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Osteoporosis treatment with denosumab in routine clinical practice in Poland

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Abstract

Introduction: The receptor activator for nuclear factor κ B ligand (RANKL) inhibitor denosumab is approved for the treatment of osteoporosis in postmenopausal women and men at increased fracture risk. The objectives were to describe the characteristics of patients with osteoporosis initiating denosumab in Polish clinical practice and their clinical management during the first 12 months of denosumab treatment.
Material and methods: This prospective, observational study enrolled denosumab-naïve women and men in Poland with osteoporosis, who had received at least one denosumab injection in the 8 weeks prior to enrolment. Patients were enrolled from specialist osteoporosis treatment centres, and orthopaedic, rheumatological, and family doctor centres. Outcomes included patient characteristics, denosumab treatment patterns, bone mineral density (BMD), and fracture; all analyses were descriptive.
Results: The study enrolled 463 patients; most (96%) were women, aged ≥ 65 years (84%), with prior fractures (88%). Approximately two-thirds of the women had received prior osteoporosis therapy, with the main reasons for discontinuation being adverse events (75%) and lack of effect (73%). Across all patients, the most common reasons for prescribing denosumab were low bone mineral density (BMD/T-score) (93%) and history of osteoporotic fracture (78%). Mean BMD at denosumab initiation ranged from T-score –3.00 (lumbar spine) to T-score –2.6 (total hip), and BMD increased by 2.8–6.2% at month 12. Most patients completed follow-up (86%) and were due to receive a third denosumab injection (81%).
Conclusion: The article presents detailed sociodemographic and disease-related characteristics of patients who routinely implemented denosumab therapy. Most of them continued denosumab for at least 12 months, with increased BMD T-scores. **(Endokrynol Pol 2023; 74 (3): 243–253)**

Key words: *denosumab; osteoporosis; postmenopausal osteoporosis; therapy*

Introduction

Osteoporosis is a chronic disease of the skeletal system, characterized by low bone mineral density, which leads to an increased risk of fractures. Osteoporosis is more common among women (mainly in the postmenopausal period) than in men [1, 2], and its prevalence increases with age. In 2018, the estimated number of people in Poland with osteoporosis was 2.1 million, of whom 1.7 million were women [3].

In many cases, the early stages of osteoporosis are asymptomatic and the disease is not diagnosed until a pathological fracture occurs. Therefore, screening for high fracture risk is important to identify affected patients and initiate treatment to prevent osteoporotic fractures [4].

Osteoporosis diagnosis is primarily based on bone mineral density (BMD), which is typically presented as the T-score, i.e. the number of standard deviations (SD) by which the BMD in an individual deviates from the mean value expected in young healthy individuals. A T-score value ≤ −2.5, assessed at the femoral neck or spine, indicates osteoporosis [5, 6].

Osteoporosis management should be carried out by both primary care physicians (screening, fracture risk assessment) and specialists (differential diagnostics, treatment choices). Osteoporosis treatment may involve orthopaedics, pharmacological treatment, analgesics, rehabilitation, and dietary modifications [4, 6, 7].

Pharmacological therapy should be implemented in patients with high risk of hip or vertebral fractures, T-scores ≤ –2.5, or, in postmenopausal women and men

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age 50 years or older, with low bone mass and high fracture probability [5, 8]. Besides calcium and vitamin D supplementation, osteoporosis treatments involve various mechanisms of action, including bisphosphonates and hormonal or biological therapies, such as the receptor activator for nuclear factor κ B ligand (RANKL) inhibitor denosumab [4, 5, 8]. In Europe, denosumab is indicated for the treatment of osteoporosis in postmenopausal women and in men with high risk of fracture [9].

We conducted a prospective, observational study in Poland to describe the characteristics of patients with osteoporosis initiating denosumab in routine clinical practice, and the clinical management of these patients during the first 12 months of denosumab treatment. Additionally, we present data for specialized osteoporosis treatment centres and small orthopaedic, rheumatological, or family doctor outpatient centres.

Material and methods

Patients

Our study included denosumab-naïve women with a clinical diagnosis of postmenopausal osteoporosis, and men with a clinical diagnosis of osteoporosis. Patients were enrolled within 8 weeks of the first dose of denosumab. All patients were required to give informed consent before enrolment. Patients with glucocorticoid-induced osteoporosis and patients participating in an ongoing or previous clinical trial of denosumab or participating in any clinical or device trial within the previous 6 months were excluded.

Study design

This multi-centre, single country (Poland), non-interventional, prospective, observational study was performed between August 2017 (study initiation date) and January 2020 (the last subject's last visit), including a 12-month follow-up period.

