

Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma: Updated Phase 1b Results From RedirecTT-1 With >1 Year of Follow-Up

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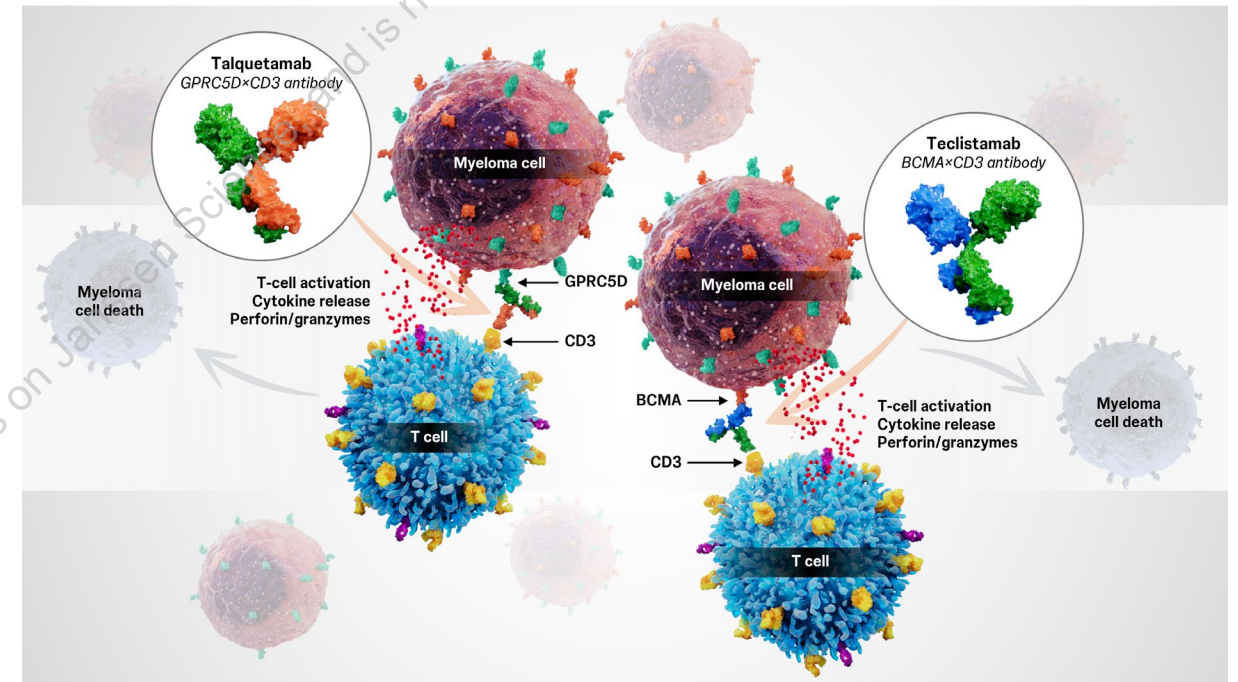
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RedirecTT-1 Tal + Tec: Dual Targeting of GPRC5D and BCMA

- Talquetamab (tal), the only approved GPRC5D-targeting BsAb, showed an ORR of $\geq 70\%$ with low rates of severe infections^{1,2}
- Teclistamab (tec), the first approved BCMA-targeting BsAb with the longest follow-up, showed deep and durable responses (ORR, 63%; \geq CR, 46%)^{3,4}
- Dual antigen targeting may overcome some resistance mechanisms to monotherapy
- Initial results of tal + tec in RedirecTT-1 showed promising efficacy in RRMM⁵
 - Safety profile of tal + tec was similar to that of each agent as monotherapy⁵
- Updated phase 1 results from RedirecTT-1 are reported, including in patients with EMD, with ~ 20 months of follow-up



ClinicalTrials.gov identifier: NCT04586426.

BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CR, complete response; EMD, extramedullary disease; GPRC5D, G protein-coupled receptor family C group 5 member D; ORR, overall response rate; RP2R, recommended phase 2 regimen; RRMM, relapsed/refractory multiple myeloma. 1. Rasche L, et al. Presented at EHA; June 13–16, 2024; Madrid, Spain & Virtual. 2. TALVEY (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2023. 3. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022. 4. Garfall AL, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. 5. Cohen YC, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual.



RedirecTT-1 Tal + Tec: Study Design

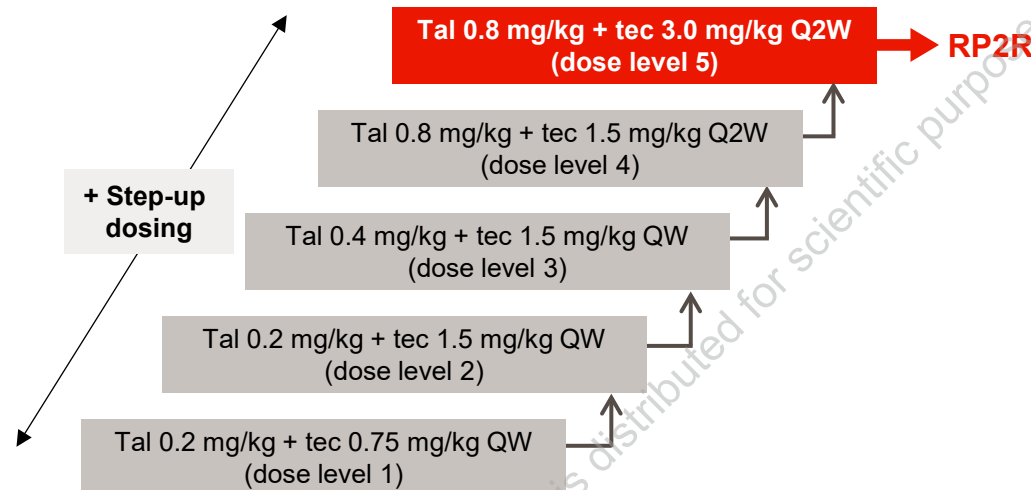
Key eligibility criteria

- Measurable MM
- EMD permitted (≥ 1 nonradiated, bone-independent lesion ≥ 2 cm)
- RR or intolerant to established therapies, including last LOT
- Triple-class exposed (prior PI, IMiD, anti-CD38)

