Bispecific antibodies ASH updates 2025

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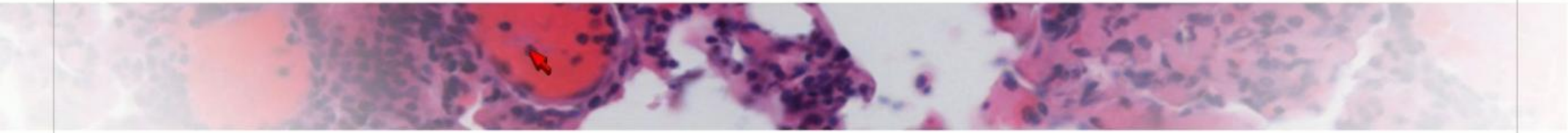


A phase 2 study of teclistamab in combination with daratumumab in elderly patients with newly diagnosed multiple myeloma: the IFM2021-01 TecLille trial, cohort A

S. Manier, J. Lambert, M. Macro, T. Chalopin, M. Dib, A. Rumpler, J. Gay, J.-N. Bastie, C. Jacquet, C. Sonntag, L. Vincent, A. Perrot, C. Mariette, L. Montes, S. Rigaudeau, N. Bigot, M. Doyle, D. Santra, P. Smirnov, C. Albrecht, C. Touzeau, J. Corre, P. Moreau, H. Avet-Loiseau, C. Hulin, X. Leleu, T. Facon

Abstract #367

ASH 2025, Orlando

ifm

CHU LILLE

IFM 2021-01 - Background

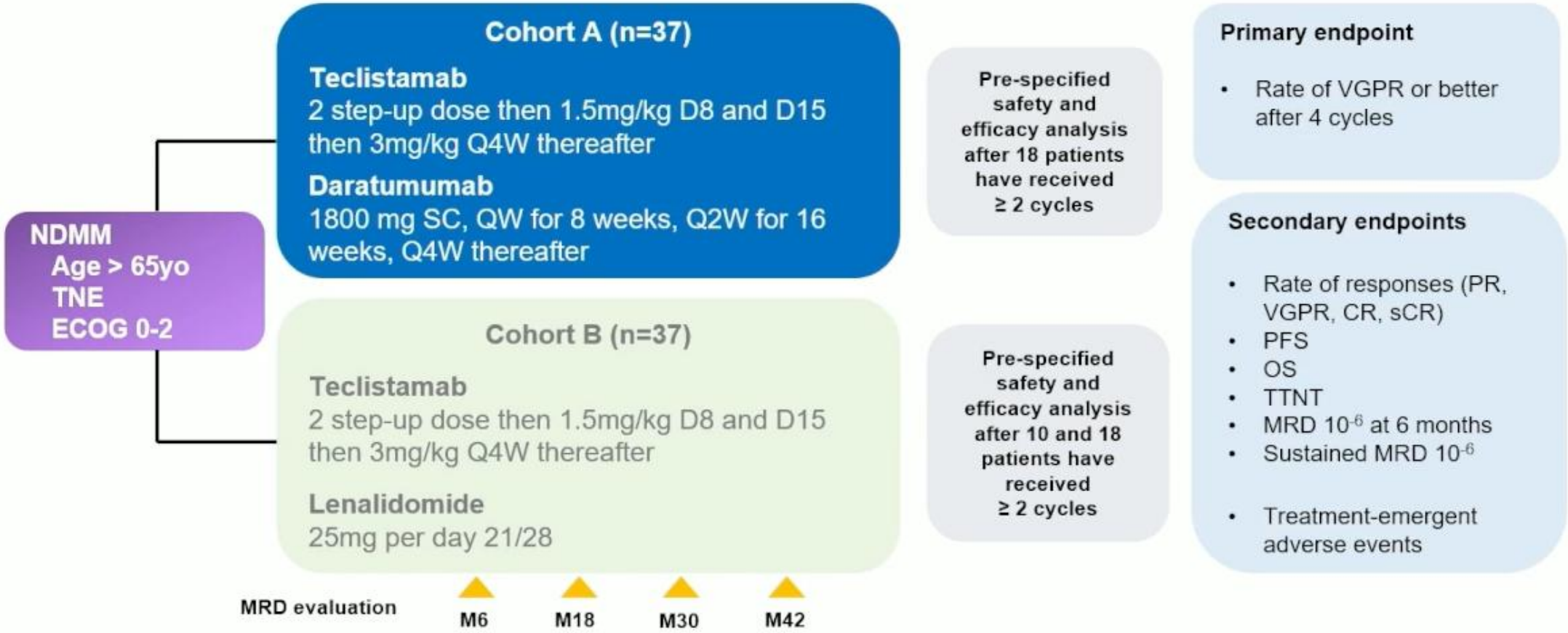
- The current standard-of-care regimens in elderly patients with newly diagnosed multiple myeloma (NDMM) include the triplet DRd (MAIA[1]) or quadruplet D-/Isa-VRd (CEPHEUS/IMROZ[2,3])
- These regimens show remarkable efficacy with 32% to 61% MRD negativity at 10^{-5} and prolonged PFS and OS[1,2,3]
- However, as patients ultimately relapse and treatments are given continuously, further optimization remains key
- Recently, the combination of teclistamab and daratumumab (Tec-Dara) has demonstrated strong efficacy in the relapsed setting with deep and durable responses[4]
- Most frontline trials currently evaluate triplet combinations of BCMA-directed bispecific antibodies with daratumumab and lenalidomide (MajesTEC-7 and MagnetisMM-6)

Here we made the hypothesis that a doublet with teclistamab-daratumumab (cohort A) – an "all-antibody" regimen - will be effective and limit toxicity in elderly patients with NDMM

[1]Facon et al. *NEJM* 2019, [2]Usmani et al. *Nature Med* 2025, [3]Facon et al. *NEJM* 2024, [4]Rodriguez-Otero et al. ASCO 2022