We planned to enrol 420 patients from osteoporosis treatment centres (Type I) and small orthopaedic, rheumatological, or family doctor outpatient centres (Type II) in a 1:1 ratio. Sites were selected based on their type and geographic location. Participating physicians were asked to enrol consecutive patients treated with denosumab at their centre.

At the enrolment visit, patient's informed consent, socio-demographics, and medical history data were collected directly or from medical records. Follow-up data were collected when patients returned to the clinic to receive subsequent denosumab injections/prescription at 6 and 12 months. These follow-up visits were part of routine clinical practice — no study specific visits were required.

The study outcomes are listed below:

- sociodemographic: age, sex, educational level, employment status, living situation;
- osteoporosis-related: body mass index (BMI), fractures, prior falls, BMD;
- denosumab treatment-related: number of doses received, osteoporosis-related laboratory examinations and radiological bone assessments pre-treatment;
- safety: incidence of adverse events (AEs) and serious AEs (SAEs), with AEs coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 22.1.

Statistical analysis

All statistical analyses were descriptive in nature. Data were summarized overall and by centre type. For categorical data, the number and percentage of patients in each category were summarized. For continuous variables, the number of non-missing values, mean and SD, median, and minimum and maximum values were summarized.

To evaluate changes in T-score during therapy, the baseline T-score was defined as the measurement closest to, and within 6 months prior to, the first administration of denosumab. Change from baseline T-score was then calculated for patients with a baseline and month 12-BMD assessment and defined as increased, decreased, or stable.

Ethics

The study protocol and informed consent form were reviewed and approved by the Bioethics Committee (decision number 81/2017/KB/VII).

Results

Patient disposition

The study was conducted in 24 sites across Poland, comprising 11 Type I (osteoporosis) centres and 13 Type II (orthopaedic, rheumatological, or family doctor outpatient) centres. Of 491 patients enrolled, 275 were from Type I centres and 216 from Type II centres. Of these, 463 subjects (260 from Type I centres and 203 from Type II centres) were included in our analysis; 28 patients were excluded due to protocol deviations (n = 25), data entry mistakes (n = 2), and investigator withdrawal (n = 1) (Fig. 1).

Most patients (400/463 [86.4%]) completed the 12-month follow-up visit (4 of them slightly later than the 3rd visit); 63 (13.6%) patients discontinued the study prematurely, with 42 (9.1%) lost to follow-up and 18 (3.9%) withdrawing their informed consent.

Patient characteristics

Patient characteristics are summarized in Table 1. Most patients (96.3%) were female, and almost half (45.1%) were aged ≥ 75 years. As per the study inclusion criteria, all women enrolled in the study were post-menopausal. Mean (SD) age at menopause was 49.3 (4.3) years; post-menopausal osteoporosis (PMO) was diagnosed, on average, 20 years later. BMI ranged from 15.8 to 47.8 kg/m^2, with the mean and median approximately 25 kg/m^2.

Most (92.7%) patients were retired and lived at home with their spouse or family (57.7%), or at home alone (28.9%).

Osteoporosis-risk factors

The presence of osteoporosis risk factors at enrolment are summarized in Table 2. The majority of patients had at least one past or current comorbidity (57.0% and 69.5%, respectively). At enrolment, the most common comorbidities were cardiovascular, gastrointestinal, metabolic, and musculoskeletal disorders (49.9%, 28.5%, 22.0%, and 12.3%, respectively).