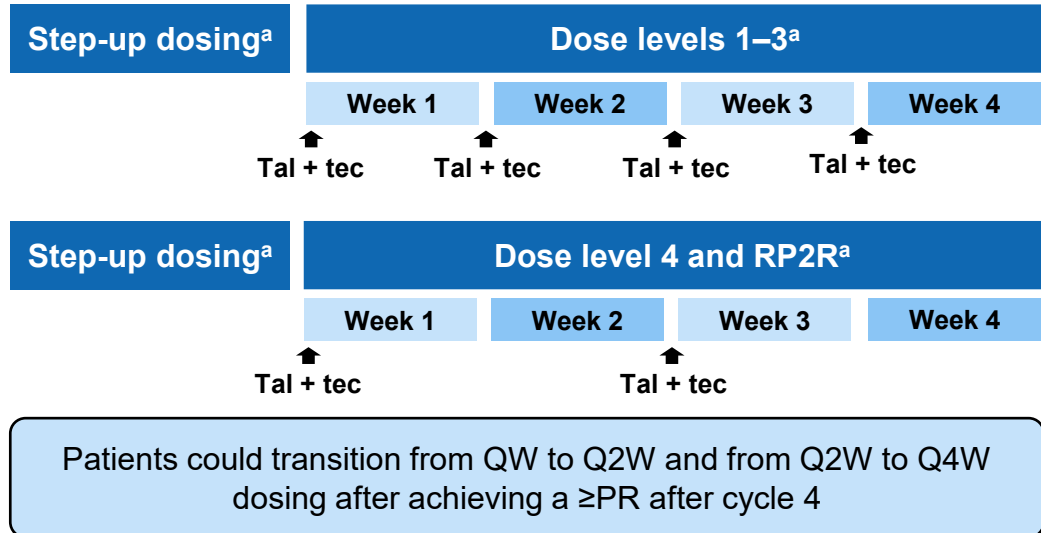
Key objectives

- Safety, including DLTs
- Identify RP2R(s)
- ORR, DOR, time to response, PK, immunogenicity
- PFS

Phase 1 dose escalation



Dosing schedule



^aTal and tec administered on the same day, 30 (± 10) minutes apart, for all step-up and full treatment doses. DLT, dose-limiting toxicity; DOR, duration of response; EMD, extramedullary disease; IMiD, immunomodulatory drug; LOT, line of therapy; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PR, partial response; Q4W, monthly, Q2W, every other week; QW, weekly; RP2R, recommended phase 2 regimen; RR, relapsed/refractory.



RedirecTT-1 Tal + Tec: Heavily Pretreated and a High Proportion of EMD

Characteristic	RP2R (n=44)	All doses (N=94)
Age (years), median (range)	63.0 (41–80)	64.5 (39–81)
Male, n (%)	23 (52.3)	49 (52.1)
Race, n (%)		
White	32 (72.7)	75 (79.8)
Black/African American	0 (0)	1 (1.1)
Asian	12 (27.3)	17 (18.1)
Unknown	0 (0)	1 (1.1)
Extramedullary plasmacytomas ≥ 1 , ^a n (%)	18 (40.9)	34 (36.2)
High risk cytogenetics, ^b n (%)	8 (42.1)	21 (41.2)
ISS stage, ^c n (%)		
I	19 (46.3)	38 (44.7)
II	14 (34.1)	26 (30.6)
III	8 (19.5)	21 (24.7)
Median years since diagnosis (range)	5.5 (0.3–12.9)	6.1 (0.3–14.6)

Characteristic	RP2R (n=44)	All doses (N=94)
Median prior LOT, n (range)	4.0 (2–10)	4.0 (1–11)
Exposure status, n (%)		
Belantamab mafodotin	5 (11.4)	18 (19.1)
CAR-T therapy ^d	2 (4.5)	4 (4.3)
Bispecific antibody ^e	2 (4.5)	7 (7.4)
Any BCMA-directed therapy	9 (20.5)	27 (28.7)
Triple class	44 (100.0)	94 (100.0)
Penta drug	28 (63.6)	61 (64.9)
Refractory status, n (%)		
Proteasome inhibitor	41 (93.2)	85 (90.4)
Immunomodulatory drug	41 (93.2)	91 (96.8)
Anti-CD38	43 (97.7)	93 (98.9)
Triple class	37 (84.1)	81 (86.2)
Penta drug	13 (29.5)	31 (33.0)
To last line of therapy	39 (88.6)	87 (92.6)

Triple-class exposed population, 36% with extramedullary plasmacytomas

Data cut-off date: March 15, 2024. Percentages were calculated with the number of patients with available data as the denominator.

