

## DATA FROM THE MYRIAM REGISTRY

# MULTIPLE MYELOMA: ANTIRESORPTIVE THERAPY IN PATIENTS WITH OSTEOLYTIC LESIONS AND IMPAIRED RENAL FUNCTION

## INTRODUCTION

In multiple myeloma (MM), renal impairment is common and persistent reduction of renal function negatively impacts prognosis. According to DGHO, IMWG and EMN guidelines, patients with MM and osteolytic bone disease should be treated with antiresorptive therapy (ART). Whereas bisphosphonates are challenging in patients with renal impairment, denosumab (RANKL inhibitor), approved in 2018 for prevention of skeletal related events in adults with advanced malignancies involving bone, provides a treatment option with known lower rates of renal complications.

As published by Terpos et al. (2013), in patients with severe renal insufficiency, i.e. creatinine clearance (CrCl) <30 mL/min, bisphosphonates are not recommended. Denosumab is a suggested alternative because it is not cleared by the kidneys. However, there are only very limited data in myeloma patients with CrCl <30 mL/min (Dimopoulos et al., 2021, supplementary material).

## PATIENTS AND METHODS

Between 2017 and 2026, about 2,200 patients with MM starting first- (1L), second- (2L) or third-line (3L) systemic therapy will be recruited in 150 sites (hospitals, office-based practices) and followed for a maximum of 5 years. Patient and disease characteristics, including the presence of osteolytic lesions or renal comorbidities, as well as details on all systemic treatments and their effectiveness are documented throughout the observation time. In addition, details on the use of ART are collected. The study was approved by ethics committees and is registered at clinicaltrials.gov (NCT03308474). Here, we present data on the use of ART, with a special focus on patients with moderate or severe renal insufficiency (database cut: 30.09.2022).

### Specific definitions

Normalized estimated glomerular filtration rate (eGFR) was calculated according to the CKD-EPI formula (Inker et al., 2021) from the serum creatinine value as documented at start of first-line treatment. This calculation is the method currently recommended by nephrological societies for the eGFR in adult patients. Renal function was categorized based on estimated glomerular filtration rate (eGFR) according to the staging of chronic kidney disease (CKD) (KDIGO, 2013):

- Normal renal function: Estimated glomerular filtration rate (eGFR)  $\geq$  90 mL/min/1.73m<sup>2</sup>.
- Impaired renal function: Estimated glomerular filtration rate (eGFR) 60 to < 90 mL/min/1.73m<sup>2</sup>.
- Moderate renal insufficiency: Estimated glomerular filtration rate (eGFR) 30 to < 60 mL/min/1.73m<sup>2</sup>.
- Severe renal insufficiency: Estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m<sup>2</sup>.
- Missing: No categorization of estimated glomerular filtration rate (eGFR) possible due to unknown or not (yet) documented serum creatinine value.

## RESULTS

In total, 1,482 patients had been recruited for first-line treatment, whereof 894 (60%) patients were not planned for stem cell transplantation (non-SCT) and 588 (40%) were scheduled for SCT.

### Patients not planned for SCT (non-SCT)

Overall, 53% (n=474/894) of patients (non-SCT) had reported osteolytic lesions (Figure 1). Of these patients, 34% (n=162/474) further had moderate (eGFR 30-60 mL/min/1.73m<sup>2</sup>) or severe (eGFR < 30 mL/min/1.73m<sup>2</sup>) renal insufficiency (Figure 5). Basic patient characteristics are displayed in Table 1.

The majority of patients (non-SCT) with osteolytic lesions received ART: At database cut, for 67% (n=317/474) of patients ART was documented. Due to ongoing treatment, further 20% (n=95/474) may still receive ART within the course of treatment ("potential" or yet missing data) (Table 1 / Figure 3).

Patients with osteolytic lesions not planned for SCT most frequently received zoledronic acid (34%, n=159/474), denosumab (18%, n=87/474) or ibandronate (11%, n=52/474) as ART, a pattern also observed in pts with osteolytic lesions and moderate or severe renal impairment (Figure 7). With regard to patients with osteolytic lesions not planned for SCT who received ART (n=317, Table 1) the frequencies were: zoledronic acid (50%, n=159/317), denosumab (27%, n=87/317) or ibandronate (16%, n=52/317).

