Chemokine Receptor 4–Targeted ^{68}Ga-Pentixafor PET/CT in Response Assessment of Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma

Comparison to ^{18}F-FDG PET/CT

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Purpose: ^{68}Ga-pentixafor PET/CT was reported to have a high sensitivity in detecting tumor involvement of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL) in our previous study. We aimed to further investigate its value in response assessment in WM/LPL.

Patients and Methods: Fifteen patients with WM/LPL were recruited in a prospective cohort study and underwent both ^{68}Ga-pentixafor and ^{18}F-FDG PET/CT at baseline and posttreatment. PET/CT-based responses were analyzed with visual assessments and compared with clinical response.

Results: At baseline, all of the 15 patients had a positive ^{68}Ga-pentixafor PET/CT scan, whereas ^{18}F-FDG PET/CT was positive in 11/15 patients. After chemotherapy, the overall response rate was 86.7% (13/15), and ^{68}Ga-pentixafor PET/CT showed different degree of tumor response from baseline in these patients. In the 2 patients with progressive disease, ^{68}Ga-pentixafor PET/CT detected new lesions or remarkable increase of ^{68}Ga-pentixafor uptake in tumor involvements. However, ^{18}F-FDG PET/CT failed to detect the improvement of disease in 6/13 patients and missed disease progression in 1 of the 2 patients.

Conclusions: ^{68}Ga-pentixafor PET/CT outperformed ^{18}F-FDG PET/CT in response assessment of WM/LPL.

Key Words: Waldenström macroglobulinemia, CXCR4, ^{68}Ga-pentixafor, PET/CT, response assessment

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Waldenström macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL) is an uncommon indolent non-Hodgkin lymphoma characterized by the accumulation of lymphoplasmacytic cells producing excessive monoclonal immunoglobulin in the bone marrow. The diagnosis of WM/LPL requires the histologic evidence of bone marrow infiltration of lymphoplasmacytic cells and the serum presence of monoclonal gammopathy (mostly monoclonal IgM protein). Similar to other indolent lymphomas, treatment is indicated for WM/LPL in cases of symptomatic disease, and serum monoclonal IgM protein level is the major determinant for disease response.[1]

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^{18}F-FDG PET/CT, a standard technique in the management of lymphoma, is recommended for staging and response assessment in FDG-avid nodal lymphomas.[2] However, it is not indicated for WM/LPL, as it is usually not FDG avid.[2,3] A study on the role of ^{18}F-FDG PET/CT in WM/LPL showed a sensitivity of only 43% in detection of bone marrow involvement; moreover, this study found there was no statistical correlation between ^{18}F-FDG PET/CT response and monoclonal protein response.[4]

Chemokine receptor 4 (CXCR4), a key factor for tumor growth and metastasis, is overexpressed in at least 20 different types of solid cancers and hematopoietic malignancies.[5] As a high level of CXCR4 expression in the B cells of patients with WM/LPL was determined,[6,7] we previously conducted a prospective cohort study and reported that ^{68}Ga-pentixafor, a CXCR4-targeted PET probe, was obviously more sensitive than ^{18}F-FDG in detecting tumor involvement of WM/LPL (100% vs 58.8%).[8–10] We also noted significant reduction of ^{68}Ga-pentixafor uptake in WM/LPL after chemotherapy in several patients, and some residual disease detected on ^{68}Ga-pentixafor PET/CT.[8,11] Thus we wonder if ^{68}Ga-pentixafor PET/CT can accurately assess the treatment response of WM/LPL. Herein, we reported the result of our prospective cohort study in response assessment with ^{68}Ga-pentixafor PET/CT after chemotherapy in patients with WM/LPL and to compare it with the performance of ^{18}F-FDG PET/CT, which served as a reference.

