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Research Article

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Oral Domiciliary Therapy of Multiple Myeloma with Cyclophosphamide, Pomalidomide and Dexamethasone Regimen in the Covid Era - A Pilot Study

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Abstract

Background: *Multiple myeloma is the 11th most common cancer in India, with a prevalence of 1.1% and a diagnosis age range of 65 to 74 years. Various doublet or triplet combinations of steroids, immunomodulatory medications, proteasome inhibitors, and monoclonal antibodies are used in standard myeloma therapy. Covid 19 pandemic has been extremely challenging especially when it comes to the management of cancer patients. As the incidence of multiple myeloma (MM) is increasing rapidly in Asian countries, and the Asian patients seem to respond differently compared to the western population to the various commonly used treatment regimens, these patients require special consideration and care to ensure optimum treatment and at the same time, precautions must be taken to decrease their exposure to COVID-19. Considering these aspects, we decided to use an all-oral treatment of CyPomDexa (Cyclophosphamide, Pomalidomide and Dexamethasone) for the treatment of myeloma both as a first-line regimen as well as for relapsed and refractory patients who had not been exposed to this regimen in the past, and to observe the feasibility and efficacy of domiciliary, oral treatment with cyclophosphamide, pomalidomide and dexamethasone (Cy-Pom-Dex) for myeloma patients during the COVID-19 pandemic.*

Methods: *A Prospective, observational, single-arm, pilot study was conducted from 1st March 2020 to 30th September 2020 in patients who were newly-diagnosed (NDMM) or relapsed multiple myeloma (RMM) at a tertiary care Centre in Bengaluru. The patients were started on oral treatment with CyPomDexa during lockdown mandated by the COVID-19 pandemic. This regimen was chosen as a replacement for cyclophosphamide, bortezomib, dexamethasone (CyBorD), which was the previous standard of care in our centre. Haematological and biochemical parameters of the patients were checked pre-treatment. Weekly complete blood counts and biochemistry was checked with home collection of blood samples. This was combined with weekly video consultations. Face-to-face visits were conducted monthly, and myeloma parameters were checked at the end of every 2 months.*

Results: *6 patients underwent the planned treatment. Among these 4 had NDMM and 2 had RMM. 1 patient who received CyPomDexa from the first cycle was lost to follow-up (COVID 19 positive). Among the remaining 5 patients ,3 (50%) achieved VGPR (very good partial response) and 2 (33.33%) achieved SCR (Stringent Complete Response) after 4 cycles of therapy.*

Conclusion: *This regimen achieved good disease control in all the evaluable patients, within 4 cycles. A larger, prospective study is however required to draw definitive conclusions.*

1. Introduction

Multiple myeloma is the 11th most common cancer in India, with a prevalence of 1.1% and a diagnosis age range of 65 to 74 years [1]. The prognosis and treatment of myeloma have been studied extensively in the last decade which led to better understanding of the disease and development of novel agents [2]. Various doublet or triplet combinations of steroids, immunomodulatory medications, proteasome inhibitors, and monoclonal antibodies are

used in standard myeloma therapy. CyBorD (Cyclophosphamide, Bortezomib, and Dexamethasone) and RVD (Lenalidomide, Bortezomib, and Dexamethasone) are two of the most used regimens, which have also been found to improve overall survival and progression-free survival in myeloma patients [2]. These require parenteral administration and hospital admission for its administration.

Covid-19 pandemic has been extremely challenging especially when it comes to the management of cancer patients. These patients require special consideration and care to ensure optimum treatment and at the same time, precautions must be taken to decrease their exposure to COVID-19. Multiple myeloma patients should be risk stratified and Covid-19 screening should be indicated in all patients, according to a report released by Mayo Clinic during current pandemic. Multiple myeloma patients are always at a higher risk of infection, according to the study [3].

Considering these aspects, we decided to use an all-oral treatment of CyPomDexa (Cyclophosphamide, Pomalidomide and Dexamethasone) for the treatment of myeloma both as a first-line regimen as well as for relapsed and refractory patients who had not been exposed to this regimen in the past. Earlier this regimen has only been used in the treatment of relapsed/refractory myeloma patients. This pilot study was planned, and Ethics Committee Approval was obtained. The Aim of this study was to understand the feasibility and efficacy of domiciliary, oral treatment with Cyclophosphamide, Pomalidomide and Dexamethasone (CyPomDexa) for myeloma patients during the COVID-19 pandemic.

2. Materials and Methods

A Prospective, observational, single-arm, pilot study was conducted from 1st March 2020 to 30th September 2020 in patients who were Newly-Diagnosed (NDMM) or Relapsed Multiple Myeloma (RMM) at a tertiary care Centre in Bengaluru. The patients were started on oral treatment with CyPomDexa during lockdown mandated by the COVID-19 pandemic. This regimen was chosen as a replacement for Cyclophosphamide, Bortezomib, Dexamethasone (CyBorD), which was the previous standard of care in our centre.

