Scholar Publishing Group
International Journal of Public Health and Preventive Medicine
https://doi.org/10.38007/IJPHPM.2020.010301
ISSN 2789-8377 Vol. 1, Issue 3: 1-12

Effectiveness of Isazomil Combined with Lenadomide and Dexamethasone in the Treatment of Recurrent and Refractory Multiple Bone Marrow

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Keywords: Multiple Myeloma, Thalidomide and Dexamethasone and Lenalidomide, Light Chain

Abstract: With the increasing morbidity and mortality of patients with multiple myeloma (MM), new immunomodulatory agents, new-generation proteasome inhibitors, monoclonal antibodies and other new drugs have been introduced, but the therapeutic effects are not obvious. Ixazosamine, lenalidomide and dexamethasone are among the drugs for the treatment of MM patients. In order to find a more effective method for the treatment of MM, this article collected 21 patients with relapsed and refractory MM who received oxazide combined with lenalidomide and dexamethasone regimen from June 2014 to April 2018 in the Department of Hematology, Jinhua People's Hospital, Zhejiang Province. MM patients were treated with oxazolamide, lenalidomide and dexamethasone. In the MM patients in the study, 7 patients in the thalidomide exposure group and 6 patients in the unexposed group, the response rates of the two groups were 71% (5/7) and 67% (4/6), respectively. For thalidomide-resistant patients, the combination group still showed higher ORR and longer TTP and PFS than the dexamethasone monotherapy group. Lenalidomide combined with dexamethasone was effective in patients with relapsed and refractory MM with mild adverse reactions. This article also analyzed the efficacy of 61 patients with light chain, 153 patients with IgG and 39 patients with IgA MM who underwent autologous stem cell transplantation. The results showed that the median OS of patients with light chain MM was 2.8 years and the EFS was 1.2 years. Shorter than IgG-type MM patients (4.5 years, P = 0.03 and 2.1 years, P = 0.03).

1. Introduction

Multiple myeloma (MM) is the most common type of malignant plasma cell disease. In recent years, the incidence of multiple myeloma has been increasing year by year. However, multiple

myeloma remains an incurable malignant blood disease, and some patients will relapse and develop resistance. The current natural course of progressive multiple myeloma is approximately 6 months, and the median survival of patients treated with conventional chemotherapy regimens such as MP and VAD is 3 years. The use of new drugs (thalidomide, bortezomib, etc.) and therapeutic measures (hematopoietic stem cell transplantation) has improved efficacy and prolonged patient survival. The median survival of the initial report may be extended to about 5 years.

In response to the pathogenesis of multiple myeloma and the severity of treatment, many research teams at home and abroad have begun in-depth research. In [1], the authors randomly assigned 722 patients with relapsed, refractory, relapsed, and refractory multiple myeloma who received either oxazolidine plus lenalidomide-dexamethasone (ixazomib group) or placebo plus Lenalidomide-dexamethasone (placebo group). The benefit of progression-free survival was observed using the ixazolidine regimen in all pre-specified patient subgroups, including in patients with high-risk cytogenetic abnormalities, compared to placebo regimens. In [2], the authors randomly assigned 569 patients with multiple myeloma who underwent one or more treatment regimens, receiving lenalidomide and dexamethasone alone (control group) or with daratumumab (daratumumab group). The results showed that in the median analysis assigned to the protocol, the median follow-up time was 13.5 months, and the score was $P < 0.001$ by the hierarchical log-rank test. In [3], the authors extracted endothelial cells (EC) from the bone marrow of 57 patients with active multiple myeloma (MM) by a lectin-based approach, and with their healthy resting counterparts, human umbilical veins EC (HUVEC) for comparison. The results indicate that they can secrete secretory growth and invasive factors of plasma cells, signaling through kinases for the development of new blood vessels. In [4], the authors evaluated thalidomide as a single agent in myeloma, myelodysplastic syndrome (MDS), and histiocytosis, a blood disorder characterized by increased angiogenesis, and prospectively A number of alternative angiogenic markers were measured. The results showed that clinical reactions were observed in 7 of 17 myeloma patients and 2 of 5 MDS patients, and some reactions were observed in histiocytosis patients. In [5], the authors' study showed improved progression-free survival and overall survival in patients receiving interferon and glucocorticoid maintenance therapy compared with interferon alone. The authors also compared the rate of remission of two different dose levels (10 mg versus 50 mg) of alternating daily oral prednisone in previously untreated myeloma patients. In [6], the authors compared the combination of carfilzomib and dexamethasone with bortezomib and dexamethasone in the treatment of patients with relapsed or refractory multiple myeloma. In a multicenter study, patients with relapsed or refractory multiple myeloma had one to three treatments, randomized (1:1), and received a randomized protocol (4 sizes) to receive cardinol Rice and dexamethasone (carfilzomib group) or bortezomib and dexamethasone (bortezomib group).

