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A Dual Targeting BCMA and CD19 FasTCAR-T (GC012F/AZD0120) as First-line Therapy for Newly Diagnosed Multiple Myeloma

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Background

1. CAR-T therapy has demonstrated substantial efficacy in relapsed / refractory multiple myeloma (RRMM) and revolutionized treatment outcomes for patients[1]

2. However, the role of CAR-T in newly diagnosed multiple myeloma (NDMM), particularly those with high-risk features or advanced age, remains to be defined

3. Early CAR-T treatment may enable ‘early truncation’ of tumor heterogeneity, delaying the emergence of drug resistance[2]

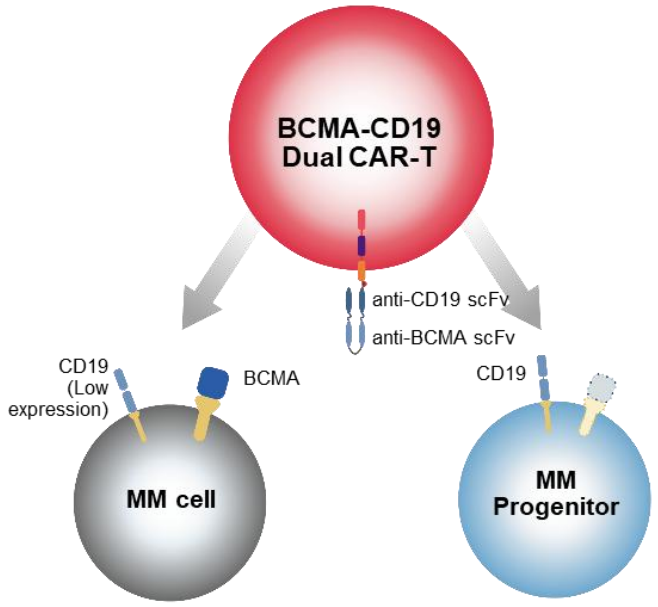
1. Swan D, et al. *Blood Cancer J* 2024;14:206. 2. Cordas Dos Santos DM, et al. *Nat Rev Cancer* 2024;24:867–886.

GC012F/AZD0120: BCMA/CD19 dual targeting CAR-T

BCMA
Universally expressed on malignant plasma cells and a well-established target

+

CD19
Expressed on majority MM cells and progenitor cells [1-3]



Next generation manufacturing
based on FAST CAR platform

Faster availability to patients

- Manufactured in <3 days

Enhanced T-cell fitness

- Younger, fitter, naïve T cells

- GC012F/AZD0120 is an autologous CAR-T therapy that targets both BCMA and CD19
- GC012F/AZD0120 has demonstrated deep and durable responses with a manageable safety profile in RRMM patients[4]

1. Boucher K, et al. *Clin Cancer Res*. 2012;18:6155–6168. 2. Garfall AL, et al. *JCI Insight* 2018;3:e120505. 3. Jiang H, et al. Presented at: ASH Annual Meeting 2020; December 5–8, 2020; virtual. Oral presentation 178. 4. Juan Du, et al. Presented at: EHA2023 Congress; June 8-11, 2023; Frankfurt & Virtual. Poster presentation P869.
MM, multiple myeloma; RRMM, relapsed / refractory multiple myeloma.

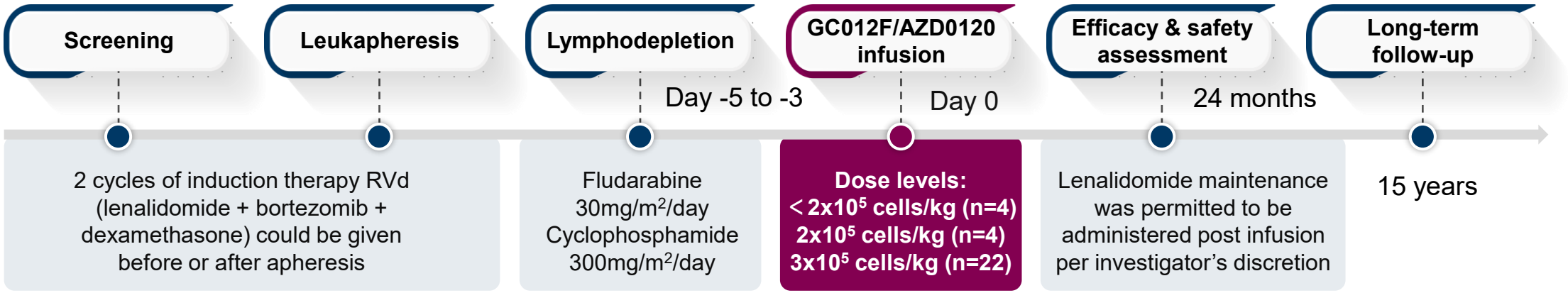
Study design
Two Phase 1 studies in NDMM