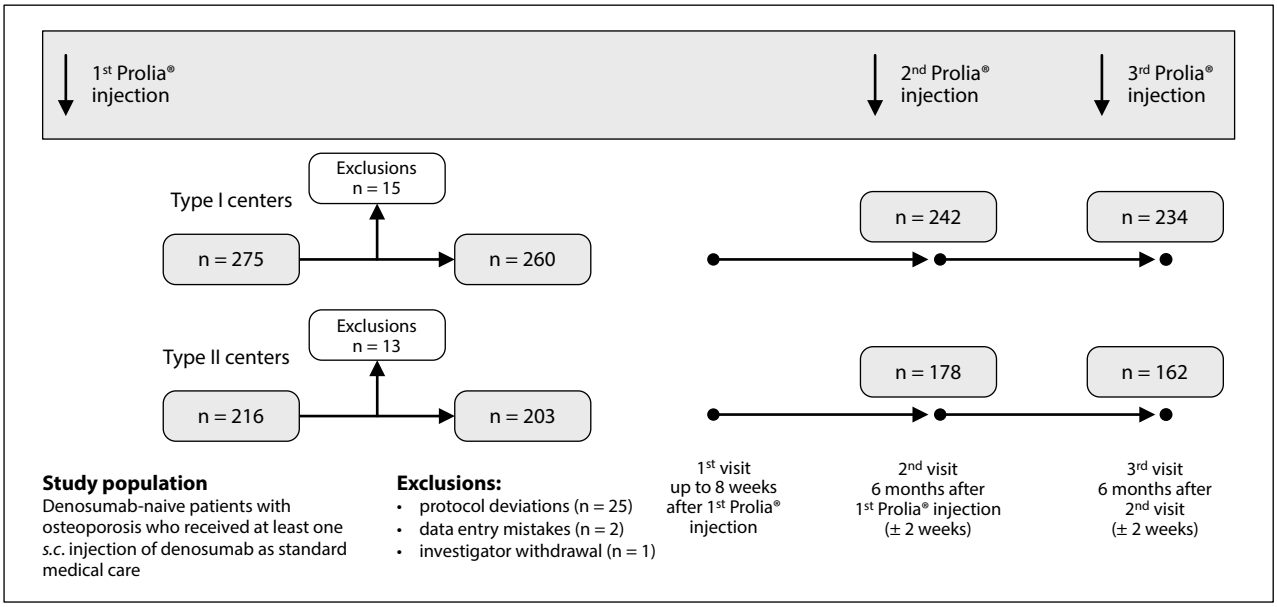

Figure 1. *Study schema and patient disposition. s.c. — subcutaneus*

Height loss was reported for two-thirds of patients; mean (SD) 4.92 (3.2) cm. Only 20.5% of patients reported prior falls; few patients reported immobility episodes or parental hip fracture (8.9% and 6.9%, respectively). Secondary osteoporosis was reported in 7 (1.5%) patients; in all cases this was due to endocrine disorders. Approximately 20% of enrolled patients were former or current smokers; few (< 1%) reported drinking 3 or more units of alcohol per day.

Table 1. *Patient characteristics*

		Overall (n = 463)	Type I centres (n = 260)	Type II centres (n = 203)
Sex, n (%)	Female	446 (96.3%)	249 (95.8%)	197 (97.0%)
	Male	17 (3.7%)	11 (4.2%)	6 (3.0%)
Age, years	Mean (SD)	73.3 (8.6)	73.0 (8.6)	73.6 (8.6)
	Median	73.0	73.0	73.0
	Range	43-95	43-92	52-95
Age group, years	< 65, n (%)	75 (16.2%)	44 (16.9%)	31 (15.3%)
	≥ 65 to < 75, n (%)	179 (38.7%)	103 (39.6%)	76 (37.4%)
	≥ 75, n (%)	209 (45.1%)	113 (43.5%)	96 (47.3%)
Age at menopause, years	n	414	236	178
	Mean (SD)	49.3 (4.3)	49.1 (4.5)	49.6 (4.1)
	Median	50.0	50.0	50.0
	Range	32-65	32-62	33-65
Cause of menopause, %	n	446	249	197
	Natural onset	90.1%	86.7%	94.4%
	Iatrogenic	8.1%	10.8%	4.6%
	Unknown	1.8%	2.4%	1.0%
Age at PMO diagnosis, years	n	423	241	182
	Mean (SD)	68.3 (9.8)	67.7 (9.5)	69.1 (10.2)
	Median	68.0	68.0	68.0
	Range	39-95	39-89	44-95

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Table 1. *Patient characteristics*

		Overall (n = 463)	Type I centres (n = 260)	Type II centres (n = 203)
BMI, kg/m^2	n	453	251	202
	Mean (SD)	25.30 (4.18)	25.7 (4.6)	24.8 (3.5)
	Median	24.84	25.2	24.6
	Range	15.8–47.8	15.8–47.8	16.6–36.2
Height, cm	n	453	251	202
	Mean (SD)	156.9 (6.31)	156.2 (6.71)	157.8 (5.69)
	Median	157.0	156.0	158.0
	Range	137–178	137–178	138–174
Educational level, n (%)	Elementary	91 (19.7%)	45 (17.3%)	46 (22.7%)
	Secondary	227 (49.0%)	135 (51.9%)	92 (45.3%)
	University	130 (28.1%)	80 (30.8%)	50 (24.6%)
	Unknown	15 (3.2%)	0	15 (7.4%)
Employment status, n (%)	Employed	25 (5.4%)	15 (5.8%)	10 (4.9%)
	Retired	429 (92.7%)	239 (91.9%)	190 (93.6%)
	Self-employed	7 (1.5%)	5 (1.9%)	2 (1.0%)
	Unemployed	2 (0.4%)	1 (0.4%)	1 (0.5%)
Living situation, n (%)	At home alone	134 (28.9%)	88 (33.8%)	46 (22.7%)
	At home with care/support	60 (13.0%)	5 (1.9%)	55 (27.1%)
	At home with spouse/family	267 (57.7%)	166 (63.8%)	101 (49.8%)
	Nursing home	2 (0.4%)	1 (0.4%)	1 (0.5%)