PATIENTS AND METHODS

Study Design and Patients

This is a prospective cohort study evaluating the role of ^{68}Ga-pentixafor PET/CT in WM/LPL approved by the Institutional Review Board of Peking Union Medical College Hospital (protocol ZS-1113) and registered at ClinicalTrials.gov (NCT 03436342). A total of 15 patients with newly diagnosed WM/LPL at the Department of Hematology, Peking Union Medical College Hospital, were consecutively recruited from March 2018 to June 2020. Written informed consent was obtained from each patient. Laboratory tests and bone marrow evaluation for WM/LPL was done at enrollment. Patients were then referred for ^{18}F-FDG and ^{68}Ga-pentixafor PET/CT for baseline evaluation that were performed within 1 week after enrollment. Chemotherapy against WM/LPL was started within 2 weeks thereafter. After completion of chemotherapy, all the patients underwent follow-up ^{18}F-FDG and ^{68}Ga-pentixafor PET/CT. In the meantime, clinical response was evaluated according to the consensus response criteria on WM/LPL.[12] The response category was classified as complete response (CR), very good partial response (VGPR), partial response (PR), minimal response (MR), stable disease (SD), and progressive disease (PD) mainly based on monoclonal IgM protein level described as follows: CR is defined as absence of serum monoclonal IgM protein by immunofixation; VGPR is monoclonal IgM protein detectable ≥90% reduction in serum IgM level from baseline; PR is

defined as monoclonal IgM protein detectable ≥50% but <90% reduction in serum IgM level from baseline; MR means monoclonal IgM protein detectable ≥25% but <50% reduction in serum IgM level from baseline; SD is monoclonal IgM protein detectable <25% reduction and <25% increase in serum IgM level from baseline; and PD is defined as ≥25% increase in serum IgM level from lowest nadir.

PET/CT Study

The DOTA-CPCR4-2 peptide was purchased from CSBio Co (Menlo Park, CA). The radiolabeling of ^{68}Ga-pentixafor was performed manually before injection according to the procedures as previously published.[8] ^{18}F-FDG was synthesized in house with an 11-MeV cyclotron (CTI RDS 111; Siemens, Germany). The PET scans were performed with dedicated PET/CT scanners (Biograph 64 Truepoint TrueV; Siemens, Germany; Polestar m660, SinoUnion, China) from the tip of the skull to the middle thigh. For ^{18}F-FDG PET/CT, the patients fasted for at least 6 hours, and the blood glucose levels were monitored (4.7–6.9 mmol/L) before an injection of ^{18}F-FDG (5.55 MBq/kg). The PET/CT images (2 min/bed) were acquired with an uptake time of 75.0 ± 13.2 (mean ± standard deviation) minutes. For ^{68}Ga-pentixafor PET/CT, imaging was performed (2–4 min/bed) with an uptake time of 45.9 ± 19.7 minutes after an injection of 85.1 ± 27.4 MBq of ^{68}Ga-pentixafor. The acquired data were reconstructed using the ordered subset expectation maximization method (Biograph 64: 2 iterations, 8 subsets, Gaussian filter, image size of 168 × 168; Polestar m660: 2 iterations, 10 subsets, Gaussian filter, image size of 192 × 192).

Imaging Analysis

Two experienced nuclear medicine physicians (Y.L. and Q.P.) visually assessed the PET/CT images and were in consensus for image interpretation. As previously described,[8,13] positive bone marrow involvement was defined as the presence of focal lesions with positive PET results or diffuse bone marrow patterns (homogeneous bone marrow uptake) with uptake higher than liver. The presence of positive lymph nodes and other extramedullary involvement were recorded. After completion of chemotherapy, the response of ^{18}F-FDG and ^{68}Ga-pentixafor PET/CT was assessed independently, and the 2 nuclear medicine physicians were blinded from clinical response when reading PET/CT images. According to the Lugano classification,[2,14] 5-point Deauville scale was used in visual assessment of PET/CT-based response (using mediastinal blood pool and liver as the comparators in both ^{18}F-FDG and ^{68}Ga-pentixafor PET/CT). PET/CT-based response cannot be assessed if the baseline scan was negative unless disease progression was noted.

RESULTS

Clinical Characteristics

Fifteen patients with newly diagnosed WM/LPL (12 men and 3 women; 60.9 ± 8.6 [range, 48–76] years) were analyzed in the present study. Anemia and thrombocytopenia was found in 13/15 and 1/15 patients, respectively; 2/15 patients (patients 4 and 9) had renal impairment caused by amyloidosis secondary to WM/LPL. Peripheral neuropathy induced by paraprotein in WM/LPL was found in 2/15 patients (patients 1 and 3), and 1 of them (patient 1) also had Bing-Neel syndrome (WM involving the central nervous system). The median proportion of infiltrated lymphoplasmacytic cells found from bone marrow aspiration was 10.25% (range, 2.5%–80.5%). Mutation of myeloid differentiation primary response 88 (MYD88), which has been identified in more than 90% of WM/LPL patients,[15] was identified in all patients in the present study. Four patients (26.7%) were found to have a CXCR4 mutation. The clinical characteristics and biochemical investigations are summarized in Table 1.

