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Original Research Article

A Retrospective Study was Conducted to Evaluate the Long-Term Effects of 177-Lutetium Labelled Somatostatin Analogues on Toxicity, Treatment Response, and Survival Outcomes in Patients Diagnosed with Progressive Neuroendocrine Tumors

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Abstract

Background: Peptide receptor radionuclide therapy (PRRT) has obtained approval in the United States for the therapeutic management of gastroenteropancreatic neuroendocrine tumours (NETs). However, there is a paucity of available data regarding the outcomes of PRRT specifically within populations residing in the United States. The objective of this study was to perform a comprehensive analysis of survival rates, toxicity patterns, and therapeutic response in patients who have received a minimum of three cycles of peptide receptor radionuclide therapy at a Tertiary Care centre located in Mumbai.

Methods: A retrospective and prospective study was conducted over a one-year duration, focusing on a cohort of 87 individuals who underwent three or more cycles of 177Lu DOTATATE therapy (PRRT). The study encompassed data from the centre between 2008 and May 2016 (retrospectively), as well as data collected from June 2016 to June 2017 (prospectively).

Results: Among the entire cohort of 87 individuals, 52.9% of the patients exhibited disease stabilisation. 20.7% of the patients exhibited a partial response to the therapeutic intervention.14.9% incidence of disease progression was observed among the patient population. Overall median survival was determined to be 45 months, and median survival from the date of the first cycle of therapy was 27.5 months. According to the results of our analysis, no significant haematological toxicity was observed.

Conclusion: Our study showed that PRRT is overall well tolerated with most recipients experiencing only mild to moderate toxicity if the necessary precautions are undertaken. It should be considered earlier in the course of metastatic disease (in combination with other treatment options) and not as the modality of last resort.

Keywords: Toxicity, Response, Survival, Neuroendocrine Tumour, Long Term Analysis.

Introduction

Neuroendocrine tumours (NETs) are an infrequent manifestation of hormone-secreting neoplasms, characterised by diverse clinical syndromes. Additionally, these cells exhibit cell surface peptide receptors that play a crucial role in both diagnostic and therapeutic applications.

The assessment of neuroendocrine tumours (NET) primarily revolves around acquiring histopathological confirmation and subsequently identifying cases that may be amenable to surgical resection. Surgical resection is the preferred treatment option if the patient's overall health and extent of tumour presence allow for it. These neoplasms frequently manifest with distant metastasis, and due to the plethora of therapeutic modalities at our disposal, the management of metastatic disease is becoming progressively intricate [1-4]. Somatostatin analogues are extensively utilised in the medical field for the treatment of metastatic neuroendocrine tumours (NETs).

These analogues have demonstrated efficacy in impeding disease progression and enhancing symptoms associated with the condition [5, 6].

Additional therapeutic options for metastatic neuroendocrine tumours (NETs) encompass systemic chemotherapy, liver-directed therapy, surgical intervention, and peptide receptor radionuclide therapy (PRRT) [7, 8, 9].

Systemic chemotherapy has demonstrated efficacy in select patient populations, particularly individuals diagnosed with poorly differentiated neuroendocrine tumours (NETs) or neuroendocrine carcinoma (grade 3, WHO 2010), as well as those with progressive pancreatic NETs. Nevertheless, in the context of well differentiated midgut neuroendocrine tumours (NETs) with a grade of 1 or 2 according to the World Health Organisation (WHO) classification of 2010, the efficacy of chemotherapy is limited, with response rates ranging from 7% to 20%. Furthermore, no evidence of improved survival outcomes has been observed [10]. Peptide receptor radionuclide therapy (PRRT) involves the utilisation of a radionuclide conjugated with a somatostatin analogue. This approach enables precise administration of radiotherapy to neuroendocrine tumours (NETs) that express somatostatin receptors, encompassing the majority of NET cases. The clinical efficacy of peptide receptor radionuclide therapy (PRRT) in the NETTER 1 trial [1] resulted in the authorization of 177Lu-DOTATATE for the management of well-differentiated gastroentero-pancreatic (GEP) neuroendocrine tumours (NETs). The NETTER 1 study was conducted on patients with well-differentiated G1 and G2 midgut neuroendocrine tumours (NETs) that had metastasized or were locally advanced and showed signs of disease progression at the beginning of the study. Peptide receptor radionuclide therapy (PRRT) demonstrated a significant advantage over high dose somatostatin analogues (SSA) in accordance with the significance of employing a suitable targeted and biologically active treatment [11].

