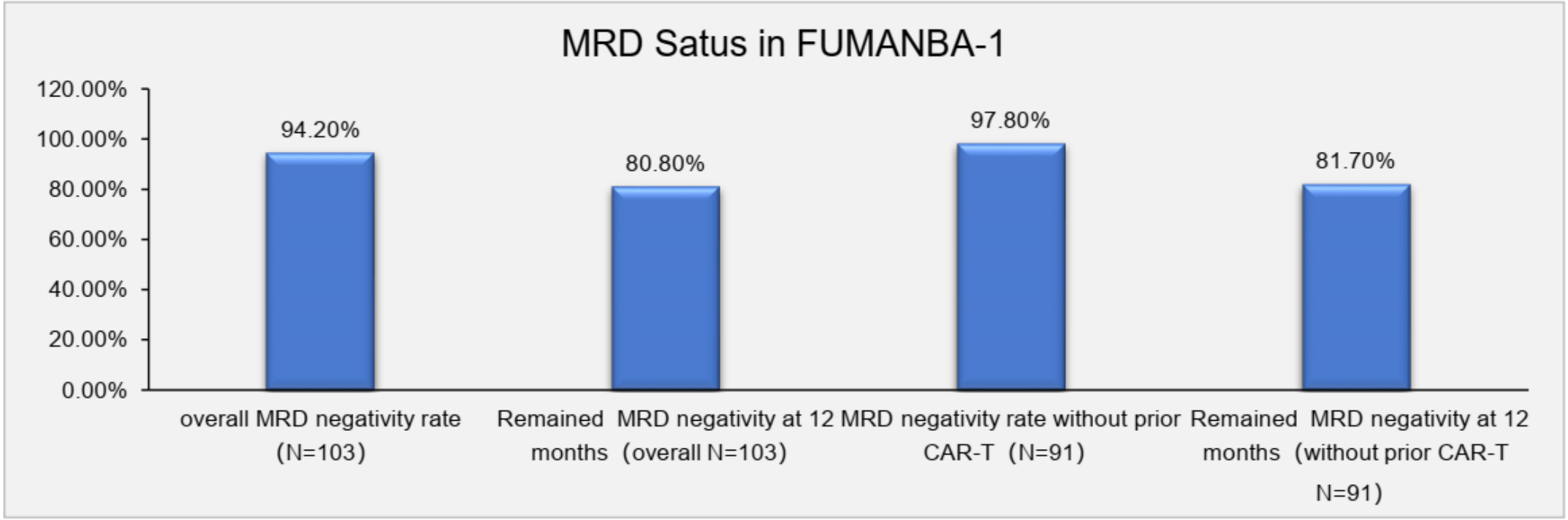
24 Month：40.0%

Lower ADA results in a prolonged persistence of CAR-T



1.Blood (2022) 140 (Supplement 1): 7435–7436.
2.Munshi NC, et al. N Engl J Med. 2021 Feb 25;384(8):705-716.
3.Mi JQ, et al. J Clin Oncol. 2023 Feb 20;41(6):1275-1284.

Overall MRD Results in FUMANBA-1



- 94.2% patients achieved MRD negativity
- 80.8% remained MRD negative at 12 months after infusion.
- 97.8% patients without prior CAR-T achieved MRD negativity
- 81.7% remained MRD negative at 12 months after infusion.

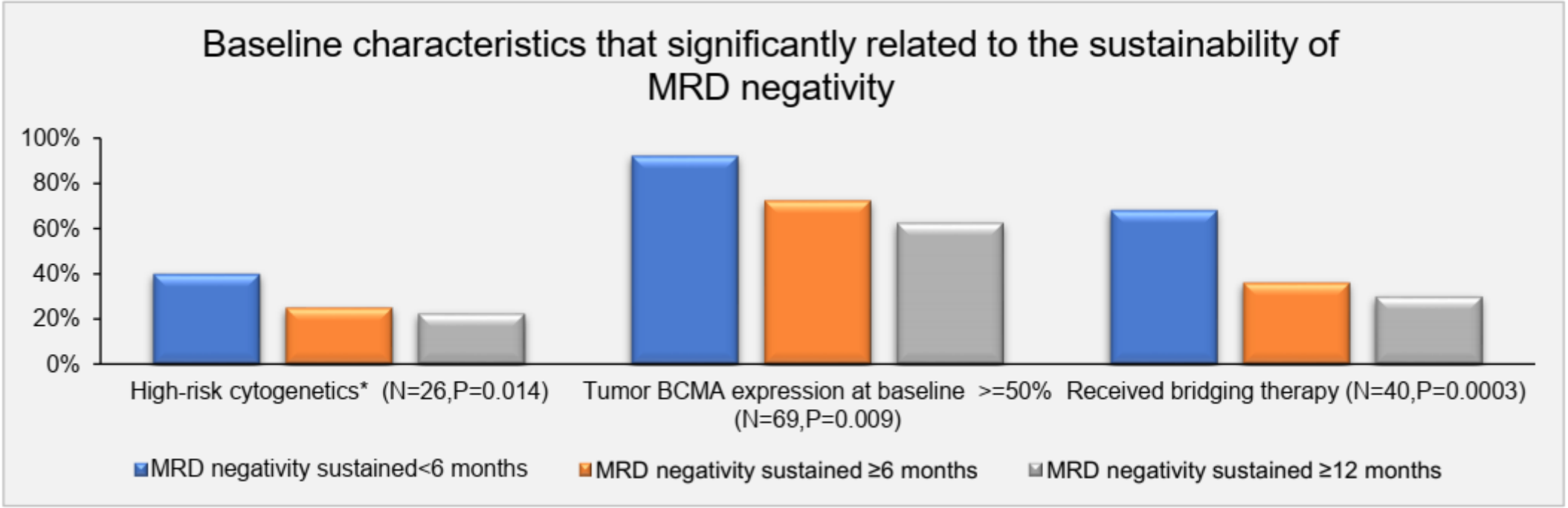
Of the 89 pts without prior CAR-T who achieved MRD negativity, the sustained MRD negativity were:

- 64 patients for ≥6 months
- 40 patients for ≥12 months
- 25 patients for <6 months

1. 2023 ASH Aabstract #173427 Oral #761

MRD Negativity Subgroups Analysis

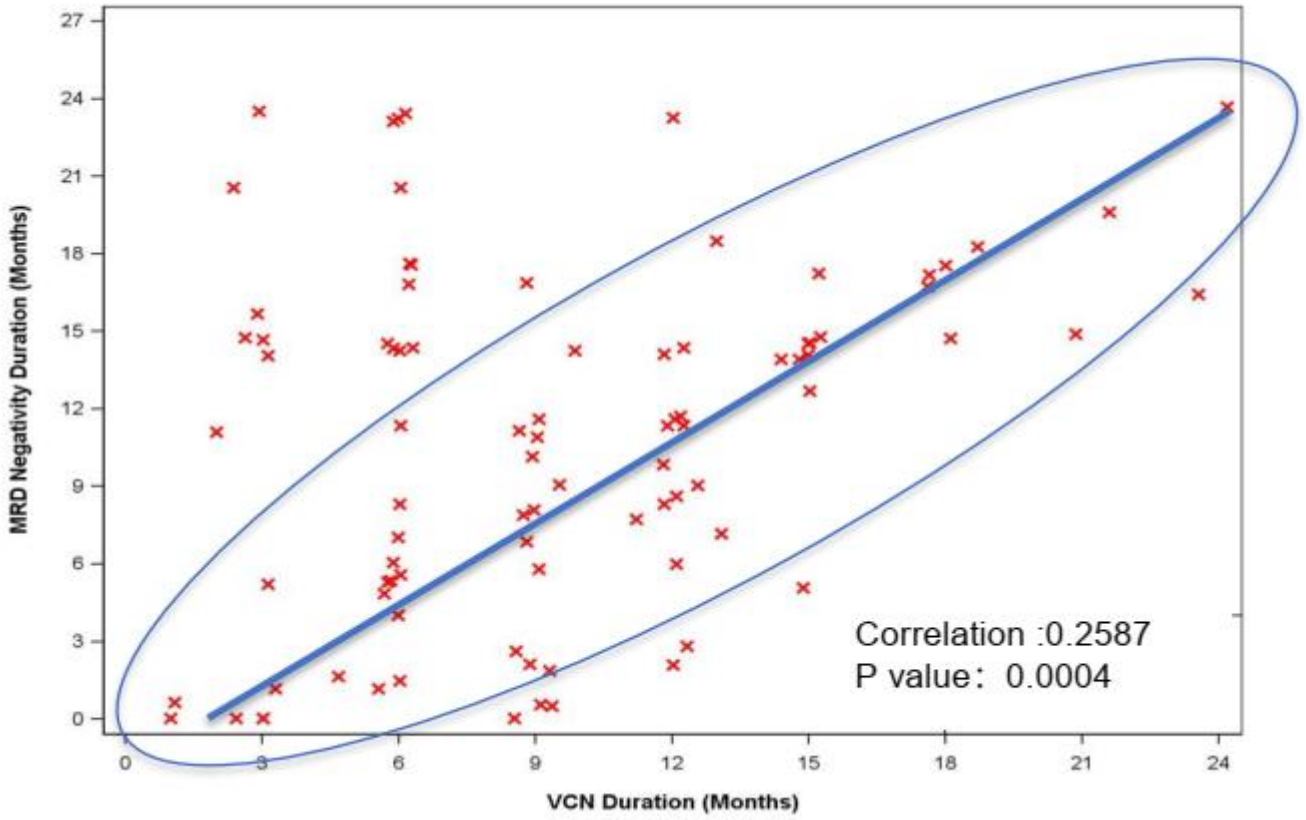
Baseline characteristics such as age, ECOG performance status, disease stage, tumor burden, number of prior therapies, refractory status, autologous stem cell transplant (ASCT) history, cytogenetic profiles, extramedullary myeloma (EMM), BCMA expression levels, and bridging therapy were evaluated as potential prognostic factors using the Cox regression model and log-rank test.