A phase II study (JCOG0904) showed that the total effective rate of bortezomib combined with dexamethasone was 77.3%, and in the third-grade adverse events, cytopenia and sensory peripheral neuropathy were 54.5 and 22.7%, respectively; the total effective rate of thalidomide combined with dexamethasone was 40.9%; indicating that although bortezomib and thalidomide increased the response rate of patients, adverse reactions were not negligible. Lenalidomide is an analogue of thalidomide, which has better curative effect than thalidomide. It mainly inhibits the proliferation of tumor cells through anti-tumor, anti-angiogenesis, erythropoiesis and immune regulation.

In order to find the most suitable drugs for the treatment of multiple myeloma, many research teams at home and abroad have conducted various research and analysis on esamizomib, lenalidomide and dexamethasone. In [7], the authors sought 46 hospitalized Japanese MM patients (25 males and 21 females) to participate in the study and developed a model that can predict

multiple myeloma using a limited sampling strategy (MM) the area under the lenalidomide plasma concentration-time curve (AUC) in patients. In [8], the authors attempted to determine the combined effect of MYC interference therapy with lenalidomide/dexamethasone, and analyzed the combination of the BET bromodomain inhibitor CPI203 and the lenalidomide/dexamethasone regimen in myeloma cell lines. Potential therapeutic effects. It was found that CPI203 exerts a dose-dependent cell growth inhibitory effect in cell lines characterized by G1 cell cycle arrest and concomitant inhibition of MYC and Ikaros signaling. In [9], the authors assessed in the bone marrow by multicolor flow cytometry or sequencing, and by imaging the extramedullary disease. It was found that maintenance of lenalidomide to progression prolonged progression-free and overall survival of standard-risk multiple myeloma and added proteasome inhibitors to treat high-risk disease. The study is evaluating the value of early and late transplantation and minimal residual disease (MRD) as therapeutic goals. In [10], the authors evaluated the safety, efficacy, and pharmacokinetics of elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM) in Japan. The maximum (median) duration of study treatment in Group 1 was 36.6 (35.2) months, and in Group 2 was 28.3 (9.2) months. As a result, leukopenia and lymphopenia were observed in all patients. In [11], the authors reported a case of a 54-year-old woman with POEMS syndrome with pulmonary hypertension who successfully and safely treated lenalidomide and dexamethasone (Ld) and then proceeded with a large Dosing chemotherapy and autologous stem cell transplantation improve pulmonary hypertension. Therefore, it is concluded that Ld can be considered safe and effective for pulmonary hypertension in POEMS syndrome. In [12], the authors gave a regimen of bortezomib in a MM patient, which is considered to be the first choice for treatment of MM with renal failure. However, his condition is that bortezomib is difficult to cure, renal function deteriorates (creatinine 12.55mg / dl), and hemodialysis needs to be started. Subsequently, the authors gave adjusted doses of lenalidomide and dexamethasone. Dialysis can be stopped after 3 cycles of lenalidomide treatment. After 4 cycles, he achieved a strict complete response (sCR) with a creatinine level of 1.85 mg / dl. This case demonstrates that lenalidomide is an effective drug for multiple myeloma and bortezomib in patients with refractory renal insufficiency.