IFM 2021-01 TecLille - Study design

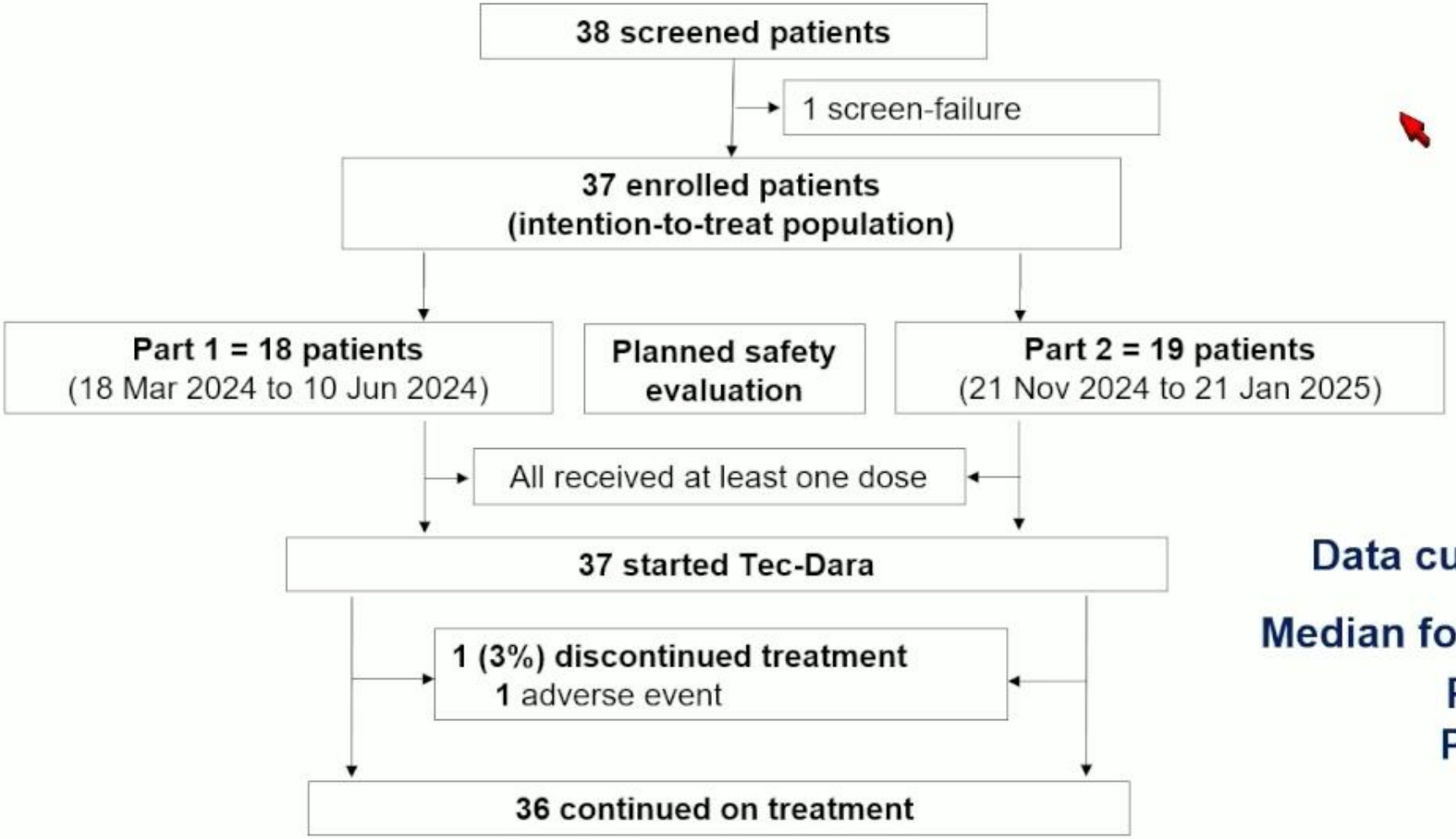
Phase 2 study of Tec-Dara and Tec-Len in TNE NDMM (n = 74)



Current amendment:
Teclistamab 3mg/kg Q8W after C13 if CR or better and treatment interruption if 2-years sustained MRD -

NCT05572229

IFM 2021-01 TecLille – cohort A: Tec-Dara
Patients disposition



Data cut-off on 04 Nov 2025

Median follow-up of 10.3 months

Part 1 mFU = 17 mo

Part 2 mFU = 9.5 mo

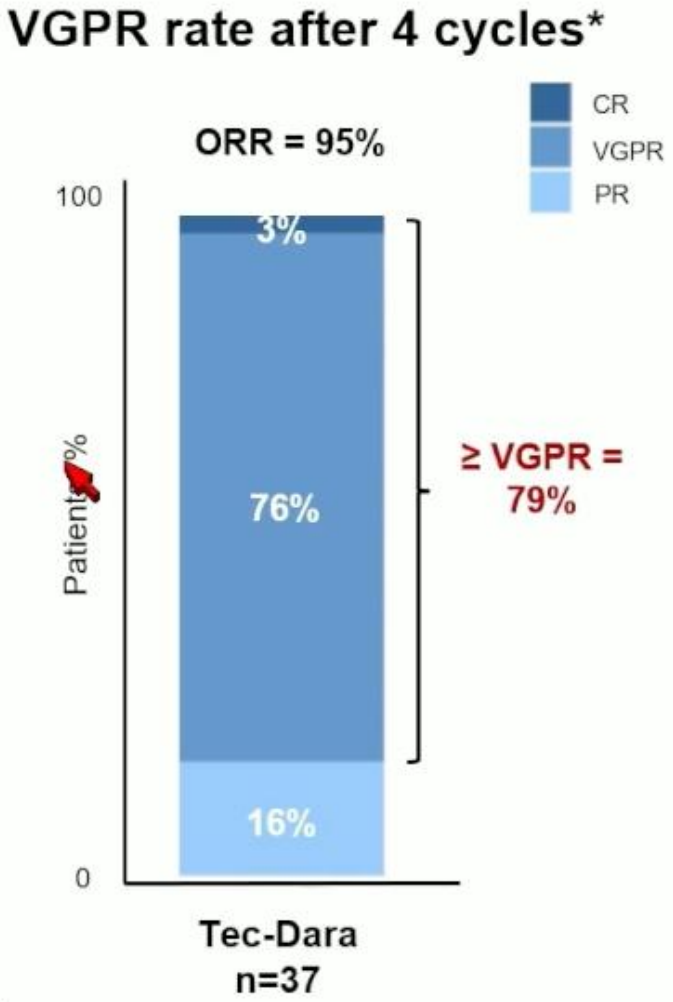
IFM 2021-01 TecLille – cohort A: Tec-Dara
Patients and disease characteristics