Subgroups characterized by high-risk cytogenetics, elevated BCMA expression, and those who underwent bridging therapy demonstrated a significantly higher hazard ratio regarding the sustainability of MRD negativity.

1. 2023 ASH Aabstract #173427 Oral #761

Correlation between VCN Persistence and MRD-Duration

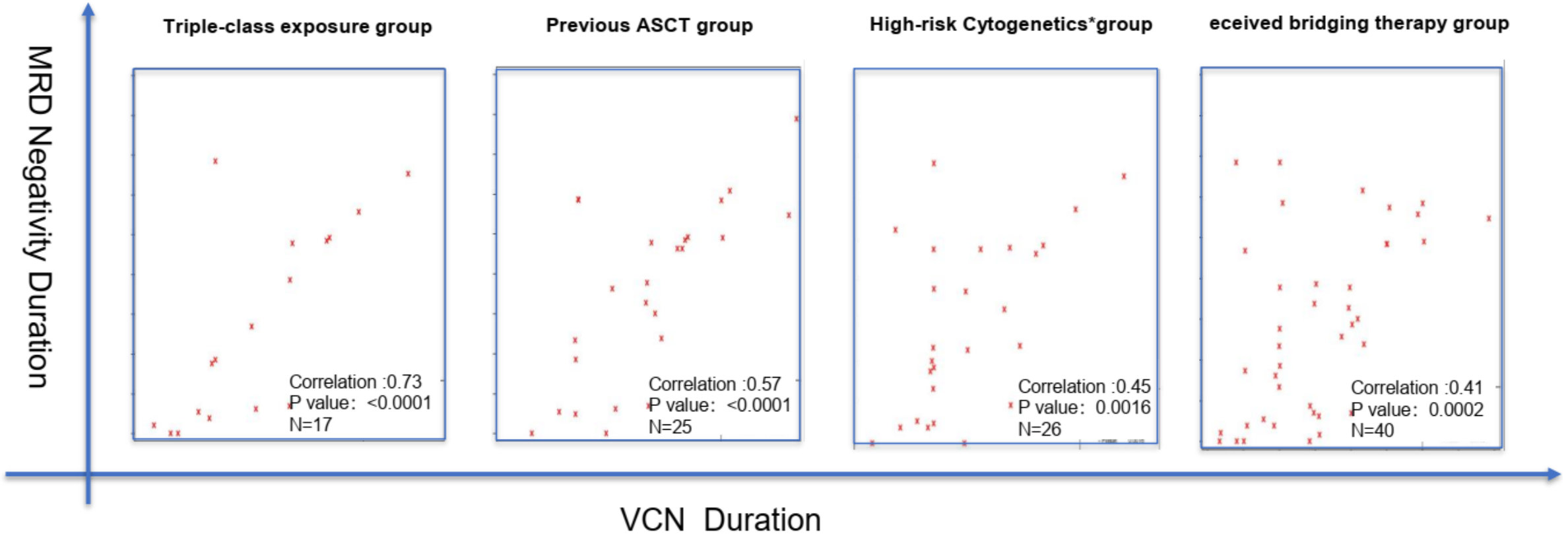


- Overall, a weak positive correlation was observed between the duration of MRD negativity and vector copy number (VCN) persistence.
- This correlation was more pronounced in certain patients.

1. 2023 ASH Aabstract #173427 Oral #761

Correlation between VCN Persistence and MRD-Duration

In subgroups with prior autologous stem cell transplantation (ASCT), triple-class refractory status, high-risk cytogenetics, or those who received bridging therapy, a medium to strong positive correlation was noted.