Baseline PET/CT

In WM/LPL, bone marrow is the predominant site of involvement, which was confirmed by bone marrow aspiration and biopsy in all patients. All of the patients had markedly increased uptake of ^{68}Ga-pentixafor in bone marrow (SUV_{max}, 7.9 ± 2.5; range, 5.1–14.8), and lymph node involvement was detected in 12/15 patients. Three patients (patients 1, 9, 10) had paramedullary disease

TABLE 1. Patients' Clinical Characteristics and Biochemical Investigation Results

Patient	Age/Sex	ISS-WM*	Cytogenetics†	M-Protein Type	IgM, g/L	M-Protein, g/L	β2-Microglobulin, mg/L	sFLC, mg/L
1	61/M	Intermediate	$MYD88^{L265P}$	IgMκ	30.49	18.5	6.13	637.5 (κ)
2	72/M	High	$MYD88^{L265P}$	IgMκ	5.78	2.1	8.93	1629.1 (κ)
3	72/M	Intermediate	$MYD88^{L265P}$	IgMλ	15.2	10.5	3.27	27.2 (λ)
4	64/M	Intermediate	$MYD88^{L265P}$	IgMλ	23.69	10.6	5.71	151.3 (λ)
5	64/M	Intermediate	$MYD88^{L265P}$	IgMκ	53.3	32.5	5.27	159 (κ)
6	48/F	NA	$MYD88^{L265P}$ $CXCR4^{s338X}$	IgDκ	6.67 (IgD)‡	6.67	NA	527.5 (κ)
7	55/F	Low	$MYD88^{L265P}$ $CXCR4^{s338X}$	IgMκ	82.49	35.6	2.93	25.7 (κ)
8	52/F	Intermediate	$MYD88^{L265P}$	IgMκ	38.13	21.6	3.34	99.4 (κ)
9	58/M	Intermediate	$MYD88^{L265P}$	IgMκ	43.48	27.9	12.6	NA
10	48/M	Intermediate	$MYD88^{L265P}$	IgMλ	50.9	32.5	6	114 (λ)
11	62/M	High	$MYD88^{L265P}$	IgMκ	33.42	23.7	6	NA
12	76/M	High	$MYD88^{L265P}$	IgMλ	96.02	62.8	3.6	7440 (λ)
13	53/M	Intermediate	$MYD88^{L265P}$ $CXCR4^{s338X}$	IgMλ	79.89	56.5	3.5	2940 (λ)
14	64/M	Intermediate	$MYD88^{L265P}$ $CXCR4^{s338X}$	IgMλ	52.73	30.6	5.9	1950 (λ)
15	64/M	Intermediate	$MYD88^{L265P}$	IgMκ	7.57	3.6	3.5	56.3 (κ)

*International Staging System for WM (ISS-WM) prognostic scoring includes age of >65 years, β2-microglobulin level of >3 mg/L, hemoglobin level of ≤11.5 g/dL, platelet count of ≤100 × 10^9/L, and IgM level of >7 g/dL.

†MYD88 and CXCR4 warts, hypogammaglobulinemia, infections, and myelokathexis syndrome–like somatic mutations were tested.

‡Serum IgD level was measured as IgD-type M-protein level.

sFLC, serum-free light chain.

affecting the soft tissues around the sternum, thoracic and lumbar vertebrae, and presacral space. Among them, 1 patient (patient 1) also had involvement of thoracic and sacral nerve roots that was confirmed by electromyography; the other 2 patients (patients 9 and 10) had additional focal hepatic or pancreatic lesions. Spleen was involved in another 2 patients (patients 8 and 13). All of the above extramedullary disease showed markedly increased uptake of ^{68}Ga-pentixafor (SUV_{max}, 10.1 ± 4.6; range, 4.0–18.8); however, most of them were not FDG avid (SUV_{max} of the detected lesions; 3.5 ± 0.7; range, 3.0–4.6). Only 10/15 patients had increased FDG uptake (uptake higher than liver) in bone marrow involvement (SUV_{max}, 3.4 ± 0.9; range, 2.1–5.3). ^{18}F-FDG PET/CT did not detect additional lesions. Consequently, all of the patients had a positive scan of ^{68}Ga-pentixafor PET/CT, whereas ^{18}F-FDG PET/CT was interpreted as being positive in 11/15 patients (73.3%) at baseline.