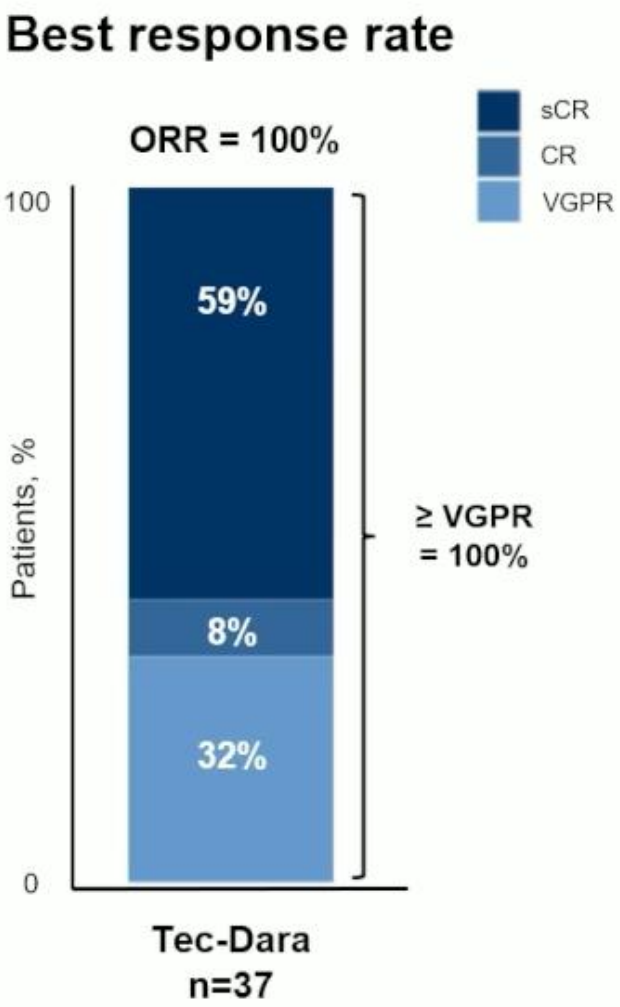
Patients characteristics	Tec-Dara (n=37)
Median age (range) - yr	73 (66-87)
Age category – no. (%)	
65 to < 70 yr	7 (19%)
70 to < 75 yr	18 (49%)
≥ 75 yr	12 (32%)
Sex - no. (%)	
Female	20 (54%)
Male	17 (46%)
ECOG – no. (%)	
0	9 (24%)
1	24 (65%)
2	4 (11%)
Frailty score (IMWG) – no. (%)	
Fit	16 (44%)
Intermediate	12 (33%)
Frail	8 (22%)
Creatinine clearance – no. (%)	
30 to < 60mL/min	14 (38%)
≥ 60 mL/min	23 (62%)

Disease characteristics	Tec-Dara (n=37)
Type of measurable disease – no (%)	
IgG	22 (59%)
IgA	8 (22%)
SFLC only	7 (19%)
ISS disease stage – no. (%)	
I	13 (35%)
II	19 (51%)
III	5 (14%)
Cytogenetic risk (IMWG/IMS) – no (%)	
Standard risk	25 (68%)
High risk	12 (32%)
del17p	4 (14%)
TP53 mutation	3 (10%)
t(4;14)	1 (3%)
t(14;16)	1 (3%)
t(14;20)	1 (3%)
gain 1q	11 (38%)
del1p32	2 (7%)
Extramedullary disease – no (%)	
No	35 (95%)
Yes	2 (5%)

Patients were representative of the TNE NDMM population

IFM 2021-01 TecLille – cohort A: Tec-Dara
Response rates





* primary endpoint

All patients achieved VGPR or better at best response

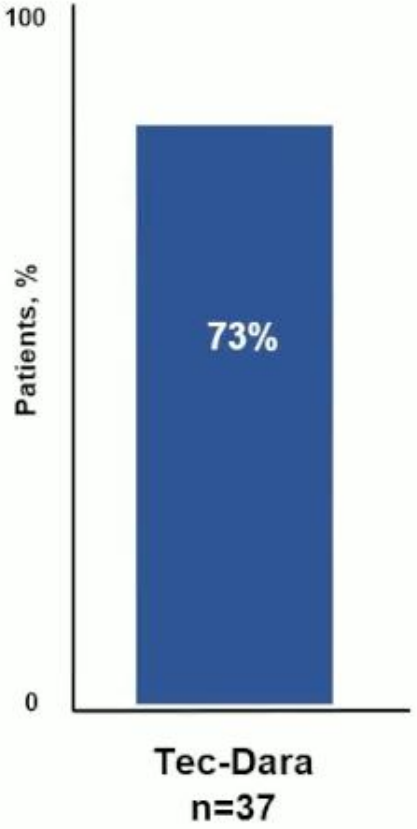
IFM 2021-01 TecLille – cohort A: Tec-Dara
MRD NGS 10^{-6} evaluation

All 37 patients had MRD evaluation by NGS (Clonoseq®) at 6 months. For technical reason, 27 patients were evaluable at 10^{-6}:

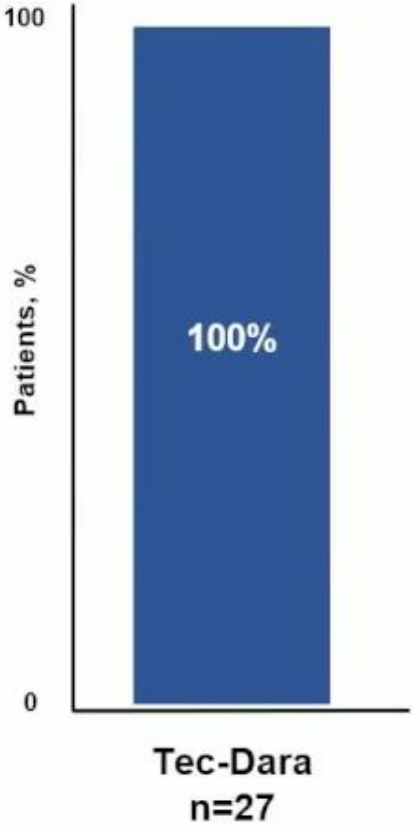
Missing causes	n
Calibration failure	4
Missing samples	3
Only evaluable at 10^{-5}	3

No patients had a positive MRD status.

MRD by NGS 10^{-6} at 6 months
ITT



MRD by NGS 10^{-6} at 6 months
Evaluable samples



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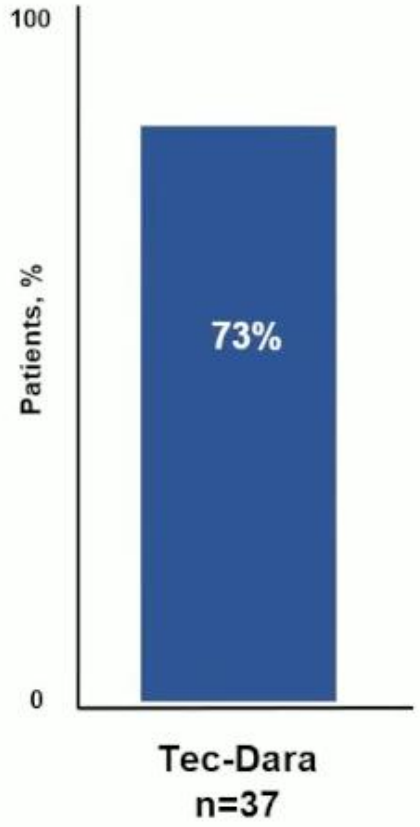