### Patients scheduled for SCT

Overall, 69% (n=403/588) of patients among the planned SCT group had reported osteolytic lesions (Figure 2). Of these patients, 20% (planned SCT, n=79/403) further had moderate (eGFR 30-60 mL/min/1.73m<sup>2</sup>) or severe (eGFR < 30 mL/min/1.73m<sup>2</sup>) renal insufficiency (Figure 6). Basic patient characteristics are displayed in Table 2.

The majority of patients with osteolytic lesions received ART: At database cut, for 74% (n=298/403) of patients ART was documented. Due to ongoing treatment, further 24% (n=95/403) may still receive ART within the course of treatment ("potential" or yet missing data) (Table 2 / Figure 4).

Patients with osteolytic lesions scheduled for SCT most frequently received zoledronic acid (49%, n=197/403) or denosumab (13%, n=54/403) as ART (Figure 8). However, due to smaller patient numbers in this group, the pattern of drugs varied in patients with osteolytic lesion and moderate or severe renal insufficiency (Figure 8). With regard to patients with osteolytic lesions scheduled for SCT who received ART (n=298, Table 2) the frequencies were: zoledronic acid (66%, n=197/298) or denosumab (18%, n=54/298).

## LIMITATIONS

Proportion and type of ART was analyzed regardless of the timing. Thus, ART might have been started during later line treatment. For this analysis, patients were classified as having moderate or severe renal impairment at the start of first-line treatment. This has not been re-evaluated during the course of disease.

## CONCLUSION

MYRIAM provides essential insights into use of antiresorptive therapy (ART) in patients with osteolytic lesions and MM, with or without impaired renal function in daily practice in Germany. Osteolytic lesions were present in nearly 2/3 of patients with MM. Of these about 1/3 were diagnosed with moderate / severe renal insufficiency.

Antiresorptive therapy is widely used indicating that the majority of patients is treated according to guidelines. Renal function should play an important role in the selection of antiresorptive therapy with currently a substantial proportion of patients with severe renal impairment still being treated with bisphosphonates.

**Abbreviations:**  
ART: antiresorptive therapy | CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration | CrCl: creatinine clearance | eGFR: estimated glomerular filtration | DGHO: Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie | EMN: European Myeloma Network | IMWG: International Myeloma Working Group | KDIGO: Kidney disease: Improving Global Outcome | mL: milliliter | min: minute | MM: multiple myeloma | pts: patients | RANKL: Receptor Activator of Nuclear Factor Kappa B Ligand | SCT: stem cell transplantation | SID: standard deviation.

**References:**  
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**Conflicts of interest, general:**  
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### Footnotes to Figure 1/2/5/6

Patients with no osteolytic lesions comprise patients with normal bone structure, diffuse osteoporosis, unknown bone structure or missing data. eGFR: Estimated glomerular filtration rate.

**Categories:**  
Normal renal function: eGFR  $\geq$  90 mL/min/1.73m<sup>2</sup>.  
Impaired renal function: eGFR 60 to < 90 mL/min/1.73m<sup>2</sup>.  
Moderate renal insufficiency: eGFR 30 to < 60 mL/min/1.73m<sup>2</sup>.  
Severe renal insufficiency: eGFR < 30 mL/min/1.73m<sup>2</sup>.  
Missing: No categorization of eGFR possible due to unknown or not (yet) documented serum creatinine value.

Figure 1 Flow chart of patient subgroups (non-SCT)