Response Assessment With PET/CT After Chemotherapy

After baseline PET/CT, all of the 15 patients received chemotherapy, and follow-up PET/CT were performed after completion of treatment. The intervals between the last cycle of chemotherapy and the follow-up PET/CT were 2 weeks to 10 months (median, 7 weeks). According to the consensus response criteria for WM/LPL,[12] 5 patients achieved CR or VGPR after chemotherapy, 8 patients were evaluated as PR or MR, and 2 patients had PD at follow-up.

In the 5 patients who achieved CR or VGPR after chemotherapy, 4 of them had normalized uptake of ^{68}Ga-pentixafor in bone marrow (SUV_{max}, 2.6 ± 0.9; range, 2.3–3.6), and all of the extramedullary disease with intense uptake of ^{68}Ga-pentixafor at baseline were no longer seen in the follow-up scan (example in Fig. 1). In ^{18}F-FDG PET/CT, the bone marrow uptake decreased from score of 3 to 4 to score of 2 in these 4 patients. The remaining 1 patient (patient 11, Fig. 2) with clinical VGPR had markedly reduced uptake of ^{68}Ga-pentixafor in bone marrow (SUV_{max} of bone marrow at baseline and follow-up, 14.8 vs 7.4) with diminished involved lymph nodes on follow-up ^{68}Ga-pentixafor PET/CT. However, the intensity of FDG uptake in bone marrow in this patient did not change markedly (SUV_{max} of bone marrow at baseline and follow-up, 3.9 vs 4.3).

Eight patients had clinical PR or MR after chemotherapy. All of these patients showed different degree of reduction in bone marrow uptake of ^{68}Ga-pentixafor compared with the baseline (SUV_{max} of bone marrow at baseline and follow-up, 7.1 ± 1.4 vs 4.1 ± 1.7) (example in Fig. 3). However, there was no change of the FDG uptake in bone marrow in 5/8 patients. The lymph node involvement was detected in 7/8 patients by ^{68}Ga-pentixafor PET/CT (most of them were missed by ^{18}F-FDG PET/CT), and there was a complete remission of the lymph node disease in 5 patients; the other 2 patients had remnant lymph nodes but were fewer, smaller, and less avid for ^{68}Ga-pentixafor at follow-up than the baseline PET/CT. Two patients (patients 8 and 13) with splenic involvement showed a significant reduction in the volume of the spleen. The patient