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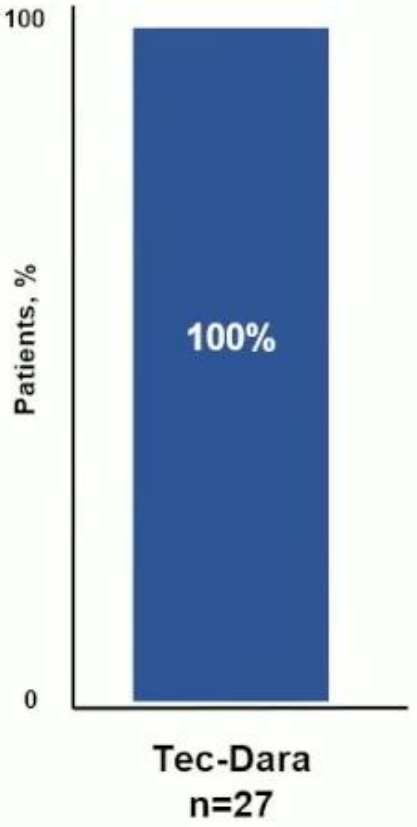
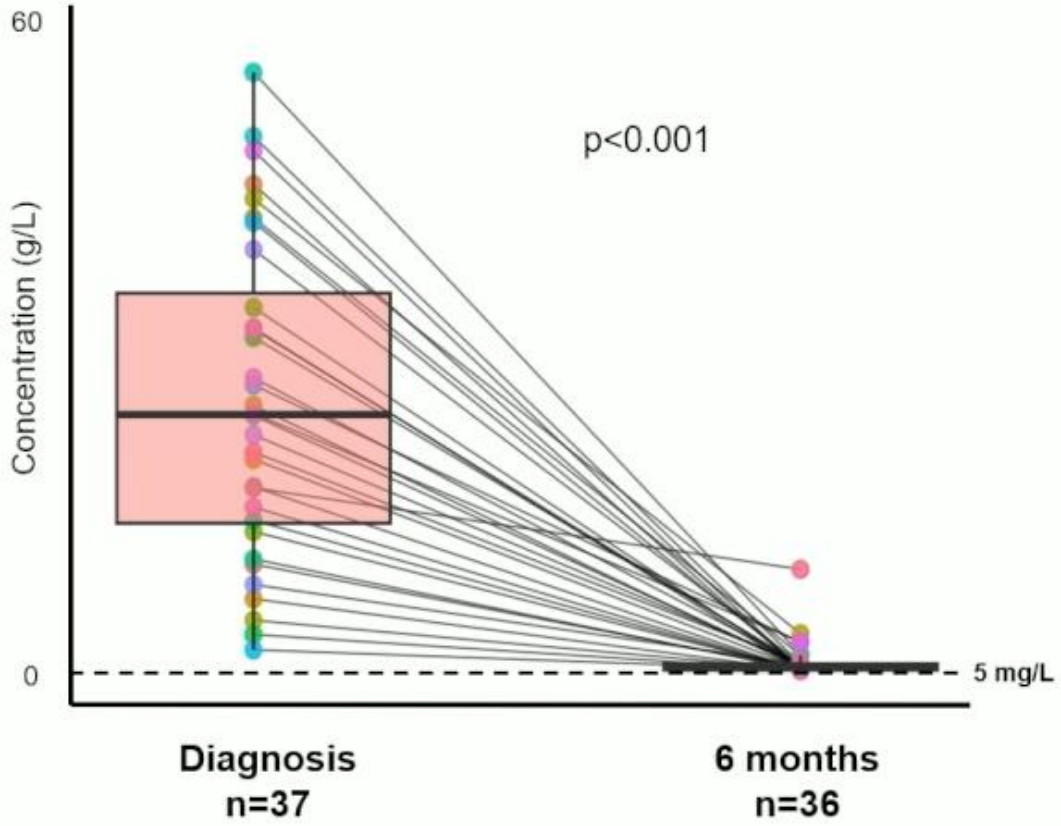


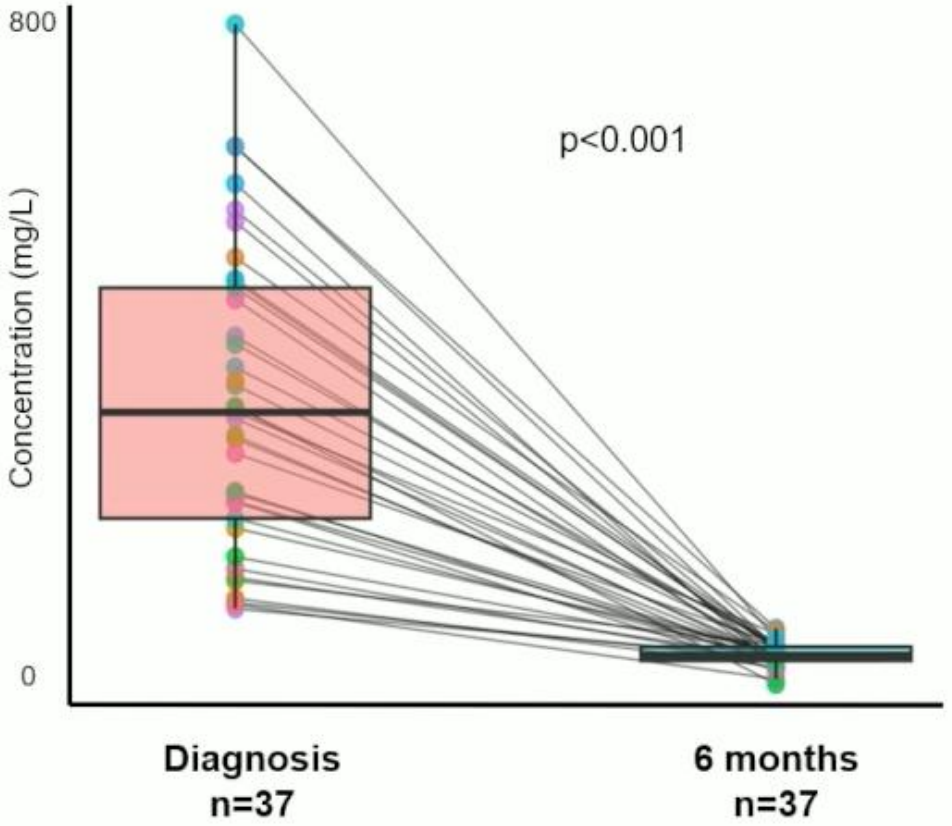
All evaluable samples were MRD negative at 10^{-6} by NGS at 6 months