Key eligibility criteria

- Diagnosed with MM per IMWG criteria
- ECOG PS ≤3
- Measurable disease
- **Study 1 (NCT04935580): high risk (HR)* transplant eligible (TE) NDMM (N=22)**
- **Study 2 (NCT05840107): transplant ineligible (TI) NDMM (N=8)**

Key endpoints

- **Safety:** incidence and severity of Aes
- **Efficacy:** ORR, per 2016 IMWG criteria
- CRR; MRD negativity rate
- DoR, OS, PFS



* High-risk was defined as meeting at least one of the following: a) R-ISS stage II or III; b) High-risk cytogenetics: del17p, t(4;14), t(14;16), or 1q21 ≥4 copies; c) Extramedullary disease; d) IgD or IgE subtype; e) High-risk definition according to mSMART3.0; f) LDH > the upper limit of normal.

IMWG: International Myeloma Working Group; ECOG PS: Eastern Cooperative Oncology Group Performance Status; AE: A22erse events; ORR: Overall response Rate; CRR: Complete Response Rate; MRD: Minimal Residual Disease; PFS: Progression Free Survival; DOR: Duration of Response: OS: Overall Survival.

Baseline characteristics

Baseline characteristics		All (N=30)	TE HR NDMM (N=22)	TI NDMM (N=8)
Age (years), median (range)		64 (43–78)	59 (43–69)	72 (70–78)
Male, n (%)		19 (63)	14 (64)	5 (63)
Induction therapy (IT), n (%)	2 cycles RVd	29 (97)	21 (95)	8 (100)
Response to induction therapy	ORR, %	93.3	90.9	100
R-ISS stage, n (%)	II / III	25 (83)	20 (91)	5 (63)
Cytogenetics†, n (%)	High risk	14 (48)	11 (52)	3 (37)
Plasmacytomas, n (%)	All	17 (57)	12 (55)	5 (63)
	Soft tissue related	3 (10)	3 (14)	0 (0)
ECOG PS, n (%)	0–1	22 (73)	16 (73)	6 (75)
	≥2	8 (27)	6 (27)	2 (25)
Apheresis, n (%)	Before IT	4 (13)	4 (18)	0 (0)
	After 1 cycle of IT	16 (53)	8 (36)	8 (100)
	After 2 cycles of IT	10 (33)	10 (45)	0 (0)