^a ≥ 1 nonradiated, bone-independent lesion ≥ 2 cm. Patients with para-skeletal plasmacytomas were permitted but not counted as EMD. ^bFISH or karyotype testing in n=51 (all doses) and n=19 (RP2R). Defined as del(17p), t(4;14), or t(14;16). ^cIn n=85 (all doses) and n=41 (RP2R). ^dAcross all doses: BCMA-directed CAR-T (n=2) and not specified (n=2). ^eAcross all doses: alnuctamab (n=4), WV-T078 (n=2), and teclistamab (n=1). BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; EMD, extramedullary disease; ISS, International Staging System; LOT, line of therapy; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: CRS and ICANS Mostly Low Grade

	RP2R (n = 44)	All doses (N = 94)
Patients with CRS, ^a n (%)	33 (75.0)	74 (78.7)
Grade 1	23 (52.3)	50 (53.2)
Grade 2	10 (22.7)	22 (23.4)
Grade 3	0 (0)	2 (2.1)
Median days to onset ^b (range)	2 (1–4)	2 (1–733)
Median duration in days, (range)	2 (1–5)	2 (1–8)
Supportive measures, ^c n (%)	28 (63.6)	61 (64.9)
Tocilizumab	10 (22.7)	24 (25.5)
IV fluids	8 (18.2)	11 (11.7)
Corticosteroids	1 (2.3)	3 (3.2)
Oxygen	1 (2.3)	1 (1.1)
Vasopressor	0 (0)	1 (1.1)

- Most CRS events occurred during step-up and C1D1 doses
 - All events recovered, apart from 1 event that was recovering as of data cut-off date
- ICANS occurred in 3 patients (3.2%)
 - 1 grade 3 event
 - 2 events concurrent with CRS
- All ICANS events occurred during step-up doses
 - Median time to onset: 2–2.5 days
 - Median duration: 3 days
 - All events recovered

CRS and ICANS occurred early and were low grade, consistent with tal and tec monotherapy

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 20.3 months (all doses).

^aCRS and ICANS were graded per American Society for Transplantation and Cellular Therapy criteria. ^bRelative to the most recent dose. ^cPatients could receive >1 supportive therapy. Other supportive measures received by 12 patients (RP2R) and 26 patients (all doses). C1D1, cycle 1 day 1; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IV, intravenous; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: Safety Consistent With Known Profiles of Tal and Tec

Most common AEs (≥35% overall), ^a n (%)	RP2R (n=44)		All doses (N=94)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
CRS	33 (75.0)	0 (0)	74 (78.7)	2 (2.1)
Taste changes ^b	22 (50.0)	NA	61 (64.9)	NA
Nonrash skin AEs ^c	25 (56.8)	0 (0)	57 (60.6)	0 (0)
Nail-related AEs ^d	21 (47.7)	0 (0)	49 (52.1)	0 (0)
Pyrexia	14 (31.8)	1 (2.3)	48 (51.1)	2 (2.1)
Diarrhea	21 (47.7)	2 (4.5)	45 (47.9)	3 (3.2)
Cough	13 (29.5)	0 (0)	42 (44.7)	1 (1.1)
Dry mouth	18 (40.9)	0 (0)	40 (42.6)	0 (0)
COVID-19	21 (47.7)	6 (13.6)	38 (40.4)	17 (18.1)
Rash AEs ^e	14 (31.8)	1 (2.3)	37 (39.4)	1 (1.1)
Pneumonia	14 (31.8)	7 (15.9)	34 (36.2)	19 (20.2)

- 3 DLTs: oral herpes (dose level 1), elevated ALT/AST (dose level 3), and thrombocytopenia (RP2R)
- Discontinuations due to AEs:
 - 13.6% (n=6; RP2R), 16.0% (n=15; all doses)
- Grade 5 AEs:
 - 11.4% (n=5; RP2R), 14.9% (n=14; all doses)
 - Most (11/14) due to infections

Consistent safety profile between RP2R and all doses

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 20.3 months (all doses).

^aAEs graded by CTCAE v5.0; CRS per ASTCT criteria. ^bIncludes dysgeusia, ageusia, hypogeusia, and taste disorder; maximum grade for taste changes is 2 per CTCAE. ^cIncludes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. ^dIncludes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasia, nail dystrophy, nail toxicity, and nail ridging. ^eIncludes rash, maculopapular rash, erythematous rash, and erythema. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; NA, not applicable; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: Hematologic AEs Consistent With Monotherapies

Most common AEs (≥40% overall), ^a n (%)	RP2R (n=44)		All doses (N=94)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Neutropenia	30 (68.2)	25 (56.8)	69 (73.4)	64 (68.1)
Anemia	18 (40.9)	11 (25.0)	53 (56.4)	36 (38.3)
Thrombocytopenia	12 (27.3)	9 (20.5)	40 (42.6)	28 (29.8)

- Cytopenia profile expected with combination of tal + tec
- Low incidence of febrile neutropenia (12.8%)

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 20.3 months (all doses).