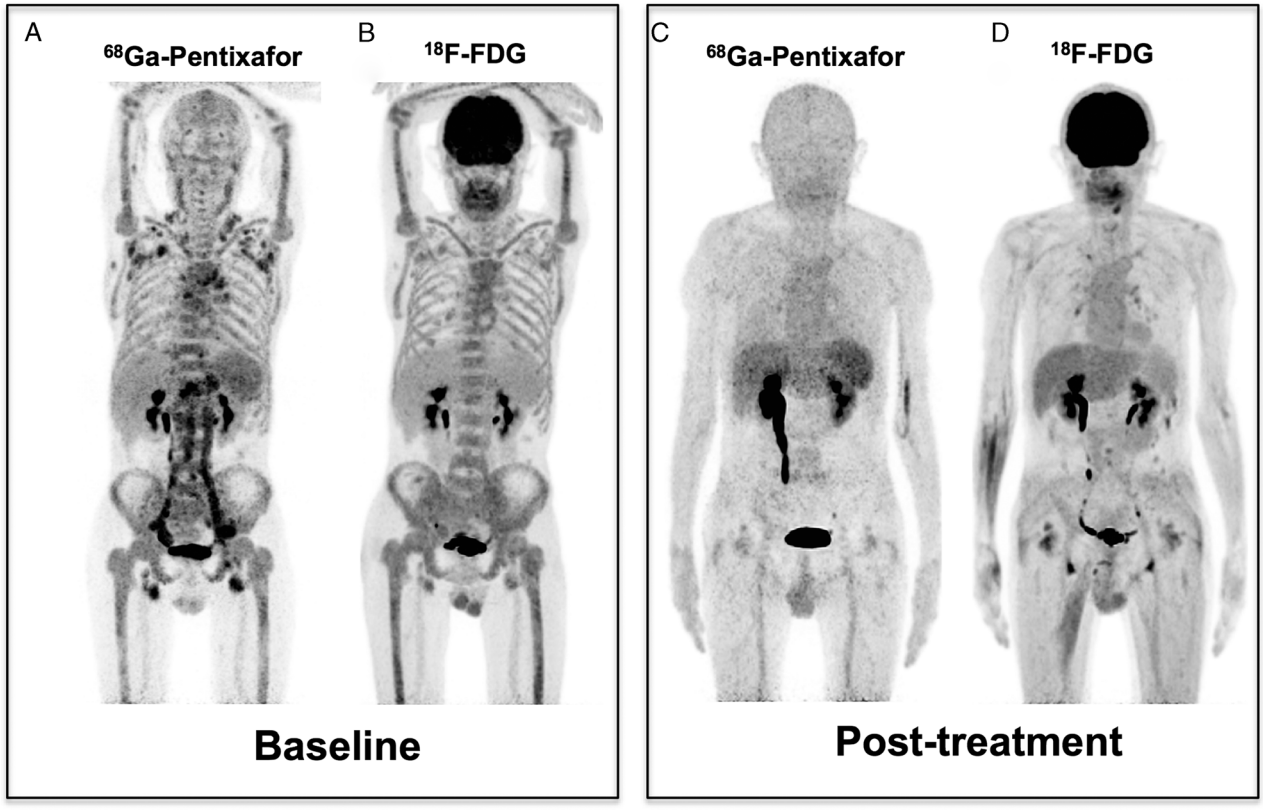

FIGURE 1. Patient 1 (male, 61 years, intermediate risk of ISS-WM) with clinical CR after 6 cycles of chemotherapy (5 cycles of R-FC, 1 cycle of R-DC). Baseline ^{68}Ga-pentixafor (**A**) and ^{18}F-FDG (**B**) PET/CT showed diffusely increased uptake in bone marrow. ^{68}Ga-pentixafor PET/CT also detected lymph nodes, paramedullary, and nerve root involvement. Four months after completion of chemotherapy both of the follow-up ^{68}Ga-pentixafor (**C**) and ^{18}F-FDG (**D**) PET/CT showed CR of the bone marrow and extramedullary disease (ISS-WM, International Staging System for WM; R, rituximab; F, fludarabine; C, cyclophosphamide; D, dexamethasone).

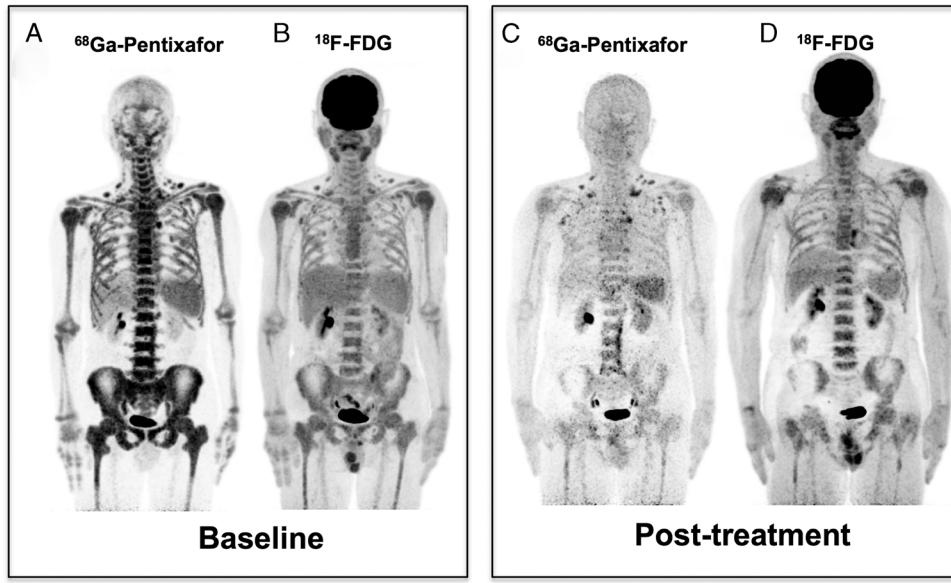

FIGURE 2. Patient 11 (male, 62 years, high risk of ISS-WM) with clinical VGPR after 4 cycles of chemotherapy with DRC. At baseline, ^{68}Ga-pentixafor (**A**) and ^{18}F-FDG (**B**) PET/CT detected diffuse bone marrow disease and multiple lymph node involvement, with more intense uptake of ^{68}Ga-pentixafor than the ^{18}F-FDG uptake in these lesions. After completion of chemotherapy, the follow-up ^{68}Ga-pentixafor PET/CT (**C**) showed markedly reduced uptake of ^{68}Ga-pentixafor in bone marrow and diminished lymph nodes. However, ^{18}F-FDG PET/CT at follow-up (**D**) did not detect significant change of the bone marrow uptake intensity (D, dexamethasone; R, rituximab; C, cyclophosphamide).

