First Results From the RedirecTT-1 Study With Teclistamab + Talquetamab Simultaneously Targeting BCMA and GPRC5D in Patients With Relapsed/Refractory Multiple Myeloma

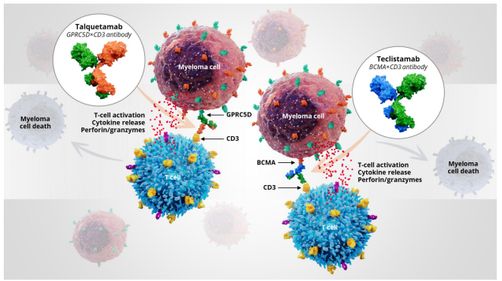
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INTRODUCTION

- Teclistamab (tec) is the only approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody (BsAb) with a personalized, weight-based dosing schedule for the treatment of triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM)[1]
  - Overall response rate (ORR) of 63% in MajesTEC-1[2]
- Talquetamab (tal) is the first approved G protein–coupled receptor family C group 5 member D (GPRC5D)-directed BsAb, with promising efficacy in patients with RRMM[3,4]
  - ORR of >70% in MonumenTAL-1[3]
- Targeting 2 distinct antigens may overcome some resistance mechanisms to monotherapy[5] (**Figure 1**)
- We report the first results from the phase 1b RedirecTT-1 trial (NCT04586426) in patients with RRMM, including a subset with extramedullary disease (EMD)

FIGURE 1: Teclistamab and talquetamab mechanism of action



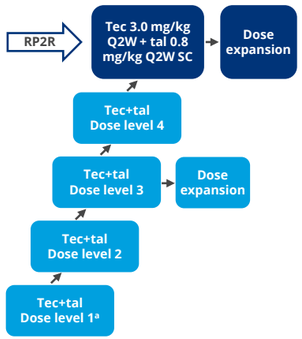
METHODS

Primary objectives
- Evaluate safety
- Identify recommended phase 2 regimen(s) (RP2R) and schedule for the combination (**Figure 2**)

Secondary objectives
- Preliminary anticancer activity of each study treatment at RP2R(s) in Part 2
- Pharmacokinetics
- Immunogenicity

Key eligibility criteria
- Measurable multiple myeloma per International Myeloma Working Group (IMWG) 2016 criteria[6]
- Relapsed/refractory or intolerant to established therapies, including last line of therapy
- Exposed to a proteasome inhibitor, immunomodulatory drug, and anti-CD38 monoclonal antibody

FIGURE 2: RedirecTT-1 study design



[a]Step-up doses were administered 2–4 days apart, similar to those used in the monotherapy studies.
Q2W, every other week; SC, subcutaneous.

MULTIPLE MYELOMA

RESULTS

Study population
- As of March 16, 2023, 93 patients were treated with tec+tal across all dose levels
  - Characteristics of patients treated at the RP2R (n=34) were consistent with those of the overall study population

Safety
- The safety profile was clinically manageable and consistent with that of the monotherapies (**Table 1**)
  - Febrile neutropenia occurred in 12.9% of patients across all dose levels, including 8.8% at the RP2R
  - No discontinuations due to hematologic TEAEs
- Rates of grade 3/4 nonhematologic TEAEs were low
  - 5 immune effector cell–associated neurotoxicity syndrome events occurred in 3 patients: 1 transient grade 3 event (non-RP2R); all others grade 1
- The majority of CRS events occurred during step-up dosing or cycle 1; all CRS events resolved (**Table 2**)
- Rates of discontinuations and death due to drug-related TEAEs were low
- Infections occurred in 83.9% of patients overall; 38.2% grade 3/4 at the RP2R (**Table 3**)
  - 81.7% with ≥1 post-baseline IgG value <400 mg/dL or hypogammaglobulinemia TEAE (all grade 1 or 2); 85.3% at the RP2R
  - Intravenous immunoglobulin was given to 37 patients (39.8%), including 15 (44.1%) at the RP2R

Efficacy
- Efficacy was assessed in response-evaluable patients (82/93)
  - 11/93 nonevaluable patients: 6 were ongoing without a postbaseline assessment at data cut-off; 5 discontinued before disease assessment (2 due to AEs, 3 withdrew consent)
- ORR was high (86.6%) across all dose levels and 96.3% at the RP2R (**Figure 3** and **Table 4**)
- At data cut-off, 61% (57/93) of patients remained on treatment