IFM 2021-01 TecLille – cohort A: Tec-Dara
Tumor burden biomarkers

Clonotypic mass spec (M-insight®, Sebia) at 6 months



sBCMA by ELISA at 6 months

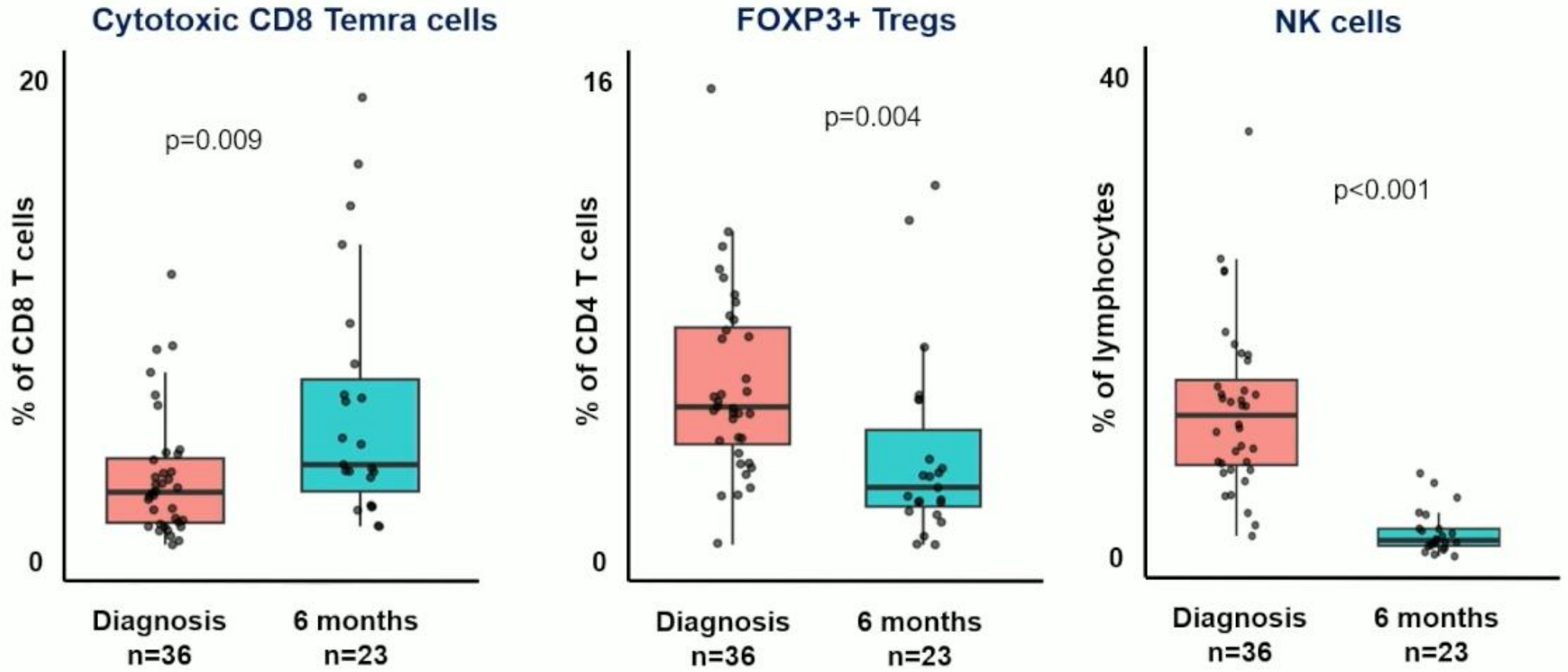


Deep decrease of clonotypes and sBMCA at 6 months

Only 3 patients had a clonotype < 5mg/L (equiv. MRD 10^{-5}) at this early time point

IFM 2021-01 TecLille – cohort A: Tec-Dara
Immune biomarkers

Flow cytometry immunomonitoring

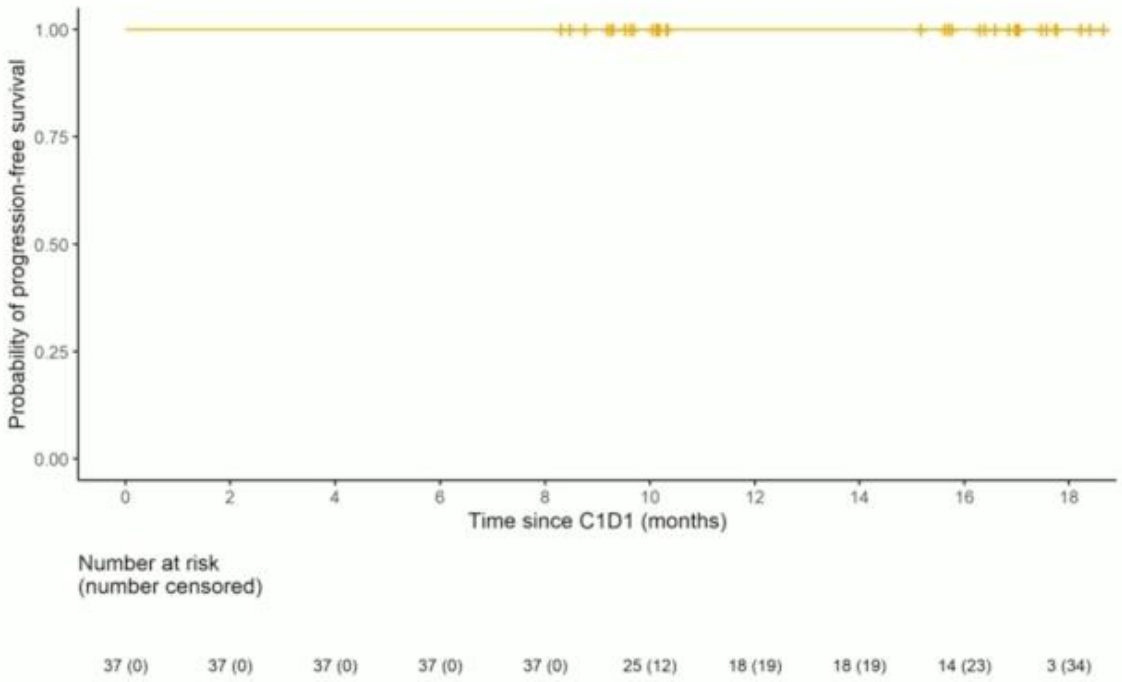


Immune remodeling at 6 months with increase of terminal effector memory T cells, and decrease of Tregs and NK cells

