Matching-Adjusted Indirect Treatment Comparison of Teclistamab Versus Selinexor-Dexamethasone for the Treatment of Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

Philippe Moreau[1], Saad Z Usmani[2], Niels WCJ van de Donk[3], Alfred L Garfall[4], Michel Delforge[5], Albert Oriol[6], Ajay K Nooka[7], Laura Rosiñol[8], Nizar Bahlis[9], Paula Rodríguez-Otero[10], Thomas G Martin[11], Joris Diels[12], Suzy Van Sanden[12], Lixia Pei[13], Eric M Ammann[14], Katherine Chastain[13], Alexander Marshall[14], Mary Slavcev[14], Anil Londhe[15], Amrita Krishnan[16]

[1]University Hospital Hôtel-Dieu, Nantes, France; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [4]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [5]University of Leuven, Leuven, Belgium; [6]Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [7]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [8]Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain; [9]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, Alberta, Canada; [10]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [11]University of California San Francisco, San Francisco, CA, USA; [12]Janssen Pharmaceutica NV, Beerse, Belgium; [13]Janssen Research & Development, Raritan, NJ, USA; [14]Janssen Global Services, Raritan, NJ, USA; [15]Janssen Research & Development, Titusville, NJ, USA; [16]City of Hope Comprehensive Cancer Center, Duarte, CA, USA

INTRODUCTION

- Teclistamab is the first approved B-cell maturation antigen × CD3 bispecific antibody, with precision dosing for the treatment of patients with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM)[1-3]
- In the phase 1/2 MajesTEC-1 study (NCT03145181/NCT04557098), teclistamab demonstrated deep and durable responses at 22.8 months median follow-up (mFU)[4]:
  - Overall response rate (ORR): 63.0%
  - Complete response or better (≥CR): 45.5%
  - Median duration of response (DOR): 22 months
  - Median progression-free survival (PFS): 11 months
  - Median overall survival (OS): 22 months
- Although there is currently no clear standard of care for patients with TCE RRMM, selinexor-dexamethasone is an approved, novel therapeutic option that has demonstrated efficacy (ORR, 26%) in penta-exposed, triple-class refractory MM in the phase 2b STORM part 2 trial (NCT02336815)[5-7]
- In the absence of head-to-head trials, a matching-adjusted indirect comparison (MAIC) can be used to compare treatments indirectly, adjusting for cross-trial differences in baseline characteristics[8]

OBJECTIVE

- To assess the comparative efficacy of teclistamab in MajesTEC-1 vs selinexor-dexamethasone in STORM phase 2 for patients with TCE RRMM

METHODS

Data sources

- Individual patient-level data (IPD) for patients who received teclistamab were compared with published summary-level data from treated patients in STORM part 2 (**Figure 1**)
- IPD from MajesTEC-1 patients meeting STORM part 2 eligibility criteria were included, weighted to match aggregated STORM part 2 baseline characteristics

FIGURE 1: Summary of trials for comparison

MajesTEC-1 (N=165)[4]	STORM part 2 (N=122)[7]
Teclistamab (1.5 mg/kg)[a] *CCO: Jan 4, 2023 (22.8 months mFU)*	Selinexor (80 mg) + dexamethasone (20 mg)[b] *CCO: Aug 17, 2018*[c]

[a]Patients in MajesTEC-1 received teclistamab at the recommended phase 2 dose, 1.5 mg/kg subcutaneously weekly, and could switch to every-other-week (Q2W) dosing if they achieved a partial response or better (≥PR) after ≥4 cycles (phase 1) or ≥CR for ≥6 months (phase 2); patients could further switch to monthly (Q4W) dosing if they demonstrated continued response on the Q2W schedule. [b]Patients in STORM part 2 received oral selinexor in combination with dexamethasone on days 1 and 3, weekly, and in 4-week cycles until disease progression, death, or discontinuation. [c]mFU not reported. CCO, clinical cut-off.

