COMPARISON BETWEEN MP-THALIDOMIDE AND MP-BORTEZOMIB IN REAL LIFE: ANALYSIS OF 16 PRIVATE FRENCH CLINICAL CENTERS

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Abstract

Background. Therapeutic options for elderly patients with multiple myeloma (MM) have expanded in the recent years with the introduction of novel agents as thalidomide (T), bortezomib (V) in association with melphalan/prednisolone (MP) and recently lenalidomide. Although their efficacy has been demonstrated in clinical trials, there are no prospective up-front studies comparing MPT in patients with MM older than 65 years old. We proposed to compare in the real life and in clinical private French centers the overcoming of those patients treated with MPT or MPV.

Patients and Methods. From February 2017 until May 2017, the majority of French private clinical centers (N: 16) collected the data of patients who received a specific treatment for MM in first line. Patients were treated with MPT (Melphalan: 0.25mg/kg and prednisolone : 60 mg/m² for 4 days every 6 weeks; Thalidomide: 100 mg by day) for 12 cycles or MPV(Melphalan: 025 mg/kg and prednisolone: 60 mg/m² for 4 days every 6 weeks; Velcade: 1.3 mg/m² D1-8-15-22) for 9 cycles as the VISTA protocol. We did a statistical analysis for elderly patients in first line (MPT versus MPV) and compared clinical and biological characteristics, main prognostic factors and results in terms of PFS and OS.

During this period, 181 patients were treated in first line for a symptomatic MM with MPT (n: 47) or MPV (n : 134). Median age was 75.4 years for the whole population without any statistical difference between the two groups (*P* : NS) neither for the sex ratio (85/94), type of MM or ISS.

No difference was found between two groups in terms of cytogenetic factors (Del 17p; Del 13q) excepted for t(4 ;14) more important in the MPV than the MPT group (4/78 versus 0/16 ;*P* : 0.014). However, More patients were treated with MPV when they have a renal failure > grade 2 (20/99) than in the MPT group (1/35) (*P* : 0.01)

Results. No difference in response was observed in proportion of patients receiving MPT or MPV. 29 patients were considered in CR (5 *versus* 24), 69 patients in VGPR (19 *vs* 50) and 43 in PR (13 *vs* 30) without any statistical difference between the two groups. One hundred and forty one (141) patients were considered as responders to the specific treatment allowed with 104/134 in the MPV group and 37/47 in the MPT group without any statistical difference (*P*: 0.1). No difference was observed in PFS between the two groups (26.9 *versus* 36.5 months; *P:* 0.3)

Conclusions. We conclude that the two treatments MPT or MPV have a good efficacy in real life and we found no difference in terms of response or PFS in our patients treated in French clinical centers. Further prospective studies are warranted to compare oral treatments (MPT or Revlimid-Dex) versus subcutaneous treatment as MPV.

Rational and method

- In newly diagnosed multiple myeloma (ndMM), for patients ineligible for front-line autologous stem cell transplantation (ASCT), melphalan and prednisone (MP) with Thalidomide ((MPT) or bortezomib (MPV) are standard first-line therapeutic options.
- New treatment combinations incorporating proteasome inhibitors and immunomodulatory drugs are challenging the role of alkylators in ndMM treatment. For instance, lenalidomide (R) combined with low-dose dexamethasone (Rd) is an effective therapeutic option for these patients and is an approved therapeutic option by the US Food and Drug Administration and European Medicines Agency.
- However, to date no head-to-head randomized controlled trial have compared MPT versus MPV.
- From February to May 2017, the HLA Group (*Hematologues Libéraux Associés*) decided to study his population of patients treated for multiple myeloma. During these 4 months, 722 cases were recorded by 16 centers in total. After several descriptive analyzes, it has been decided to focus on the first-line treatment of elderly subjects (aged 65 and over).
- As it was found that MPV and MPT regimens were the main treatments administered and considering the few studies available on the topic, it seemed interesting to compare the response to treatment and progression-free survival for these two groups of patients.

Patients characteristics

Retrospective observational cohort study with patients treated from 2005 to 2017 with data collected on a 4 months period

	Total N=181	MPV arm N=134	MPT arm N=47	P values
Median Age	75.4	75.6	75.4	NS[1]
Sex ratio	85/94	64/68	21/26	NS[2]
Type of MM IgG IgA Free light chains K L Non secreting others(PMO)	 113 46 11 6 4 1	 80 34 10 6 3 1	 33 12 1 0 1 -	 NS[2]
B2 mic	3.2	3.25	3.2	NS[1]
ISS 1 2 3	 90 68 23	 64 52 18	 26 16 5	 NS[2]
Cytogenetic Not done T(4 ;14) Del17p Del 13q others	 87 4/94 7/94 11/94 20/94	 56 4/78 6/78 9/78 16/78	 31 0/16 1/16 2/16 4/16	 0.014[2] NS 0.015[2] 0.016[2]
Bone lesions	105/134	79/99	26/35	NS[2]
Anemia	80/134	59/99	24/35	NS[2]
Renal insufficiency	21/134	20/99	1/35	0.01[2]
Hypercalcemia	18/134	11/99	7/35	NS[2]