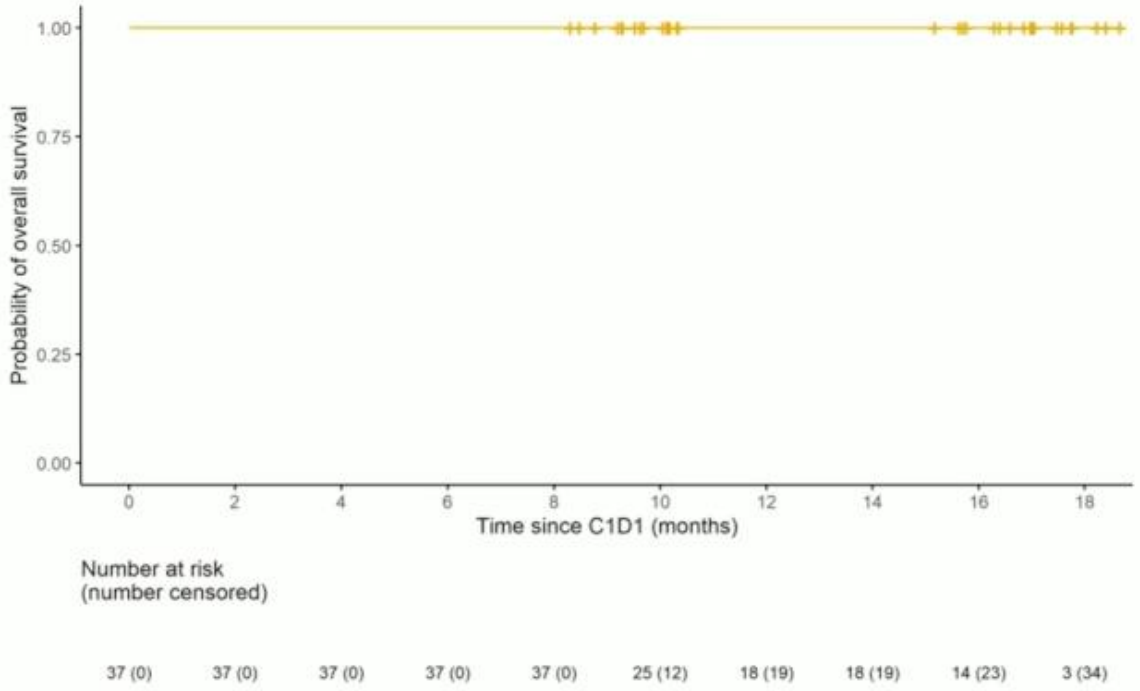
IFM 2021-01 TecLille – cohort A: Tec-Dara
PFS and OS

Median follow up time = 10.3 months

PFS



OS



No event of progression or death occurred

IFM 2021-01 TecLille – cohort A: Tec-Dara
Most common AEs

Grade ≥ 3 AEs

AEs, n(%)	Tec-Dara (n=37) Grade ≥ 3
All grade ≥ 3 AEs	29 (78%)
All grade ≥ 3 SAEs	10 (27%)
Grade 5	-
Hematologic AEs	26 (70%)
Lymphopenia	21 (57%)
Neutropenia	16 (43%)
Anemia	2 (5%)
Thrombocytopenia	1 (3%)
Non-hematologic AEs	10 (27%)
Infection	5 (14%)
Hepatic cytolysis	2 (5%)
Skin rash	2 (5%)

All grade AESI

	Tec-Dara (n=37)		
AESI, n(%)	All grade	Grade 1-2	Grade ≥ 3
Infections	24 (65%)	19 (52%)	5 (14%)
Bronchitis	6 (16%)	6 (16%)	-
COVID-19	5 (14%)	4 (11%)	1 (3%)
Urinary tract infection	5 (14%)	5 (14%)	-
Sinusitis	4 (11%)	4 (11%)	-
Pneumonia	3 (8%)	2 (5%)	1 (3%)
GI salmonella	1 (3%)	-	1 (3%)
Peritonitis	1 (3%)	-	1 (3%)
HHV6 infection	1 (3%)	-	1 (3%)
CRS	22 (59%)	G1: 13 (35%) G2: 9 (24%)	-
ICANS	-	-	-
Injection site reaction	7 (19%)	7 (19%)	-
Second primary malignancy	1 (3%)	1 (3%)	-

	Tec-Dara (n=37)
Treatment discontinuation due to AE*, n (%)	1 (3%)

* GI infection to salmonella

IFM 2021-01 TecLille – cohort A: Tec-Dara Conclusions

- The IFM2021-01 TecLille study demonstrates that an “all-antibody regimen” of teclistamab and daratumumab is highly effective and well-tolerated in TNE patients with NDMM
- With a median follow up of 10.3 months:
  - 100% of patients achieved a VGPR or better
  - All evaluable samples were MRD negative at 10^{-6} by NGS at 6 months
  - PFS and OS were 100%
  - No grade ≥ 3 CRS and no ICANS occurred
  - The rate of grade ≥ 3 infections was 14% with systematic IVIG prophylaxis

These results support further exploration in phase 3 clinical trial of frontline combination of BCMA/CD3 bispecific with anti-CD38 monoclonal antibodies

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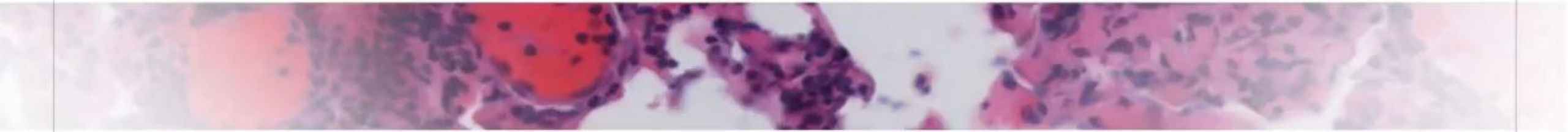

A Phase 2 Trial of Abbreviated Fixed-Duration (Default 4 Cycles) Linvoseltamab Immuno-Consolidation to Deepen Responses Post Newly Diagnosed Multiple Myeloma Combination Therapy for Minimal Residual Disease Positivity (NCT06376526): The ***IMMUNOPLANT™*** Study

Dickran Kazandjian*, Benjamin Diamond, James Hoffman, Abhishek Pandey, David Coffey, Marcella Kaddoura, Brian Walker, David Lessen, Yaharini, Rodriguez, Caterine Diaz, Stephanie Mompoint, Sindy Gutierrez, Jennifer Chapman, Yi Zhou, Mike Georgiou, Russ Kuker, Kellye Koubek, Andrew Kowalski, Leslie Gallardo, Stephanie Fernandes, Fiorela Flores, Rabia Bukhari, Sunwoo Han, Michelle Armogan, **Ola Landgren**

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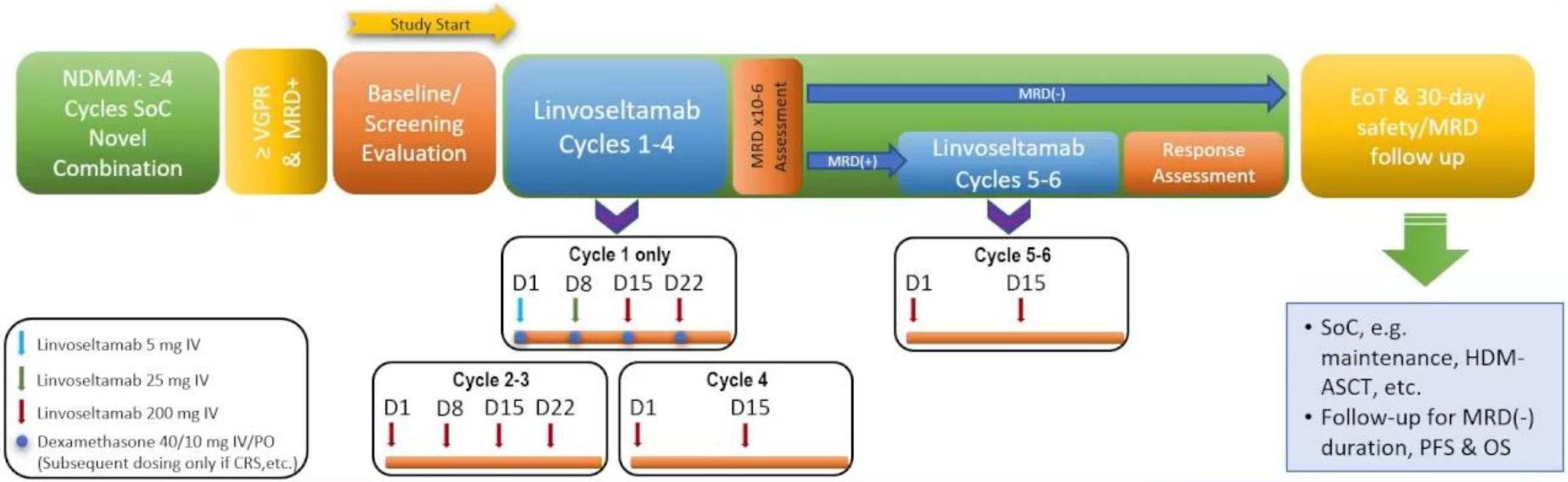
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM
MYELOMA INSTITUTE