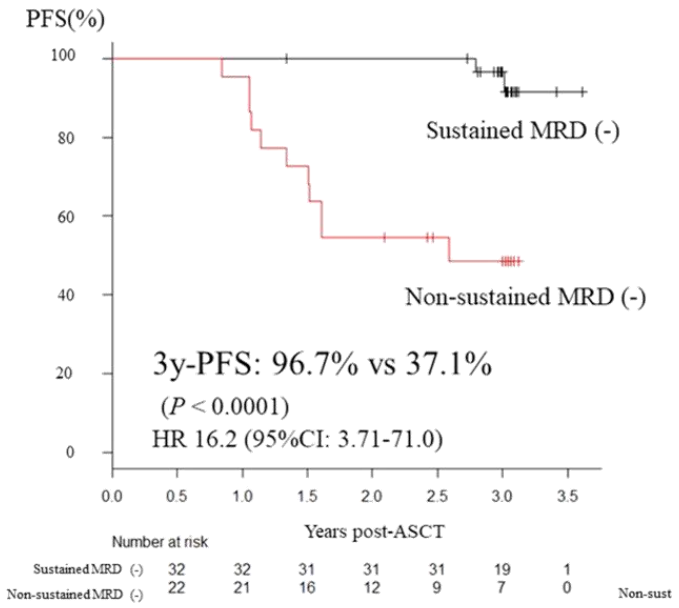
2023 ASH Aabstract #173427 Oral #761

Sustained MRD-negative patients show markedly better survival outcomes

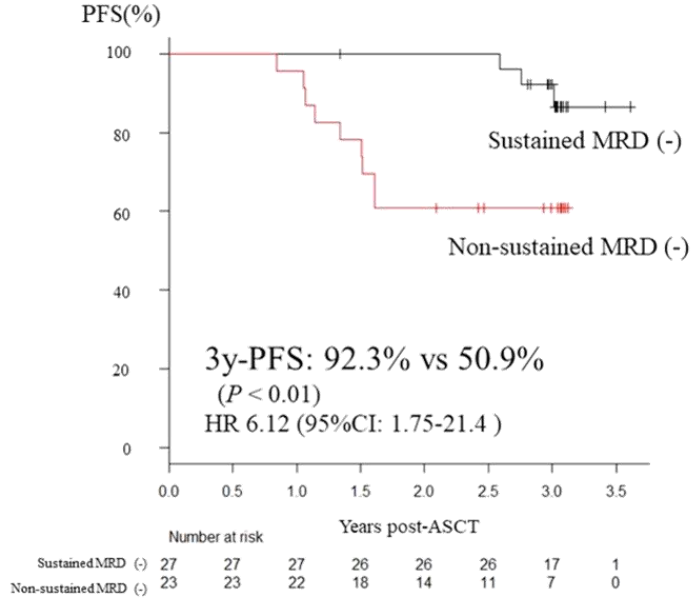
Regardless of NGF or NGS detection:

- Patients achieving any MRD negativity show a significantly better 3-year PFS than MRD-positive patients.
- Those with MRD negativity for 6+ months have a notably higher 3-year PFS than non-sustained MRD-negative patients.

EuroFlow-NGF



NGS

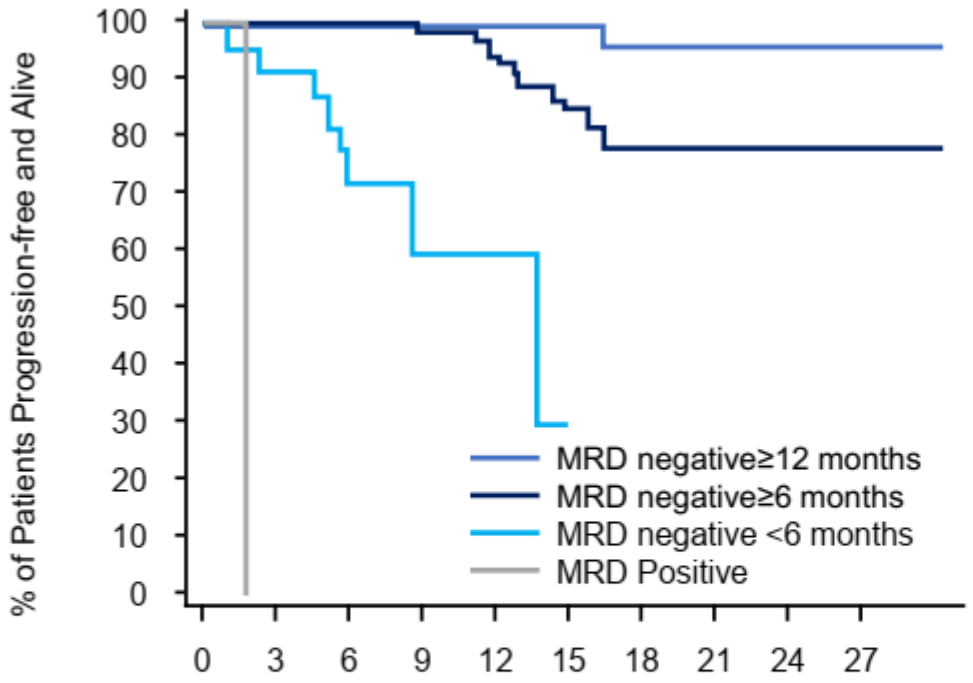


A Japanese prospective, multicenter study enrolled 60 NDMM patients post-bortezomib induction, ASCT, and lenalidomide maintenance, reaching CR or sCR within 100-365 days post-ASCT. MRD was assessed post-CR, at 1 and 2 years post-ASCT.

Takeshi Yoroidaka, et al. 2021 ASH, Poster 3946.