Statistical tests:

[1] : Mann Withney median comparison

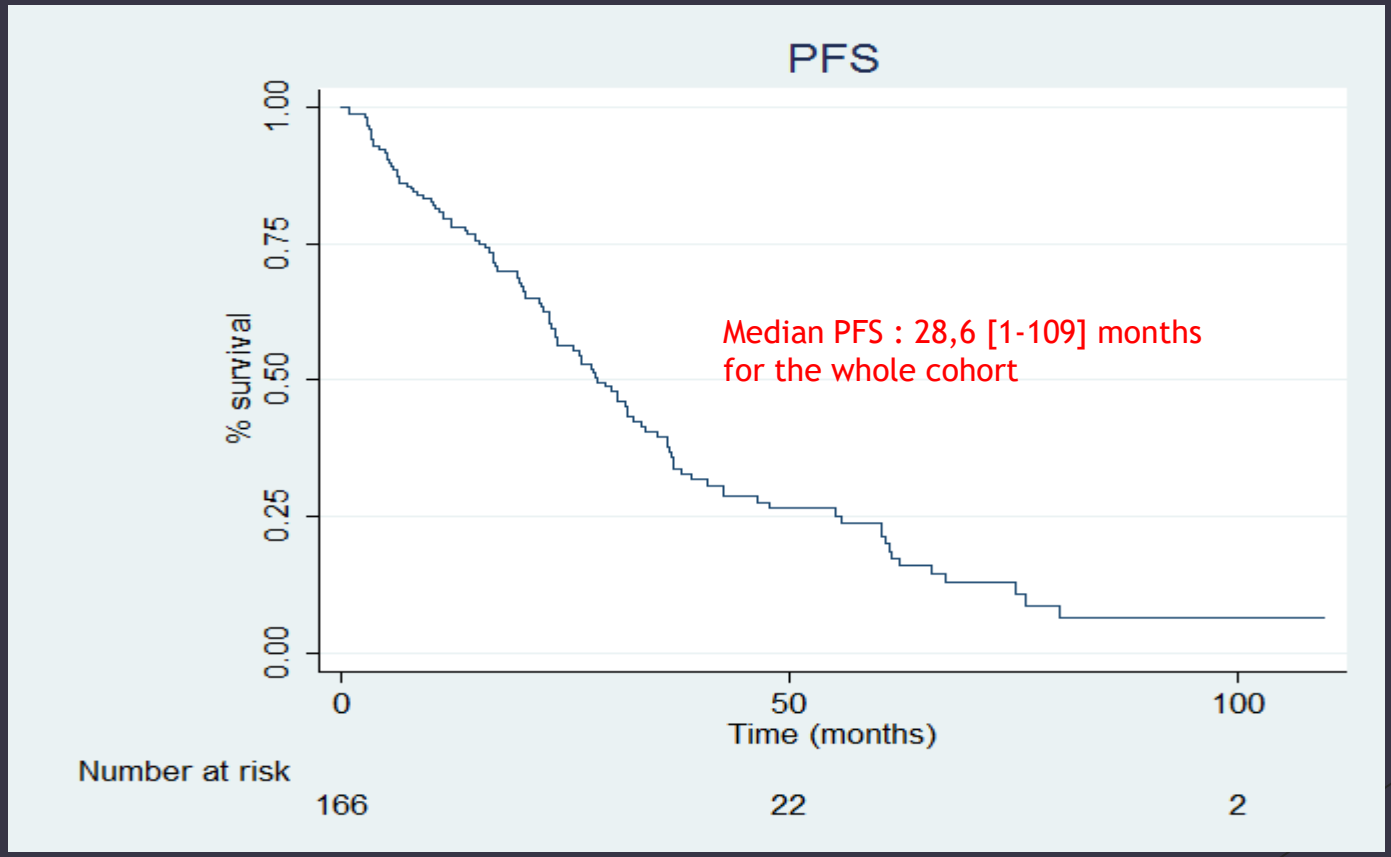
[2] : Fisher exact test

[3] : Logistic regression

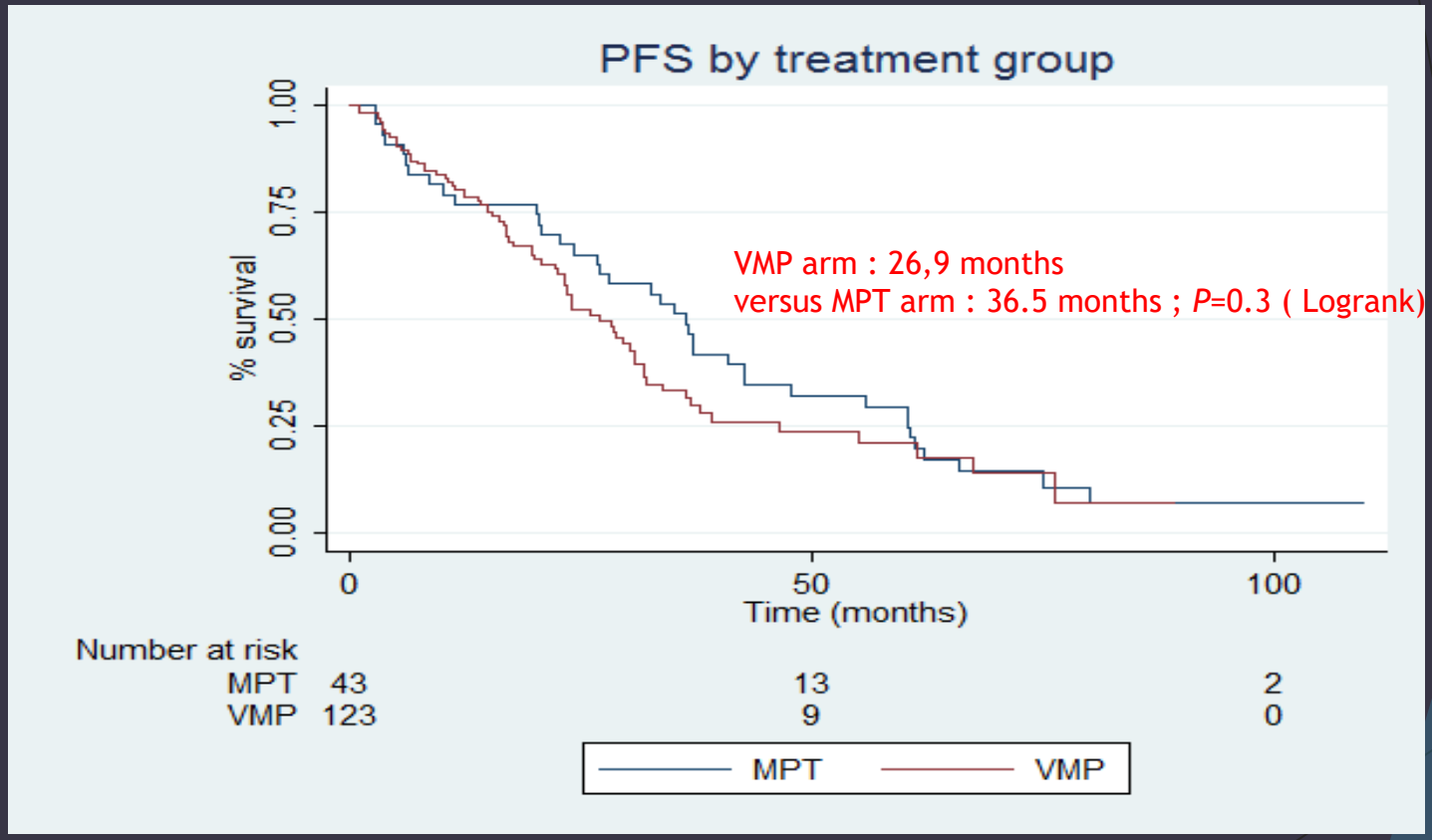
Response to treatment

	Total N=181	MPV arm N=134	MPT arm N=47	P values
CR	29	24	5	NS[2]
VGPR>=90%	69	50	19	
PR>=50% and< 90%	43	30	13	
SD	21	16	5	
Progression	14	10	4	
Not assessable	5	4	1	
ORR	141	104	37	NS[2, 3]

PFS for the whole population



PFS by treatment group



Analysis

- To our knowledge, this is the first real-life study comparing MPT to MPV for newly diagnosed MM.
- This not randomised study, well-balanced between two groups, found that majority of patients were treated with MPV (134/181) because of renal impairment, less neurologic toxicity described in this population and medical use.
- Otherwise, no difference was found in term of response and PFS between MPV and MPT. We expect that treatment decisions continue to be made on an individual basis, taking disease features and co-morbidities into consideration. Some patients subgroups may better benefit from one regimen to another.
- However, these data are clinically important in a setting in wich alkylating agents have long been considered as standard treatment.
- Of note, in addition to favorable efficacy and safety parameters[1] , the Rd regimen has shown significant improvements in clinical relevant quality of life measurements[2], wich is a considerable value in the context of elderly patients with an incurable disease as MM.

1 Benboubker L, Dimopoulos MA, Dispenzieri A, et al. Lenalidomide and dexamethasone in transplant-ineligible patients with myeloma. *N Engl J Med*. 2014;371:906–917.

2 Delforge M, Minuk L, Eisenmann JC, et al. Health-related quality-of-life in patients with newly diagnosed multiple myeloma in the FIRST trial: lenalidomide plus low-dose dexamethasone versus melphalan, prednisone, thalidomide. Haematologica. 2015;100:826–833.

Conclusions

- These data are clinically important in a setting in wich alkylating agents have long been considered as standard treatment.
- This retrospective observational study is well-balanced between the two groups, excepted for cytogenetic and renal failure more present in the MPV group. Less neurologic toxicity is described in this population.
- Despite the cytogenetic imbalance , MPV and MPT regimens seem to provide similar outcome in term of PFS. More data are necessary to have an answer to the question of benefit of bortezomib for poor cytogenetic MM patients.
- MPT will be less used in the future, replaced by Rd regimen in occidental countries.

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