(patient 9) with focal hepatic and pancreatic lesions detected by ^{68}Ga-pentixafor PET/CT (which was missed by ^{18}F-FDG PET/CT) showed remarkable improvement of these lesions.

Two patients (patients 10 and 15) had clinical progression after chemotherapy. Patient 15 with bone marrow involvement alone had emerging lesions involving bilateral iliac lymph nodes detected in both ^{68}Ga-pentixafor and ^{18}F-FDG PET/CT, whereas the bone marrow uptake of both tracers remained unchanged (Fig. 4). Patient 10 had disease in bone marrow, lymph nodes, paramedullary, and liver in baseline ^{68}Ga-pentixafor PET/CT, and the above disease

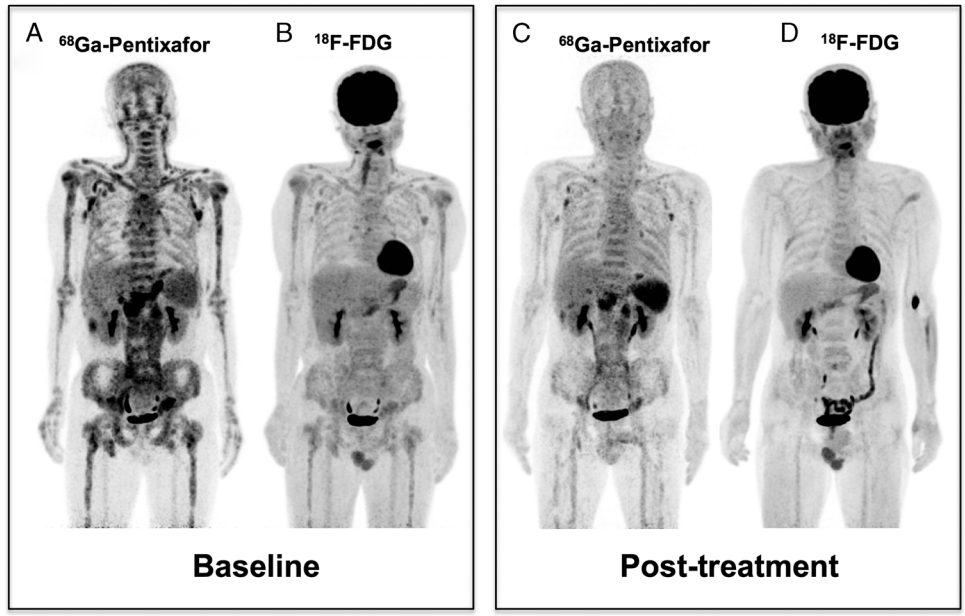

FIGURE 3. Patient 9 (male, 58 years, intermediate risk of ISS-WM) with clinical PR after 5 cycles of chemotherapy with rituximab and lenalidomide. At baseline, ^{68}Ga-pentixafor PET/CT (**A**) showed involvement in bone marrow, paramedullary disease, lymph nodes, liver, and pancreas; meanwhile ^{18}F-FDG PET/CT (**B**) missed most of the extramedullary disease, and only revealed moderately increased uptake in bone marrow involvement. Nine months after completion of chemotherapy, ^{68}Ga-pentixafor PET/CT (**C**) showed remarkable reduced uptake in bone marrow and PR of the extramedullary disease. The follow-up ^{18}F-FDG PET/CT (**D**) also revealed some reduction in bone marrow uptake and PR in some lymph nodes.