Currently, a multitude of treatment protocols are available, each characterised by distinct study designs. The primary benefit for individuals diagnosed with terminal stage cancer can be evaluated through the analysis of long-term outcomes and survival rate statistics, which are currently insufficient in availability. Greater emphasis should be placed on the assessment of the quality of life that can be afforded by these novel therapeutic interventions. Through this study, our objective is to evaluate the clinical efficacy of Peptide Receptor Radionuclide Therapy (PRRNT) in relation to the overall survival rate observed in patients following treatment with 177Lu DOTATATE. The objective of this study was to perform a comprehensive analysis of survival rates, toxicity patterns, and treatment response in patients who have received a minimum of three cycles of peptide receptor radionuclide therapy at a Tertiary Care centre located in Mumbai.

Methods

The present retrospective prospective study was undertaken at the Department of Nuclear Medicine and Positron Emission Tomography/Computed Tomography (PET/CT), Jaslok Hospital, Mumbai. All individuals aged 15 to 100 years who have undergone peptide receptor radionuclide therapy as inpatients at a nuclear medicine department within a tertiary care centre in Mumbai for the treatment of progressive neuroendocrine tumours. The present investigation was carried out from 2008 to June 2016, encompassing a retrospective component, and from June 2016 to January 2017, incorporating a prospective component.

Inclusion criteria

All patients who have undergone 3 or more than 3 cycles of 177Lu DOTATATE therapy (PRRT) from the centre.

Exclusion criteria

Patients who have undergone less than 3 cycles of 177Lu DOTATATE therapy. All pregnant ladies and teenagers and children (<15 years of age).

Sampling method

In the retrospective component of the study, all patients who satisfy the predefined inclusion criteria and for whom consecutive data are accessible for analysis are included in the study cohort. In the prospective component of the study, sequential data of patients who have provided informed consent will be included from June 2016 to January 2017.

Study tools and procedure

The retrospective analysis involved the examination of pre-therapy assessments, therapy records, and post-therapy follow-up records of all patients who had received therapy at the tertiary centre before June 2016. The individuals who received three cycles of treatment subsequent to June 2016 were prospectively enrolled in the study following the provision of informed consent. Data pertaining to these patients were collected in a prospective manner. A patient information sheet and clinical record form have been developed. The study assessed the patient characteristics, response patterns, and toxicity profiles of individuals who underwent Peptide Receptor Radionuclide Therapy (PRRT) at a prominent tertiary healthcare facility starting from 2008. The inclusion criteria for this study involved the selection of patients who had undergone a minimum of three cycles of peptide receptor radionuclide therapy (PRRT). This criterion was established to ensure a suitable evaluation of treatment response.

Statistical Analysis

Continuous variables were evaluated using the median and range, while discrete variables were examined using counts or percentages, unless stated

otherwise. Survival was evaluated based on the date of diagnosis and the date of initiation of the initial peptide receptor radionuclide therapy (PRRT) cycle. The Kaplan-Meier life tables were employed to compute the probabilities of survival. The 'time' variable represents the duration from the initial day of the first cycle to either the month of demise or the day of communication for subsequent evaluation. The log-rank tests were utilised to examine the presence of a disparity in survival curves among the various response groups. In order to evaluate response, it is necessary to include only patients who have undergone a minimum of three cycles of peptide receptor radionuclide therapy (PRRT) and have undergone at least one post-therapy restaging somatostatin receptor (SSTR) functional imaging assessment. All p-values were calculated using a two-sided test, and a significance level of $p<0.05$ was deemed statistically significant in this study. The data analysis was conducted using the SPSS statistical software package.

Results

Our research comprised a cohort of 87 patients who have successfully undergone a minimum of three cycles of Peptide Receptor Radionuclide Therapy (PRRT), with pending administration of subsequent cycles.