BMI — body mass index; cm — centimetres; kg — kilograms; m — meters; n — number; PMO — postmenopausal osteoporosis; SD — standard deviation; Type I centres — osteoporosis centres; Type II centres — orthopaedic, rheumatological, or family doctor outpatient clinics

Table 2. *Presence of clinical risk factors for osteoporosis at enrolment*

	Overall (n = 463)	Type I centres (n = 260)	Type II centres (n = 203)
Any past comorbidities, n (%)			
Yes	264 (57.0%)	160 (61.5%)	104 (51.2%)
No	184 (39.7%)	91 (35.0%)	93 (45.8%)
Not available	15 (3.2%)	9 (3.5%)	6 (3.0%)
Any current comorbidities, n (%)			
Yes	322 (69.5%)	199 (76.5%)	123 (60.6%)
No	134 (28.9%)	59 (22.7%)	75 (36.9%)
Not available	7 (1.5%)	2 (0.8%)	5 (2.5%)
Type of current comorbidities[a], n (%)			
Cardiovascular	231 (49.9%)	149 (57.3%)	82 (40.4%)
Gastrointestinal	132 (28.5%)	92 (35.4%)	40 (19.7%)
Metabolic	102 (22.0%)	76 (29.2%)	26 (12.8%)
Musculoskeletal	57 (12.3%)	34 (13.1%)	23 (11.3%)
Central nervous system	36 (7.8%)	27 (10.4%)	9 (4.4%)
Respiratory	26 (5.6%)	21 (8.1%)	5 (2.5%)
Endocrinological	20 (4.3%)	5 (1.9%)	15 (7.4%)
Renal	17 (3.7%)	12 (4.6%)	5 (2.5%)
Neoplasm	7 (1.5%)	4 (1.5%)	3 (1.5%)

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Table 2. *Presence of clinical risk factors for osteoporosis at enrolment*

	Overall (n = 463)	Type I centres (n = 260)	Type II centres (n = 203)
Ophthalmological	6 (1.3%)	4 (1.5%)	2 (1.0%)
Haematological	5 (1.1%)	5 (1.9%)	0
Other	4 (0.9%)	2 (0.8%)	2 (1.0%)
Allergy	3 (0.6%)	3 (1.2%)	0
Dermatological	3 (0.6%)	3 (1.2%)	0
Laryngological	2 (0.4%)	1 (0.4%)	1 (0.5%)
Mental disorder	2 (0.4%)	1 (0.4%)	1 (0.5%)
Autoimmune	1 (0.2%)	1 (0.4%)	0
Height loss [cm]			
Yes	307 (66.3%)	187 (71.9%)	120 (59.1%)
Mean (SD)	4.92 (3.20)	5.54 (3.25)	3.94 (2.88)
Median	4.0	5.0	3.0
Prior fracture, n (%)			
Yes	406 (87.7%)	235 (90.4%)	171 (84.2%)
No	55 (11.9%)	24 (9.2%)	31 (15.3%)
Not available	2 (0.4%)	1 (0.4%)	1 (0.5%)
Falls, n (%) experienced (last 12 months), n (%)			
Yes	95 (20.5%)	67 (25.8%)	28 (13.8%)
No	366 (79.0%)	192 (73.8%)	174 (85.7%)
Not available	2 (0.4%)	1 (0.4%)	1 (0.5%)
Immobility episodes (during last 12 months), n (%)			
Yes	41 (8.9%)	25 (9.6%)	16 (7.9%)
No	419 (90.5%)	233 (89.6%)	181 (91.6%)
Not available	3 (0.6%)	2 (0.8%)	1 (0.5%)
Parent fractured hip, n (%)			
Yes	32 (6.9%)	24 (9.2%)	8 (3.9%)
No	400 (86.4%)	215 (82.7%)	185 (91.1%)
Not available	31 (6.7%)	21 (8.1%)	10 (4.9%)
Coexisting secondary osteoporosis, n (%)			
Yes	7 (1.5%)	5 (1.9%)	2 (1.0%)
No	451 (97.4%)	253 (97.3%)	198 (97.5%)
Not available	5 (1.1%)	2 (0.8%)	3 (1.5%)
Current smokers, n (%)			
Yes	48 (10.4%)	24 (9.2%)	24 (11.8%)
No	414 (89.4%)	236 (90.8%)	178 (87.7%)
Not provided	1 (0.2%)	0	1 (0.5%)
Former smokers, n (%)			
Yes	52 (11.2%)	34 (13.1%)	18 (8.9%)
No	362 (78.2%)	202 (77.7%)	160 (78.8%)
Not applicable	49 (10.6%)	24 (9.2%)	25 (12.3%)
Alcohol ≥ 3 units per day, n (%)			
Yes	3 (0.6%)	2 (0.8%)	1 (0.5%)
No	458 (98.9%)	257 (98.8%)	201 (99.0%)
Not provided	2 (0.4%)	1 (0.4%)	1 (0.5%)

cm — centimetres; SD — standard deviation; n — number; Type I centres — osteoporosis centres; Type II centres — orthopaedic, rheumatological, or family doctor outpatient clinics. [a]Patients can have multiple comorbidities; therefore, the percentages do not sum to 100%