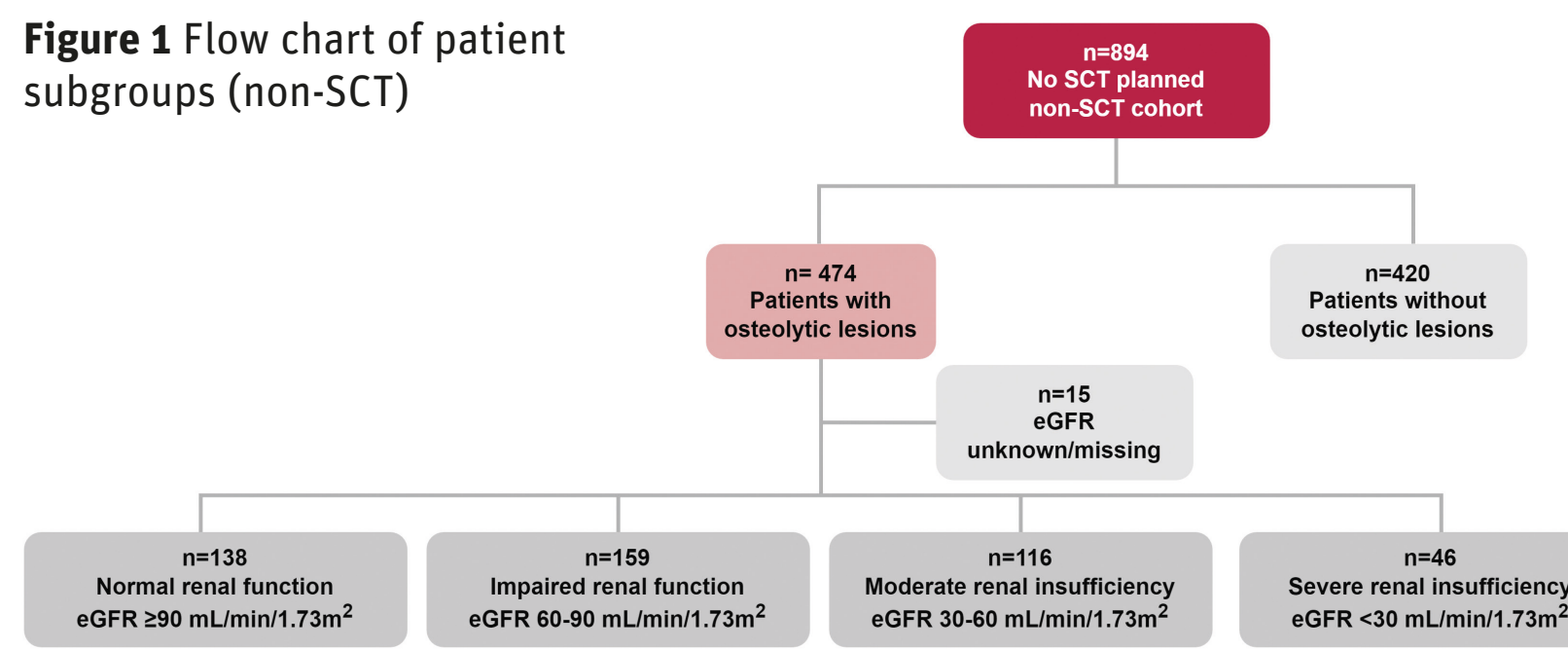


Table 1: Patient characteristics (non-SCT) at start of 1L and administration of antiresorptive therapy

	Patients with osteolytic lesions	Patients with osteolytic lesions and moderate renal insufficiency	Patients with osteolytic lesions and severe renal insufficiency
<b>Patients</b>	<b>474</b>	<b>116</b>	<b>46</b>
<b>Sex</b>			
Male n (%)	276 (58.2%)	67 (57.8%)	26 (56.5%)
Female n (%)	198 (41.8%)	49 (42.2%)	20 (43.5%)
<b>Age at start of first-line-treatment</b>			
Mean ± SD (years)	76.1 ± 7.18	76.6 ± 7.23	76.9 ± 8.17
Median (years)	77.4	77.5	78.5
25-75% quantile (years)	72.1 - 81.0	71.5 - 81.7	72.0 - 83.7
< 65 years / ≥ 65 years n (%)	37 (7.8%) / 437 (92.2%)	8 (6.9%) / 108 (93.1%)	4 (8.7%) / 42 (91.3%)
< 70 years / ≥ 70 years n (%)	88 (18.6%) / 386 (81.4%)	22 (19.0%) / 94 (81.0%)	10 (21.7%) / 36 (78.3%)
<b>Administration of antiresorptive therapy</b>			
Yes n (%)	317 (66.9%)	86 (74.1%)	25 (54.3%)
No n (%)	62 (13.1%)	11 (9.5%)	13 (28.3%)
Potential for ART * n (%)	89 (18.8%)	17 (14.7%)	7 (15.2%)
Missing * n (%)	6 (1.3%)	2 (1.7%)	1 (2.2%)

\* Potential: Number of patients with ongoing documentation and no documented antiresorptive therapy (antiresorptive therapy may still be performed within the course of treatment).  
\* Missing: Number of patients with completed documentation and no available answer to the respective parameter.