Background

- PI, IMiD, and CD38 -based quadruplet therapies have delivered unparalleled clinical benefit independent of ASCT eligibility in NDMM treatment
- However, about half of patients do not attain MRD negativity after initial combination therapy
- Although ASCT remains an option for some patients, we developed a study using abbreviated fixed-duration (default 4 cycles) immunotherapy as a strategy to deliver deep and durable responses (MRD negativity $<10^{-6}$) after initial combination therapy
- Linvoseltamab is a T cell redirecting BiSpecific Ab (CD3xBCMA) approved for Relapsed/Refractory MM after ≥4 prior lines in the US and ≥3 prior lines in the EU
- IMMUNOPLANT™ is an on-going Investigator-Sponsored Study evaluating fixed short duration linvoseltamab consolidation in NDMM
- The pre-specified Stage 1 efficacy threshold was met and Stage 2 enrollment completed, herein we present these results as of Nov 1, 2025

Study Design: Schema

Immuno-consolidation for newly diagnosed **M**ultiple **M**yeloma **U**sing lack of MRD **N**egativity after initial c**O**mbination therapy to **P**ursue deeper responses with **L**invoseltamab **AN**d delay **T**ransplant:
The Phase 2 **IMMUNOPLANT™ Study**)



Key Eligibility

–PI/IMiD/anti-CD38 triplet/quad
–≥4 cycles with MRD+ ≥VGPR
–adequate organ function

Statistical Hypothesis:

- Simon Minimax 2-Stage Design: Target MRD(-) Rate: 30%; null MRD(-) Rate: 10%
- Stage I: ≥2 of 15 patients with response--> continue enrollment
- Stage II: total ≥6 of 25 patients with response→ reject null hypothesis
- One sided alpha = 0.05; Power = 80%

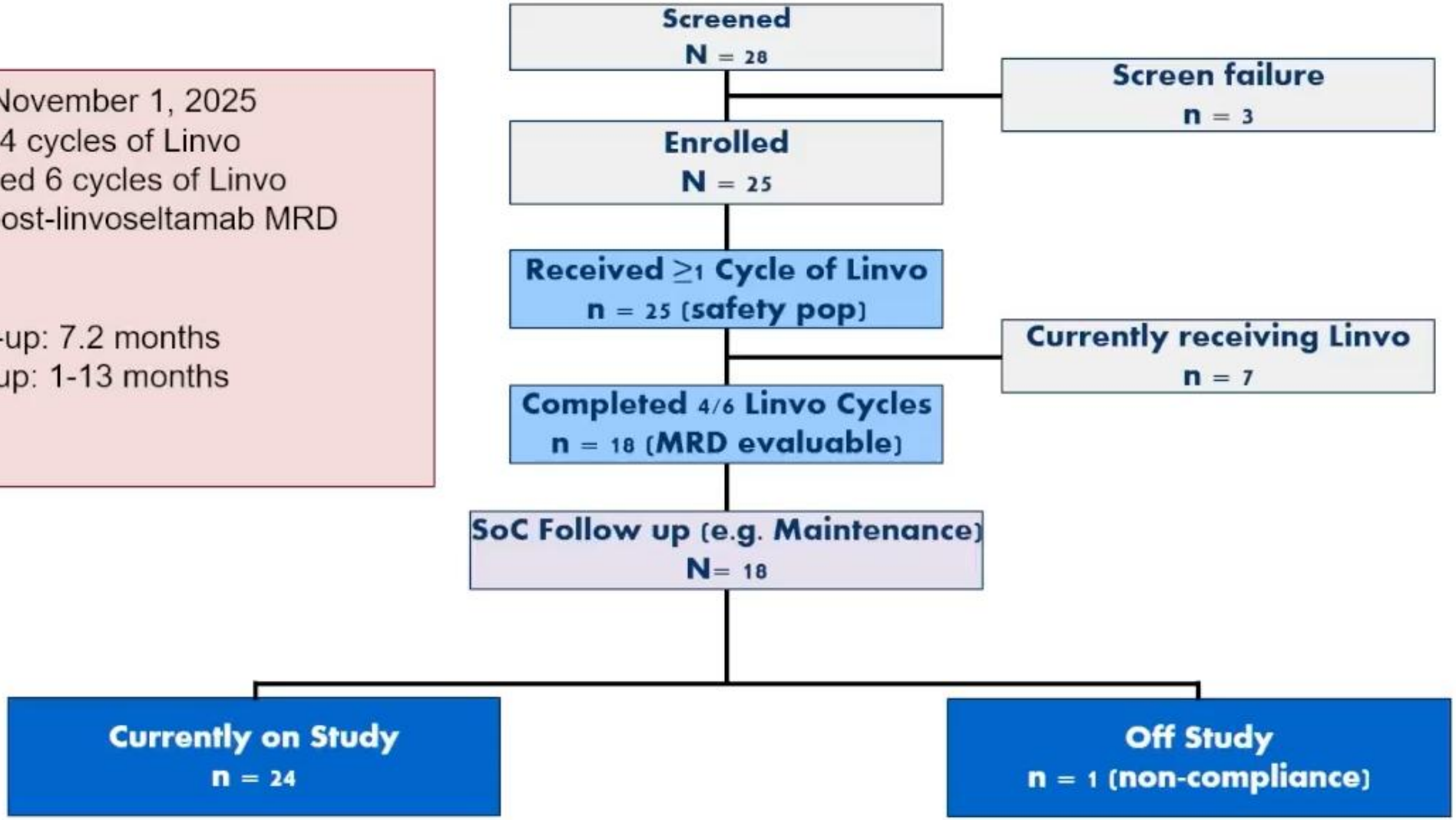
Endpoints:

Primary: MRD- 10^{-6}conversion rate
Secondary: Safety, sustained MRD negativity, PFS, OS

