Effectiveness and safety of teclistamab in triple-class exposed relapsed/refractory multiple myeloma: results of the French real-world RetrosTECtive study

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INTRODUCTION

Teclistamab, a B-cell maturation antigen (BCMA) x CD3 directed bispecific antibody, has demonstrated high response rates and prolonged survivals in patients with relapsed/refractory multiple myeloma. FDA and EMA approved teclistamab based on the phase I/II MajesTEC-1 trial[(1)]. Teclistamab was available in France since October 2022 through an early access.

Most previous studies of real-world use have reported the results of cohorts of smaller numbers of patients than the original trial, often with a shorter follow-up.

Here, we report retrospective analyses on efficacy and safety among 303 consecutive patients, triple-class exposed who initiated teclistamab between 14 October 2022 and 14 September 2023.

OBJECTIVE

Evaluate the effectiveness and safety of teclistamab used in real world setting in France through the early access program.

METHODS

Retrospective multicenter observational study : 31 centers in France.

Data of all patients who initiated teclistamab between October 14, 2022 and September 14, 2023, and did not object, were retrospectively collected. The study was submitted to the French Health Data Hub.

Teclistamab was administered every week at 1.5 mg/kg following two step-up doses of 0.06 and 0.3 mg/kg including premedication according the EMA recommendations. 303 patients were included in this IFM2024-09 RetrosTECtive study.

RESULTS

Patient characteristics in IFM2024-09 and MajesTEC-1 [(1,2)]

Characteristics	IFM 2024-09 (n=303)	Majestec-1 (n=165)
Age (years), median [range]	70 [37-88]	64 [33-84]
> 75 years, n (%)	90 (29.7%)	24 (14.4%)
Sex Male, n (%)	151 (49.9%)	96 (58.2%)
Female, n (%)	152 (50.1%)	69 (41.8%)
Median prior lines of therapy [range]	4 [2-11]	5 [2-14]
Previous autologous transplant	171 (56.4%)	135 (81.8%)
IMiDs exposed	302 (99.7%)	165 (100%)
IMiDs refractory	208 (68.6%)	152 (92.1%)
PIs exposed	303 (100%)	165 (100%)
PIs refractory	194 (64%)	142 (86.1%)
Anti-CD38 antibody exposed	295 (97.4%)	165 (100%)
Anti-CD38 antibody refractory	165 (54.5%)	148 (89.7%)
Anti-BCMA exposure	41 (13.6%)	0
ECOG > 2 at the initiation of teclistamab	26 (8.5%)	0
Severe renal failure at the initiation of teclistamab	30 (9.9%)	0
Ineligibility to Majestec-1	86 (28.4%)	0
High-risk cytogenetics, n (%)		
Del(17p)	34/179 (19%)	23/148 (15.5%)
Del(17p) and/or TP53 mutation	54/179 (30.2%)	NA
t(4;14)	27/188 (14.3%)	16/148 (10.8%)
t(14;16)	4/97 (4%)	4/148 (2.7%)
Circulating plasma cells, n (%)	39 (13.8%)	NA
EMD, n (%)	34 (11.8%)	28 (17%)
PMD, n (%)	70 (25.5%)	NA
Median follow-up, months [range]	11.9 [9.2-14.8]	22 then 30.4

ORR, PFS and OS

Median follow-up: 11.9 months [95% CI, 9.2- 14.8]
ORR rate: **68.8%** including 61.4% VGPR or better
Median PFS: 11.3 months [95% CI, 8.9 - 14.9] in the overall population
17 months [95% CI, 16.4 - NA] in the 175 responding patients
Median OS: 17 months [95% CI, 13.8 - NA]

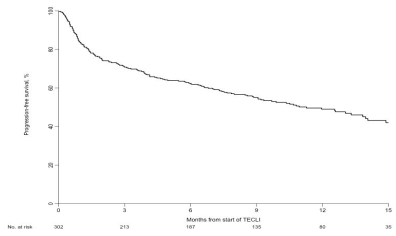

Figure 1a. Progression-Free Survival

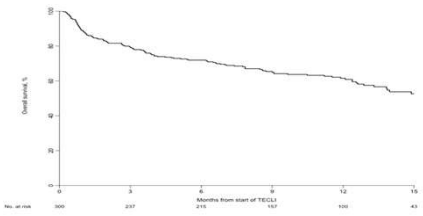

Figure 1b. Overall Survival

Subgroups analyses

Subgroups	Median PFS	
Age < 75	9.1 months (6.3-13)	p = 0.007
Age 75 or more	16.4 months (10.7-NR)	
Extra medullary disease	3.7 months (2-NR)	
No extra medullary disease	11.3 months (8.8-16.2)	p = 0.057
Paramedullar disease	16.2 months (9.3-NR)	
No paramedullar disease	9.2 months (7.3-13.3)	p = 0.103
Circulating plasmacytosis	4.7 months (1.7-10.5)	
No circulating plasmacytosis	12.6 months (9.7-16.4)	p = 0.001
del(17p) or TP53 mutation	5.2 months (2.9-9.1)	
No del(17p), no mutation TP53	16.4 months (4.1-NR)	p = 0.009
Ineligibility to MAJESTEC-1	3.9 months (2.3-7.9)	
Eligibility to MAJESTEC-1	14.9 months (11.3-NR)	p < 0.001
No previous Auto Transplant	12.5 months (9.7-NR)	
Previous Auto Transplant	9.1 months (6.3-16.2)	p = 0.357

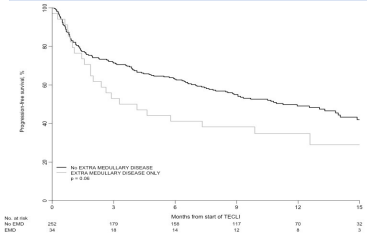

Figure 2. PFS according the extramedullary disease status

Safety

No new safety signals were observed, particularly regarding the occurrence of cytokine release syndrome (CRS) or immune effector-cell associated neurotoxicity syndrome (ICANS).

A total of 107 patients (36%) received tocilizumab and/or dexamethasone for CRS and/or ICANS.

Among 294 patients with available data, 186 (61.4%) received immunoglobulin (Ig) supplementation, including 122 (41.8%) as primary prophylaxis.

Infections led to the definitive discontinuation of teclistamab in 13% of patients; 99 patients (29.9%) were readmitted at least once for infections.

CONCLUSIONS

Our analysis encompassed a very large cohort of patients treated in both university and community hospitals.
The response rate in triple-class exposed RRMM was identical to that of Majectec-1.
The PFS was also very similar to the pivotal study for approval, considering that fewer than 29% of our patients would have been excluded from Majectec-1.
The OS rate was also noteworthy and compared favorably to that of Majestec-1.
A high proportion of patients received Ig supplementation, which is now highly recommended in the management of such therapies in heavily pretreated patients[(3-4)].

Despite some limitations (retrospective design, heterogeneity in institutional practices for toxicity management, response assessment without independent review committee and minimal residual disease analyses), our study clearly confirms, on a very high number of patients treated in the real-world settings and with almost the same follow-up as Majectec-1, the reasonable safety and good efficacy of Teclistamab in patients with RRMM.

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