Table 2: Patient characteristics (planned SCT) at start of 1L and administration of antiresorptive therapy

	Patients with osteolytic lesions	Patients with osteolytic lesions and moderate renal insufficiency	Patients with osteolytic lesions and severe renal insufficiency
<b>Patients</b>	<b>403</b>	<b>52</b>	<b>27</b>
<b>Sex</b>			
Male n (%)	250 (62.0%)	33 (63.5%)	15 (55.6%)
Female n (%)	153 (38.0%)	19 (36.5%)	12 (44.4%)
<b>Age at start of first-line-treatment</b>			
Mean ± SD (years)	61.6 ± 7.99	63.7 ± 7.82	58.5 ± 6.77
Median (years)	63.0	65.0	57.6
25-75% quantile (years)	57.0 - 67.4	58.9 - 70.5	53.8 - 63.4
< 65 years / ≥ 65 years n (%)	246 (61.0%) / 157 (39.0%)	26 (50.0%) / 26 (50.0%)	22 (81.5%) / 5 (18.5%)
< 70 years / ≥ 70 years n (%)	354 (87.8%) / 49 (12.2%)	38 (73.1%) / 14 (26.9%)	25 (92.6%) / 2 (7.4%)
<b>Administration of antiresorptive therapy</b>			
Yes n (%)	298 (73.9%)	35 (67.3%)	16 (59.3%)
No n (%)	10 (2.5%)	2 (3.8%)	2 (7.4%)
Potential for ART * n (%)	95 (23.6%)	15 (28.8%)	9 (33.3%)
Missing * n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

\* Potential: Number of patients with ongoing documentation and no documented antiresorptive therapy (antiresorptive therapy may still be performed within the course of treatment).  
\* Missing: Number of patients with completed documentation and no available answer to the respective parameter.

Figure 2: Flow chart of patient subgroups (planned SCT)