In order to find a cure for the treatment of MM patients, the collection was performed in the Department of Hematology, Jinhua People's Hospital, Zhejiang Province from June 2014 to April 2018, in combination with lenalidomide and dexamethasone (Rd) regimen. 21 patients with relapsed and refractory MM. Patients with relapsed refractory MM. Specific treatment plan: lenalidomide: 25mg/d, continuous oral 21 days, rest 7 days; dexamethasone 40mg / w, oral 4 weeks. According to the previous chemotherapy regimen, the patients were divided into thalidomide exposure group and non-exposed group (7 patients in the exposed group and 6 patients in the unexposed group), all of whom received LD regimen chemotherapy (lenidamide 10-15 mg/d, 1 to 21 days, dexamethasone 20 mg, days 1 to 4, days 15 to 18, 1 cycle every 28 days for a total of 4 cycles). According to the results of immunofixation electrophoresis, MM is divided into five types: IgG, IgA, IgD, IgM, IgE, and is divided into κ chain and λ chain according to the presence or absence of single immunoglobulin light chain secretion; no M protein in serum or urine. It is called non-secretory MM. Finally, R (3.3.1) software was used to conduct meta and summary analysis of the clinical efficacy and safety of DARA.

2. Information and Methods

2.1. Clinical Data

(1) Research object

From June 2014 to April 2008, 21 patients with relapsed/refractory MM admitted to our department (Basic information of patients is shown in Table 1.). The initial diagnosis was in accordance with the MM diagnostic criteria established by the International Myeloma Working Group (IMWG) in 2008, 9 of which were MM recurrence and 4 were refractory MM. Of the relapsed patients, 2 had undergone autologous stem cell transplantation and allogeneic stem cell transplantation. Thirteen patients had previously received at least 1 course of chemotherapy (including VAD, MP/MPT, arsenic trioxide + thalidomide, valence + dexamethasone, and thalidomide alone) with or without thalidomide regimen Medicine maintenance, etc.). There were 7 males and 6 females with a median age of 65 years (49-80 years), 4 cases of IgGκ, 4 cases of IgGλ, 2 cases of IgAκ, 1 case of IgAλ, 1 case of κ light chain, and 1 case of λ light chain. The ECOG score is ≤ 2 points. All patients were staged using the ISS staging system, including 4 cases in stage II, 9 cases in stage III, and DS stage: 4 cases in stage IIA, 8 cases in stage IIIA, and 1 case in stage IIIB. All patients had normal liver function before treatment, and 1 patient with κ light chain had renal dysfunction; no patients had grade 2 or higher peripheral neuropathy (PN).

Table 1. Basic information and clinical characteristics of patients

Patient Basic Information		
Age	Moderate	65
	Range	49~80
Gender	Male	7
	Female	6
Number of chemotherapy before enrollment	Moderate	7
	Range	1~12
Thalidomide exposure (N)	Yes	7
	No	6
Previously accepted transplant (N)	Yes	2
	No	11
ISS staging (N)	Ⅱ	4
	Ⅲ	9
DS staging (N)	Ⅱ A	4
	Ⅲ A	8
	Ⅲ B	1
Classification (N)	IgG κ	4
	IgG λ	4
	IgA κ	2
	IgA λ	1
	κ light chain	1
	λ light chain	1

(2) Main selection criteria

1) Age 18-75 years old, voluntarily participate in clinical trials and sign informed consent.

2) Patients diagnosed with Durie-Salmon stage II or stage III multiple myeloma who have undergone at least two cycles of systemic anti-myeloablative therapy with disease progression or relapse after treatment.

3) Serum myeloma lesion protein reaches measurable level (serum M protein ≥ 0.5g / dl or urine M protein ≥ 200mg / 24h; or serum free light chain determination: in the case of abnormal serum free light chain ratio, affected free Light chain level ≥ 10mg/dl).

4) Absolute blood neutrophil count (ANC) ≥ 1.0 X109 / L; platelets ≥ 50 X109 / L.