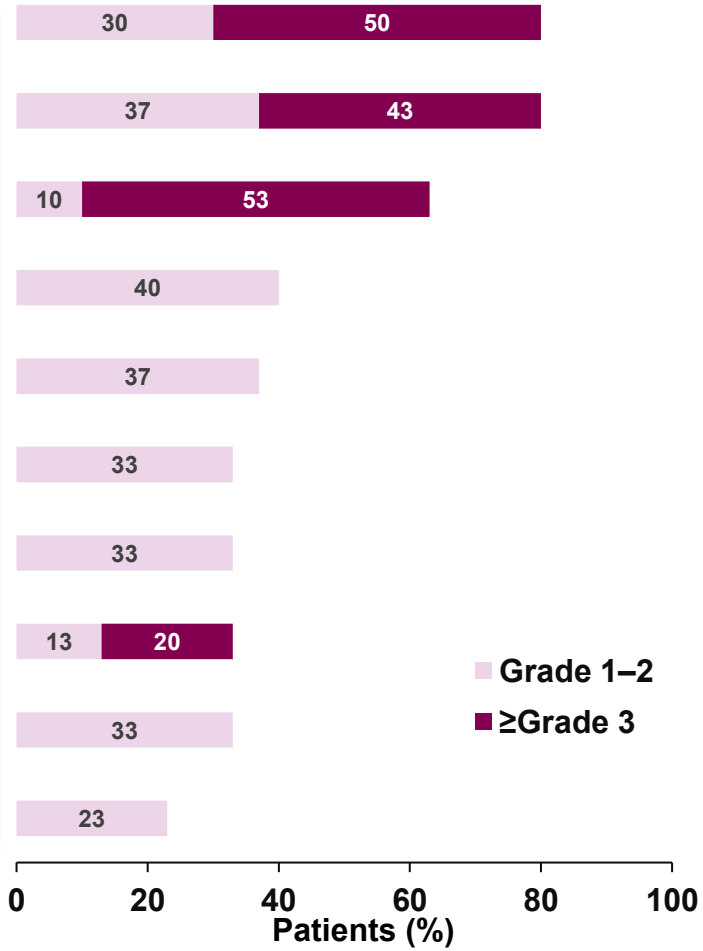
Median time from diagnosis to infusion was 3 months (range, 2–5 months)

*One patient received one cycle of PAD (bortezomib, doxorubicin, and dexamethasone) and one cycle of RVd.
†The definition of high-risk cytogenetics: del (17p), t (4;14), t (14;16), amp (1q21).
ECOG, eastern cooperative oncology group performance status; HR, high risk; NDMM, newly diagnosed multiple myeloma;
R-ISS, revised international staging system; RVd, lenalidomide + bortezomib + dexamethasone; IT, induction therapy; TE, transplant eligible; TI, transplant ineligible.

