DESCRIPTIVE ANALYSIS OF BORTEZOMIB USE IN THE TREATMENT OF MULTIPLE MYELOMA IN FOUR ADULT UNIVERSITY TEACHING HOSPITALS IN QUÉBEC, CANADA

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BACKGROUND

Bortezomib, a reversible inhibitor of the 26S proteasome widely used in the treatment of multiple myeloma, is now being used in various other indications. Pharmacy directors gave the Therapeutic Drug Management Program (TDMP / *Programme de Gestion Thérapeutique des Médicaments (PGTM)* - www.pgtm.qc.ca) the mandate to evaluate bortezomib use in four university teaching hospitals in Quebec, Canada.

OBJECTIVES

Primary objectives

- Describe bortezomib use for all indications in our hospitals and review its use in the treatment of multiple myeloma.

Secondary objectives

- Assess clinical use of bortezomib
  - Therapeutic regimen description (dose, route of administration, frequency)
  - Number of cycles received by patients (treatment duration)
  - Response rate
  - Adverse events

DESIGN

A review of pharmacy databases was performed to identify patients who received bortezomib between June 1st 2012 and May 31st 2013. Pharmacy and medical records of every patient who received bortezomib during the study period were reviewed retrospectively to assess the treatment, response and adverse events.

RESULTS

GLOBAL STUDY POPULATION

A total of 232 bortezomib regimens were administered to 227 different patients during the study period.

Figure 1: Indications for Bortezomib use in the global study population

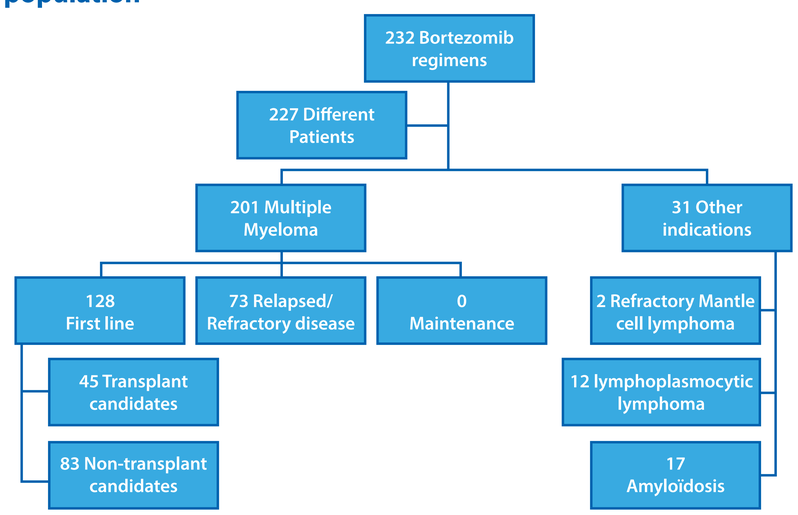


Table 1: Patients characteristics in the global study population

	NUMBER OF PATIENTS (N = 232)
Male / Female (%)	124 / 108 (53.4% / 46.6%)
Mean age (range)	68 (61-75)
Median body surface area (range)	1.80 m² (1.66-1.95)
Patient deceased at the end of study period (%)	36 (15.5%)

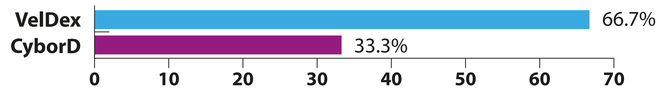
**At the time of data analysis, 81 of patients (35%) were still treated with bortezomib, 58 had finished (25%) their planned treatment and 78 (34%) had discontinued treatment. The main reasons for discontinuation were adverse events and disease progression.*

FIRST LINE MULTIPLE MYELOMA POPULATION (128 PATIENTS)

TRANSPLANT CANDIDATES (45 PATIENTS)

Forty five transplant candidates received bortezomib for multiple myeloma. Of these patients, 7 (15.5%) discontinued therapy, 3 because of side effects, 2 due to disease progression and 2 for other unknown reasons.

Figure 2: First Line Regimens used in transplant candidates



NON-TRANSPLANT CANDIDATES (83 PATIENTS)

Eighty three non-transplant candidates received bortezomib for multiple myeloma. Of these patients, 27 (32.5%) discontinued therapy, 11 because of adverse events, 7 for remission or stable disease, 2 due to disease progression, and 7 for other reasons.

Figure 3: First Line Regimens used in non-transplant candidates

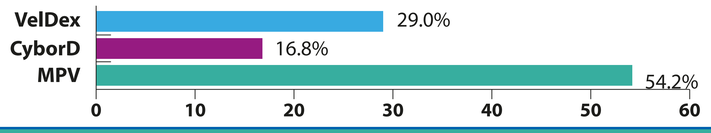


Table 2: Dosage and treatment duration in First Line Multiple Myeloma population

		TRANSPLANT CANDIDATES NUMBER OF PATIENTS (N = 45)	NON-TRANSPLANT CANDIDATES NUMBER OF PATIENTS (N = 83)
Initial dose	1.3 mg/m² 1.5 mg/m² 1.0 mg/m²	31 (68.9%) 13 (28.9%) 1 (2.2%)	67 (80.7%) 10 (12.1%) 6 (7.2%)
Route of Administration	IV SC IV then SC SC then IV	14 (31.1%) 24 (53.4%) 6 (13.3%) 1 (2.2%)	18 (21.7%) 57 (68.7%) 8 (9.6%) 0
Median treatment duration days (Interquartile range)		111 days (61-199)	118 days (39-258)
Median number of cycles (Interquartile range)		4 cycles (2.5-5.5)	3 cycles (1-6)
		NUMBER OF PATIENTS WHO COMPLETED TREATMENT (N = 28)	NUMBER OF PATIENTS WHO COMPLETED TREATMENT (N = 15)
Mean number of cycles received by patients that completed treatment (range)		4.6 cycles (2-11)	8.8 cycles (1-13)