Statistical analyses

- An unanchored MAIC adjusted for baseline characteristics of prognostic significance (primary analysis):
  - Refractory status
  - Cytogenetics
  - Revised International Staging System stage
  - Extramedullary disease
  - Number of prior lines of therapy (LOT)
- A fully adjusted model further adjusted for: years since MM diagnosis, age, prior autologous hematopoietic stem cell transplant, Eastern Cooperative Oncology Group performance status, race, sex, type of MM, creatinine clearance, percent bone marrow plasma cells, and time since discontinuation of last LOT
- Comparative efficacy was estimated for ORR, very good partial response or better (≥VGPR) rate, ≥CR rate, DOR, PFS, and OS
- For binary endpoints, relative effects were quantified using an odds ratio (OR), 95% CI, and risk ratio (RR) derived from a weighted logistic regression analysis
- For time-to-event endpoints, hazard ratios (HRs), including 95% CI, were estimated using a weighted Cox proportional hazards model

MULTIPLE MYELOMA

RESULTS

Patients and baseline characteristics

- Baseline characteristics for reweighted patients from MajesTEC-1 were balanced with the STORM part 2 population

Efficacy outcomes

- Patients treated with teclistamab were 1.9-, 7.5-, and 23.9-fold more likely to achieve ORR, ≥VGPR, and ≥CR, respectively, compared with those treated with selinexor-dexamethasone; results were consistent between the primary and fully adjusted analyses (**Figure 2** and **Table 1**)
- DOR and OS were significantly longer and PFS was numerically longer for patients treated with teclistamab vs selinexor-dexamethasone; results were consistent between the primary and fully adjusted analyses (**Figure 3** and **Table 2**)
- Cross-trial differences in baseline characteristics led to a relatively low effective sample size (n=43) after adjustment, resulting in wide CIs for some outcomes