Safety profile: TEAEs

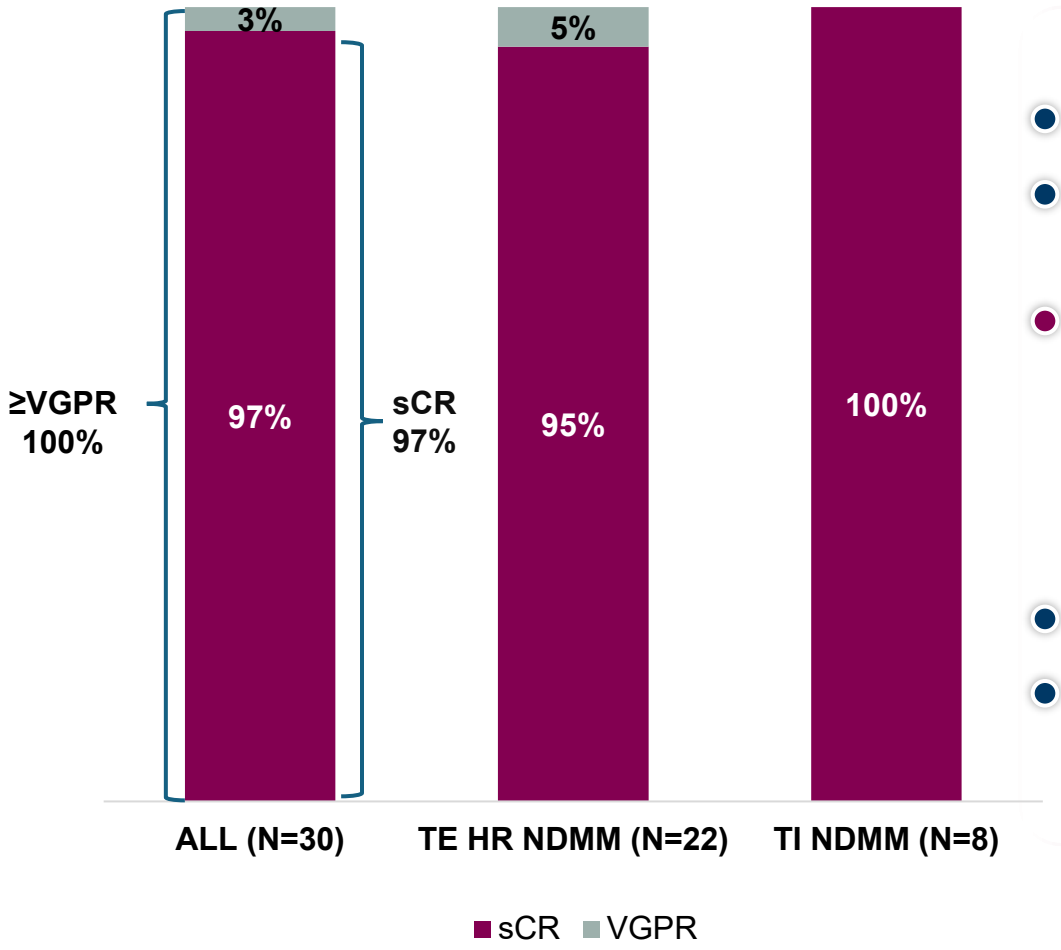
- GC012F was well tolerated and mostly low-grade CRS
- Grade 1 CRS: 30% (9/30), grade 2 CRS: 3% (1/30), grade ≥3 CRS: 0
  - Four patients with CRS were treated with tocilizumab
  - Median time to onset: 8 days (range, 6–18 days)
  - Median duration: 2 days (range, 1–8 days)
- No ICANS or IEC-HS or IEC-EC observed
- No delayed neurotoxicities or secondary primary malignancies observed to date