5) Liver function serum AST or ALT ≤ 3 times the upper limit of normal; serum total bilirubin ≤ 34umol / L (2.0mg / dl).

6) The estimated survival time is ≥ 3 months.

7) ECOG fitness status score 0, 1 or 2.

2.2. Ttreatment Plan

(1) Dose and usage

Lenalidomide: starting dose 25mg, once a day, after 21 days of continuous oral administration, rest for 7 days, 28 days a cycle until the disease progresses. It can be taken with food or on an empty stomach and should be taken at roughly the same time every day. Capsules should not be opened, destroyed and chewed. Capsules should be swallowed completely with water.

Dexamethasone: 40 mg orally on days 1, 8, 15 and 22 of the 28-day treatment cycle.

(2) Accompanying medications and methods

The bisphosphonate can be used to protect the bone during the study; other treatments deemed necessary for the health of the subject can be performed with the consent of the study physician, including antibiotics, analgesics, antihistamines drugs or other drugs, granulocyte colony-stimulating factor (GCSF), are used to support pre-medication neutrophil counts and infusion of red blood cells, platelets, or fresh frozen plasma to help treat concomitant complications associated with multiple myeloma or other treatments. Subjects at risk of thromboembolic (VTE) events should receive daily preventive treatment during the trial. The choice of treatment depends on the investigator's judgment and should consider thrombosis analysis, bleeding risk, and patient compliance with VTE prevention. Individualized treatment that is tailored to the individual's individual risk/benefit situation after sex.

2.3. Eefficacy Indicators

(1) MR: negative immunoelectrophoresis in serum and urine, disappearance of soft tissue plasmacytoma, proportion of plasma cells in bone marrow <5%; patients who rely solely on serum free light chain (FLC) level as measurable lesions, except above in addition to the CR standard, the FLC ratio is also required to return to normal (0.26-1.65). All of the above indicators need to be evaluated twice in succession.

(2) PR: serum M decreased by 25%-49%, 24h urinary light chain decreased by 50%-89%; if there is soft tissue plasmacytoma at baseline, plasmacytoma is required to be reduced by 25%-49%; number of osteolytic lesions and no increase in size (allowing for the occurrence of compressive bone).

(3) ORR:(Overall response rate, ORR). Does not meet the CR, VGPR, PR and PD standards. If imaging studies are performed, there should be no evidence of new bone lesions or progression of

the original bone lesions.

(4) VGPR: (Very good partial response rate, VGPR). Protein electrophoresis does not detect M protein, but serum and urine immunofixation electrophoresis is positive; or serum M protein is reduced by ≥90% and urinary M protein is <100mg/24h; in patients who rely solely on serum FLC levels as measurable lesions, in addition to the above VGPR criteria, the difference between the affected and unaffected FLC is required to be reduced by >90%, and the above indicators need to be evaluated twice in succession.

(5) CR: negative for immunofixation electrophoresis in serum and urine, disappearance of soft tissue plasmacytoma, ratio of plasma cells in bone marrow <5%; patients who rely solely on serum free light chain (FLC) levels as measurable lesions, in addition to meeting the above CR criteria in addition, the FLC ratio is required to return to normal (0.26-1.65). All of the above indicators need to be evaluated twice in succession.

2.4. Statistical Methods

Since some of the trials belonged to Phases I and II without the control group, a summary analysis was performed on all clinical trials, and a meta-analysis was performed on the RCT containing the control group. Describe the effectiveness and safety of the test group (single arm and RCT) by using remission or incidence (ORR, at least VGPR, and AE incidence); use OR to describe the effectiveness of the test group relative to the control group (RCT) (ORR and at least VGPR); RR was used to describe the safety of the test group relative to the control group (RCT) (AE incidence); HR was used to describe the effectiveness of the test group relative to the control group (RCT) (PFS and OS).