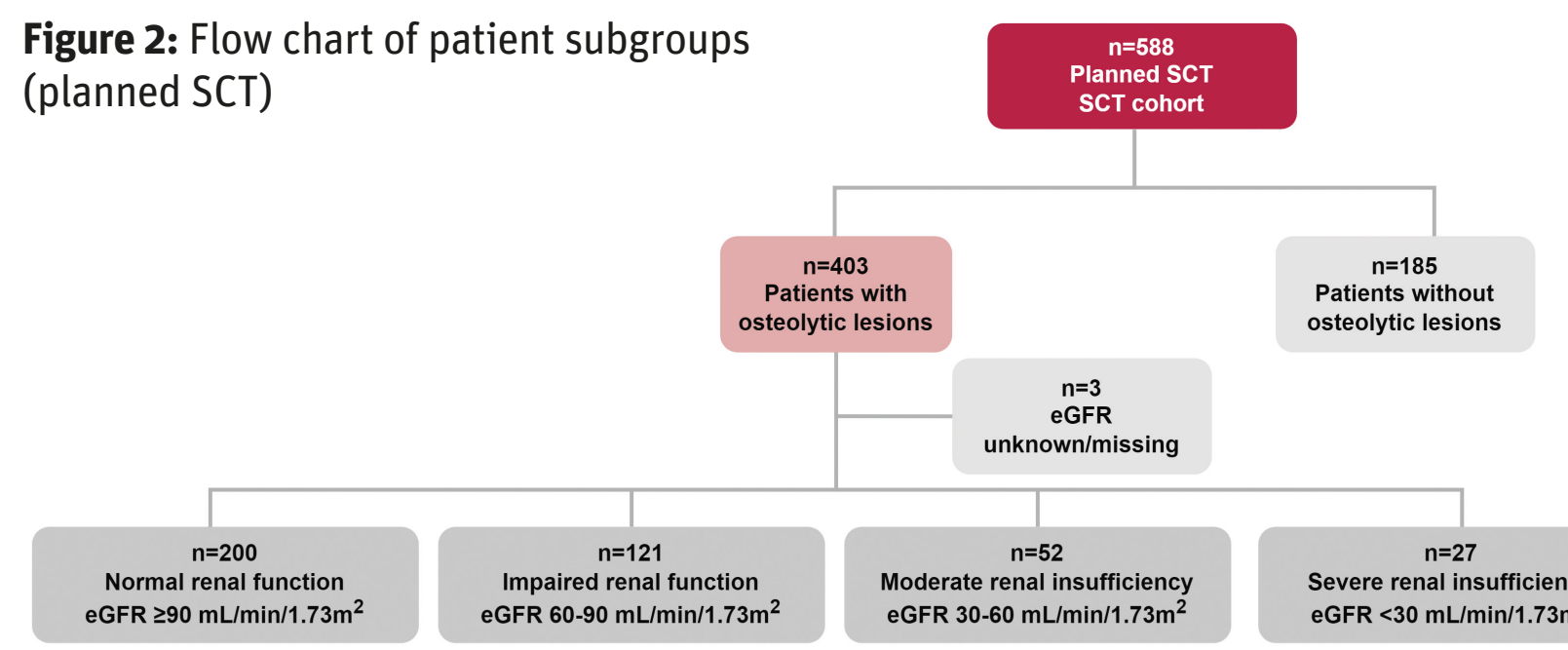


Figure 3: Patients with osteolytic lesions (non-SCT): Treatment with antiresorptive therapy (ART)

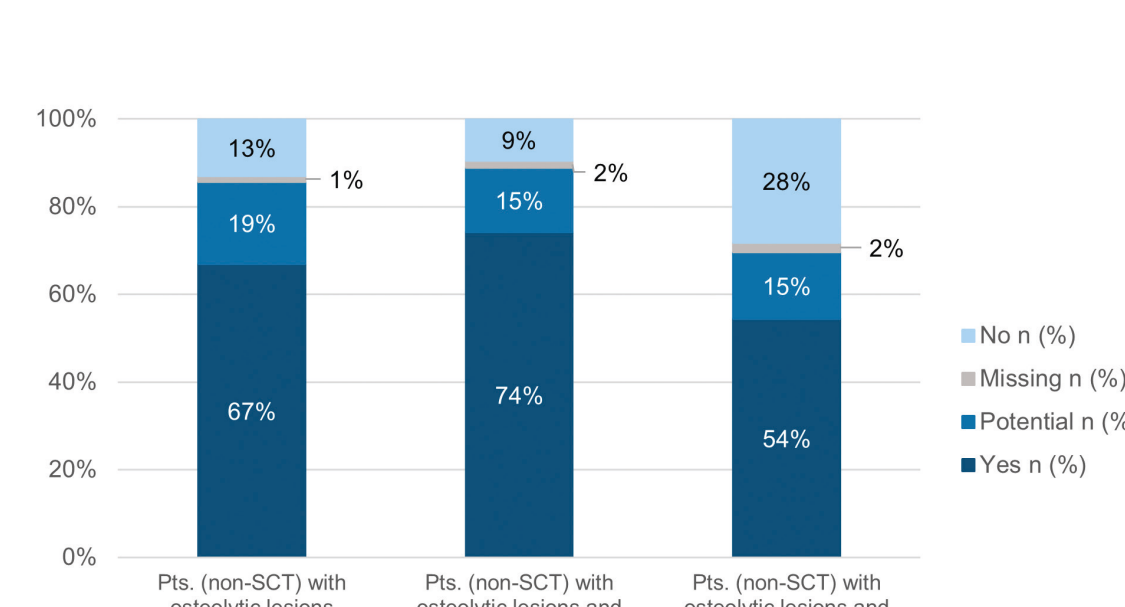


Figure 4: Patients with osteolytic lesions (planned SCT): Treatment with antiresorptive therapy (ART)