TEAEs, n (%)	All grades	Grade ≥3
Neutropenia	24 (80)	15 (50)
Leukopenia	24 (80)	13 (43)
Lymphopenia	19 (63)	16 (53)
LDH increased	12 (40)	0
Thrombocytopenia	11 (37)	0
Hypoalbuminemia	10 (33)	0
Anemia	10 (33)	0
Infection	10 (33)	6 (20)
CRS	10 (33)	0
Hypocalcemia	7 (23)	0



AEs were graded according to CTCAE v5.0.
AE, adverse event; ASTCT, American society for transplantation and cellular therapy; CRS, cytokine release syndrome, graded by ASTCT consensus; CTCAE, common terminology criteria for adverse events; ICANS, immune effector cell-associated neurotoxicity syndrome, graded by ASTCT consensus; IEC-EC, immune effector cell–associated encephalopathy; IEC-HS, immune effector cell–associated hemophagocytic syndrome; LDH, lactase dehydrogenase; TEAE, treatment-emergent adverse event.

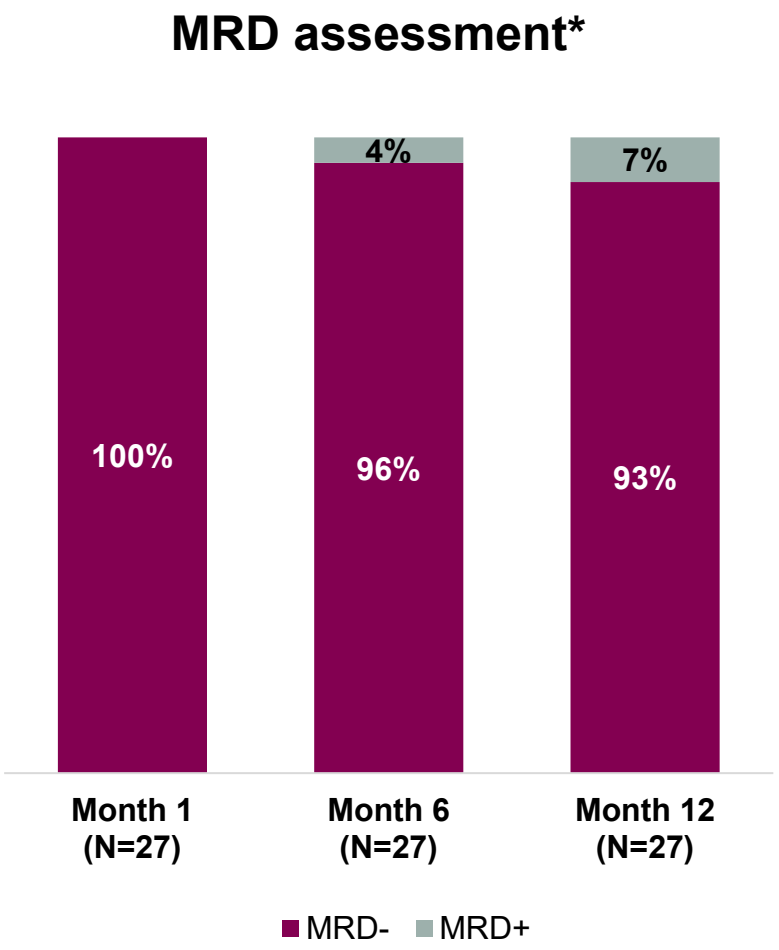
100% ORR in both cohorts



- Fast and deep responses were achieved in both groups
- As of October 15, 2025, the median follow-up time since diagnosis was 36.5 months (19.6–53.9)
- **ORR=100% (30/30):**
  - **100% ≥VGPR**
  - **97% (29/30)** sCR (1 VGPR patient still in response)
- Median time to first response post infusion was 28 days
- Median time to best response post infusion was 68 days

HR, high risk; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; sCR, stringent complete response; TE, transplant eligible; TI, transplant ineligible; VGPR, very good partial response.