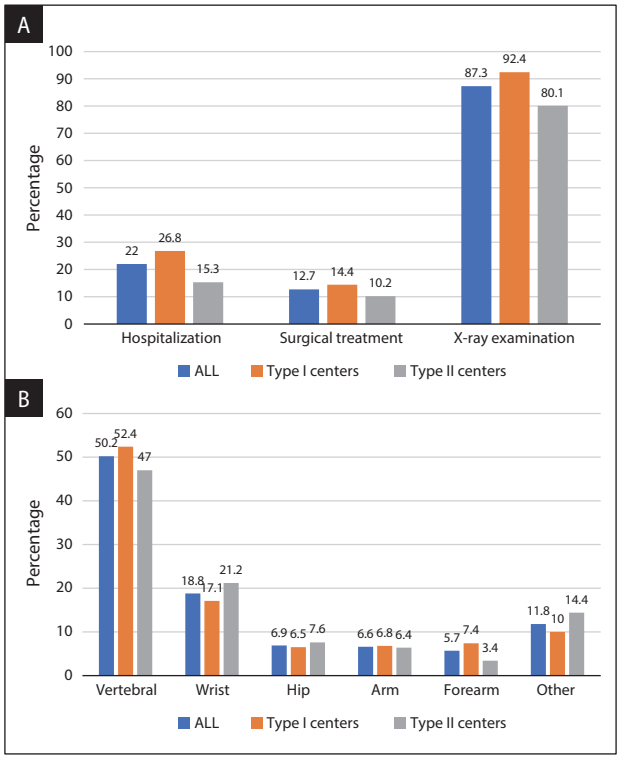

Figure 2. *Prior fracture location (***A***) and management (***B***). Data presented in (%). Percentages calculated from the total number of fractures. Type I centres — osteoporosis centres; Type II centres — orthopaedic, rheumatological, or family doctor outpatient clinics*

Fracture (prior to and after denosumab initiation)

Most patients (87.7%) reported a prior osteoporotic fracture (90.4% of patients in Type I centres, 84.2% in Type II centres), with a total of 576 prior fractures recorded in patients' medical history (340 in Type I centres and 236 in Type II centres). Half [289/576 (50.2%)] of all prior fractures were vertebral fractures (Fig. 2); most [503/576 (87.3%)] were X-ray examined, and only a minority required hospitalization [127/576 (22.0%)] or surgical treatment [73/576 (12.7%)].

Only 8 new fractures were recorded at month 6 (6 in Type I centres and 2 in Type II centres), and 4 new fractures were recorded at month 12 (3 in Type I centres and one in Type II centres). Due to the small number of new fractures, there were insufficient data to describe post-fracture treatment patterns.

Prior osteoporosis therapy

Data on prior osteoporosis therapies were only available for women, and they are presented in Table 3. Approximately two-thirds (65.7%) of women enrolled in the study had received prior osteoporosis therapy with a different mechanism of action than denosumab. Of these, over three-quarters had started a prior osteoporosis treatment in the 12 months before enrolment and two-thirds (63.1%) had discontinued treatment.

The most commonly reported prior osteoporosis therapies were the bisphosphonates ibandronate (150 mg/month) and alendronate (70 mg/week) (75.1% and 42.3%, respectively). The most commonly reported reasons for discontinuing prior osteoporosis therapy were AEs (75.1%) and lack of efficacy (73.0%).

Calcium and vitamin D supplementation

At enrolment, most patients reported taking calcium and/or vitamin D supplements (413/463 [89.2%] and 446/463 [96.3%], respectively). In Type I and Type II centres, the frequency of calcium supplementation was 96.9% (252/260) and 79.3% (161/203), respectively, and for vitamin D it was 98.8% (257/260) and 93.1% (189/203), respectively. The most frequently reported doses of calcium were 1000 mg and < 500 mg (230/413 [55.7%] and 86/413 [20.8%], respectively). The most commonly reported doses of vitamin D were 2000 and 4000 IU (256/446 [57.4%] and 49/446 [11.0%], respectively).

Denosumab treatment

Denosumab treatment patterns are summarized in Table 4. The majority (67.1%) of patients had initiated denosumab more than 12 months after their most recent fracture. The most common reasons for prescribing denosumab were low BMD T-score (92.9%) and/or a history of osteoporotic fracture (78.2%).