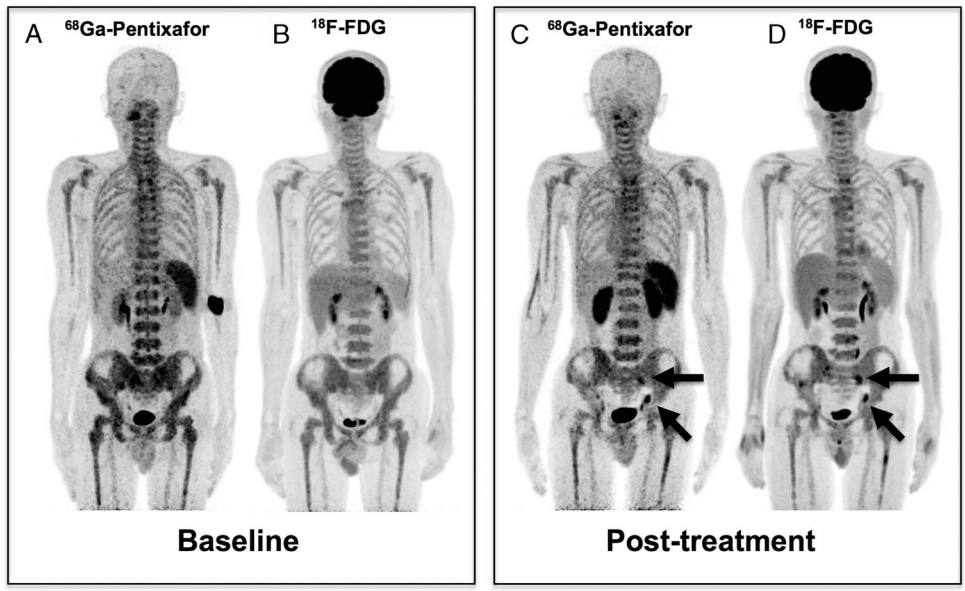

FIGURE 4. Patient 15 (male, 64 years, intermediate risk of ISS-WM) with clinically PD after 5 cycles of chlorambucil. At baseline, ^{68}Ga-pentixafor (**A**) and ^{18}F-FDG (**B**) PET/CT showed increased uptake in bone marrow without extramedullary involvement. After chemotherapy, there were emerging lesions involving bilateral iliac lymph nodes in both ^{68}Ga-pentixafor (**C**, arrows) and ^{18}F-FDG PET/CT (**D**, arrows), whereas the bone marrow uptake of both ^{68}Ga-pentixafor and ^{18}F-FDG remained unchanged.

persisted with increased uptake of ^{68}Ga-pentixafor at follow-up (SUV_{max} at baseline and follow-up, 9.4 vs 13.7). In ^{18}F-FDG PET/CT, only bone marrow involvement was detected (score of 4) in this patient, which remained unchanged at follow-up. The involvement of disease, chemotherapy regimen, clinical, and PET/CT response of each patient are shown in Table 2.

DISCUSSION

The role of ^{18}F-FDG PET/CT is limited in WM/LPL due to its indolent nature and the difficulty in detecting diffuse bone marrow disease; in particular, bone marrow is primarily involved in WM/LPL. In our previous study,[8] we reported that more than 40% of the WM/LPL patients did not present any hypermetabolic disease in ^{18}F-FDG PET/CT; conversely, ^{68}Ga-pentixafor PET/CT showed significantly higher sensitivity in detecting tumor involvements of WM/LPL. Consistently, in the current study, ^{68}Ga-pentixafor PET/CT detected more extensive tumor involvement of the bone marrow and extramedullary disease with higher intensity of radioactivity than ^{18}F-FDG PET/CT did at baseline, which further added evidence of the superiority of ^{68}Ga-pentixafor to ^{18}F-FDG in staging of WM/LPL with PET/CT.

TABLE 2. Clinical Response and PET/CT-Based Response After Chemotherapy

Patient	Involvement at Baseline	Chemotherapy Regimens (Cycles)	Clinical Response	PET/CT-Based Response	
				^{68}Ga-Pentixafor	^{18}F-FDG
1	BM, LN, PMD, nerve root	R-FC (5) + R-DC (1)	CR	CR	CR
2	BM, LN	DRC (7)	PR	PR	NA*
3	BM	DRC (6)	VGPR	CR	NA*
4	BM, LN	BRD (6)	CR	CR	CR
5	BM, LN	DRC (8)	VGPR	CR	NA*
6	BM, LN	DRC (6)	PR	PR	CR
7	BM, LN	DRC (1) + BRD (4) + BD (1)	PR	PR	SD
8	BM, spleen	DRC (6)	PR	PR	CR
9	BM, LN, liver, pancreas, PMD	R2 (5)	PR	PR	PR
10	BM, LN, liver, PMD	DRC (6)	PD	PD	SD
11	BM, LN	DRC (4)	VGPR	PR	SD
12	BM, LN	BRD (8)	PR	PR	NA*
13	BM, LN, spleen	Chlorambucil (2) + BCD (5)	MR	PR	PR
14	BM, LN	BRD (4) + DRC (2)	PR	PR	PR
15	BM	Chlorambucil (5)	PD	PD	PD

*PET/CT-based response cannot be assessed because baseline PET/CT was negative.