Efficacy profile: MRD

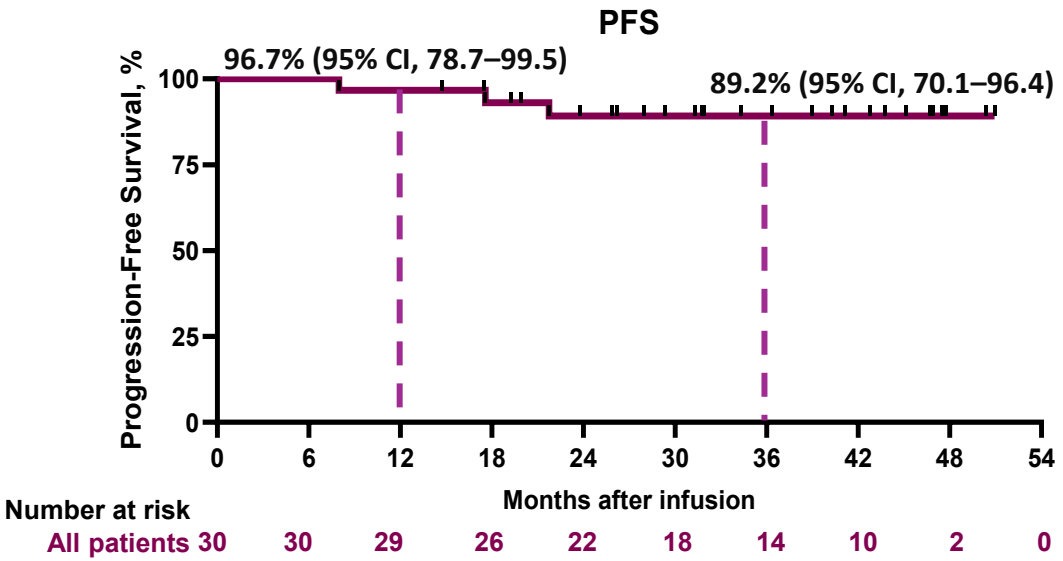


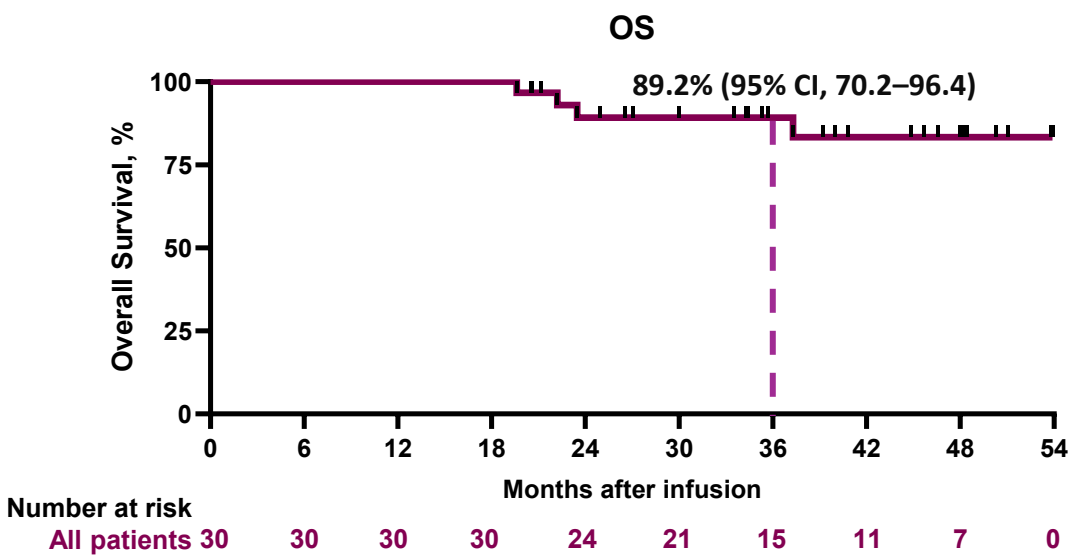
- MRD was tested by Euroflow at a sensitivity of 10^{-6}
- 100% (30/30) of MRD evaluable patients achieved MRD negativity in all dose levels at least 1 time point of measurement
- 100% (27/27) of MRD evaluable patients achieved MRD negativity at Month 1 post infusion
- All patients achieved MRD negativity before lenalidomide maintenance initiation
- 83% (25/30) patients had ≥ 12 months sustained MRD negativity

*The subjects who did not complete the MRD testing at Month 1, 6, and 12 were different.
MRD, minimal residual disease.