Denosumab treatment duration ranged from 6 to 14 months, with mean and median treatment duration approximately 12 months. A third injection of denosumab was planned in most patients (at least 80.8%); the most common reasons for denosumab discontinuation were patient decision (9/463 [1.9%]), loss to follow-up (7/463 [1.5%]), economic reasons (5/463 [1.2%]), and investigator's decision (3/463 [0.7%]).

Bone mineral density

Patients enrolled in our study had a total of 740 BMD assessments recorded prior to enrolment (477 in Type I and 263 in Type II centres). At months 6 and 12, 141 and 263 BMD assessments were recorded, respectively (Type 1 centres, 101 and 201, respectively; Type II centres 40 and 62, respectively). At each timepoint, the most common locations for BMD testing were femoral neck (baseline — 47.0%; month 6 — 51.1%; month 12 — 43.0%) and lumbar spine (baseline — 44.5%; month 6 — 46.8%; month 12 — 46.8%), and the least common location was total hip (baseline — 8.5%; month 6 — 2.1%; month 12 — 10.3%).

BMD values are summarized in Figure 3. Due to the small number of patients with measurements at month 12, BMD data are reported for the overall

Table 3. *Prior osteoporosis therapy in women*

	Overall (n = 443)	Type I centres (n = 249)	Type II centres (n = 197)
Prior osteoporosis therapy, n (%)			
n	446	249	197
Yes	293 (65.7%)	195 (78.3%)	98 (49.7%)
No	149 (33.4%)	52 (20.9%)	97 (49.2%
Not available	4 (0.9%)	2 (0.8%)	2 (1.0%)
Prior osteoporosis therapy in the 12 months prior to denosumab initiation, n (%)			
n	293	195	98
Yes	227 (77.5%)	154 (79.0%)	73 (74.5%)
No	61 (20.8%)	39 (20.0%)	22 (22.4%)
Not available	5 (1.7%)	2 (1.0%)	3 (3.1%)
Discontinuation of prior osteoporosis therapy, n (%)			
n	293	195	98
Yes	185 (63.1%)	120 (61.5%)	65 (66.3%)
No	107 (36.5%)	74 (37.9%)	33 (33.7%)
Not available	1 (0.3%)	1 (0.5%)	0
Reasons for discontinuation, n (%)			
n	185	120	65
Adverse events	139 (75.1%)	98 (81.7%)	41 (63.1%)
Lack of effect	135 (73.0%)	77 (64.2%)	58 (89.2%)
Physician decision	29 (15.7%)	24 (20.0%)	5 (7.7%)
Switch to other treatment	27 (14.6%)	22 (18.3%)	5 (7.7%)
Poor adherence	11 (5.9%)	1 (0.8%)	10 (15.4%)
Other	6 (3.2%)	2 (1.7%)	4 (6.2%)
Economical reason	3 (1.6%)	2 (1.7%)	1 (1.5%)
Patient's decision	3 (1.6%)	3 (2.5%)	0
Prescribed medication, n (%)			
n	293	195	98
Ibandronate	220 (75.1%)	147 (75.4%)	73 (74.5%)
Alendronate	124 (42.3%)	85 (43.6%)	39 (39.8%)
Risedronate	28 (9.6%)	13 (6.7%)	15 (15.3%)
Strontium ranelate	11 (3.8%)	10 (5.1%)	1 (1.0%)
Zoledronate	2 (0.7%)	2 (1.0%)	0
Calcitonin	2 (0.7%)	1 (0.5%)	1 (1.0%)
Other	1 (0.3%)	1 (0.5%)	0

n — number; Type I — osteoporosis centres; Type II — orthopaedic, rheumatological, or family doctor outpatient clinics

study population and not summarized by centre type. Overall, the mean BMD and T-score increased on denosumab treatment (Fig. 3).

Among patients with a BMD assessment at baseline and month 12, most (132/182 [72.5%]) experienced an increase in BMD T-score, with increases most likely at the total hip, (82.4% [14/17]), followed by the lumbar spine (79.5% [66/83]), and the femoral neck (63.4% [52/82]). BMD T-score decreased in 16.5% (30/182) of patients and remained stable in 11.1% (20/182) of patients. At month 12, 42.7% (35/82), 39.8% (33/83), and 52.9% (9/17) of patients had a BMD T-score >-2.5 (the threshold differentiating osteoporosis and osteopaenia) at the femoral neck, lumbar spine, and total hip, respectively. The percentage change in BMD ranged from 2.82% to 6.21%, being highest at the lumbar spine (Fig. 4).

Concomitant medications

Overall, during the study period 71.9% of patients took concomitant (other than denosumab) therapies.

