PF747

Talquetamab Immunogenicity and Impact on Exposure, Efficacy, and Safety: Analyses From Patients With Relapsed/Refractory Multiple Myeloma in MonumenTAL-1

Jue Gong[1], Thomas Renaud[2], Sheetal Khedkar[3], Brandi W Hilder[1], Tara J Masterson[1], Michela Campagna[4], Bonnie W Lau[2], Bonnie Wu[1], Jenny Zhang[1], Nahor Haddish-Berhane[1], Indrajeet Singh[5]

[1]Johnson & Johnson, Spring House, PA, USA; [2]Johnson & Johnson, Raritan, NJ, USA; [3]Johnson & Johnson, Horsham, PA, USA; [4]Johnson & Johnson, Madrid, Spain; [5]Johnson & Johnson, La Jolla, CA, USA

Key Takeaway

Incidence of ADA and/or NAb did not appear to affect the benefit-risk balance of talquetamab for patients with RRMM

Conclusions

Although treatment-emergent ADA and NAb were observed in 35.8% and 18.2%, respectively, of patients with RRMM treated at the talquetamab RP2Ds, there was no apparent clinically meaningful impact of ADA or NAb on the PK, efficacy, or safety of talquetamab

These results, including data generated using a revised and highly sensitive NAb assay in line with regulatory requirements, were consistent with previously reported immunogenicity results[4]

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Poster

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Acknowledgments

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Disclosures

JG is an employee of Johnson & Johnson.

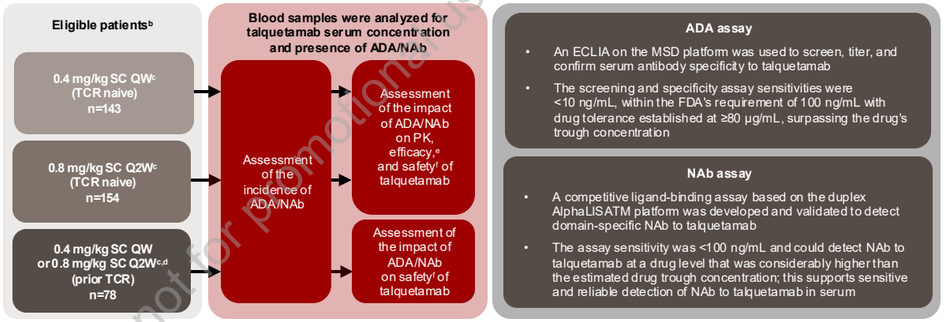
Introduction

- Talquetamab is the first approved bispecific antibody targeting G protein–coupled receptor class C group 5 member D for the treatment of relapsed/refractory multiple myeloma (RRMM)[1,2]
- In the phase 1/2 MonumenTAL-1 study (data cutoff: Jan 2024; median follow-up, 21–30 months), talquetamab showed high overall response rates (ORRs) of >66% and durable responses in patients with and without prior T-cell redirection (TCR) therapy[3]
- In previously reported immunogenicity results (data cutoff: Jan 2023), antidrug antibodies (ADA) were seen in patients treated with talquetamab at the recommended phase 2 doses (RP2Ds) but had no apparent impact on the pharmacokinetics (PK), efficacy, or safety of talquetamab[4]

We report updated immunogenicity results (data cutoff: Sept 2024), including data generated using a revised neutralizing antibody (NAb) assay, and their impact on the PK, efficacy, and safety of talquetamab in MonumenTAL-1

Methods

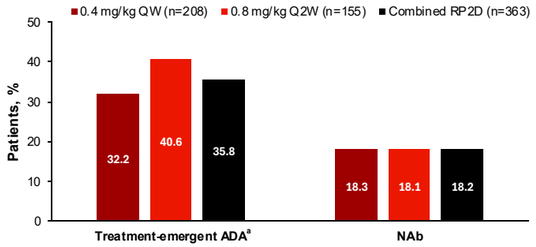
MonumenTAL-1[a] phase 1/2 study design and immunogenicity analyses