A comprehensive analysis was conducted on a cohort comprising 87 individuals, consisting of 50 males and 37 females. The cohort encompassed individuals aged 25 to 82 years, with a mean age of 52.87 years.

Table 1: Sex distribution

Sex	No. of patients	% of patients
Male	50	57.5
Female	37	42.5

Table 2: Age distribution

Variable	Minimum	Maximum	Mean±SD	Std. Deviation
Age	25.0	82.0	52.87±13.26	13.2602

Table 3: Tumour types

	No of patients	Percentage
Thoracic NET		
Bronchial carcinoid	3	3.4
Mediastinal Carcinoid	1	1.1
Neuroendocrine tumor		
Duodenal NET	6	6.9
Gastric net	2	2.3
Pancreatic NET	22	25.3
Gall bladderNET(GB)	1	1.1
Jejunal NET	3	3.4
Ileal NET	13	14.9
Rectosigmoid NET	1	1.1
Retroperitoneal NET	1	1.1
Renal NET	1	1.1
Unknown Primary	1	1.1
Paraganglioma		
Pheochromocytoma	1	1.1
SporadicParaganglioma	1	1.1
FamalialParaganglioma	1	1.1
Other Tumors with SSTR Expression		
Meningioma	2	2.3
MedullaryThyroidCancer	4	4.6
HurtleCellCarcinoma	1	1.1

Table 4: Kaplan–Meier survival analysis showing SSTR response after 3 or 4 cycles: Log rank Test, p=0.003

SSTR Response After 3 Or 4 Cycles	Total N	N of Events	Censored	
			N	Percent
Complete	1	0	1	100.0%
Partial	18	3	15	83.3%
Progression	13	11	2	15.4%
Stable	48	9	39	81.3%
Overall	80	23	57	71.3%