Meta analysis and summary analysis were done through Rstudio software (3.3.1, meta package). The heterogeneity between studies was obtained by Cochran Q and I2 test: when P>0.1, I2<50%, it can be considered that there is homogeneity between multiple studies, and a fixed effect model can be selected for meta-analysis; <0.1, I2> 50%, it can be considered that there is a certain heterogeneity between multiple studies, and a random effects model can be selected.

3. Results

3.1. Analysis of the Effectiveness of Three Drugs

Next, two RCTs (CASTOR and POLLUX trials, including a total of 1031 patients) were analyzed by meta, and the remission rate and survival of the DARA-based triple regimen relative to the dual standard regimen were obtained (Figure 1). The overall weight of the triple regimen relative to the standard regimen ORR, at least VGPR and MRD negative rate (10-5) OR values were 3.27 (95% CI: 2.34-4.56), 3.82 (95% CI: 2.93-4.99) and 3.52 (95% CI: 2.21-5.63). At the same time, the HR value of PFS is 0.36 (95% CI: 0.27-0.47). The OS has an HR value of 0.71 (95% CI: 0.58-0.87) and OS outcomes are subject to longer-term follow-up. The results showed that DARA monotherapy (16 mg/kg) had a very good effect in the treatment of MM patients with advanced relapse and refractory treatment. Despite this, the patient response rate (ORR and at least VGPR) of the triple regimen was significantly better than that of the single drug. By comparing ORR, at least VGPR, MRD negative rates, and PFS, OS, the DARA-based triple regimen (DRd and DVd) was significantly better than the standard regimen (Rd and Vd).

Table 2. Meta-analysis of the efficacy of DARA triple therapy in the treatment of relapsed/refractory multiple myeloma

		OR	95%Cl	Weight
ORR	Odds Ratio	2.82	[1.84;4.33]	62.8%
		4.02	[2.36;6.85]	37.2%
		3.27	[2.34;4.56]	100.0%
VGPR	Odds Ratio	3.54	[2.41;5.18]	50.1%
		4.10	[2.83;5.95]	49.9%
		3.82	[2.93;4.99]	100.0%
MRD	Odds Ratio	4.38	[1.45;13.23]	17.9%
		3.34	[1.99;5.60]	82.1%
		3.52	[2.21;5.63]	100.0%
		HR	95%Cl	Weight
PFS	Hazard Ratio	0.31	[0.29;0.33]	51.1%
		0.41	[0.37;0.46]	48.9%
		0.36	[0.27;0.47]	100.0%
OS	Hazard Ratio	0.77	[0.59;1.01]	56.1%
		0.64	[0.47;0.87]	43.9%
		0.71	[0.58;0.87]	100.0%

A: OR of triple drug versus control ORR; B: OR of at least VGPR of triple drug versus control group; C: negative rate of MRD of triple drug versus control group (10-5); D: triple drug versus control Group HR of PFS; E: HR of triple drug versus control OS.

3.2. Analysis of the Efficacy of Each of the Three Drugs

According to the patient's age/gender/typing, the curative effect between different age groups/gender/type patients was analyzed. According to the relapse/refractory condition of the patients, the relapsed group and the refractory group were compared, and the relapsed/refractory patients were compared. According to whether the patient had previously received thalidomide / lenalidomide / esamizomib, divided into thalidomide exposure group / thalidomide unexposed group, lenalidomide exposure group / the lenalidomide unexposed group, the oxazomib exposure group and the oxazomib-exposed group were specifically analyzed for the efficacy between the groups; show Tables 3 to 7 for details.