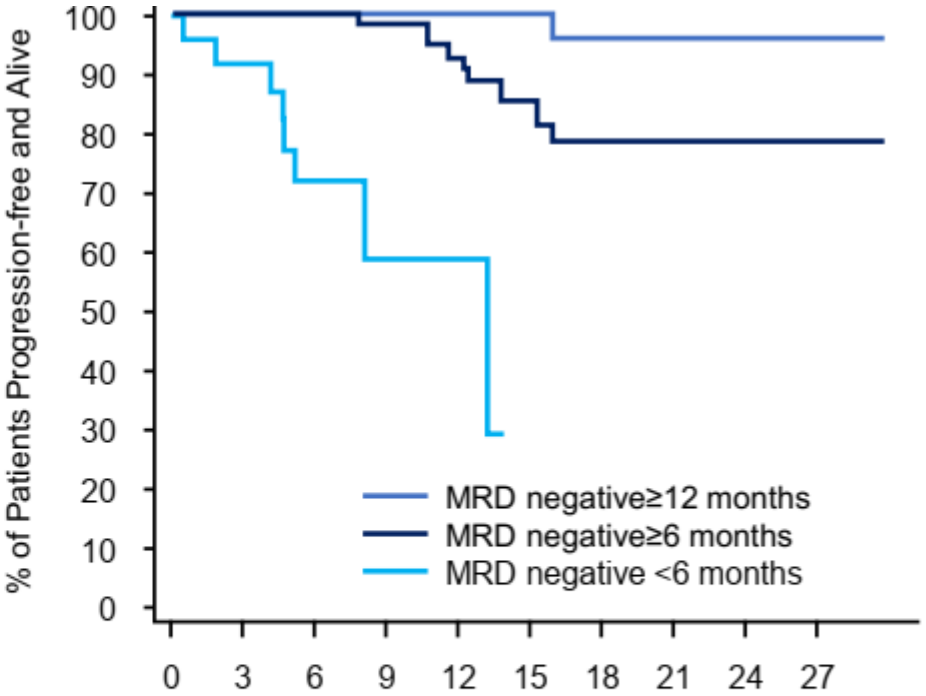
The Efficacy of FUCASO® according to MRD negativity

Subtained MRD negativity(≥6 moths,and ≥12 months)conferred prognostic PFS&DOR benefit.



Patients at risk

MRD negative≥12 months	40	40	40	40	40	33	19	10	1	1
MRD negative≥6 months	64	64	64	61	53	35	19	10	1	1
MRD negative <6 months	25	22	13	8	5	0	0	0	0	0
MRD Positive	1	0	0	0	0	0	0	0	0	0



Patients at risk

MRD negative≥12 months	40	40	40	40	40	24	14	9	1	1
MRD negative≥6 months	64	64	64	58	46	26	14	9	1	1
MRD negative <6 months	25	19	11	5	2	0	0	0	0	0

1. 2023 ASH Aabstract #173427 Oral #761

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Contents

Superior efficacy and safety compared to other BCMA-targeted CAR-T therapies.

FUCASO® offers "Fast & Persistence" in overwhelming efficacy, addressing unmet needs in MM treatment, along with a favorable safety profile.

Approved Product	FUCASO	Abecma	Carvykyi
Data Source	Ph1b/2	Ph2	Ph1b/2
Patient #	91	100	97
Median follow-up	18.07m	10.7m	12.4m/18m
ORR	98.9%	72%	96.9%/97.9%
CR/sCR	**82.4%**	**28%**	**67.0% at 12.4m follow-up /80.4% at 18m follow-up**
MRD	**80.8%**	**15%**	**55%**
12m PFS Rate	**85.5%**	**<50%**	**76.6%**
Median time to response	**16d**	**1 m**	**1 m**
MRD- Rate	98%, 100% for CR	26%,79% for CR	91.8%
≥3 CRS	**1%**	**9%**	**5%**
ICANS	**2.2%**	**28%**	**23%**
≥3 ICANS	**0%**	4%	**5%**

1. Data presented in 2023 IMS meeting, at the median follow-up of 18.07 months

FUCASO has efficacy and safety advantages compared to BCMA bispecific antibody products