Table 4. *Denosumab treatment patterns*

	Overall (n = 463)	Type I centres (n = 260)	Type II centres (n = 203)
Reasons for prescribing denosumab, n (%)			
Contraindications for other osteoporosis therapy	52 (11.2%)	41 (15.8%)	11 (5.4%)
Failed other available osteoporosis therapy	177 (38.2%)	131 (50.4%)	46 (22.7%)
History of osteoporotic fracture	362 (78.2%)	208 (80.0%)	154 (75.9%)
Intolerant to other osteoporosis therapy	140 (30.2%)	91 (35.0%)	49 (24.1%)
Low BMD/T-score	430 (92.9%)	237 (91.2%)	193 (95.1%)
Multiple risk factors for fracture	146 (31.5%)	94 (36.2%)	52 (25.6%)
Patient's decision	2 (0.4%)	2 (0.8%)	0
Previous therapy unavailable	3 (0.6%)	3 (1.2%)	0
Other	1 (0.2%)	1 (0.4%)	0
Time since most recent previous fracture to 1st denosumab injection, n (%)			
< 12 months	121/368 (32.9%)	68/228 (29.8%)	53/140 (37.9%)
≥ 12 months	247/368 (67.1%)	160/228 (70.2%)	87/140 (62.1%)
Not available	38/406 (9.4%)	7/235(3.0%)	31/171 (18.1%)
Time of treatment, months			
n	420	242	178
Mean (SD)	11.8 (1.4)	11.9 (1.1)	11.6 (1.8)
Median	12.0	12.0	12.0
Range	6–14	6–14	6–14
Subjects who completed 12 months of observation, n (%)	400/463 (86.4%)	235/260 (90.4%)	165/203 (81.3%)
Subjects with next denosumab injection planned, n (%)			
Yes	374/463 (80.8%)	210/260 (80.8%)	164/203 (80.8%)
Not	27/463 (5.8%)	20/260 (7.7%)	7/203 (3.4%)
Not provided	62/463 (13.4%)	30/260 (11.5%)	32 (15.8%)

BMD — bone mineral density; n — number; SD — standard deviation; Type I — osteoporosis centres; Type II — orthopaedic, rheumatological, or family doctor outpatient clinics

At baseline the median number of prescription medication was 2, and the most common concomitant medications were those for the cardiovascular system (50.7% of medications, 49.7% of patients) and the alimentary tract and metabolism (16.4% of medications, 27.0% of patients). This pattern persisted until month 12.

Osteoporosis-related laboratory examinations

At enrolment, the most commonly reported laboratory tests were blood calcium (34.1% of patients), phosphate (20.3%), and vitamin D (16.6%), followed by bone-specific alkaline phosphatase (ALP) (15.8%), thyroid tests (12.1%), and parathyroid hormone (PTH) (11.7%). These laboratory tests were performed less frequently at months 6 and 12 follow-up visits (blood calcium, 10.5% and 10.9%; phosphate, 4% and 3%; vitamin D, 5.7% and 9.8%; ALP, 1.9% and 0.5%; thyroid tests, 0.7% and 1%; parathyroid hormone, 0.5% and 2.5%).

Safety evaluation

Two patients reported adverse events during the 12-month follow-up. One patient reported poor tolerance to denosumab [System Organ Class (SOC): general disorders and administration site conditions, preffered term (PT): asthenia, nausea], which the physician judged to be treatment-related and of moderate severity. The second AE was a fatal lung neoplasm [SOC: neoplasms benign, malignant, and unspecified (incl. cysts and polyps); PT: lung neoplasm malignant], which the physician considered unrelated to denosumab treatment.

Discussion

With a global aging population, the prevalence of osteoporosis will increase, posing a great clinical and economic burden to healthcare systems. Therefore, effective clinical management of osteoporosis is important, and understanding the characteristics and treatment