Table 3. Comparison of the efficacy of patients

Project	Effective (13)	Invalid (8)	Test Value	P
Median age	57.9(48-69)	59.4(48-69)		
≤58 years old	7(53.8%)	4(50%)	0.290	1.0
>58 years old	6(46.2%)	4(50%)		
Male	7(53.8%)	4(50%)	0.290	1.0
Female	6(46.2%)	4(50%)		
Light chain	4(30.8%)	2(25%)	0.081	1.0
Heavy chain	9(69.2%)	6(75%)		

Table 4. Comparison of curative effect between relapse group and refractory group

Efficacy evaluation	Recurrent group (16)	Refractory group (5)	Test Value	P
PR	10(62.5%)	1(20%)		
MR	2(12.5%)	0		
ORR	12(75%)	1(20%)	4.887	0.047

Table 5. Comparison of the efficacy of thalidomide exposed group and thalidomide unexposed group

Efficacy evaluation	Thalidomide exposure group (15)	Thalidomide unexposed group (6)	Test Value	P
PR	8(53.3%)	3(50.05%)		
MR	1(6.7%)	1(16.7%)		
ORR	9(60.0%)	4(66.7%)	0.081	1.0

Table 6. Comparison of efficacy between lenalidomide exposed group and lenalidomide unexposed group

Efficacy evaluation	Lenalidomide exposed group (11)	Lenalidomide unexposed group (10)	Test Value	P
PR	4(36.4%)	7(70.0%)		
MR	1(9.1%)	1(10.0%)		
ORR	5(45.5%)	8(80.0%)	2.651	0.183

Table 7. Comparison of efficacy between ezazizomi exposed group and oxazomib-exposed group

Efficacy evaluation	Ishazomi exposed group (5)	Ishazomi unexposed group (16)	Test Value	P
PR	4(80.0%)	7(43.8%)		
MR	0	2(12.5%)		
ORR	4(80.0%)	9(56.3%)	0.911	0.606

Efficacy analysis between patients of different age groups/sex/scores showed that the older/female/heavy chain patients had poorer efficacy, and the difference was not statistically significant; the ORR of the relapsed group and the refractory group were 75% VS 20%, respectively. The difference was statistically significant (P=0.047); the ORR of the renal insufficiency group/normal renal function group was 71.4% vs 57.2%, respectively, and the difference was not statistically significant (P=0.656); the ORR of the diabetic group/no diabetes group the difference was 66.7% vs 61.1%, the difference was not statistically significant (P=1.0); the ORR of thalidomide exposed group/thalidomide unexposed group was 60% vs 66.7%, respectively, the difference was not statistically significant (P =1.0); the ORR of the lenalidomide exposed group and the lenalidomide unexposed group were 80% vs 45.5%, respectively, and the difference was not statistically significant (P=0.183); oxazomib exposed group and the ORR of the ixazozomib unexposed group was 80% vs 56.3%, respectively, and the difference was not statistically significant (P=0.606).

3.3. Relapse Refractory Patients

(1) Comparison of the effects of light chain and non-light chain

Figure 1 is a comparison of the efficacy of the two groups in the initial treatment group and the relapsed and refractory group. In this study, there were 22 cases of non-light chain type MM, 4 cases of light chain type MM, and 1 case of non-secretory type. Non-secretory patients and patients who were unable to assess efficacy were not included in the comparison of light-chain and non-light-chain effects. Among the cases that can be used for analysis, 18 patients were non-light chain patients, including 11 males (61.11%), 7 females (38.89%), 1 patient (5.56%), and 1 patient (5.56%). In the third stage, 16 cases (88.89%), the median age was 66 (47-86) years old, the median course of treatment was 4 (1-6), the first diagnosis group was 14 cases (77.78%), and the recurrence group was 4 cases (22.22%). There were 5 patients with CR (27.78%), 9 patients with VGPR (50%), and 1 patient with PR (5.56%). The total effective rate was 83.33%. There were 4 patients with light chain type, 2 males (50%), 2 females (50%), 1 patient (25%), 3 patients (75%), and median age 53 (49-66). The number of median courses was 2 (2-3), 2 (50%) in the newly diagnosed group, 2 (50%) in the recurrent group, 1 (25%) in the VGPR, and 2 (50%) in the PR. The total effective rate is 75%. The ORR rates of the two groups were analyzed and compared, and statistical analysis showed no significant difference (p=0.4462).