Efficacy profile: PFS & OS

Median study follow-up: 36.5 months



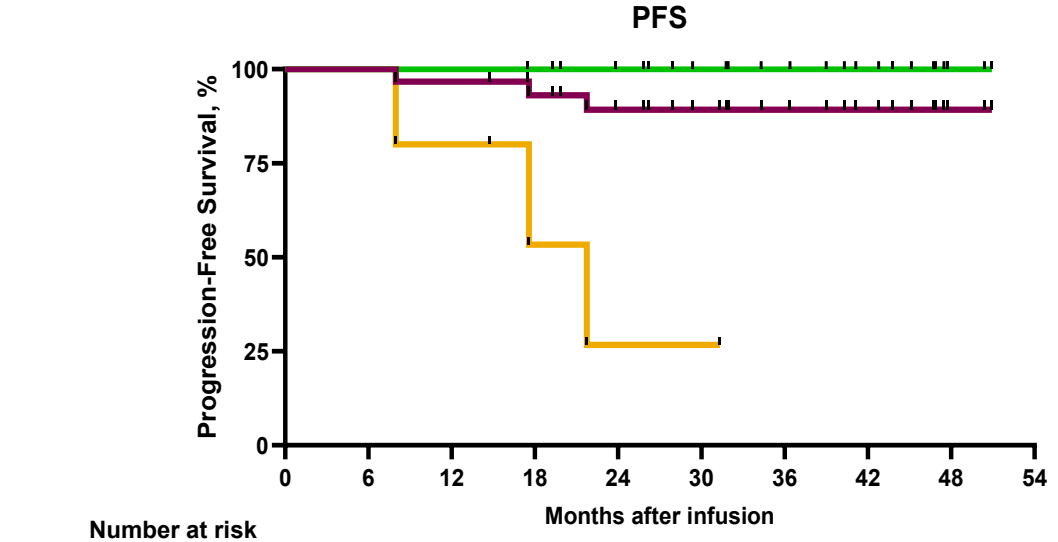


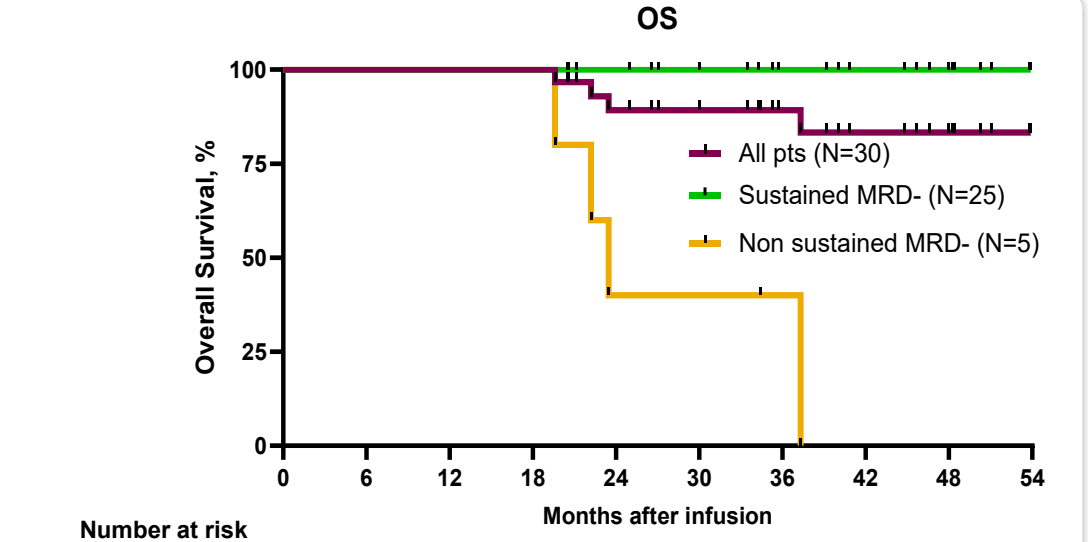
- **No patients died within 12 months of AZD0120 infusion**
- **23 patients (77%) received lenalidomide maintenance (median time to initiation was 6 months post infusion)**
  - Two patients progressed and then died
- **7 patients did not receive lenalidomide maintenance, 5 of them remain in disease-free survival.**
  - One experienced PD and subsequently died
  - One died without documented PD

OS, overall survival; PD, progressive disease; PFS, progression-free survival.

Patients with ≥ 12 months sustained MRD negativity have superior survival outcomes