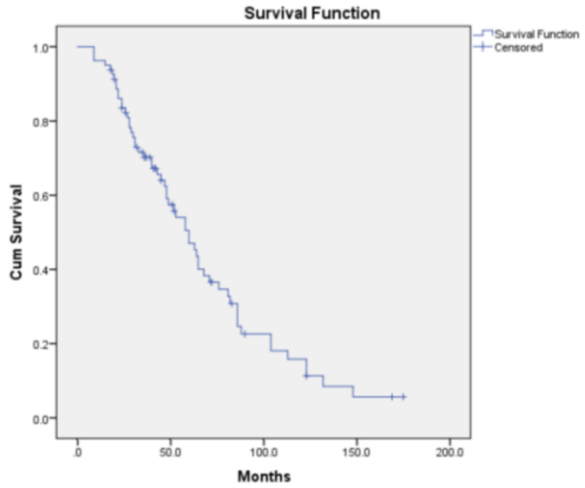

Figure 1: Kaplan–Meier survival curve for overall survival

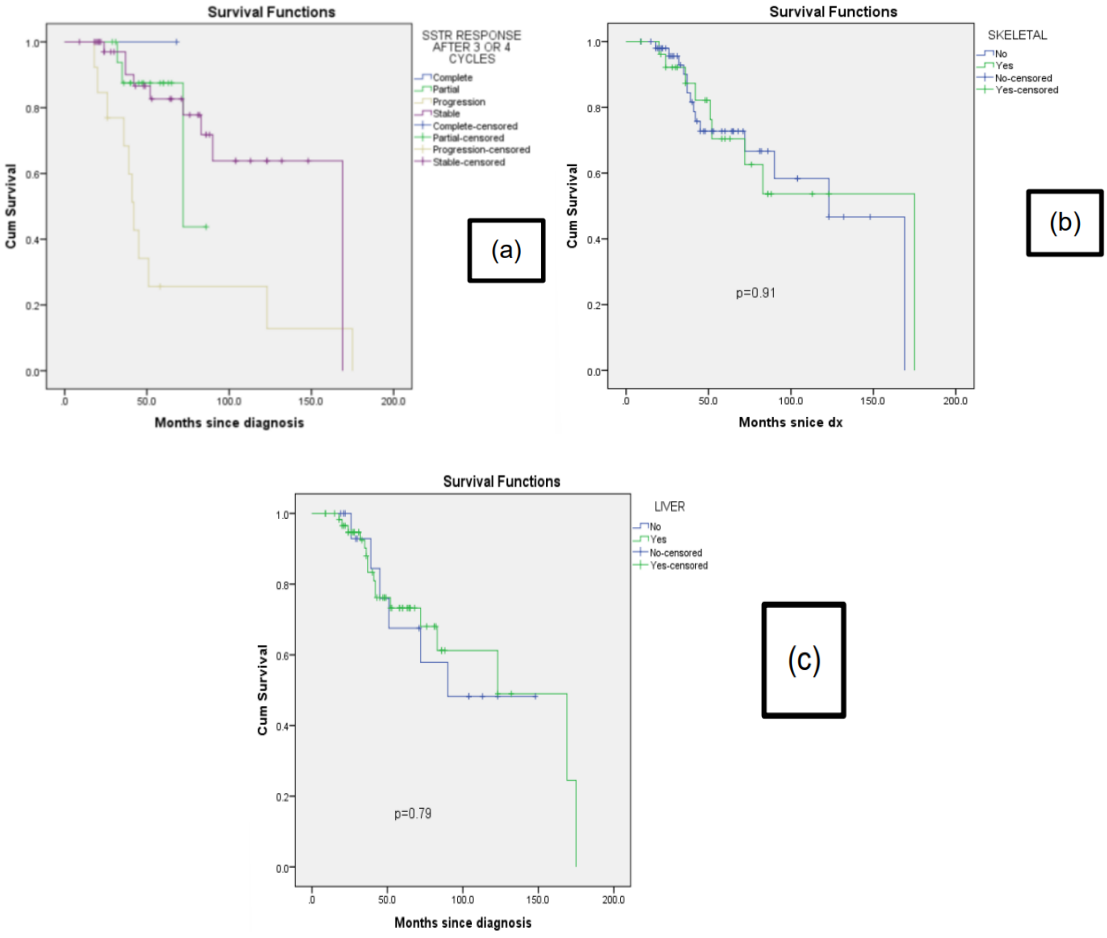

Figure 2: OS stratified by (a) Radiological response to PRRT therapy, (b) Skeletal and (c) Liver metastasis

Table 5: Toxicity Cycle 1

2 weeks(n=65)					
	Grade 0	**Grade 1**	**Grade2**	**Grade 3**	**Grade 4**
Hb	43(66.15)	15(23.07)	7(10.77)	0	0
PLC	63(96.92)	1(1.54)	0	0	1(1.54)
WBC	61(93.85)	3(4.61)	1(1.54)	0	0
S.Cr	64(98.46)	1(1.54)	0	0	0
SGOT	63(96.92	2(3.08)	0	0	0
SGPT	63(96.92	2(3.08)	0	0	0

ALP	62(95.38)	3(4.61)	0	0	0
4 weeks(n=64)					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	42(65.62)	16(25)	6(9.37)	0	0
PLC	63(96.92)	1(1.56)	0	0	0
WBC	61(95.31)	3(4.69)	0	0	0
S.Cr	63(98.44)	1(1.56)	0	0	0
SGOT	64(100)	0	0	0	0
SGPT	64(100)	0	0	0	0
ALP	63(96.92)	1(1.56)	0	0	0
6 weeks(n=86)					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	58(67.44)	19(22.09)	9(10.46)	0	0
PLC	84(97.67)	2(2.32)	0	0	0
WBC	78(90.69)	7(8.14)	1(1.16)	0	0
S.Cr	86(100)	0	0	0	0
SGOT	84(97.67)	2(2.32)	0	0	0
SGPT	84(97.67)	2(2.32)	0	0	0
ALP	81(94.18)	3(3.49)	2(2.32)	0	0