Product	Eque-cel		Tecvayli	Elrexfio	Talvey	
Molecule	IASO BIOTHERAPEUTICS		Johnson&Johnson	Pfizer	Johnson&Johnson	
Company	**BCMA CAR-T**		**BCMA/CD3 BsAb**	**BCMA/CD3 BsAb**	**GPRC5D BsAb**	
Phase	P1b/2 (China)	P1b/2 (China) (w/o prior CAR-T pts)	P1/2(US)	P2(US)	P1/2(US)	
Patient #	103	93	165	123	143	145
Dose	1×10^6 CAR-T cells/kg		1.5 mg/kg	76 mg	0.4 mg/kg QW	0.8 mg/kg Q2W
Median follow-up	18.1m	17.6m	14.1m	14.7m	18.8m	12.7m
ORR	96.1%	98.9%	63.0%	61%	74.1%	71.7%
CR/sCR	77.7%	82.4%	39.4%	35%	33.6%	38.7%
MRD-rate	80.8%	81.7%	26.7%	/	/	/
mTTR (Time to Response)	16d	16d	1.2m	/	/	/
mPFS/PFS rate	12m 80.0%	12m 85.5%	11.3m	NR, 12m 56.6%	NR, 34.9% at 12m	NR, 54.4% at 12m
≥3 CRS	1%	1.1%	0.6%	0	2.1%	0.7%
ICANS	1.9%	1.1%	3%	3.4%	10.7%	11%
≥3 ICANS	0	0	0	0	/	/

Source: :Eque-cel: internal data, cut off date: 2022-12-31. Tecvayli: N Engl J Med 2022;387:495-505. Elrexfio: ASCO 2023 #8039. Talvey: ASCO 2023#8036
; Abbreviations: ORR: overall response rate; (s)CR: (stringent) complete response; ; TTR: Time to response; mPFS: median progression-free survival; CRS: cytokine release syndrome; ICANS: Immune effector cell-associated neurotoxicity syndrome; NR: Not reached; NA: Not applicable

Conclusions

- MRD negativity is linked to improved survival and is a recognized efficacy endpoint.
- CAR-T therapy offers specificity, overcomes immune tolerance, clears myeloma cells, and improves immune surveillance, delivering breakthrough MRD outcomes in R/R MM
- The first fully human BCMA CAR-T, Eque-cel, avoids immunogenicity and sustains higher memory T cell levels, promoting CAR-T proliferation and durability, offering deeper remission and potential cures in R/R MM

Elevated

Achieves an ORR of 98.9%*

Profound

Attains a ≥CR rate of 78.7%, with all patients at ≥CR reaching MRD negativity

Sustained

Median response duration extends to 307.5 days, with 82.4% of patients maintaining MRD negativity beyond 12 months

Endurance

Demonstrates a 12-month PFS rate at 84.4%*

* 89pts without prior CAR-T

Optimizing the timing of CAR-T therapy within the MM treatment continuum, including early-line application, can enhance the role of CAR-T in MM therapy. Related research is currently underway.

About IASO BIO

A commercial-stage biopharma with a pipeline consisting **autologous CAR-T, allogeneic CAR-NK and biologics**, dedicated to developing breakthrough therapies for **cancers and autoimmune diseases**.

- Equel-cel received the NMPA BLA approval on June 30th as the first BCMA CAR-T in China.
- The **1st fully human DualCAR-T** product (CD19/22) to have entered **phase I clinical trial in China**
- **GPRC5D CAR-T** product in clinical trial
- **A global leader** in applying CAR-T to **autoimmune diseases**

Focus on Addressing Unmet Medical needs

- 2 FDA **Orphan Drug Designations (ODD)**
- 1 China NMPA **Breakthrough Therapy Designation (BTD)**

Reaching **400+** employees within 6 years' rapid development

4 drug candidates in clinical trials with First-in-Class/Best-in Class potential and **10+** assets under development