^aAEs were graded by Common Terminology Criteria for Adverse Events v5.0. AEs are listed in descending order of frequency. AE, adverse event; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: Grade 3/4 Infections Lower at RP2R

Most common AEs (≥5% overall), ^a n (%)	RP2R (n=44)		All doses (N=94)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Infections	38 (86.4)	21 (47.7)	84 (89.4)	60 (63.8)
COVID-19	21 (47.7)	6 (13.6)	38 (40.4)	17 (18.1)
Pneumonia	14 (31.8)	7 (15.9)	34 (36.2)	19 (20.2)
Upper respiratory tract infection	11 (25.0)	0 (0)	23 (24.5)	3 (3.2)
Nasopharyngitis	4 (9.1)	0 (0)	14 (14.9)	0 (0)
Sinusitis	4 (9.1)	0 (0)	12 (12.8)	1 (1.1)
Rhinovirus infection	2 (4.5)	0 (0)	10 (10.6)	3 (3.2)
Bronchitis	3 (6.8)	1 (2.3)	9 (9.6)	3 (3.2)
Respiratory tract infection	3 (6.8)	1 (2.3)	9 (9.6)	5 (5.3)
Urinary tract infection	7 (15.9)	1 (2.3)	9 (9.6)	1 (1.1)
Oral candidiasis	2 (4.5)	0 (0)	7 (7.4)	2 (2.1)
Sepsis	4 (9.1)	4 (9.1)	7 (7.4)	7 (7.4)
Septic shock	1 (2.3)	1 (2.3)	7 (7.4)	6 (6.4)

- Grade 3/4 infections:
 - 47.7% (RP2R), 63.8% (all doses)
- Grade 5 infections:
 - 6.8% (n=3; RP2R), 11.7% (n=11; all doses)
- Infection prophylaxis given per institutional guidelines
 - 81.9% received antiviral prophylaxis (all doses)
- 56.6% had hypogammaglobulinemia^b
 - 56.6% received ≥1 dose of IVIG

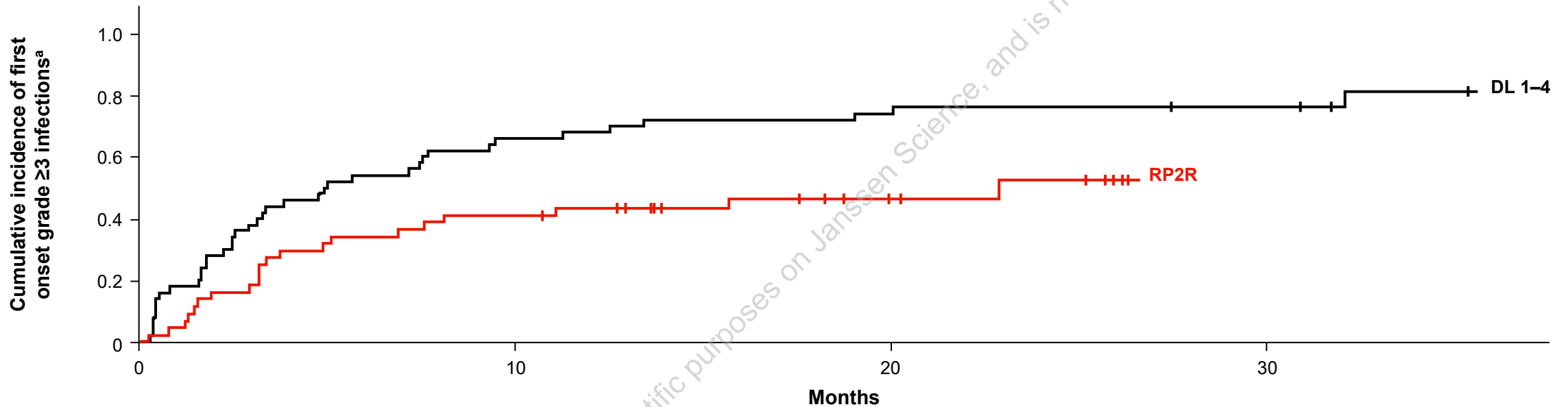
Although infections were common, lower incidence of severe infections at RP2R

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 20.3 months (all doses).

^aAEs were graded by Common Terminology Criteria for Adverse Events v5.0. ^bPost-treatment IgG <400 mg/dL or hypogammaglobulinemia treatment-emergent AE; excluded patients with IgG myeloma and after IVIG replacement. AE, adverse event; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: Cumulative Incidence of Severe Infections



Patients at risk

DL 1-4	50	33	21	17	13	11	10	8	7	7	5	5	5	5	4	4	1	1	0
RP2R	44	34	27	25	23	22	19	14	13	12	9	7	6	3	0	0	0	0	0

Cumulative incidence of grade ≥ 3 infections lowest with RP2R, leveled off at ~6 months

