AUTOLOGOUS B CELL MATURATION ANTIGEN (BCMA) AND CD19 DUAL TARGETING FASTCAR-T CELLS (GC012F/AZD0120) AS FIRST-LINE THERAPY FOR ELDERLY PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS

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INTRODUCTION

GC012F (AZD0120) – a DUAL targeting BCMA/CD19 chimeric antigen receptor (CAR)-T cell therapy

- CAR-T cell therapy has dramatically improved outcomes in patients with relapsed/refractory multiple myeloma (RRMM) and is being evaluated in newly diagnosed multiple myeloma (NDMM) patients.
- Long-term follow-up from previous trials (NCT04236011; NCT04182581; NCT04935580) strongly suggests that GC012F is effective in RRMM and high-risk transplant-eligible NDMM patients aged ≤70 years.
- However chronological age can be a common reason for exclusion in a clinical trial setting.

AIM

- To characterize the safety and feasibility of GC012F CAR-T cell therapy in elderly transplant-ineligible NDMM patients in a single-arm phase I study. (NCT05840107)

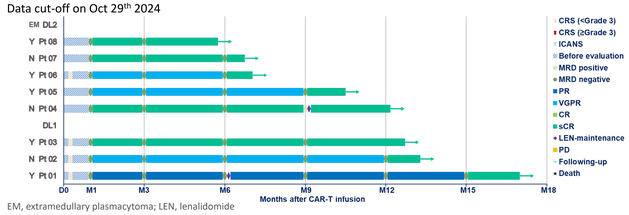
METHOD

- GC012F was manufactured on the novel FasTCAR-T platform.
- Key Eligibility Criteria:
  - Transplant-ineligible NDMM patients
  - ECOG ≤ 3
- All patients received two cycles induction therapy of VRd (bortezomib, lenalidomide, and dexamethasone) prior to CAR-T infusion.

RESULTS

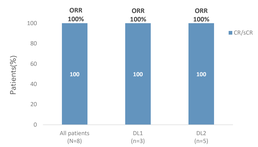
Swimmer Plot

Data cut-off on Oct 29th 2024



EM, extramedullary plasmacytoma; LEN, lenalidomide

Efficacy Profile- Response



ORR 8/8 patients **100%** all sCR

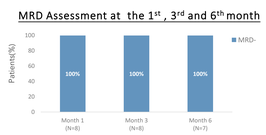
MRD- 8/8 patients **100%** sensitivity 10^{-6}

MRD- sCR 8/8 patients **100%** best response achieved to date

- Median duration of response (DOR) was not reached at data cut off
- Median duration of follow up: 10.4 months (range: 5.3 – 15.6 months)

-ORR, overall response rate; DL, dose level; sCR, stringent complete response; MRD, minimal residual disease
-MRD assessed at sensitivity of 10^{-6} using EuroFlow

Efficacy Profile- MRD Assessment



100% of MRD evaluable patients achieved MRD negativity at **Month 1**

100% of MRD evaluable patients achieved MRD negativity **in all dose levels**

All patients achieved MRD negativity before lenalidomide maintenance

Safety Profile

All CRS[1] were Grade 1 and resolved within 8 days
No ICANS or Neurotoxicity was observed[2]

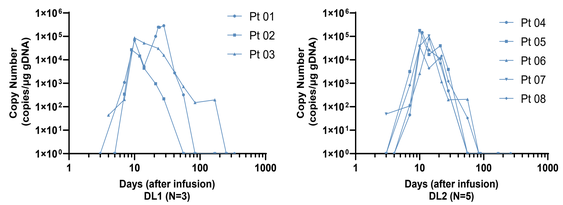
N=8	CRS[1] n (%)	ICANS[2] n (%)
Grade 1	4 (50)	0 (0)
Grade 2	0 (0)	0 (0)
Grade ≥ 3	0 (0)	0 (0)
All grade	**4 (50)**	**0 (0)**

CRS any grade	Median (days)	Range (days)
Time to onset	9	6-18
Duration	3	1-8

N=8	All Grades n (%)	Grade ≥3 n (%)
Hematologic TEAEs* (≥20% All Grades)		
Neutropenia	7 (88)	6 (75)
Leukopenia	5 (63)	3 (38)
Thrombocytopenia	5 (63)	0 (0)
Lymphopenia	2 (25)	2 (25)
Anemia	2 (25)	0 (0)
Non-Hematologic TEAEs* (≥20% All Grades)		
Infection	4 (50)	2 (25)
LDH increased	3 (38)	0 (0)
Ferritin increased	2 (25)	0 (0)

CRS - cytokine release syndrome, ICANS - immune effector cell-associated neurotoxicity syndrome
1 CRS graded by ASTCT Consensus criteria; one patient was treated with tocilizumab.
2 ICANS graded by ASTCT Consensus.
* AEs were graded according to CTCAE v5.0; TEAE - treatment emergent adverse event; LDH - lactase dehydrogenase.

Pharmacokinetics Profile

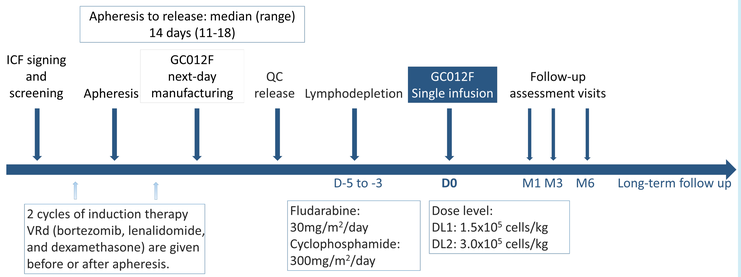


Dose Level	Tmax (days)	Cmax (copies/μg gDNA)	$AUC_{0\text{-}28day}$ (copies/μg gDNA*days)	Tlast (days)
DL1 (N=3)	10	86902	899007	56
$1.5*10^5$ cells/kg	(9-28)	(27177-285955)	(132422-2283331)	(28-168)
DL2 (N=5)	11	105109	727009	28
$3.0*10^5$ cells/kg	(10-14)	(37417-179154)	(266488-1025843)	(28-56)
ALL (N=8)	10.5 (9-28)	96005.5 (27177-285955)	744389 (132422-2283331)	42 (28-168)

Baseline Characteristics	Total N=8
Median age, years (range)	72 (70-78)
Male, n (%)	5 (63)
Type of myeloma, n (%)	
IgG	3 (38)
IgA	4 (50)
Light chain	1 (12)
Induction therapy, n (%)	
2 cycles VRd	8 (100)

High-risk, n (%)	8 (100)
R-ISS stage II/III	5 (63)
High-risk cytogenetics[1]	3 (38)
Extramedullary disease	5 (63)
High-risk as mSMART3.0	6 (75)
ECOG performance status, n (%)	
1	6 (75)
2	2 (25)

1. High-risk cytogenetics: del17p, t(4;14), t(14;16), or 1q21 ≥4 copies.



CONCLUSIONS

- GC012F/AZD0120 resulted in a very favorable safety profile and deep responses in elderly transplant-ineligible NDMM patients.
- High overall response rate ORR of 100% (8/8) and MRD- sCR rate of 100% (8/8).
- All patients achieved MRD negativity tested by EuroFlow 10^{-6} before lenalidomide maintenance.
- Age alone should not preclude patients from receiving highly effective treatments aimed at cure or long-term disease control.

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CONTACT INFORMATION

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