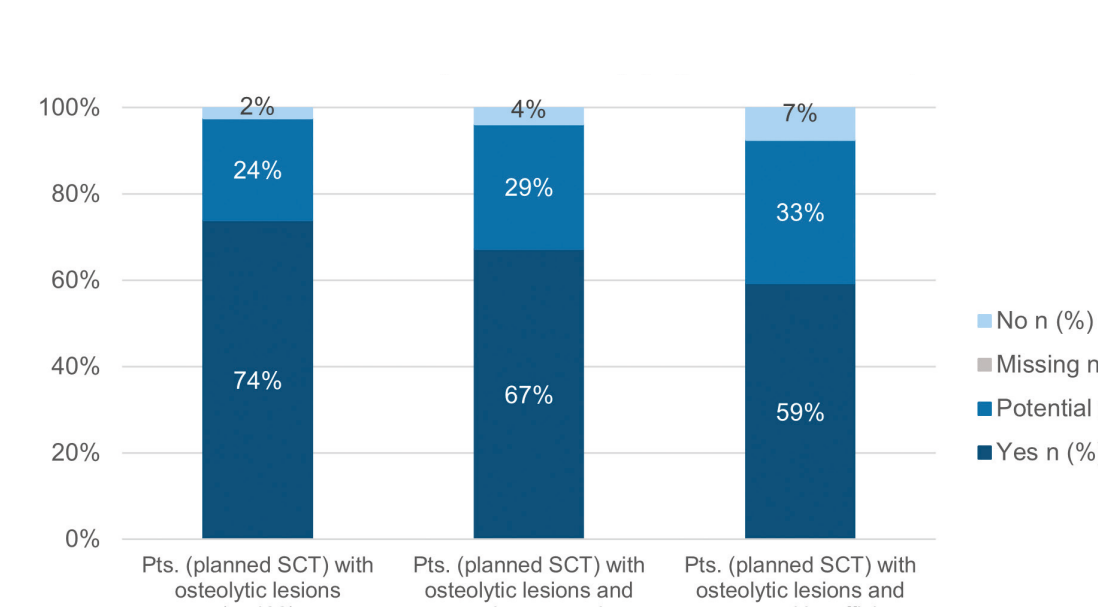


Figure 5: Patients with osteolytic lesions (non-SCT): Renal function (n=474)

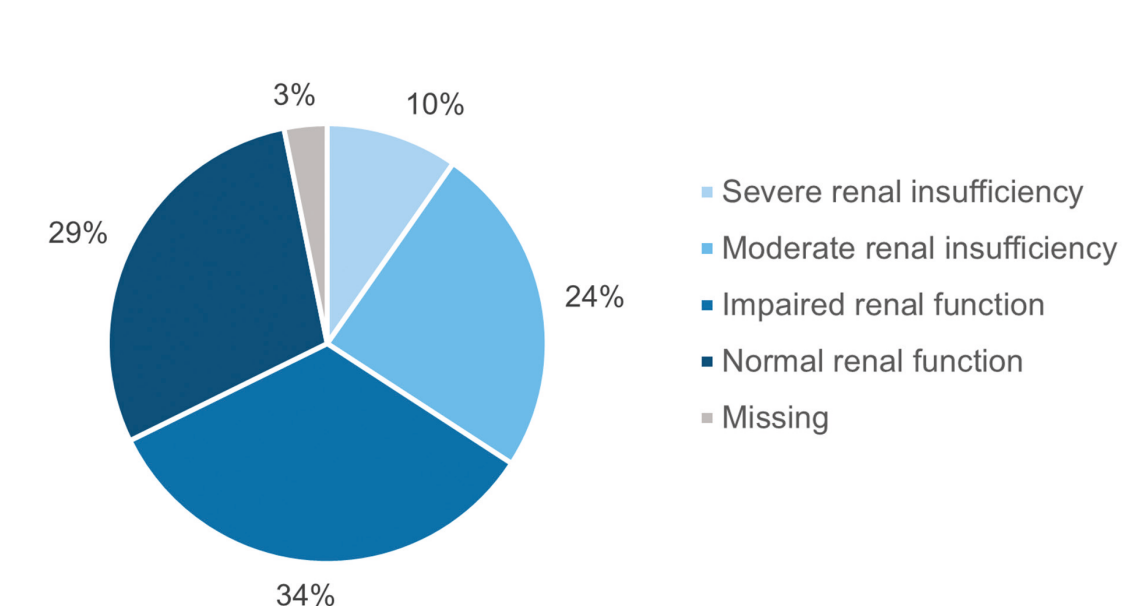


Figure 6: Patients with osteolytic lesions (planned SCT): Renal function (n=403)

