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Clinical Outcomes in Black Patients With Relapsed/Refractory Multiple Myeloma Following Talquetamab Treatment: Analyses From the Phase 1/2 MonumenTAL-1 Study

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Key Takeaway

Efficacy of talquetamab was similar between Black and White patients, whereas higher rates of dysgeusia and skin-related AEs were experienced by Black patients; small numbers of Black patients warrant confirmation of these results in larger studies

Conclusions

High ORR and deep and durable responses were observed in Black and White patients, with comparable efficacy outcomes between groups

Differences in dysgeusia and skin-related AEs (higher incidence, longer duration, and more dose modifications needed in Black patients) require further study to better inform clinical management of Black patients treated with talquetamab

Overall, no PK/PD differences were observed between Black and White patients; PROs indicated worse baseline scores in Black patients but greater improvements in many quality-of-life measures vs White patients

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Poster

Supplementary material

https://www.congresshub.com/ASH2024/Oncology/Talquetamab/Schinke

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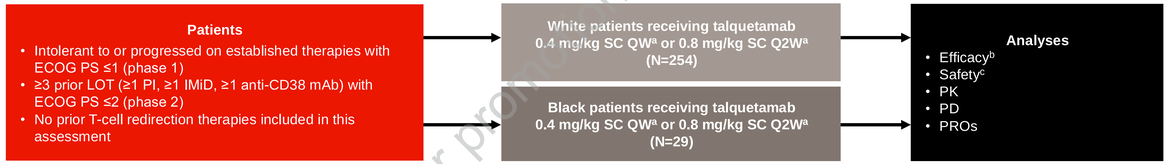
Introduction

- Talquetamab is the first approved G protein–coupled receptor class C group 5 member D (GPRC5D)-targeting bispecific antibody for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1-3]
- In the phase 1/2 MonumenTAL-1 study, talquetamab showed overall response rates (ORRs) of >71% and a clinically manageable safety profile in patients with RRMM[4]
- Black patients have a higher incidence of multiple myeloma (MM) and higher mortality due to MM but are underrepresented in MM clinical trials[5]
- Preliminary analyses have suggested similar efficacy but higher rates of GPRC5D-related adverse events (AEs) with talquetamab in Black vs White patients
- We present clinical outcomes with talquetamab among Black patients from MonumenTAL-1

Methods

- In this post hoc exploratory analysis, outcomes in Black vs White patients were assessed in the phase 1/2 MonumenTAL-1 study (NCT03399799/NCT04634552) with a data cut-off of June 20, 2024 (**Figure 1**)

Figure 1: Assessment in Black and White patients in MonumenTAL-1



[a]With 2–3 step-up doses. [b]ORR assessed by IRC using International Myeloma Working Group criteria.[6,7] PFS based on IRC assessment. [c]CRS was graded by ASTCT criteria; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PRO, patient-reported outcome; Q2W, every other week; QW, weekly; SC, subcutaneous.

Results

Baseline characteristics

- In MonumenTAL-1, majority of patients were White (86%) vs Black (10%); baseline characteristics were generally similar between Black and White patients (**Table 1**)

Table 1: Baseline characteristics

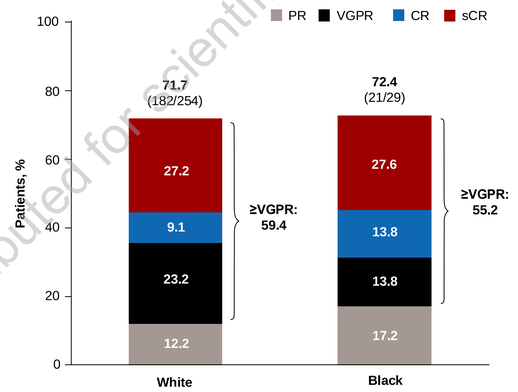
Characteristic	White (N=254)	Black (N=29)
Median age, years (range)	67 (38–84)	67 (46–86)
Male, n (%)	144 (56.7)	17 (58.6)
High-risk cytogenetics,[a] n (%)	75 (32.8)	5 (22.7)
ISS stage III,[b] n (%)	56 (22.1)	6 (20.7)
Extramedullary plasmacytomas,[c] n (%)	63 (24.8)	9 (31.0)
Median prior LOT, (range)	5 (2–17)	4 (3–10)
Refractory status, n (%)		
Triple-class[d]	191 (75.2)	17 (58.6)
Penta-drug[e]	73 (28.7)	7 (24.1)

[a]del(17p), t(4;14), and/or t(14;16); percentages calculated from n=229 for White and n=22 for Black patients. [b]Calculated from n=253 for White patients. [c]Soft tissue plasmacytomas not associated with the bone were included. [d]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [e]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ISS, International Staging System.