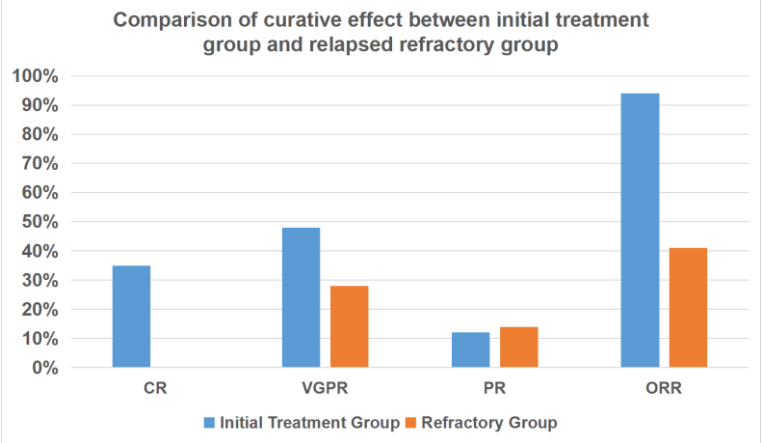

Figure 1. Comparison between the initial treatment group and the relapsed and refractory group

(2) Comparison of the efficacy of IgA and IgG

Figure 2 is a comparison of the effects of the patient after 2 courses and 4 courses. Of the 28 patients enrolled, 13 were IgA and 7 were IgG. Of the evaluable patients, 12 were IgA, including 6 males (50%) and 6 females (50%). Phase II 1 Patients (8.33%), 11 patients (91.67%) in stage III, median age 64.5 (47-86) years old, 3.5 (1-4) median courses, 8 patients (66.67%) in the newly diagnosed group, relapse group 4 For example (33.33%), 3 patients (25%) with CR and 6 patients (50%) with VGPR had a total effective rate of 75% (9/12). There were 5 cases of Ig G type, including 4 males (80%), 1 female (20%), 1 (20%) in stage I, 4 (80%) in stage III, and median age 69 (52-70). The age of middle-aged patients was 4 (2-6). All patients were newly diagnosed patients, 2 patients (40%) with CR, 2 patients (40%) with VGPR, and 1 patient with PR. The total effective rate was 100%. (5/5). The CR rates of the two groups were analyzed. The statistical results showed that there was no difference between the two groups (P=0.3555), and the ORR rate was not statistically significant (p=0.3235).

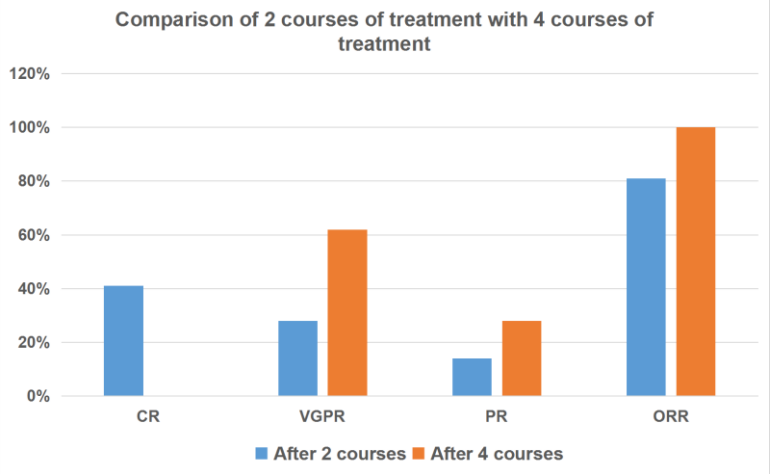

Figure 2. 2 Comparison of the course of treatment with the course of 4 courses

4. Discussions

The meta-analysis was included in the RCT to compare the differences between the triple- and third-level AEs of the triple-dose regimen and the standard-use regimen. No significant increase in AE was observed, with fatigue and diarrhea in the test group slightly higher than in the control group (P = 0.051, 0.058, respectively). A pooled analysis of all clinical trials revealed that the higher incidence of hematologic AE was neutropenia (39%, 95% CI: 16-61%), thrombocytopenia (19%, 95%) CI: 8-31%) and anemia (15%, 95% CI: 8-22%); the non-hematologic AE with a high incidence is pneumonia (8%, 95% CI: 6-10%), around Neuropathy (5%, 95% CI: 2-7%) and fatigue (4%, 95% CI: 2-6%). The results show that the safety based on the DARA regimen is acceptable, but the results need to be further expanded to confirm the sample size of the clinical patient.