Table 6: Toxicity Cycle 2

2 weeks(n=64)					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	40(62.5)	18(28.12)	6(9.37)	0	0
PLC	63(98.44)	1(1.56)	0	0	0
WBC	61(95.31)	3(4.69)	0	0	0
S. Cr	63(98.44)	1(1.56)	0	0	0
SGOT	64(100)	0	0	0	0
SGPT	63(98.44)	1(1.56)	0	0	0
ALP	61(95.31)	1(1.56)	2(3.12)	0	0
4 weeks(n=64)					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	44(68.75)	14(21.87)	6(9.37)	0	0
PLC	63(98.44)	1(1.56)	0	0	0
WBC	61	3(4.69)	0	0	0
S.Cr	63(98.44)	1(1.56)	0	0	0
SGOT	64	0	0	0	0
SGPT	63(98.44)	1(1.56)	0	0	0
ALP	61(95.31)	1(1.56)	2(3.12)	0	0
6 weeks(n=87)					
	Grade 0	**Grade1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	57(65.52)	24(27.59)	5(5.75)	1(1.15)	0
PLC	83(95.40)	3	1(1.15)	0	0
WBC	7(8.04)	13(14.94)	1(1.15)	0	0
S.Cr	87(100)	0	0	0	0
SGOT	86(98.85)	1(1.15)	0	0	0
SGPT	85(97.70)	2(2.29)	0	0	0
ALP	83(95.40)	3(3.45)	2(2.29)	1(1.15)	0

Table 7: Toxicity Cycle 3

2 weeks(n=59)					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	41(69.49)	14(23.73)	4(6.78)	0	0
PLC	53(89.83)	6(10.17)	0	0	0
WBC	54(91.52)	5(8.47)	0	0	0
S.Cr	59(100)	0	0	0	0
SGOT	58(98.30)	1(1.69)	0	0	0
SGPT	58(98.30)	1(1.69)	0	0	0
ALP	56(94.91)	2(3.39)	1(1.69)	0	0

4 weeks					
	Grade 0	**Grade1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	42(68.85)	15(24.59)	4(6.56)	0	0
PLC	55(90.16)	6(9.84)	0	0	0
WBC	56(91.80)	5(8.19)	0	0	0
S.Cr	61(100)	0	0	0	0
SGOT	60(98.36)	1(1.64)	0	0	0
SGPT	59(96.72)	2(3.29)	0	0	0
ALP	58(95.08)	2(3.29)	1(1.64)	0	0
6 weeks					
	Grade0	**Grade1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	41(61.19)	17(25.37)	6(8.95)	3(4.48)	0
PLC	57(85.07)	9(10.34)	1(1.49)	0	0
WBC	55(82.09)	11(16.42)	1(1.49)	0	0
S.Cr	66(98.51)	1(1.49)	0	0	0
SGOT	67(100)	0	0	0	0
SGPT	66(98.50)	1(1.49)	0	0	0
ALP	64(95.52)	2(2.98)	1(1.49)	0	0

Table 8: Toxicity Cycle 4

2 weeks					
Haematology	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	17(80.95)	4(19.05)	0	0	0
PLC	17(80.95)	2(9.52)	2(9.52)	0	0
WBC	21(100)	0	0	0	0
S.Cr	21(100)	0	0	0	0
SGOT	21(100)	0	0	0	0
SGPT	20(95.24)	1(4.76)	0	0	0
ALP	18(85.71)	3(14.28)	0	0	0
4 weeks					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	29(63.04)	13(28.26)	4(8.69)	0	0
PLC	21(45.65)	4(8.69)	1(2.17)	0	0
WBC	42(91.30)	1(2.17)	3(6.52)	0	0
S.Cr	46(100)	0	0	0	0
SGOT	46(100)	0	0	0	0
SGPT	44(95.65)	2(4.34)	0	0	0
ALP	44(95.65)	2(4.34)	0	0	0
6 weeks					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	29(64.44)	12(26.67)	1(2.22)	3(6.67)	0
PLC	38(84.44)	6(13.33)	1(2.22)	0	0
WBC	42(93.33)	0	2(4.44)	1(2.22)	0
S.Cr	45(100)	0	0	0	0
SGOT	45(100)	0	0	0	0
SGPT	42(93.33)	0	0	0	0
ALP	43(95.55)	2(4.45)	0	0	0