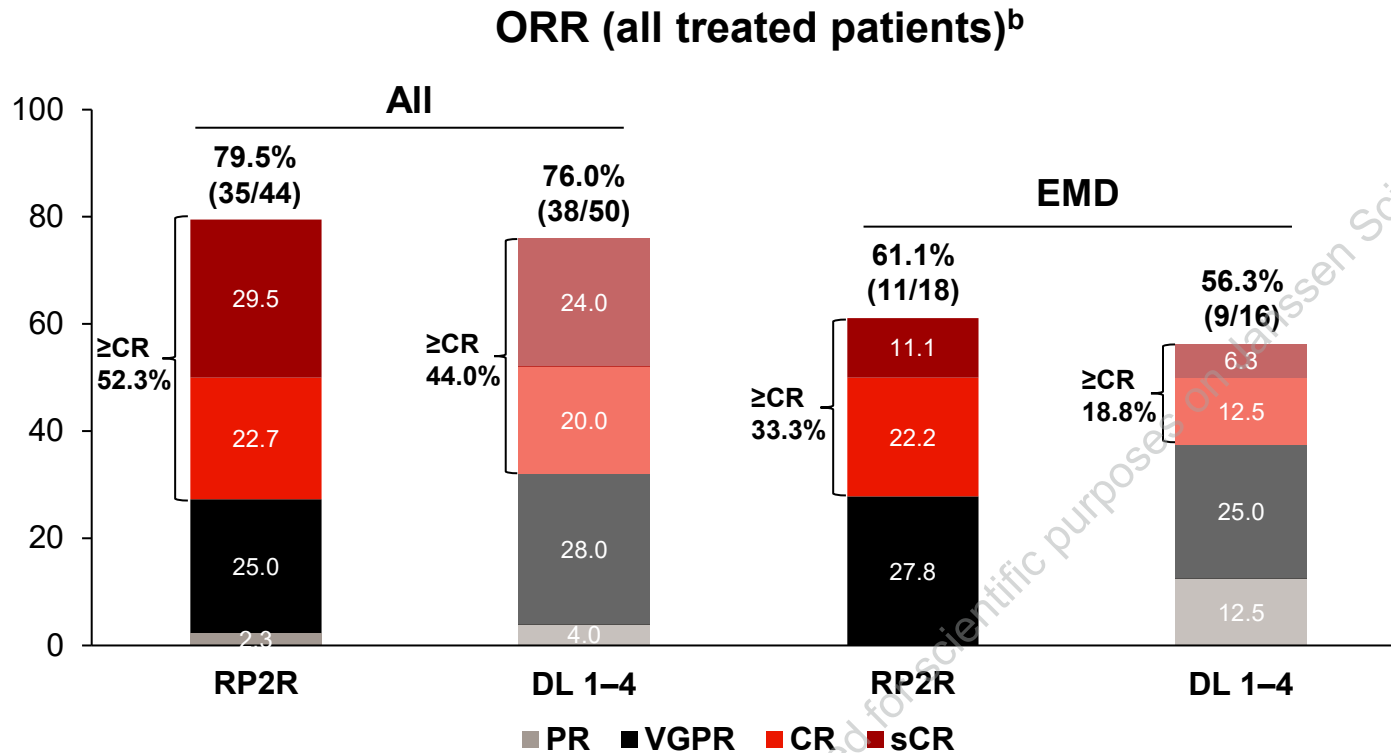
Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 29.0 months (dose levels 1-4).

^aData shown are system organ class infections and infestations and graded by Common Terminology Criteria for Adverse Events v5.0. DL, dose level; RP2R, recommended phase 2 regimen.

Presented by YC Cohen at 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil



RedirecTT-1 Tal + Tec: High ORR and Deep Responses, Including in EMD^a



All patients	RP2R (n=44)	DL 1-4 (n=50)
Median (range) follow-up, mos	18.2 (0.7-27.0)	29.0 (0.5 ^c -37.1)
Median (range) time to first response, mos	1.4 (0.3-5.1)	2.1 (1.1-7.7)
Median (range) time to best response, mos	4.9 (1.4-19.8)	4.9 (1.1-30.6)

Patients with EMD	RP2R (n=18)	DL 1-4 (n=16)
Median (range) follow-up, mos	13.6 (0.7-25.9)	18.7 (0.5 ^c -33.8)
Median (range) time to first response, mos	3.0 (1.4-5.1)	2.6 (2.1-3.8)
Median (range) time to best response, mos	6.3 (3.0-10.7)	3.9 (2.1-10.7)

ORR 79.5% (61.1% in EMD) at RP2R with rapid and deep responses

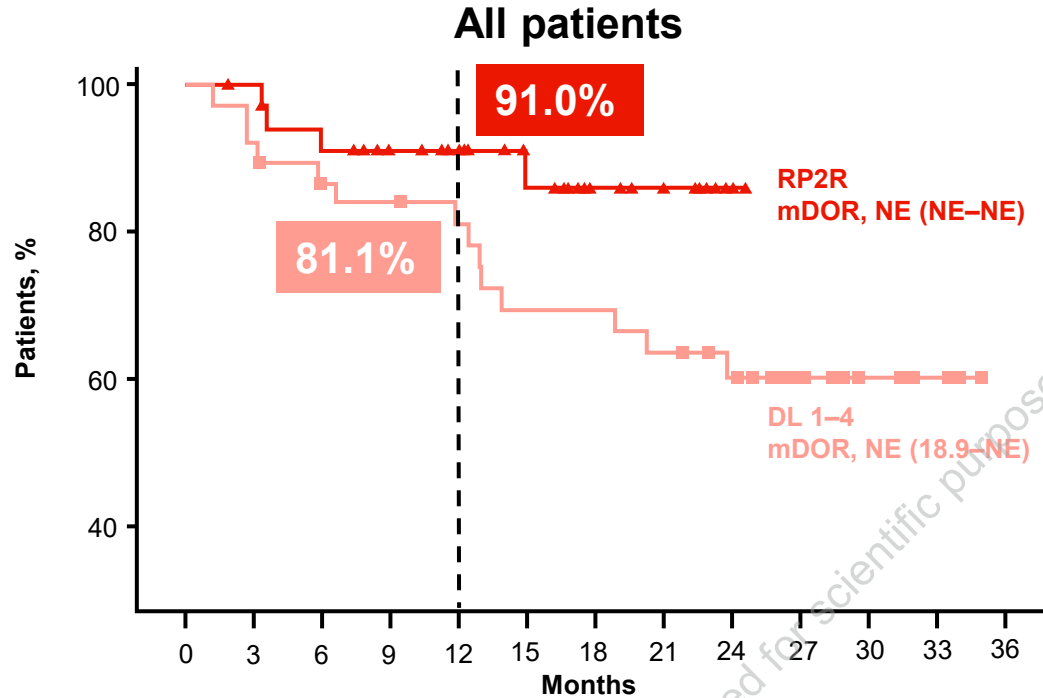
Data cut-off date: March 15, 2024.

^aEMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. ^bResponses were investigator-assessed per IMWG 2016 criteria. Data shown are confirmed responses and calculated in all treated patients. ^cDenotes patients who died. CR, complete response; DL, dose level; EMD, extramedullary disease; IMWG, International Myeloma Working Group; mos, months; ORR, overall response rate; PR, partial response; RP2R, recommended phase 2 regime; sCR, stringent complete response; VGPR, very good partial response.

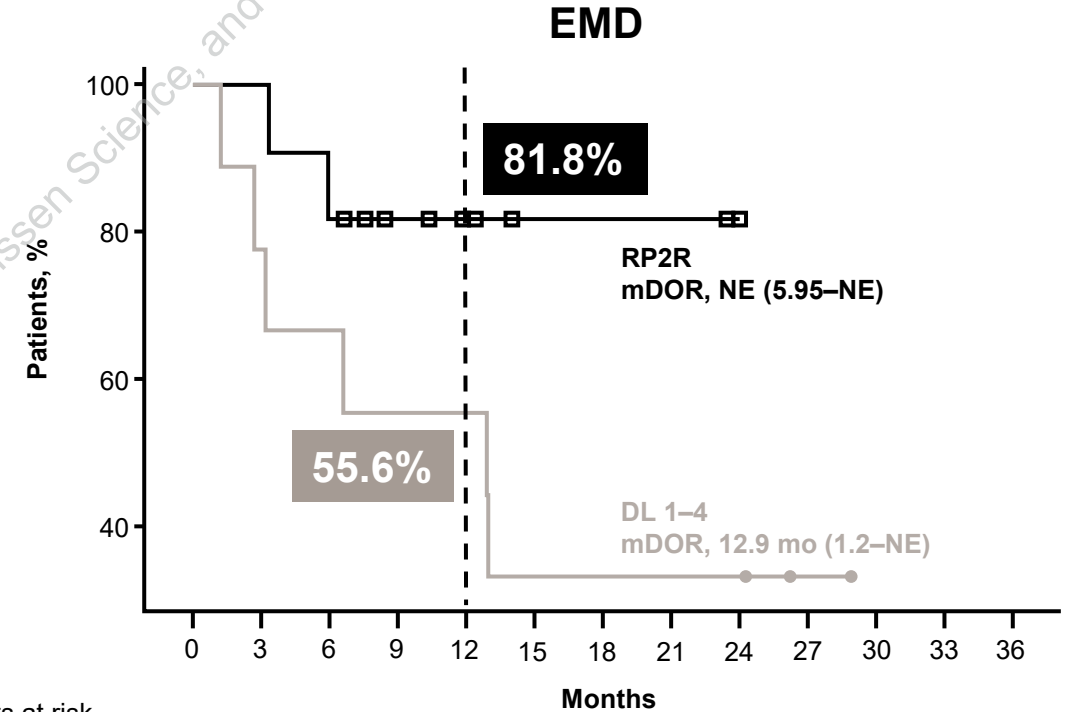


RedirecTT-1 Tal + Tec: Highly Durable Responses, Including in EMD^a

Duration of response (DOR)



Patients at risk	0	3	6	9	12	15	18	21	24	27	30	33	36
DL 1-4	38	35	31	30	28	24	24	22	18	12	5	3	0
RP2R	35	34	30	26	23	17	10	7	2	0	0	0	0



Patients at risk	0	3	6	9	12	15	18	21	24	27	30	33	36
DL 1-4	9	7	6	5	5	3	3	3	3	1	0	0	0
RP2R	11	11	9	6	5	2	2	2	1	0	0	0	0

12-mo DOR of 91.0% better at RP2R (81.8% 12-mo rate in EMD)

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 29.0 months (dose levels 1-4). **Eighteen-month DOR rates at the RP2R were 85.9% (all patients) and 81.8% (EMD patients).**

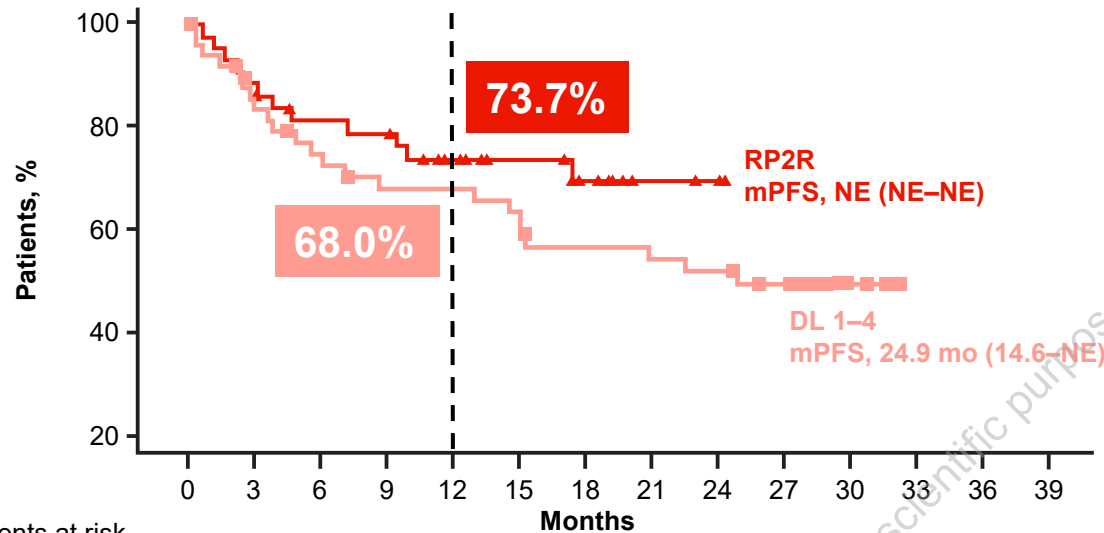
^aEMD defined as ≥ 1 nonradiated, bone-independent lesion ≥ 2 cm. DL, dose level; EMD, extramedullary disease; mDOR, median duration of response; NE, not evaluable; RP2R, recommended phase 2 regimen.