FIGURE 2: Response outcomes for teclistamab vs selinexor-dexamethasone

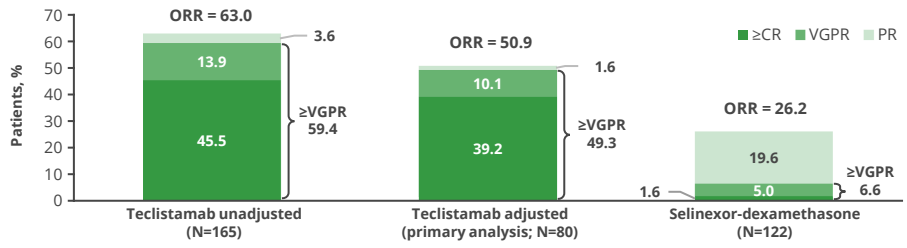


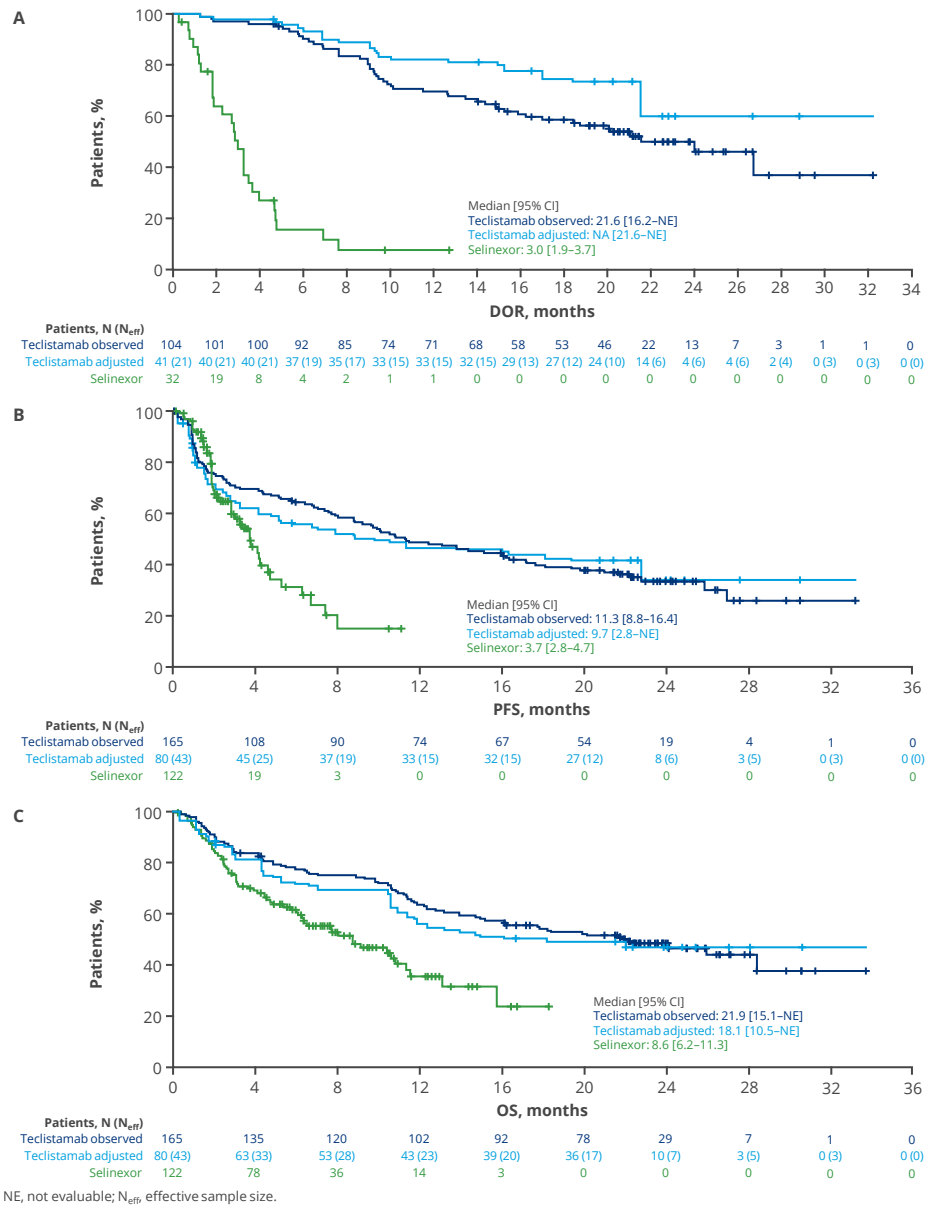
TABLE 1: Unadjusted and adjusted comparative analyses of response outcomes

Outcome/ Analysis	Teclistamab vs selinexor-dexamethasone		
	OR (95% CI)	RR	*P* value
ORR			
Unadjusted	4.80 (2.87–8.01)	2.40	<0.0001
Adjusted (primary analysis)	2.91 (1.42–5.98)	1.94	0.0036
Fully adjusted	2.51 (1.19–5.31)	1.80	0.0160
≥VGPR			
Unadjusted	20.84 (9.54–45.53)	9.06	<0.0001
Adjusted (primary analysis)	13.84 (5.45–35.17)	7.52	<0.0001
Fully adjusted	12.22 (4.69–31.80)	7.04	<0.0001
≥CR			
Unadjusted	50.00 (11.96–209.06)	27.73	<0.0001
Adjusted (primary analysis)	38.69 (8.33–179.62)	23.92	<0.0001
Fully adjusted	32.72 (6.94–154.33)	21.53	<0.0001

TABLE 2: Unadjusted and adjusted comparative analyses of time-to-event outcomes

Outcome/ Analysis	Teclistamab vs selinexor-dexamethasone	
	HR (95% CI)	*P* value
DOR		
Unadjusted	0.08 (0.05–0.15)	<0.0001
Adjusted (primary analysis)	0.06 (0.03–0.14)	<0.0001
Fully adjusted	0.06 (0.02–0.15)	<0.0001
PFS		
Unadjusted	0.52 (0.35–0.76)	0.0009
Adjusted (primary analysis)	0.61 (0.33–1.13)	0.1164
Fully adjusted	0.69 (0.36–1.30)	0.2479
OS		
Unadjusted	0.45 (0.31–0.65)	<0.0001
Adjusted (primary analysis)	0.55 (0.33–0.93)	0.0265
Fully adjusted	0.59 (0.35–1.00)	0.0483

FIGURE 3: Unadjusted and adjusted Kaplan-Meier plots for (A) DOR, (B) PFS, and (C) OS



NE, not evaluable; N_{eff}, effective sample size.