TABLE 1: TEAEs in RedirecTT-1

TEAE,[a] n (%)	All dose levels (N=93)		RP2R (n=34)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic TEAEs (≥20% overall)				
Neutropenia	61 (65.6)	57 (61.3)	19 (55.9)	15 (44.1)
Anemia	47 (50.5)	32 (34.4)	11 (32.4)	8 (23.5)
Thrombocytopenia	40 (43.0)	27 (29.0)	11 (32.4)	8 (23.5)
Nonhematologic TEAEs (≥25% overall)				
CRS	71 (76.3)	3 (3.2)	25 (73.5)	0
Dysgeusia[b,c]	57 (61.3)	–	16 (47.1)	–
Pyrexia	47 (50.5)	2 (2.2)	13 (38.2)	1 (2.9)
Skin toxicity[d]	50 (53.8)	0	18 (52.9)	0
Nail disorders[e]	43 (46.2)	0	14 (41.2)	0
Diarrhea	38 (40.9)	2 (2.2)	14 (41.2)	1 (2.9)
Cough	36 (38.7)	0	8 (23.5)	0
Dry mouth	35 (37.6)	0	11 (32.4)	0
Rash[f]	32 (34.4)	1 (1.1)	10 (29.4)	1 (2.9)
COVID-19	31 (33.3)	9 (9.7)	14 (41.2)	1 (2.9)
Pneumonia	25 (26.9)	10 (10.8)	4 (11.8)	2 (5.9)
Fatigue	24 (25.8)	7 (7.5)	6 (17.6)	2 (5.9)

[a]TEAEs were graded by CTCAE v5.0 with CRS events graded per ASTCT criteria. [b]Includes ageusia, dysgeusia, hypogeusia, and taste disorder. [c]Per CTCAE, the maximum grade of dysgeusia is 2. [d]Includes skin exfoliation, dry skin, pruritus, palmar-plantar erythrodysesthesia syndrome. [e]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, nail ridging. [f]Includes rash, rash papular, rash erythematous, erythema. ASTCT, American Society for Transplantation and Cellular Therapy; CTCAE, Common Terminology Criteria for Adverse Events.

Efficacy in EMD
- ORR was 71.4% across all dose levels for response-evaluable patients with EMD (all were soft tissue plasmacytomas) (**Figure 4**)
- At the RP2R (n=11):
  - Median DOR not reached at 7.2 months median follow-up (range, 0.7–14.2)
  - 85.7% (6/7 evaluable) ORR and 28.6% (2/7 evaluable) ≥CR

TABLE 2: Cytokine release syndrome

	All dose levels (N=93)	RP2R (n=34)
Patients with CRS,[a] n (%)	71 (76.3)	25 (73.5)
Grade 1	44 (47.3)	16 (47.1)
Grade 2	24 (25.8)	9 (26.5)
Grade 3	3 (3.2)	0
Time to onset (days),[b] median (range)	2 (1–5)	2 (1–4)
Duration (days), median (range)	2 (1–8)	2 (1–4)
Patients who received supportive measures,[c] n (%)		
Tocilizumab[d]	25 (26.9)	7 (20.6)
Steroids	4 (4.3)	0
Oxygen	7 (7.5)	0
Vasopressor	1 (1.1)	0

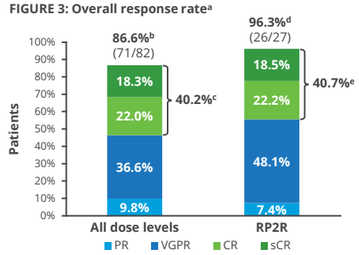
[a]CRS was graded by ASTCT criteria. [b]Relative to the most recent dose. [c]Patients could receive >1 supportive therapy. [d]Tocilizumab was allowed for all CRS events and was allowed at grade 1 CRS; the protocol did not recommend prophylactic tocilizumab use; no patients received tocilizumab prophylactically. CRS, cytokine release syndrome.