RedirecTT-1 Tal + Tec: Promising Early PFS, Including in EMD^a

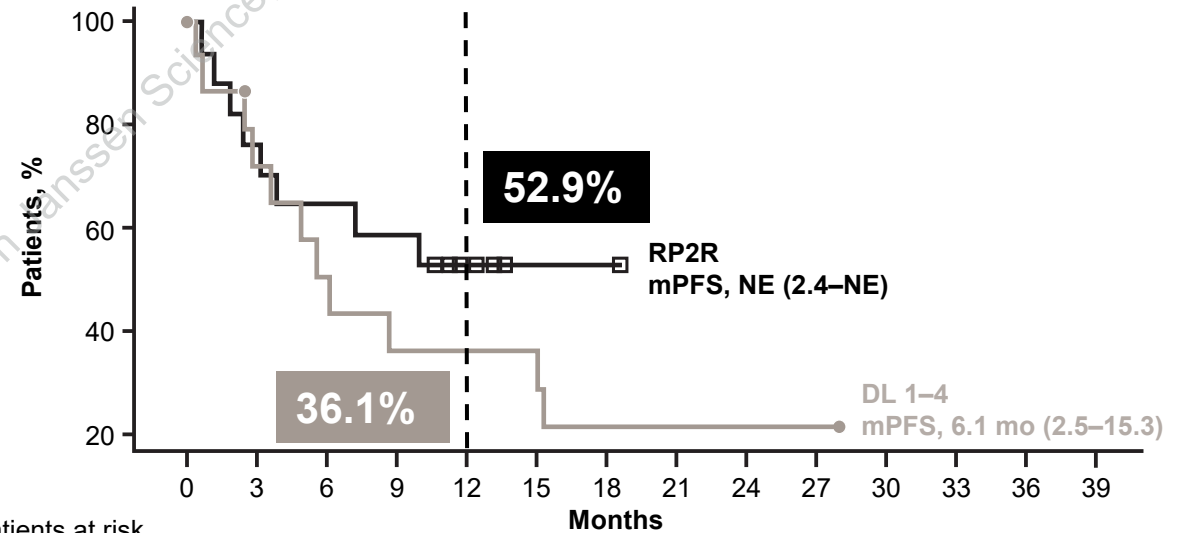
Progression-free survival (PFS)

All patients



Patients at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
DL 1-4	50	39	34	30	30	28	24	23	22	19	10	4	1	0
RP2R	44	38	33	32	26	20	16	8	7	0	0	0	0	0

EMD



Patients at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
DL 1-4	16	10	7	5	5	5	3	3	3	3	1	0	0	0
RP2R	18	13	11	10	6	3	3	2	2	0	0	0	0	0

12-mo PFS of 73.7% better at RP2R (52.9% 12-mo rate in EMD)

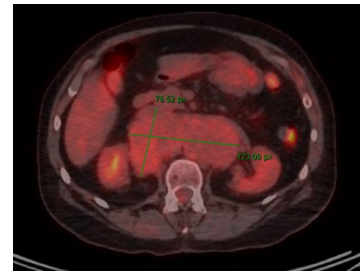
Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 29.0 months (dose levels 1-4). **Eighteen-month PFS rates at the RP2R were 69.8% (all patients) and 52.9% (EMD patients).**
^aEMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. DL, dose level; EMD, extramedullary disease; mPFS, median progression-free survival; NE, not evaluable; RP2R, recommended phase 2 regimen.



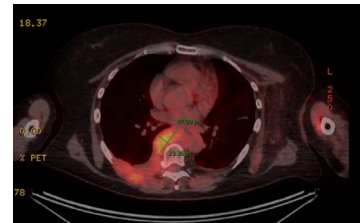
RedirecTT-1 Tal + Tec: Case Study

- 62-year-old female treated at the RP2R with 3 prior LOT (TCE). Patient in CR and ongoing treatment (C21)