Global operation with **4** offices in China and the US

$253 Mn USD capital raised in 4 rounds

National Treatment Centers Network of FUCASO in China

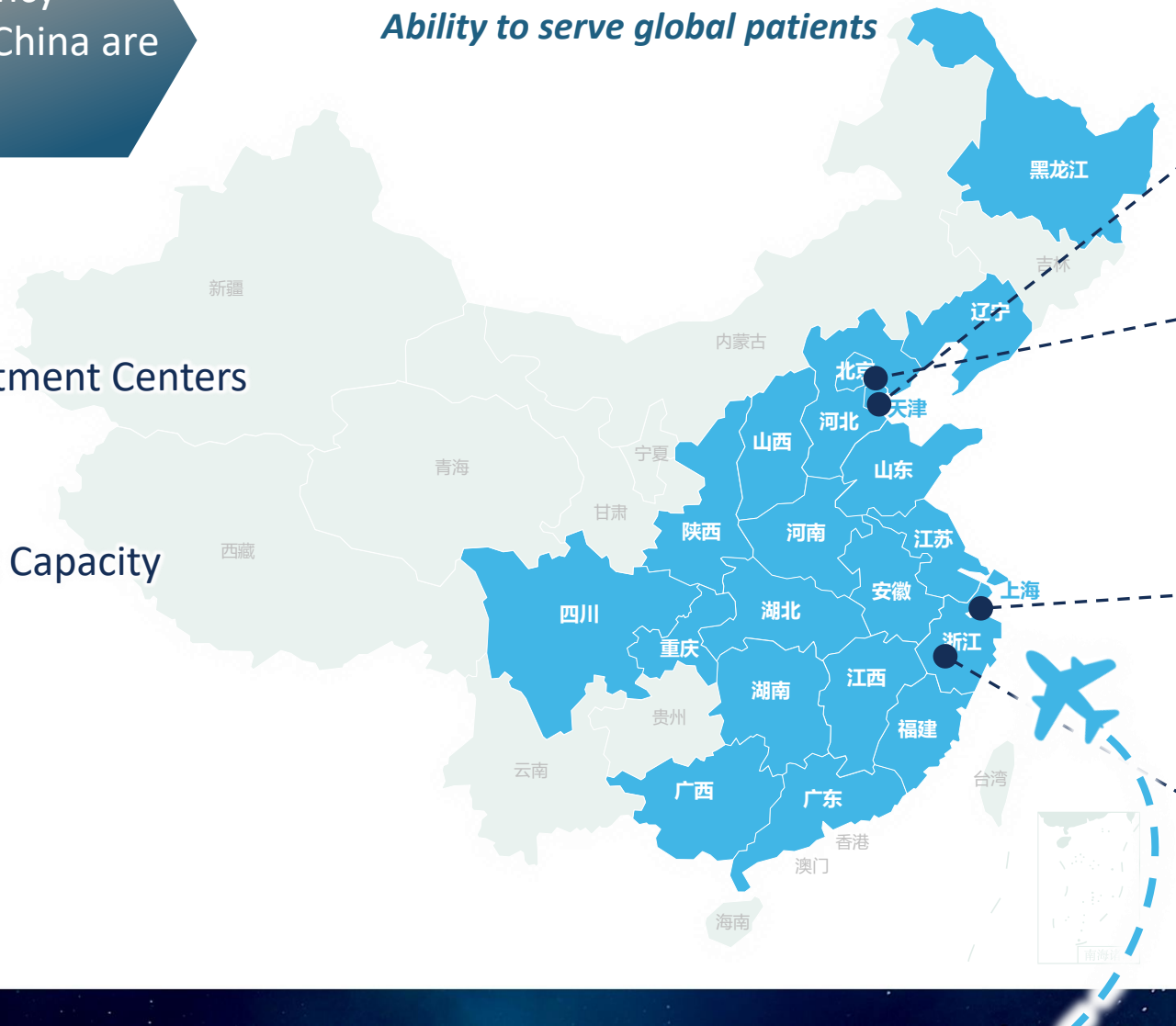
All Top Hema- Malignancy Treatment Centers in China are covered