Patient Disposition

- Data cutoff – November 1, 2025
- 19 completed 4 cycles of Linvo
- 1 of 2 completed 6 cycles of Linvo
- 18 have had post-linvoseltamab MRD assessment

- Median follow-up: 7.2 months
- Range follow-up: 1-13 months

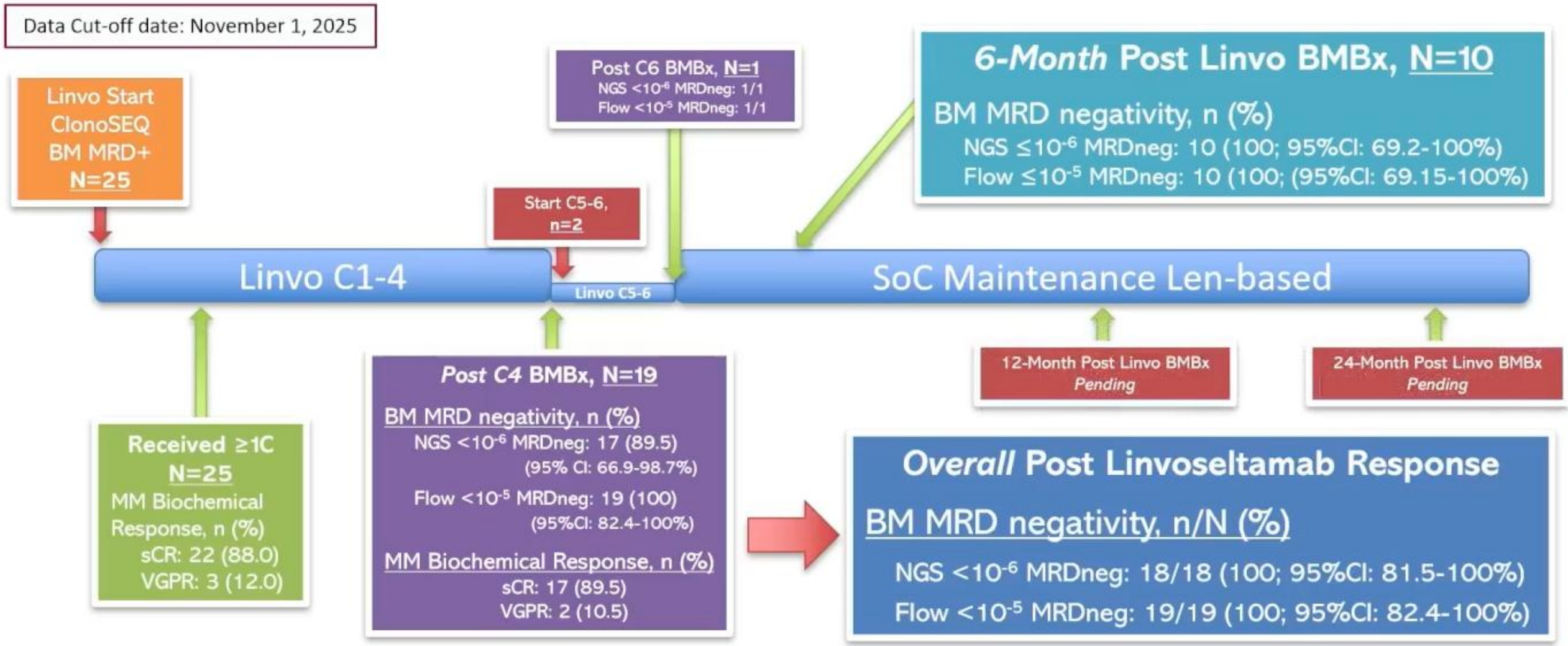


Patient Demographics and Disease Characteristics

Patient Demographics	N=25
Median age, years (range)	62 (40-77)
≥65, n (%)	8 (32)
Female, n (%)	8 (32)
ECOG PS, n (%)	
0	19 (76)
1	6 (24)
Ethnicity/Race, n (%)	
Black	4 (16)
Hispanic	11 (44)

Disease Characteristics	N = 25
MM Isotype, n (%)	
IgG	13 (52)
IgA	5 (20)
IgD	1 (4)
Light Chain only	6 (24)
FISH/Cytogenetics, n (%)	
High-Risk	7 (28)
Standard	14 (56)
Unknown	4 (16)
Median # of Initial Induction Cycles (range)	8 (6-13)
Initial NDMM Regimens, n (%)	
D-VRd	8 (32)
KRd	8 (32)
D-KRd	7 (28)
DRd	1 (4)
Isa-VRd	1 (4)
MRD+ ClonoSEQ at Study Start, n (%)	25 (100)
sCR	4 (16)
VGPR	21 (84)

Results: *Efficacy Timeline*



Results: PFS & OS

Progression-Free Survival:

- All 25 enrolled patients remain free from progression or relapse

Overall Survival:

- All 25 patients remain alive

Results: Safety & Tolerability

Common (>1 patient), Grade 3, Treatment-Related Adverse Events (N=25)		
TEAEs, n (%)	All grade	Grade 3
Neutropenia	5 (20)	2 (8)
Infection, Other (peritonsillar abscess)	1 (4)	1 (4)
Upper Respiratory Infection	7 (28)	–
ALT/AST Elevation	4 (16)	–
Diarrhea	4 (16)	–
Bone Pain	3 (12)	–
Cough	3 (12)	–
Fatigue	3 (12)	–
Nausea	3 (12)	–
Rash	3 (12)	–
Thrombocytopenia	3 (12)	–
Arthralgia	2 (8)	–
Hyperphosphatemia	2 (8)	–

Results: Safety & Tolerability

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Nausea	3 (12)	–
Rash	3 (12)	–
Thrombocytopenia	3 (12)	–
Arthralgia	2 (8)	–
Hyperphosphatemia	2 (8)	–

Results: Safety & Tolerability

- No patients had CRS/ICANS
- No patient deaths
- One patient had a Grade 3 SAE (peritonsillar abscess)
- No Grade 4 TRAEs
- Temporary dose delays occurred in 6 patients due to infection-related symptoms or neutropenia

Summary

- The IMMUNOPLANT™ Study using short/fixed (4-6cycles) duration bispecific T cell redirecting antibody, linvoseltamab, for immunoconsolidation of patients with MRD+ after initial combination induction appears to successfully convert patients to deep and potentially durable responses
  - MRD-negativity ($<10^{-6}$) rate of 100% (17 of 19 requiring only 4 linvoseltamab cycles)
  - 6-Month durable MRD negativity of 100%; 12 and 24 –month MRD evaluations upcoming
- Generally, manageable safety profile with expected toxicities and no new safety signals
- No CRS/ICANS; prophylactic one-time use of tocilizumab
- Given the magnitude of MRD negativity and favorable benefit to risk profile, the study has expanded to enroll 50 patients to more precisely determine efficacy and characterize safety