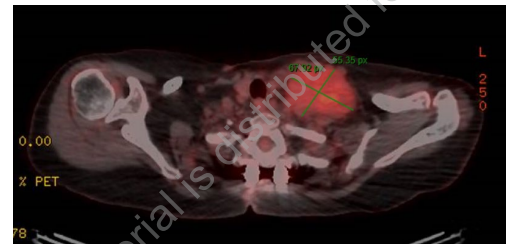
Patient with EMD treated at the RP2R



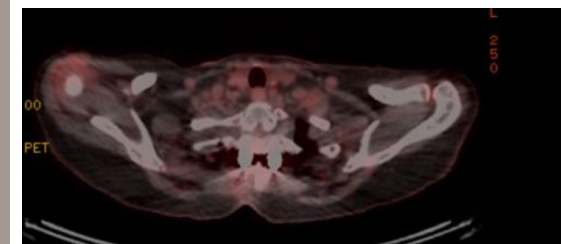
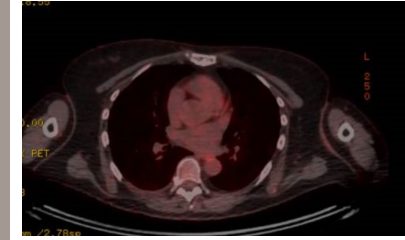
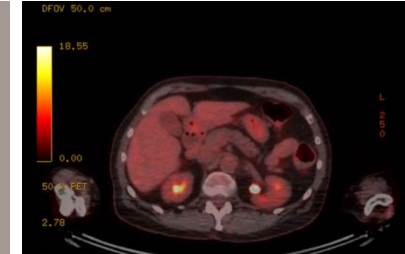
Peritoneum
12 cm × 8 cm



Paravertebral
4.4 cm × 2.3 cm



Supraclavicular
7 cm × 5.5 cm



RedirecTT-1 Tal + Tec: Findings From >1 Year Follow-up

- **Tal + tec had a safety profile generally consistent with each agent as monotherapy**
 - Infections were common but new onset grade ≥ 3 infections declined at 6 months
 - RP2R safety profile consistent with safety profile observed at all other dose levels
- **Deep and durable responses at the RP2R**
 - ORR of 79.5% (\geq CR 52.3%)
 - 12-month DOR rate of 91.0%, 12-month PFS rate of 73.7%
- **In EMD, best reported ORR and DOR for BsAb-based treatment at the RP2R**
 - ORR of 61.1% (\geq CR 33.3%)
 - 12-month DOR rate of 81.8%, 12-month PFS rate of 52.9%
- **Dual targeting of GPRC5D and BCMA may avoid antigen escape and clonal resistance**

RedirecTT-1, the first study combining 2 BsAbs to achieve dual antigen targeting, demonstrated deep and durable responses in RRMM, with impressive efficacy in hard-to-treat patients with EMD



Future Directions

Phase 2 of RedirecTT-1 at RP2R: Tal + Tec in EMD

RedirecTT-1 Phase 2 Study Design

Key eligibility criteria

- EMD (≥ 1 nonradiated, bone-independent lesion ≥ 2 cm)
- RRMM
- Triple-class exposed
- ECOG PS ≤ 2

Talquetamab (0.8 mg/kg)

+

Teclistamab (3.0 mg/kg)

Both Q2W C1–6 \rightarrow Q4W^a C7 until PD

Primary endpoint

- ORR

Key secondary endpoints

- DOR
- PFS
- OS
- Safety

^aOptional switch to Q4W dosing from C5+ if response is \geq VGPR and for any response C7+.

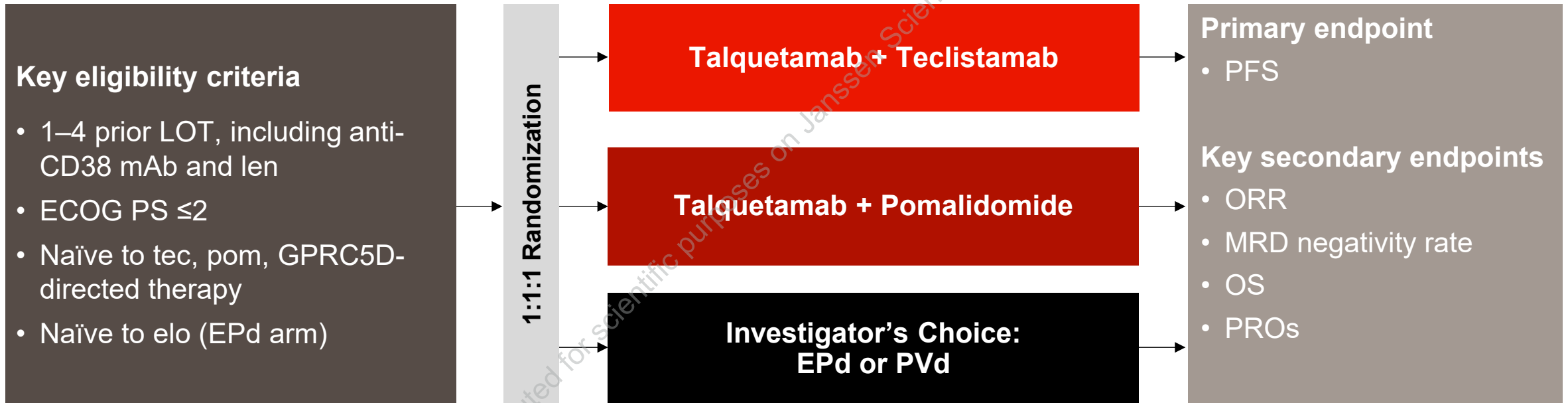
C, cycle; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EMD, extramedullary disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q4W, monthly; Q2W, every other week; RRMM, relapsed/refractory multiple myeloma; VGPR, very good partial response.



Future Directions

MonumenTAL-6: Tal + Tec in Earlier Lines

MonumenTAL-6 Study Design



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