R, rituximab; D, dexamethasone; C, cyclophosphamide; B, bortezomib; F, fludarabine; R2, lenalidomide plus rituximab; BM, bone marrow; LN, lymph node; PMD, paramedullary disease; NA, not applicable.

Our study also determined that ^{68}Ga-pentixafor PET/CT is more accurate than ^{18}F-FDG in assessing treatment response in WM/LPL. The overall response rate in the enrolled patients after different chemotherapy regimens was 86.7% (13/15). Among these patients with clinical remission, ^{68}Ga-pentixafor PET/CT showed different degree of tumor response from baseline. However, ^{18}F-FDG PET/CT failed to detect the improvement of disease in 6/13 patients (treatment response could not be assessed in 4 patients due to the false-negative baseline scan; interpretation of SD in the other 2 patients). In the 2 patients with PD, ^{68}Ga-pentixafor PET/CT detected new lesions or remarkable increase of ^{68}Ga-pentixafor uptake values; meanwhile, ^{18}F-FDG PET/CT missed disease progression in 1 patient.

The consensus-based treatment response criteria for WM/LPL, which was proposed for the first time in the second International Workshop on WM/LPL in 2002,[16] is based mainly on the degree of monoclonal IgM protein reduction, because IgM serves as a good marker for tracking disease burden in a particular patient with WM/LPL. For attainment of CR or VGPR, in addition to monoclonal IgM protein level, complete resolution of extramedullary disease on CT scan, that is, lymphadenopathy and splenomegaly if present at baseline, is required.[12] In 1 patient with clinical VGPR (patient 11), ^{68}Ga-pentixafor PET/CT showed remarkable improvement of the bone marrow disease and lymph node involvement, but residual lymph node disease avid for ^{68}Ga-pentixafor was still detected at follow-up (missed by ^{18}F-FDG PET/CT). If using ^{68}Ga-pentixafor PET/CT to evaluate the resolution of extramedullary disease, the response category of this patient would be modified into PR, and the stringency for the determination of a CR or VGPR state will be increased in such circumstances.

Discrepancies can exist between monoclonal IgM protein responses and tumor reduction in WM/LPL[12,17,18]; therefore, additional investigations are needed to confirm the disease response along with IgM levels and to help with precise identification of the depth of response and early recognition of disease progression. Further studies are warranted whether ^{68}Ga-pentixafor PET/CT could play such a role to supplement the current response criteria.

Our study has several limitations. First, the study is limited with a small patient cohort and different chemotherapy regimens for individual patient. We also did not include survival analysis, as further follow-up is needed. Second, the time interval between the end of treatment and posttreatment PET/CT was variant, ranging from 2 weeks to 10 months. Considering chemotherapy may induce downregulation of the surface expression of CXCR4,[19] we scheduled the posttreatment PET/CT at least 2 weeks after completion of chemotherapy in our study design. Affected by the pandemic of COVID-19, follow-up of some patients was delayed. However, the evaluation of clinical response, laboratory tests, and bone marrow evaluation (if needed) were performed in the same period of PET/CT, so the analysis of PET/CT response was not biased. Third, due to the considerable physiologic uptake of ^{68}Ga-pentixafor in the normal spleen, it is difficult to establish an interpretation criterion to define the splenic involvement in ^{68}Ga-pentixafor PET/CT. In our study, the involvement of spleen was established according to the presence of splenomegaly at baseline and significant reduced volume of spleen after chemotherapy, regardless of the splenic uptake of ^{68}Ga-pentixafor.

CONCLUSIONS

In the present study, we found that ^{68}Ga-pentixafor PET/CT-based response after chemotherapy was in concordance with clinical response categories in patients with WM/LPL. Further investigation is warranted to evaluate the value of ^{68}Ga-pentixafor PET/CT in patients' prognosis and survival in larger cohort of WM/LPL.

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