Median study follow-up: 36.5 months



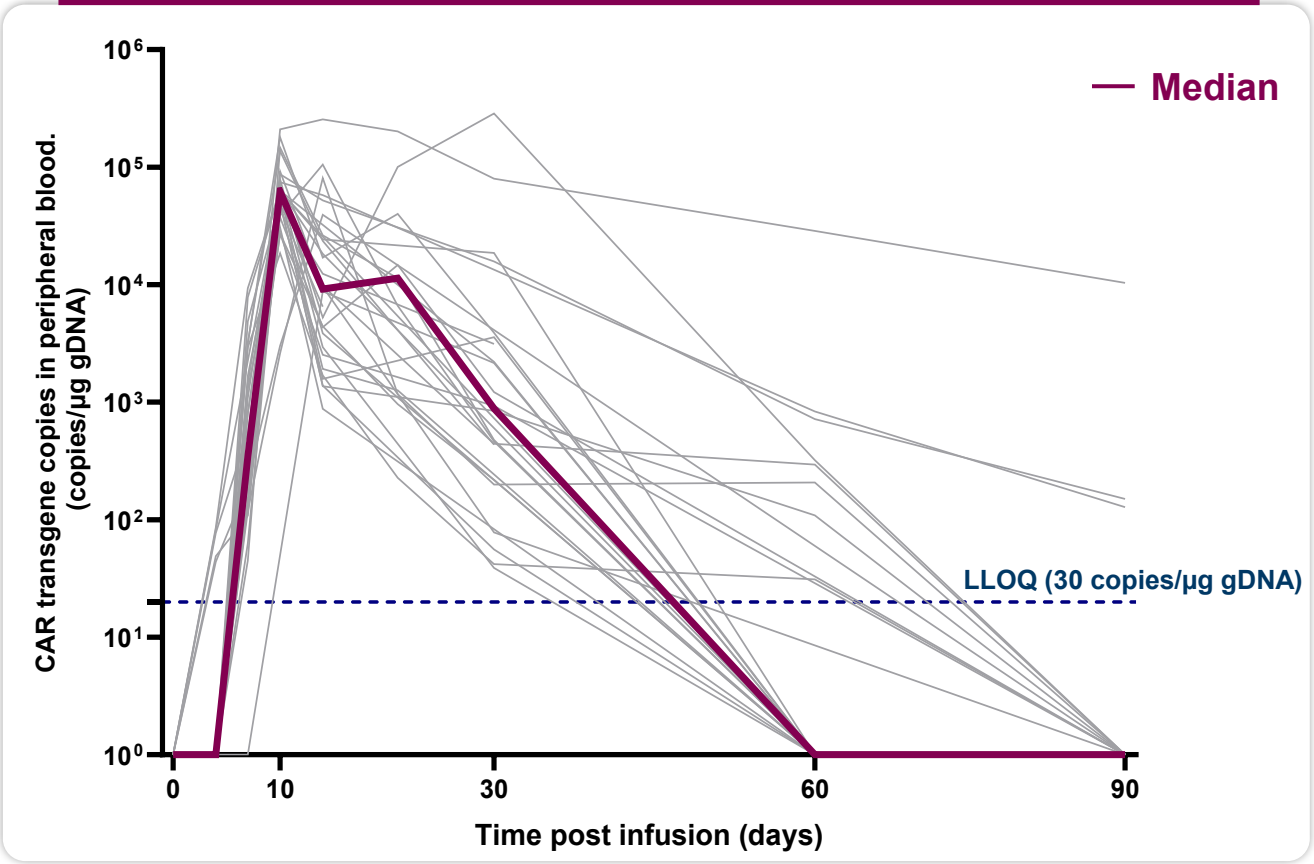


- No patients progressed or died in sustained MRD negativity group
- In non-sustained MRD negativity group, median PFS was 21.7 months and median OS was 23.5 months

*Sustained MRD is defined as maintenance of MRD negativity confirmed ≥ 12 months apart.
MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival.

Cellular kinetics profile

CAR Expansion and Persistence (N=30)



Robust CAR-T cell expansion with sustained persistence in all patients

T_{max}	Days	
10	9–28	
T_{last}	Days	
29	26–NR	
C_{max}	copies/µg gDNA	
62,644	8,754–331,159	
AUC_{0-28}	copies*days/µg gDNA	
348,671	80,181–3,985,420	

1.CK parameters expressed as median (range)
2.CAR, Chimeric Antigen Receptor; LLOQ, lower limit of quantification; NR, not reached; Cmax, Maximum Concentration; AUC, Area Under the Curve.

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Conclusions

- **In the largest ASCT-naïve CAR-T treated NDMM cohort to date, GC012F/AZD0120 demonstrated a favorable efficacy profile in NDMM patients:**
  - ORR = 100% (100% ≥VGPR rate; 97% MRD- sCR rate)
  - 100% overall MRD negative rate at a sensitivity of 10^{-6}
  - Median PFS and OS were not reached with a median follow-up time 36.5 months
- **Patients with sustained MRD negativity had superior survival outcomes compared with patients with non-sustained MRD negativity status**
  - Median OS: NR vs 23.5 months
  - Achieving sustained MRD negativity is associated with improved patient outcomes
- **With the longest follow-up of CAR-T in NDMM, GC012F/AZD0120 demonstrated a well-tolerated safety profile**
  - Mitigates intolerance associated with long-term SoC treatment
  - Broadens therapeutic options for NDMM

ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell therapy; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; NR, not reached; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response; SoC, standard of care; TI, transplant ineligible; VGPR, very good partial response.

We would like to thank the patients, their families, the investigators, all the caregivers involved in this study, and AstraZeneca / Gracell Biotechnologies for providing FasTCAR-T™ GC012F (AZD0120)

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