Table 9: Toxicity Cycle 5

2 weeks					
Haematology	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	6(75%)	2(25)	0	0	0
PLC	5(62.5)	2(25)	1(12.5)	0	0
WBC	7(87.5)	1(12.5)	0	0	0
S.Cr	8(100)	0	0	0	0
SGOT	8(100)	0	0	0	0
SGPT	8(100)	0	0	0	0
ALP	7(87.5)	1(12.5)	0	0	0

4 weeks					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	17(85)	3	0	0	0
PLC	17(85)	3	0	0	0
WBC	20(100)	0	0	0	0
S.Cr	20(100)	0	0	0	0
SGOT	20(100)	0	0	0	0
SGPT	19(95)	1(5)	0	0	0
ALP	18(90)	2(10)	0	0	0
6weeks					
	Grade0	**Grade1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	17(85)	3(15)	0	0	0
PLC	18(90)	2(10)	0	0	0
WBC	20(100)	0	0	0	0
S.Cr	20(100)	0	0	0	0
SGOT	20(100)	0	0	0	0
SGPT	20(100)	0	0	0	0
ALP	18(90)	2(10)	0	0	0

Table 10: Toxicity Cycle 6

2 weeks					
Haematology	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	7	0	0	0	0
PLC	7	0	0	0	0
WBC	7	0	0	0	0
S.Cr	7	0	0	0	0
SGOT	7	0	0	0	0
SGPT	7	0	0	0	0
ALP	7	0	0	0	0
4 weeks					
	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	5(71.43)	2(28.57)	0	0	0
PLC	4(57.14)	3(42.86)	0	0	0
WBC	6(85.71)	1(14.28)	0	0	0
S.Cr	7	0	0	0	0
SGOT	7	0	0	0	0
SGPT	7	0	0	0	0
ALP	7	0	0	0	0
6 weeks					
	Grade 0	**Grade1**	**Grade 2**	**Grade 3**	**Grade 4**
Hb	2(28.57)	5(71.43)	0	0	0
PLC	5(71.43)	2(28.57)	0	0	0
WBC	7	0	0	0	0
S.Cr	7	0	0	0	0
SGOT	7	0	0	0	0
SGPT	7	0	0	0	0

Discussion

The management of metastatic neuroendocrine tumours (NETs) poses a significant clinical dilemma due to the limited availability of therapeutic interventions. In the context of advanced and metastatic neuroendocrine tumours (NETs), the utilisation of surgical interventions, external beam radiotherapy, and chemotherapeutic agents is constrained. During the early 1990s, the administration of radiolabelled somatostatin analogues commenced as a therapeutic intervention for patients diagnosed with neuroendocrine tumours (NETs). This treatment approach was initially implemented using [111In-DTPA0] octreotide. This led to the management of symptomatic disease, although instances of partial remissions were infrequent [12].

Furthermore, it led to bone marrow suppression, myelodysplastic syndrome, renal insufficiency, and transient liver toxicity. The subsequent iteration of peptide receptor radionuclide therapy (PRRT) was formulated through the utilisation of somatostatin

receptor analogues and novel radionuclides such as Lu177 and Y90 [13, 14]. The objective of our research was to conduct a comprehensive analysis of survival rates, toxicity patterns, and therapeutic response among patients who have received a minimum of three cycles of Lu 177-based peptide receptor radionuclide therapy. The present study encompassed a cohort of 87 patients who successfully underwent a minimum of three cycles of Peptide Receptor Radionuclide Therapy (PRRT). Among the observed population, 57.5% were identified as males, while 42.5% were identified as females. The study encompassed individuals within the age range of 25 to 82 years, with a calculated mean age of 52.87 years and a standard deviation of 13.26 years. A total of 87 individuals underwent 343 administrations of 177Lu DOTATATE between the months of March 2010 and April 2017. A total of 43.7% of the patients included in the study underwent four cycles of treatment, as reported in reference [15]. In our research cohort, pancreatic neuroendocrine tumours (NETs) emerged as the prevailing subtype, constituting 25.3% of the total cases. The second most prevalent neoplasms were ileal neuroendocrine tumours (NETs), with a prevalence rate of 14.9% among the patients who underwent treatment. Among the cohort of 87 individuals, a substantial majority of 82 patients presented with metastatic disease, while a smaller subset of 5 patients exhibited locally aggressive disease that was deemed inoperable. The sites of metastatic involvement exhibited heterogeneity among individual patients. In our study cohort, the liver emerged as the predominant site of metastasis. In the study cohort, liver metastasis was observed in 75.9% of patients, while lymph node metastasis was found in 66.7% of the study participants. A total of 36% of the patients exhibited skeletal metastasis. There was no statistically significant difference observed in comparable parameters, including age, sex, the origin of tumours, site of metastases, and treatment prior to peptide receptor radionuclide therapy (PRRT).