[a]NCT03399799/NCT04634552. [b]Patients were intolerant to or progressed on established therapies and had an ECOG PS ≤1 (phase 1) or had ≥3 prior LOT (≥1 PI, ≥1 IMiD, ≥1 anti-CD38 mAb) and an ECOG PS ≤2 (phase 2). [c]With 2–3 step-up doses. [d]Patients received QW (n=70) or Q2W (n=8) dosing. [e]Assessed by IRC using IMWG criteria.[5,6] [f]CRS and ICANS were graded by ASTCT criteria[7]; all other AEs were graded by CTCAE v4.03. AE, adverse event; ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ECLIA, electrochemiluminescence-based immunoassay; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; International Myeloma Working Group; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous.

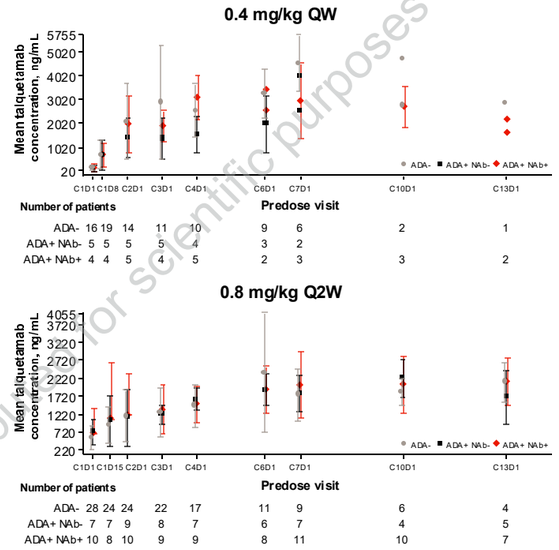
Results

Figure 1: ADA and NAb were detected in patients with and without prior TCR treated at the RP2Ds



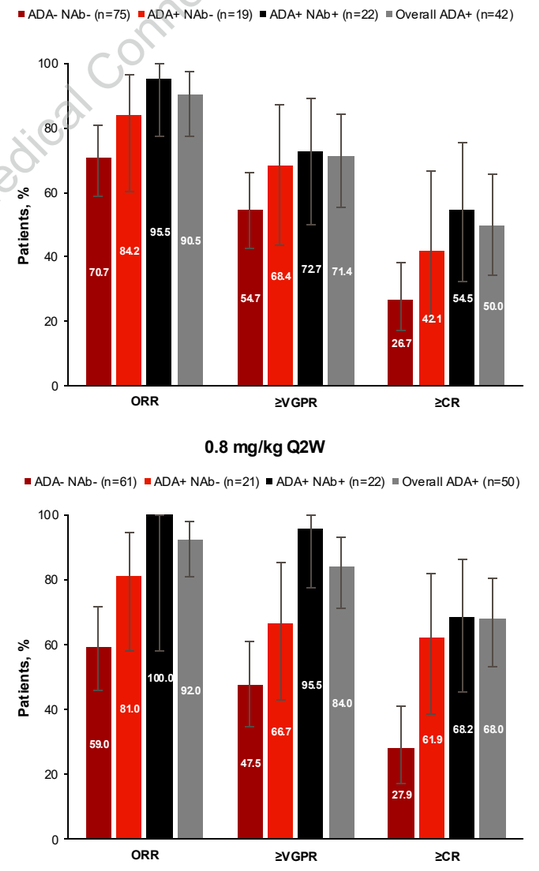
Data are reported for patients who have available immunogenicity-evaluable samples, inclusive of patients with prior TCR. [a]Treatment-emergent ADA are inclusive of treatment-induced ADA (defined as ADA positivity post talquetamab after a negative baseline sample) and treatment-boosted ADA (defined as ADA positivity post talquetamab after a positive baseline sample). In QW, Q2W, and combined RP2D cohorts, respectively, treatment-induced ADA were persistent in 20.2%, 25.2%, and 22.3%, and transient in 10.6%, 14.8%, and 12.4%. Percentages were calculated with the number of patients with immunogenicity-evaluable samples as the denominators.