Table 3: Response Rate in First Line Multiple Myeloma population

	TRANSPLANT CANDIDATES		NON-TRANSPLANT CANDIDATES	
EFFICACY	NUMBER OF PATIENTS (N = 45)	EXCLUDING PATIENTS STILL ON ACTIVE TREATMENT* (n = 36)	NUMBER OF PATIENTS (N = 83)	EXCLUDING PATIENTS STILL ON ACTIVE TREATMENT (n = 48)
Response rate (partial or complete response or stable disease)	30 (66.7%)	30/36 (83.3%)**	23 (27.7%)	23/48 (47.9%)***
Disease progression	2 (4.4%)	2/36 (5.6%)	2 (2.4%)	2/48 (4.2%)
Still on treatment at the end of study period	9 (20%)	--	35 (42.2%)	--
Unknown response (missing information)	4 (8.9%)	4/36 (11.1%)	23 (27.7%)	23/48 (47.9%)

**Twenty-eight (28) patients out of the 36 who completed treatment have undergone autologous stem cell transplant*
*** Response by specific treatment: VelDex 20/24 (83.3%); CyBorD 10/12 (83.3%)*
**** Response by specific treatment: MPV 20/28 (71.4%); VelDex 3/15 (20%)*

RELAPSED OR REFRACTORY MULTIPLE MYELOMA POPULATION (73 PATIENTS)

Seventy three patients received bortezomib for relapsed / refractory myeloma. Of these patients, 32 (43.8%) discontinued therapy, 19 due to disease progression, 8 because of adverse events and 5 for other reasons.

Figure 4: Regimens used in relapsed or refractory Multiple Myeloma population

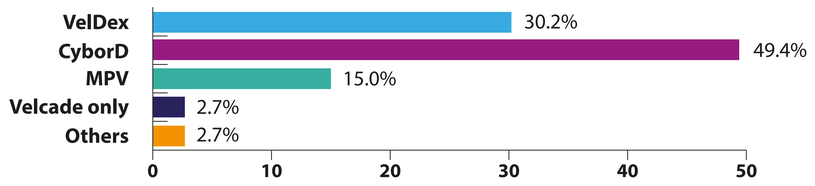


Table 4: Dosage and treatment duration in relapsed or refractory Multiple Myeloma population

DOSE, ROUTE OF ADMINISTRATION, TREATMENT DURATION		NUMBER OF PATIENTS (N = 73)
Initial dose	1.3 mg/m² 1.5 mg/m² 1.0 mg/m² Other*	43 (58.9%) 23 (31.5%) 5 (6.9%) 2 (2.7%)
Route of administration	IV SC IV then SC	20 (27.4%) 43 (58.9%) 10 (13.7%)
Median duration of treatment in days (Interquartile range)		124 days (57-223)
Median number of cycles (Interquartile range)		4 cycles (2-7)
		NUMBER OF PATIENTS WHO COMPLETED TREATMENT (N = 9)
Mean number of cycles received by patients who completed treatment (range)		7 cycles (4-9)

**1.1 mg/m² and 1.6 mg/m²*

Table 5: Response rate in relapsed or refractory Multiple Myeloma Population

EFFICACY	NUMBER OF PATIENTS (N = 73)	EXCLUDING PATIENTS STILL ON ACTIVE TREATMENT (n = 47)
Best Response (partial or complete responses or stable disease)	14(19.2%)	14/47 (29.8%)*
Disease Progression	19 (26%)	19/47 (40.4%)
Unknown response (missing information)	40 (54.8%)	14/47 (29.8%)

** Response by specific treatment: MPV 4/9 (44.4%); VelDex 6/16 (37.5%); CyBorD 4/19 (21.1%); Other treatment 0/3 (0%)*

ADVERSE EVENTS

Table 6: Treatment related adverse events in global multiple myeloma population

ADVERSE EVENTS	NUMBER OF PATIENTS (N = 201)*
Thrombocytopenia (grade 2 and more)	57 (28.4%)
Hematologic toxicity (grade 2 and more excluding thrombocytopenia)	86 (42.8%)
Peripheral neuropathy (all grades)	100 (49.8%)
Hypotension during administration	15 (7.5%)
Gastrointestinal toxicity	90 (44.8%)
Other adverse events (unlisted)	121 (60.2%)
Data not available	5 (2.5%)
Absence of adverse event	22 (10.9%)

**Seventeen patients (8.5%) of the multiple myeloma population treated with bortezomib were hospitalized and 22 patients (10.9%) had to discontinue treatment because of adverse events.*

CONCLUSION

Bortezomib is widely used in the treatment of multiple myeloma. Treatment algorithms should be developed and implemented in each center to optimize the use of bortezomib, particularly in the relapsed/refractory setting. The use of pre-printed orders for the prescription of chemotherapy regimens could help stardardize prescription (dose and frequency of each drug).

Le pGTm est une initiative des cinq centres hospitaliers universitaires du Québec

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