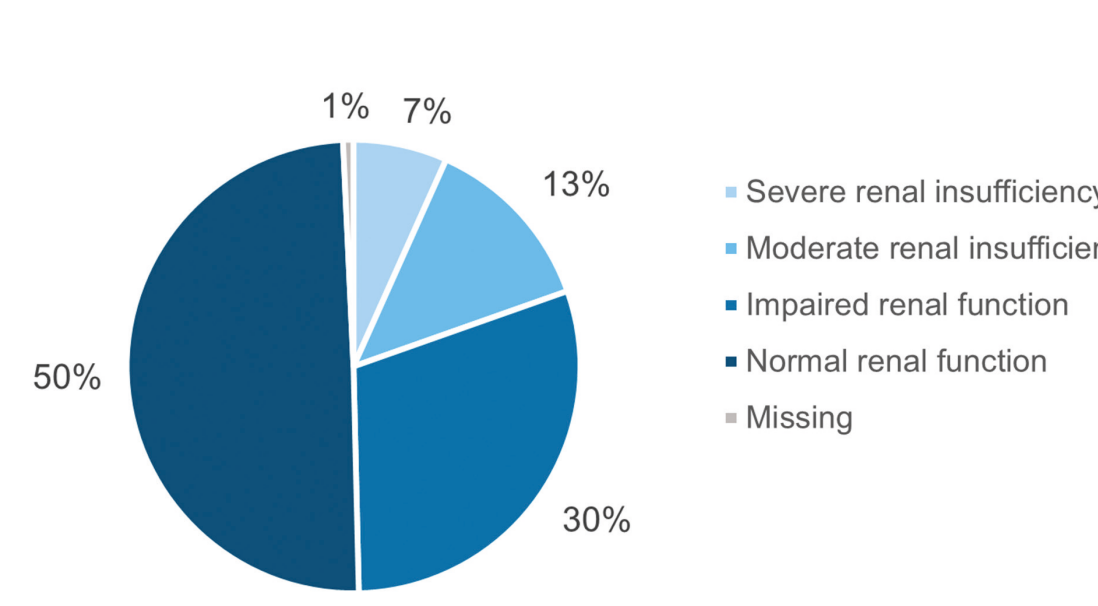


Figure 7: Patients with osteolytic lesions (non-SCT): Antiresorptive therapy

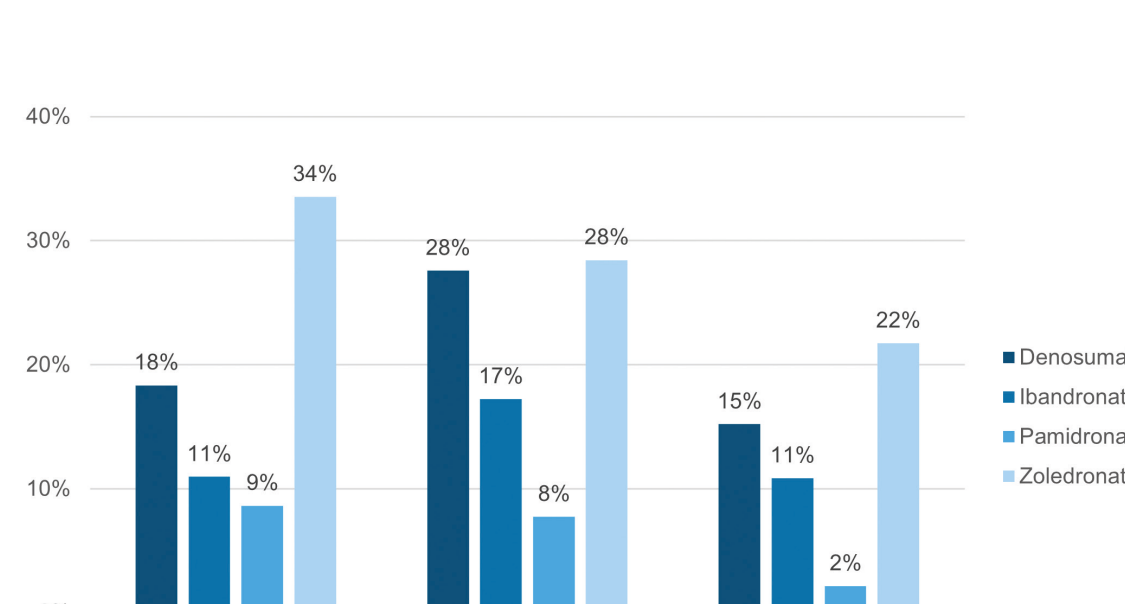


Figure 8: Patients with osteolytic lesions (planned SCT): Antiresorptive therapy