Efficacy

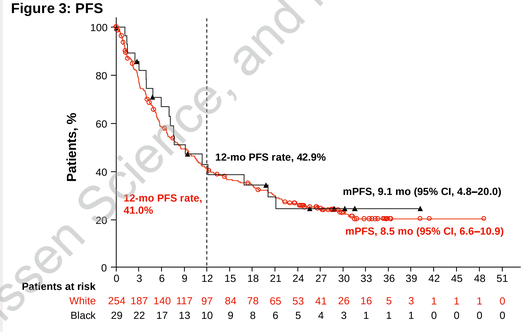
- Comparable ORR and PFS results were observed between Black and White patients (median follow-up, 26 and 31 months, respectively; **Figures 2** and **3**)

Figure 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR. CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Figure 3: PFS



mPFS, median progression-free survival.

Safety

- Approximately two-thirds of individuals of African ancestry carry the Duffy-null genotype, which leads to normal neutrophil counts at lower ranges,[8,9] but neutropenia rates were similar between Black and White patients (**Table 2**)
- Among GPRC5D-related AEs, incidence of nail- and rash-related AEs was generally similar between groups, whereas incidence of dysgeusia and skin-related AEs was higher in Black patients; no differences in severity were noted (**Table 2**)
  - Dysgeusia: Black patients had longer duration with more dose modifications and fewer events that resolved vs White patients (**Supplemental Table**)
  - Skin-related AEs: Black patients had longer duration with more dose modifications and more concomitant medications used vs White patients (**Supplemental Table**)
- Overall, comparable rates of cycle delays, dose modifications, and discontinuations due to AEs were observed between Black and White patients; no talquetamab-related deaths occurred

PK/PD

- Race was not identified as a covariate impacting the PK of talquetamab
- PD analysis indicated no differences between Black and White patients
- Although numbers were small, baseline GPRC5D expression in Black patients was higher in those who experienced skin-related AEs vs those who did not; no differences were observed in White patients (**Figure 4**)

PROs

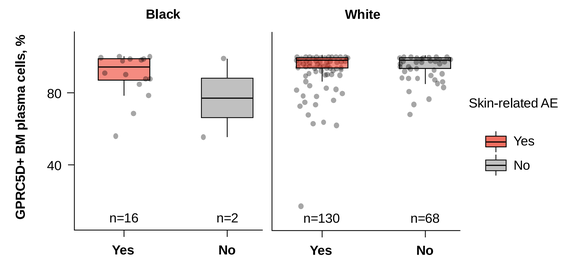
- Black patients had worse baseline values in appetite loss, constipation, dyspnea, pain, and social functioning, but reported greater improvements from baseline in these values, as well as in diarrhea (after cycle 1), fatigue, and global health status vs White patients
- With time, both Black and White patients reported improvements in disease severity; by cycle 3, most patients reported severity as "moderate," "mild," or "none"

Table 2: Hematologic and nonhematologic AEs

AEs, n (%)	White (N=254)		Black (N=29)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic AEs (≥30% in either group)				
Anemia	119 (46.9)	75 (29.5)	9 (31.0)	7 (24.1)
Lymphopenia	67 (26.4)	59 (23.2)	11 (37.9)	11 (37.9)
Neutropenia	77 (30.3)	62 (24.4)	9 (31.0)	8 (27.6)
Thrombocytopenia	77 (30.3)	53 (20.9)	5 (17.2)	3 (10.3)
Nonhematologic AEs (≥35% in either group)				
Dysgeusia[a]	178 (70.1)	NA	26 (89.7)	NA
Skin related[b]	163 (64.2)	0	25 (86.2)	0
CRS	193 (76.0)	4 (1.6)	21 (72.4)	0
Infections	168 (66.1)	57 (22.4)	18 (62.1)	6 (20.7)
Nail related[c]	142 (55.9)	0	17 (58.6)	0
Weight decreased	100 (39.4)	10 (3.9)	15 (51.7)	2 (6.9)
Fatigue	63 (24.8)	0	12 (41.4)	0
Dry mouth	80 (31.5)	0	11 (37.9)	0
Decreased appetite	60 (23.6)	0	11 (37.9)	0
Constipation	43 (16.9)	0	11 (37.9)	0
Rash related[d]	95 (37.4)	8 (3.1)	7 (24.1)	1 (3.4)

[a]Includes dysgeusia, ageusia, taste disorder, and hypogeusia. Per CTCAE v4.03, the maximum grade of dysgeusia is 2. [b]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Includes nail discoloration, nail disorder, nail toxicity, nail dystrophy, nail ridging, onychoclasis, onycholysis, and onychomadesis. [d]Includes rash, maculopapular rash, erythematous rash, and erythema. NA, not applicable.

Figure 4: Baseline GPRC5D expression in patients with and without skin-related AEs



BM, bone marrow.

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Multiple Myeloma

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