TABLE 3: Summary of infections

TEAE[a] (≥5% overall), n (%)	Total (N=93)		RP2R (n=34)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Infections	**78 (83.9)**	**49 (52.7)**	**27 (79.4)**	**13 (38.2)**
COVID-19	31 (33.3)	9 (9.7)	14 (41.2)	1 (2.9)
Pneumonia	25 (26.9)	10 (10.8)	4 (11.8)	2 (5.9)
Upper respiratory tract infection	11 (11.8)	2 (2.2)	4 (11.8)	0
Nasopharyngitis	8 (8.6)	0	2 (5.9)	0
Rhinovirus infection	8 (8.6)	2 (2.2)	2 (5.9)	0
Oral candidiasis	7 (7.5)	1 (1.1)	2 (5.9)	0
Septic shock	7 (7.5)	6 (6.5)[b]	1 (2.9)	1 (2.9)
Urinary tract infection	7 (7.5)	1 (1.1)	5 (14.7)	1 (2.9)
COVID-19 pneumonia	6 (6.5)	5 (5.4)	4 (11.8)	3 (8.8)
Bacteremia	5 (5.4)	2 (2.2)	1 (2.9)	0
Bronchitis	5 (5.4)	2 (2.2)	0	0
Sinusitis	5 (5.4)	0	1 (2.9)	0

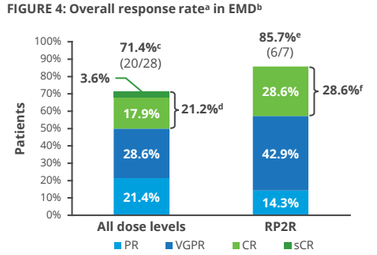
[a]TEAEs were graded by CTCAE v5.0. [b]There was 1 grade 5 septic shock.
TEAE, treatment-emergent adverse event.

FIGURE 3: Overall response rate[a]



[a]Response was assessed by investigators, based on IMWG criteria; response-evaluable patients have received ≥1 study treatment and have ≥1 adequate post-baseline response evaluation by investigator. [b]95% CI, 77.3–93.1%. [c]95% CI, 29.6–51.7%. [d]95% CI, 81.0–99.9%. [e]95% CI, 22.4–61.2%. CR, complete response; PR, partial response; sCR, stringent CR; VGPR, very good PR.

FIGURE 4: Overall response rate[a] in EMD[b]



[a]Response was assessed by investigators, based on International Myeloma Working Group criteria; response-evaluable patients have received ≥1 study treatment and have ≥1 adequate post-baseline response evaluation by investigator. [b]EMD was strictly defined as plasmacytomas originating in soft tissue. [c]95% CI, 51.3–86.8%. [d]95% CI, 8.3–41.0%. [e]95% CI, 42.1–99.6%. [f]95% CI, 3.7–71.0%.

TABLE 4: Efficacy summary

	All dose levels (N=93)	RP2R (n=34)
Follow-up (months), median (range)	13.4 (0.3–25.6)	8.1 (0.7–15.0)
DOR[a] (months), median (95% CI)	NE (NE–NE)	NE (NE–NE)
Time to first response[a] (months), median (range)	1.97 (0–7.7)	1.48 (0–4.0)
Time to best response[a] (months), median (range)	3.98 (1.1–15.7)	3.22 (1.4–10.7)
PFS[b] (months), median (95% CI)	20.9 (13.0–NE)	NE (9.9–NE)
9-month PFS rate[b] (95% CI)	70.1 (58.0–79.4)	77.1 (50.8–90.5)

[a]Includes only patients with confirmed responses. [b]All treated patients. DOR, duration of response; NE, not estimable; PFS, progression-free survival.

KEY TAKEAWAY

Teclistamab (BCMA×CD3) + talquetamab (GPRC5D×CD3) is the first-ever reported dual bispecific combination for hematologic malignancies; these results support the initiation of larger studies with the combination of teclistamab and talquetamab

CONCLUSIONS

- 96% ORR with Q2W teclistamab + talquetamab in the RP2R in TCE multiple myeloma, competitive with CAR-T cell therapies
- Notable 85.7% ORR at the RP2R in patients with extramedullary soft tissue plasmacytomas, with median DOR not reached at 7.2 months of follow-up
- The safety profile of the combination was consistent with that of monotherapies, with no new or additive toxicity

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DISCLOSURES

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