Survival Analysis

On 87 patients, a Kaplan-Meier survival analysis was performed. The aggregate median survival time for our 87 patients was 45 months (from the time of diagnosis) and 27.5 months (from the date of the first cycle of therapy). 87 patients' disease-related survival was evaluated based on treatment outcome. The survival rate of patients with progressive disease (PD) was significantly lower. Survival did not differ substantially between other treatment outcomes, including complete response, partial response, and stable disease.

We found a benefit in OS for patients treated with ^{177}Lu-octreotate, ranging from a minimum of 5 months to a maximum of 78 months from the date of the first cycle and a minimum of 9 months to 179 months from the date of diagnosis. The disadvantage of the preceding statement is that our study cohort included SSTR-expressing tumours such as meningioma.

Toxicity

Hematotoxicity

Haemoglobin level, WBC count, and platelet count were used to assess hematotoxicity. 27.9% of patients had grade 1 anaemia and 5.7% had grade 2 anaemia, according to a pre-treatment blood report evaluation. One patient had grade 1 thrombocytopenia and two patients had grade 1 neutropenia. According to the results of our analysis, no significant haematological toxicity was observed. During the entire study period, the incidence of thrombocytopenia, anaemia, and neutropenia of grade 3 or 4 was less than a maximum of 6.6% of patients. Only one patient required platelet transfusion support. During the study period, no adverse haematological toxicity, such as MDS or acute leukaemia, was observed in our study cohort.

Renal toxicity

Serum creatinine was used to determine the toxicity to the kidneys. One patient (1,1%) developed grade 1 renal toxicity with the rise in S. creatinine following the first and second cycles at the second and fourth weeks of follow-up, which improved by the sixth week. After the third cycle, one patient experienced a transient grade 1 increase in S. creatinine in the sixth week. None of our patients developed renal toxicity of grades 2, 3, or 4. Up to 26% of patients exhibited Grade 1-3 toxicity, which corresponds to the results reported in the medical literature.

Hepatoxicity

After the first, third, fourth, fifth, and sixth PRRT cycles, no patients experienced hepatotoxicity of grades 3 or 4. One patient exhibited serum alkaline phosphatase elevation of grade 3. No patient exhibited an increase in S. SGOT/SGPT of grade 2 or higher. Only a transient grade 1 increase in liver enzymes was observed following the second PRRT cycle. During the period of follow-up, no obvious hepatotoxicity was detected.

Conclusion

Peptide Receptor Radionuclide Therapy (PRRT) has emerged as a widely recognised and efficacious therapeutic approach for the management of gastrointestinal neuroendocrine tumours (GEP), bronchopulmonary tumours, and other malignancies that exhibit somatostatin receptor (SSTR) expression. This treatment modality has gained significant acceptance within the medical community over the course of the last twenty years, particularly for patients with inoperable or metastatic disease. Our research findings indicate that the intervention demonstrated a favourable

tolerability profile, as the majority of participants experienced only mild to moderate adverse effects when appropriate precautionary measures were implemented. In patients with progressive disease expressing somatostatin receptors (SSTR), the median survival is reported to be 27.5 months. Additionally, a high rate of tumour control (73.6% for partial response, stable disease, and complete response combined, and 52.9% for stable disease alone) suggests that the use of 177LuDOTATate may offer a significantly greater advantage compared to existing treatments for metastatic tumours expressing SSTR. In comparison to historical control groups, there is a notable improvement in overall survival (OS). Significantly, the absence of clinically significant bone marrow suppression and hepatotoxicity was noted. No instances of radiation-induced kidney toxicity were observed when employing suitable nephroprotective co-medication strategies.

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