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Presented at the ISPOR Europe Annual Meeting; November 12–15, 2023; Copenhagen, Denmark

KEY TAKEAWAY

Teclistamab demonstrates improved efficacy vs selinexor-dexamethasone in these MAIC analyses, highlighting the clinical benefit of teclistamab for patients with TCE RRMM, a population with a high unmet medical need

CONCLUSIONS

Teclistamab showed deeper and more durable responses and improved survival outcomes vs selinexor-dexamethasone in patients with TCE RRMM who had received ≥3 prior LOT in these comparative analyses

Results of the fully adjusted analysis were consistent with those of the primary analysis

Reduction in the effective sample size after adjustment limited the study's power and may account for some treatment-effect estimates being clinically meaningful but not statistically significant

ACKNOWLEDGMENTS

We thank the patients who participated in the study and their families and caregivers, the physicians and nurses who cared for patients and supported this clinical trial, staff members at the study sites, and staff members involved in data collection and analyses. This study was funded by Janssen Global Services, LLC. Medical writing support was provided by Kristin M Allan, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

DISCLOSURES

PM has served in a consulting/advisory role and has received honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Oncopeptides, and Sanofi. **SZU** has served in a consulting/advisory role for AbbVie, Amgen, BMS/Celgene, Celgene, Genentech, Gilead Sciences, GSK, Janssen, Karyopharm Therapeutics, Merck, and Takeda; and has received research funding from Amgen, Array BioPharma, BMS, Celgene, GSK, Merck, Pharmacyclics, Sanofi, Seattle Genetics, and SkylineDx. **NWCJvdD** has served in a consulting/advisory role for Adaptive Biotechnologies, Amgen, Bayer, BMS, Celgene, Janssen, Novartis, Roche, Servier, and Takeda; and has received research funding from Amgen, BMS, Celgene, Cellectis, Janssen, and Novartis. **ALG** has served in a consulting/advisory role for Amgen, CDR-Life, GSK, and Janssen; has patents, royalties, other intellectual property in the field of CAR-T cell therapy; has stock/other ownership interests in Cabaletta Bio; and has received research funding from CRISPR Therapeutics, Janssen, Novartis, and Tmunity Therapeutics, Inc. **MD** has served in a consulting/advisory role for Amgen, BMS, GSK, Janssen, Sanofi, Stemline, and Takeda; and has received research funding from Janssen. **AO** has served in a consulting or advisory role for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi; and has participated in speakers' bureaus for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi. **AKN** has received honoraria and has served in a consulting/advisory role for Adaptive Biotechnologies, Amgen, BeyondSpring Pharmaceuticals, BMS, Cellectar, Genzyme, GSK, Janssen, Karyopharm Therapeutics, Oncopeptides, ONK Therapeutics, Pfizer, Secura Bio, and Takeda; reports travel, accommodations, and expenses from GSK; and has received research funding from Amgen, Arch Oncology, BMS/Celgene, Cellectar, GSK, Janssen, Pfizer, and Takeda. **LR** has served in a consulting/advisory role for Amgen, Celgene, Janssen-Cilag, and Sanofi; and has received honoraria from Amgen, Celgene, GSK, Janssen-Cilag, Sanofi, and Takeda. **NB** has served in a consulting/advisory role with AbbVie, Amgen, BMS, Forus, GSK, Janssen, Pfizer, Sanofi, and Takeda, received honoraria from AbbVie, Amgen, BMS, Forus, Janssen, and Sanofi, has been a member of the steering committee at AbbVie, GSK, and Janssen, and has received research funding from Janssen and Pfizer. **PR-O** has received honoraria from or served on speakers' bureaus for Amgen, BMS/Celgene, GSK, Janssen, Oncopeptides, Regeneron, and Sanofi. **TGM** has served in a consulting/advisory role for GSK and Legend Biotech USA Inc.; and has received research funding from Amgen, Janssen, and Sanofi. **JD**, **SVS**, **LP**, **EA**, **KC**, **AM**, **MS**, and **AL** are employed by and may own stock in Janssen. **AK** has served on an advisory committee for Sutro Biopharma; has had consulting agreements with Adaptive Biotechnologies Corporation, BMS, GSK, Regeneron Pharmaceuticals Inc., and Sanofi Genzyme; has performed contracted research for Janssen; has served on speakers' bureaus for Amgen, BMS, and Takeda; and has stock options/ownership in BMS.