Figure 2: In TCR-naive patients treated at the RP2Ds, the presence of ADA and NAb had no apparent impact on talquetamab serum concentration over time



Data are reported for patients who are TCR naive and have available immunogenicity-evaluable samples. Data shown as mean and error bars represent standard deviation. Symbols (+ and -) denote positivity or negativity for ADA and/or NAb. C, cycle; D,day.

Figure 3: In TCR-naive patients, development of ADA and NAb did not affect the clinical efficacy of talquetamab at the RP2Ds



Data are reported for patients who are TCR naive and have available immunogenicity-evaluable samples. Data are shown as mean, and errors bars represent 95% CIs. Symbols (+ and -) denote positivity or negativity for ADA and/or NAb. ORR includes all patients with a sPR. Overall ADA+ includes ADA+ NAb- patients, ADA+ NAb+ patients, and patients who were ADA+ but were not evaluable for NAb. Percentages were calculated with the number of patients with immunogenicity-evaluable samples as the denominators. CR, complete response; PR, partial response; VGPR, very good partial response.

Table 1: In phase 2 analysis of TCR-naive patients, median time to treatment-induced ADA onset was ~4 months after median time to first response to talquetamab, indicating ADA had no apparent causality or impact on the efficacy of talquetamab at the RP2Ds

Parameter	0.4 mg/kg QW[a]	0.8 mg/kg Q2W[a]
Median time to first response to talquetamab, days		
ADA+ patients	35.0	41.5
ADA- patients	36.0	39.0
Median time to treatment-induced[b] ADA onset, days	148.0	155.0

Data are reported for patients who are TCR naive and have available immunogenicity-evaluable samples. Symbols (+ and -) denote positivity or negativity for ADA and/or NAb. [a]Phase 2 analysis, excluding patients treated with talquetamab 0.4 mg/kg QW and 0.8 mg/kg Q2W in phase 1. [b]Treatment-induced ADA were defined as ADA positivity post talquetamab after a negative baseline sample.

Table 2: The presence of ADA and/or NAb had no apparent impact on the incidence of key AEs of clinical interest

AE, n (%)	ADA- NAb- (n=364)	ADA+ NAb- (n=71)	ADA+ NAb+ (n=74)	Overall ADA+[a] (n=158)
CRS				
Any Grade	250 (68.7)	54 (76.1)	55 (74.3)	121 (76.6)
Grade ≥2	69 (19.0)	12 (16.9)	11 (14.9)	26 (16.5)
ISR				
Any Grade	38 (10.4)	12 (16.9)	12 (16.2)	24 (15.2)
Grade ≥3	0	0	0	0
sARR				
Any Grade	26 (7.1)	3 (4.2)	4 (5.4)	7 (4.4)
Grade ≥3	6 (1.6)	0	0	0
ICANS[b]				
Any Grade	14 (7.8)	4 (9.1)	3 (5.6)	8 (7.3)
Grade ≥2	10 (5.6)	1 (2.3)	2 (3.7)	3 (2.7)
Neurological events				
Any Grade	195 (53.6)	46 (64.8)	48 (64.9)	103 (65.2)
Grade ≥2	90 (24.7)	19 (26.8)	22 (29.7)	46 (29.1)

Data are reported for patients who have available immunogenicity-evaluable samples. Symbols (+ and -) denote positivity or negativity for ADA and/or NAb. [a]Includes ADA+ NAb- patients, ADA+ NAb+ patients, and patients who were ADA+ but were not evaluable for NAb. [b]ICANS was only assessed in phase 2; denominators were n= 179 (ADA- NAb-), n=44 (ADA+ NAb-), n=54 (ADA+ NAb+), and n=110 (overall ADA+). For all other AEs, percentages were calculated with the number of all treated patients as denominator. ISR, injection-site reaction; sARR, systemic administration-related reaction.

References

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Multiple Myeloma

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