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Updated results of a phase I open-label single-arm study of dual targeting BCMA and CD19 FasTCAR-T (GC012F/AZD0120) as first-line therapy for transplant-eligible newly diagnosed high-risk multiple myeloma

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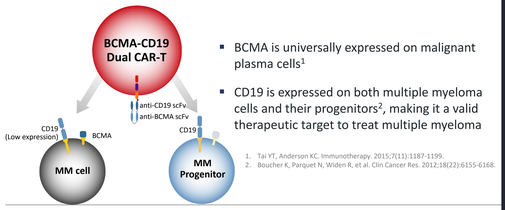
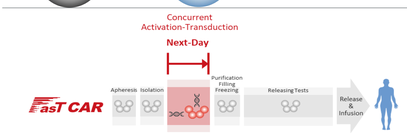
INTRODUCTION

GC012F: Targeting BCMA/CD19 is designed to drive fast, deep and durable responses in multiple myeloma (MM) patients



- BCMA is universally expressed on malignant plasma cells[1]
- CD19 is expressed on both multiple myeloma cells and their progenitors[2], making it a valid therapeutic target to treat multiple myeloma

1. Tai YT, Anderson KC. Immunotherapy. 2015;7(11):1187-1199.
2. Boucher K, Parquet N, Widen R, et al. Clin Cancer Res. 2012;18(22):6155-6168.



- Designed to address major challenges faced by conventional autologous CAR-T
- Key advantages:
  - Faster to patient
  - Enhanced CAR-T cell quality and materially higher concentration of young phenotype T cells

AIM

This is a phase I single-arm study conducted in the first-line setting for TE HR NDMM pts to evaluate the safety and feasibility of GC012F/AZD0120 CAR-T cell therapy (NCT04935580) .

METHOD

- Consent and Screening
- Apheresis
- RVd induction therapy 2 cycles
- GC012F Next Day Manufacturing
- QC Release
- Lymphodepletion D-5 to -3
- AZD0120 (GC012F) Single infusion D-0
  - DOSE LEVEL 1 1x10^5 cells/kg
  - DOSE LEVEL 2 2x10^5 cells/kg
  - DOSE LEVEL 3 3x10^5 cells/kg
- Post-infusion treatment based on PI's evaluation*
- Follow-up assessment visits

Key Eligibility Criteria:
-High-risk, transplant eligible, NDMM
-18-70 years old
-ECOG 0-2

All patients received two cycles induction therapy of RVd (bortezomib, lenalidomide, and dexamethasone) prior to CAR-T infusion.

*Lenalidomide maintenance therapy at 6 months post infusion was initiated per PI's discretion

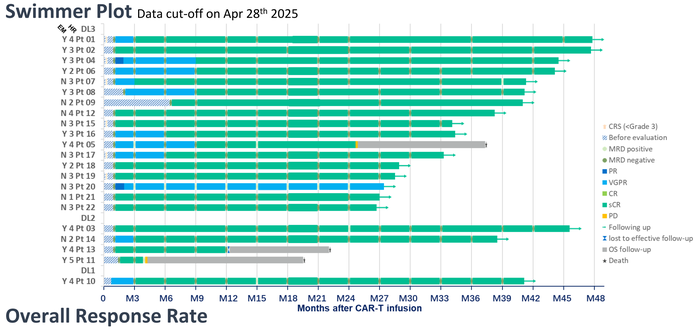
RESULTS

Baseline Characteristics	Total N=22
Median age, years (range)	59 (43-69)
Male, n (%)	14 (64)
Type of myeloma, n (%)	
IgG	9 (41)
IgA	7 (32)
IgD	2 (9)
Light chain	4 (18)
Induction therapy, n (%)	
2 cycles RVd	21 (95)
High-risk, n (%)	22 (100)
R-ISS stage II/III	20 (91)
High-risk cytogenetics[1]	11 (52)
Extramedullary disease	12 (55)
ECOG performance status, n (%)	
0	5 (23)
1	11 (50)
2	6 (27)

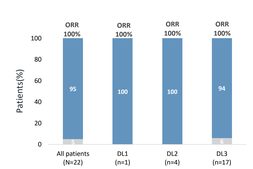
1. High-risk cytogenetics: del17p, t(4;14), t(14;16), or amp(1q21).

Efficacy Profile

Swimmer Plot Data cut-off on Apr 28th 2025



Overall Response Rate

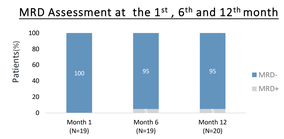


ORR 22/22 patients
95% sCR
MRD- 22/22 patients
100% sensitivity 10^{-6}

- Median duration of response (DOR) was not reached at data cut off
- Median duration of follow up: 37.1 months (range: 19.3 – 48.5 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

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

*20 pts used lenalidomide as maintenance treatment. The median time to initiation was 6 months post infusion.

Safety Profile

All CRS were Grade 1 or 2 and resolved within 4 days
No ICANS or Neurotoxicity was observed[2]

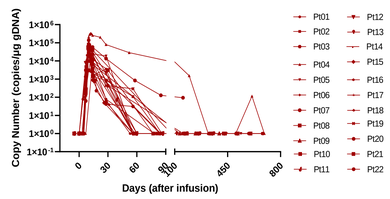
N=22	CRS[1] n (%)	ICANS[2] n (%)
Grade 1	5 (23)	0 (0)
Grade 2	1 (5)	0 (0)
Grade ≥ 3	0 (0)	0 (0)
All grade	**6 (27)**	**0 (0)**

CRS any grade	Median (days)	Range (days)
Time to onset	7	6-9
Duration	1	1-4

N=22	All Grades n (%)	Grade ≥3 n (%)
Hematologic TEAEs*		
Neutropenia	17 (77)	9 (41)
Leukopenia	19 (86)	10 (45)
Thrombocytopenia	6 (27)	0 (0)
Lymphopenia	17 (77)	14 (64)
Anemia	8 (36)	1 (5)
Non-Hematologic TEAEs*		
Infection	6 (27)	4 (18)
LDH increased	9 (41)	0 (0)
Hypoalbuminemia	9 (41)	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



- **Median Cmax** (copies/μg gDNA) : *60652 (8754–331159)*
- **Median AUC_{0-28}** (copies/μg gDNA*Days): *289685 (80181–3985420)*
- **Median Tmax** (Days): *10 (9-14)*

CONCLUSIONS

- **GC012F shows a favorable safety profile in newly diagnosed multiple myeloma patients**
  - Only 27% (6/22) patients experienced Grade 1-2 CRS
  - No Grade ≥3 CRS and no ICANS or any neurotoxicity observed
- **100% (22/22) ORR in high risk population**
  - 95% sCR
  - Patients continue being followed up for durable response
- **100% (22/22) MRD negativity at sensitivity of 10^{-6}**
- **FAST and DEEP responses with median DOR not reached**
- **GC012F BCMA/CD19 dual-targeting CAR-T cell therapy shows very encouraging anti-tumor activity in transplant-eligible, high risk, newly diagnosed multiple myeloma patients**

ACKNOWLEDGEMENT

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CONTACT INFORMATION

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