The ORR of the thalidomide exposed group/thalidomide exposed group was 60% vs 66.7%, respectively, and the difference was not statistically significant (P=1.0); lenalidomide exposed group and lenalidomide did not. The ORR of the exposed group was 80% vs 45.5%, respectively, and the difference was not statistically significant (P=0.183). The ORR of the oxazomib-exposed group and the oxazomib-exposed group were 80% vs 56.3%, respectively, academic significance (P=0.606).

This article analyzed the efficacy of 61 patients with light chain, 153 patients with IgG, and 39 patients with IgA MM who underwent autologous stem cell transplantation. The results showed that patients with light chain MM had a median OS of 2.8 years and an EFS of 1.2 years. Patients with IgG type MM (4.5 years, P = 0.03 and 2.1 years, P = 0.03). However, there was no significant difference in OS and EFS between the light chain type and IgG type MM patients who achieved CR. This shows that early detection of CR in patients with light chain MM is particularly important.

5. Conclusion

In this article, the combination of esamizomib, lenalidomide and dexamethasone in the treatment of relapsed and refractory multiple bone marrow disease leads to the following conclusions:

(1) In the MM patients in this study, 7 patients were exposed to thalidomide and 6 patients were not exposed. The response rates of the two groups were 71% (5/7) and 67% (4/6), respectively. It is suggested that patients with MM who have been treated with thalidomide for relapse may still get

better results when they receive lenalidomide. This conclusion is also confirmed in other related literature reports. In patients with thalidomide resistance, the LD combination group still showed higher ORR and longer TTP and PFS than the dexamethasone monotherapy group. However, the study still showed that the ORR of patients who had not used thalidomide before was higher than that of patients who had received thalidomide treatment (65 vs 54%), and TTP (13.9 vs 8.4 months) and PFS (13.2 vs 8.4 months) were longer, while the median OS of the two groups was similar (36.1 vs 33.3 months); in thalidomide exposure group, the ORR of patients with thalidomide exposure was higher than that of patients with thalidomide treatment (65 vs 54%). Patients who responded well to lidomide and did not progress during treatment showed better prognosis.

(2) Lenalidomide combined with dexamethasone was effective in patients with relapsed and refractory MM, and the adverse reactions were mild. Lenalidomide combined with dexamethasone was effective in patients with relapsed MM; it was effective in patients with relapsed and refractory MM with extramedullary infiltration. Lenalidomide combined with dexamethasone has a certain effect on refractory MM patients with renal insufficiency/diabetes. Patients who have previously received thalidomide/bortezomib relapse and refractory MM may also benefit from treatment with lenalidomide plus dexamethasone; patients who have previously received hematopoietic stem cell transplantation may also benefit.

(3) The efficacy of 61 cases of light chain type, 153 cases of IgG type and 39 cases of IgA type MM in autologous stem cell transplantation was analyzed. The results showed that the median OS of light chain type MM patients was 2.8 years and EFS was 1.2 years, significantly shorter than patients with IgG type MM (4.5 years, P = 0.03 and 2.1 years, P = 0.03). However, there was no significant difference in OS and EFS between the light chain type and IgG type MM patients who achieved CR. This shows that early detection of CR in patients with light chain MM is particularly important. There are currently no large clinical trials for the efficacy of VD-based chemotherapy regimens in patients with light-chain and non-light chain types. This study analyzed the efficacy of 4 patients with light chain and 18 patients with non-light chain MM. The effective rates were 75% and 83.33%, respectively. Statistics showed that the two groups were not statistically significant (p=0.4462).

Funding

This article is not supported by any foundation.

Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Conflict of Interest

The author states that this article has no conflict of interest.

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