The regimen consists of Cyclophosphamide 400 mg PO on days 1,8 and 15; Pomalidomide 4 mg PO from days 1 to 21; Dexamethasone 40 mg PO/ 20 mg PO on days 1,8,15 and 22; for every 28 days. In the presence of renal failure, CyBorD was given in the first month of treatment and CyPomDexa was initiated from the second cycle. Oral Ibandronate 50 mg daily was given to all the patients.

Haematological and biochemical parameters of the patients were checked pre-treatment. Weekly complete blood counts and biochemistry was checked with home collection of blood samples. This was combined with weekly video consultations. Face-to-face visits were conducted monthly, and myeloma parameters were checked at the end of every 2 months. Six patients underwent the planned treatment. Among these 4 had NDMM and 2 had RMM.

3. Results

Out of the 6 myeloma patients enrolled in our study, 4 (66.7%) were found to have IgG Kappa, 1 (16.67%) IgA Kappa and 1(16.67%) IgG lambda myeloma. As per International Staging System (ISS), 2 (33.33%) patients had ISS stage 2 disease and 4 (66.67%) had ISS stage 3 multiple myeloma.

Among the 4 newly diagnosed patients in the study 2 (33.33%) received CyPomDexa for the first cycle, while 2 (33.33%) had hypercalcemia and renal failure at diagnosis hence were started on CyBorD as the first cycle which was later changed to CyPomDexa from the second cycle. For the 2(33.33%) patients relapsed were given CyPomDexa for remission induction for relapse, post autologous transplant. 1 patient who received CyPomDexa from the first cycle was lost to follow-up (COVID 19 positive). Among the remaining 5 patients 3 (50%) achieved VGPR (very good partial response) after 4 cycles of therapy and 2 (33.33%) achieved SCR (Stringent Complete Response). All the patients were subsequently started on Lenalidomide maintenance.

Age and sex	Diagnosis	Stage	Presenting complaints	Comorbidities	M band	SFLC	PC	Response after cycle-4	Hypercalcemia	CYBORD (1st cycle)
Newly diagnosed										
46/f	IGG lambda	ISS-II	Bone pain, fracture	None	4.29	Lambda	35%	VGPR	No	No
74/m	IGG Kappa	ISS-III	Joint pain	Hypothyroid	2.2	Kappa	65%	VGPR	No	No
56/m	IGA Kappa	ISS-III	Bone pain, Hypercalcemia, AKI	None	4.07	Kappa	60-70%	SCR	Yes	Yes
62/f	IGG Kappa	ISS-III	Renal failure	DM	5.56	Kappa	70%	Not known	Yes	Yes
Relapsed										

55/m	IGG Kappa	ISS-II	Post-transplant, backpain	None	NORMAL	Kappa	32%	SCR	No	Yes
51/m	IGG KAPPA	ISS-III	Post-transplant, backpain	None	NORMAL	Kappa	NA	VGPR	No	Yes
Response#4- Response Assessment after 4 Cycles; PC-Plasma Cells; SFLC-Serum Free Light Chain Assay; Diag-Diagnosis										

Table

4. Discussion

In Asian myeloma network trial AMN 001, the effectiveness of Pomalidomide in combination with Cyclophosphamide and Dexamethasone has been studied among Asians as it had previously been observed that there was a difference in Asian patients tolerating immunomodulatory as compared to the Western population by having a higher hematologic toxicities and lower thromboembolic complications [4]. This study had highlighted that Pomalidomide showed good response in lenalidomide refractory MM (multiple myeloma) patients. The median PFS was 9.6 months which was longer as compared to 4.6 months in other reported studies. Addition of cyclophosphamide to PomDex combination showed longer DOR. PomDex showed better response in those MM patients with high risk cytogenetic that includes 17pdel and t (4; 14).

In the Asian study population, PomDexa and CyPomDexa were better tolerated, and the most common adverse event noted was myelosuppression which was not the case in our study population. Our patients did not experience major myelosuppression that required dose modification or admission for neutropenia. This combination of drugs has been effective across age groups and across various lines of treatment that includes latest generation of drugs [4].

2100 clinical trials were registered till 2017 February to study about multiple myeloma out of which only 3.7% of overall studies were registered using Pomalidomide [5]. CyPomDex combination has been looked at few of the studies including Baz et al, Van Oekelen O et al and Sriskandarajah et al studies. Baz et al carried out a phase 2 trial which has shown that among the 34 patients enrolled, the ORR was 64.7% with a median PFS of 9.5 months and Van Oekelen O et al conducted a phase 2 study which had 28 patients with ORR of 67% [5-7].

In our pilot study, as highlighted in the results, combination of Cyclophosphamide, pomalidomide and dexamethasone provided good control of myeloma and it was helpful as a domiciliary treatment modality in pandemic times. As discussed previously, CyPomDexa has been used commonly for relapsed/refractory myeloma treatment, but we have used this regimen as an upfront option in newly diagnosed myeloma patients. Prospective studies are required to compare this regimen with the current standard of care for Newly diagnosed multiple myeloma.

5. Conclusion

Domiciliary treatment was feasible, efficacious and cheaper in all our patients. This regimen achieved good disease control in all the evaluable patients, within 4 cycles. A larger, prospective study is however required to draw definitive conclusions [8].

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