90+ Certified Treatment Centers

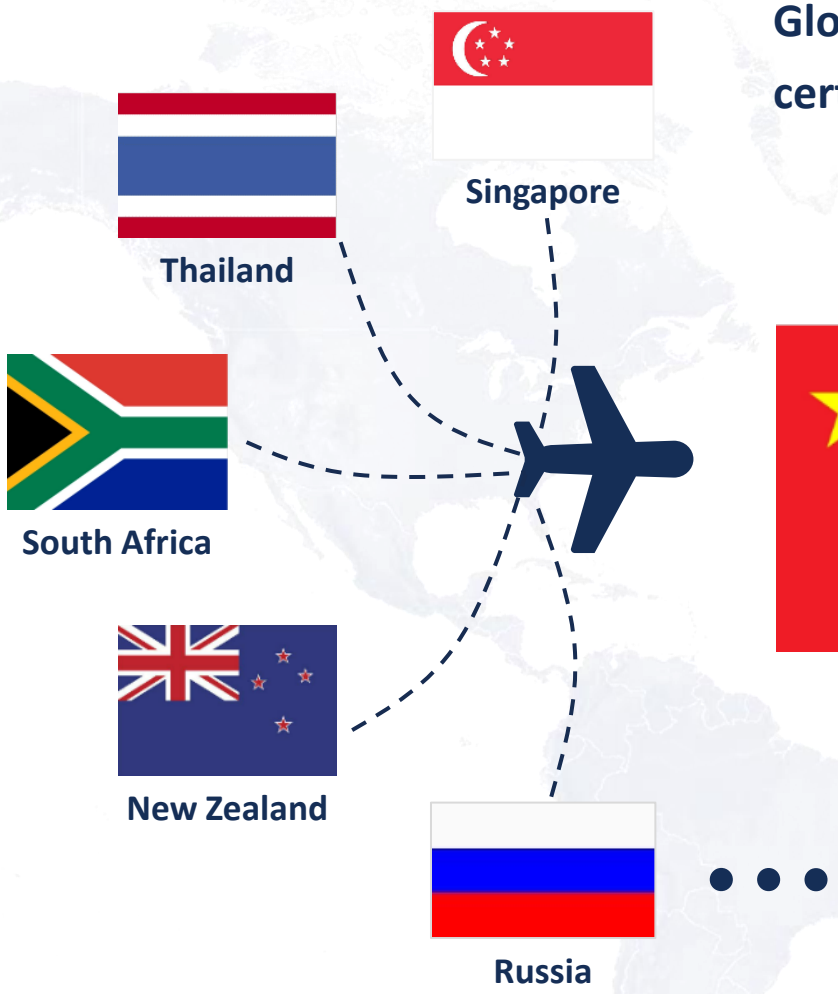
30+ Cities Landing Capacity

world-class clinical center

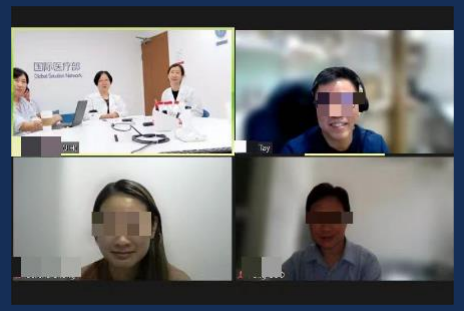
Ability to serve global patients



FUCASO Has Treated Multiple Myeloma Patients from Several Countries in 3 months



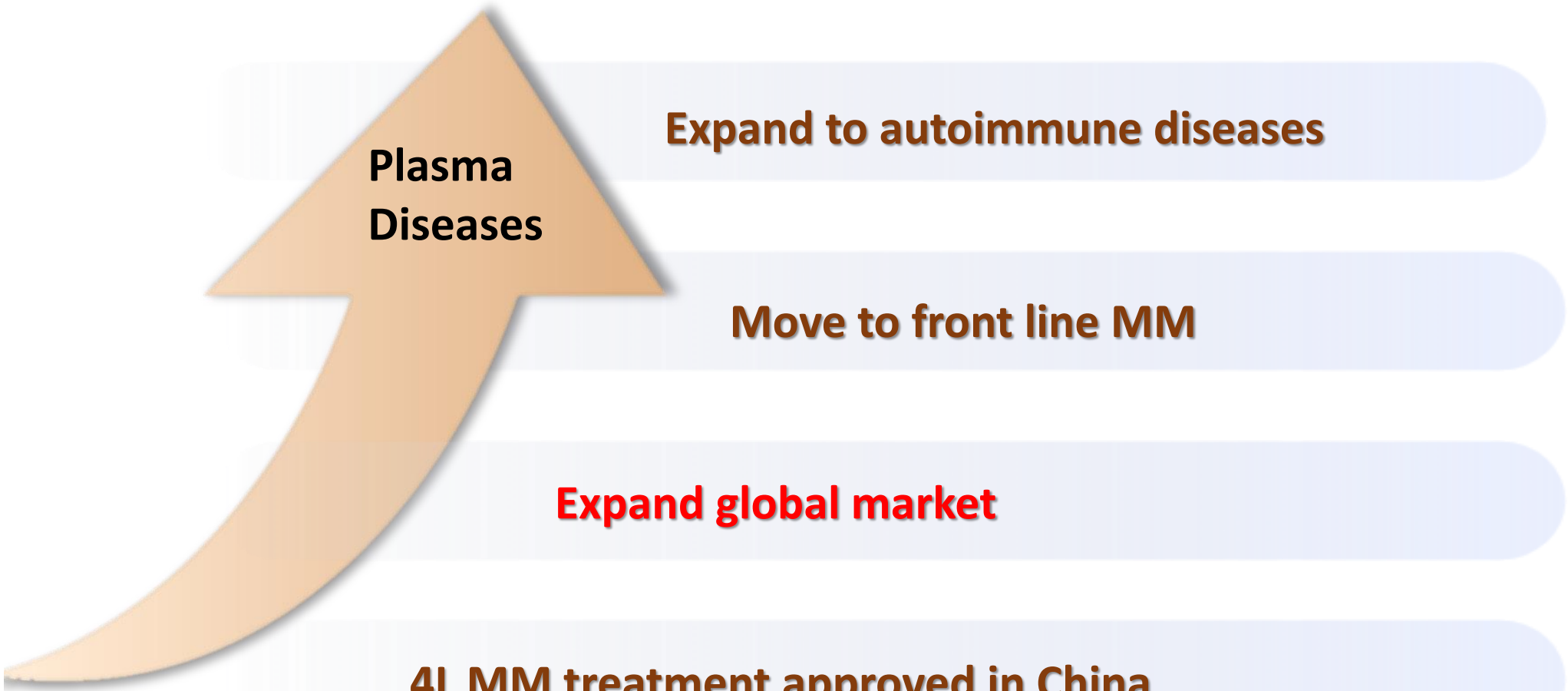
Global patients coming to China for FUCASO treatment at IASO BIO/NMPA-certified FUCASO treatment centers



In-person consultation in Shanghai

Virtual consultation to confirm treatment plan before departure

FUCASO® Clinical Development Strategies



福可苏
伊基奥仑赛注射液

IASO 驯鹿生物 Innovent 信达生物制药

THANK YOU !

全力以福 未来可苏

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