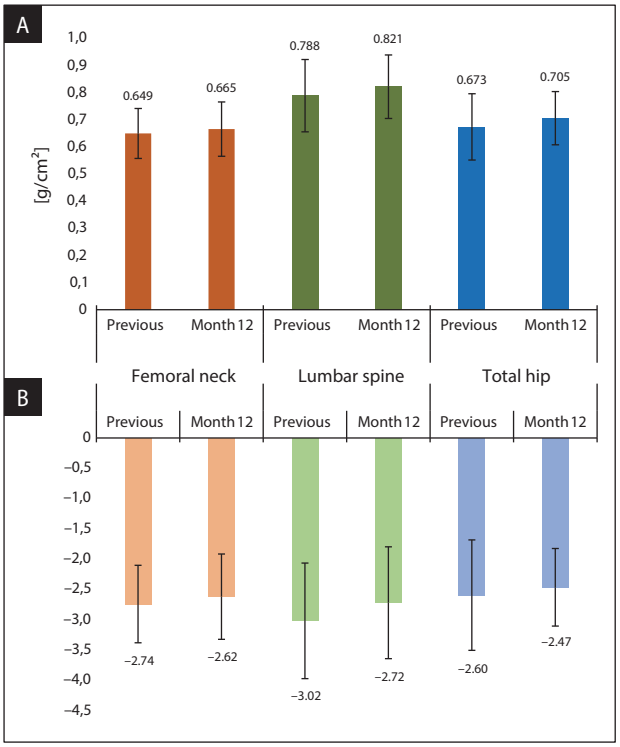

Figure 3. *Means of bone mineral density [g/cm²] (**A**) and T-score values (**B**)*

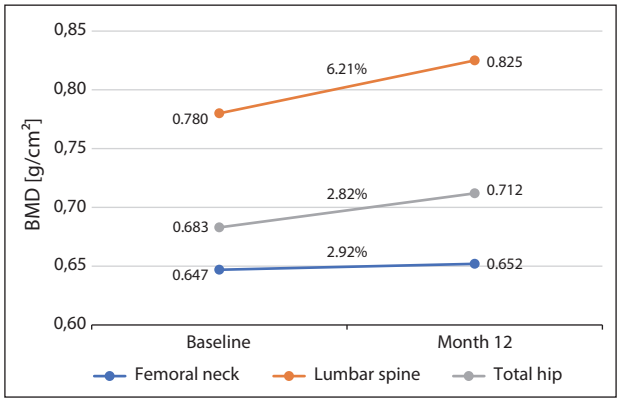

Figure 4. *Bone mineral density (BMD) changes in patients with data at baseline and month 12*

patterns of patients with osteoporosis could improve clinical practice. To our knowledge, our study is the first to evaluate the characteristics of patients receiving denosumab for the treatment of osteoporosis in clinical practice across Poland.

As expected, and consistent with other published studies, the majority of patients in our study were women [10, 11] and were over 65 years old [11, 12]. Moreover, our study population reflects local reimbursement criteria at the time of our study. At the start of our study, denosumab was reimbursed for women over 60 years of age with both PMO (T-score ≤ –2.5 measured by dual-energy X-ray absorptiometry [DXA]) and an osteoporotic fracture, having failed, or with contraindications to, oral bisphosphonates [13]. In November 2019, reimbursement criteria were modified to include women and men older than 60 years with osteoporosis (T-score ≤ –2.5 measured by DXA) or an osteoporotic fracture [14]. Therefore, had the study continued for longer, the proportion of men enrolled would likely have increased.

The prevalence of risk factors for fracture observed in our study population, such as smoking status [15], mean BMI [16, 17], the number and type of comorbidities [18, 19], age, and cause of menopause onset [17, 18, 20], was similar to previous studies, validating these risk factors.

When diagnosing osteoporosis, a BMD assessment should be performed at the femoral neck or spine [4, 6]. This is reflected in our study, whereby most patients had a BMD assessment prior to enrolment, most commonly at the femoral neck or spine. The laboratory tests recorded most frequently in our study (before study enrolment and during follow-up) were blood calcium, phosphate, and vitamin D levels. This reflects the need to optimize calcium and vitamin D in patients with osteoporosis, regardless of fracture risk [4, 21]. Indeed, the majority of patients in our study received supplementary calcium and/or vitamin D, as recommended in international [22] and Polish guidelines [4].

Two-thirds of the women enrolled in our study had received prior osteoporosis therapy, most commonly bisphosphonates, which are the recommended first-line treatment for osteoporosis. Almost two-thirds of these women discontinued prior osteoporosis therapy before enrolment into our study, mainly due to toxicity and lack of effect. This is aligned with real-world data reporting persistence to bisphosphonate therapy ranging from 28% to 74% [23]. The most common reason for initiating denosumab was low BMD T-score, followed by a history of osteoporotic fracture, failure of other osteoporosis therapies, multiple risk factors, and intolerance to other therapies. These data reflect the local reimbursement criteria at the time of the study [13]. Studies from the Czech Republic and Slovakia also reported that reimbursement criteria for denosumab impacted the baseline characteristics of enrolled patients [17].

While our study was not designed to assess the effectiveness of denosumab, it is worth noting that BMD values increased at all tested locations after 12 months. Moreover, only 8 new fractures were noted after 6 months of denosumab treatment, and 4 were reported after 6–12 months of therapy. The ability of denosumab to increase BMD and decrease risk of fractures was previously demonstrated in numerous clinical studies [24–28].

It is also noteworthy that 86% of patients persisted to denosumab therapy for 12 months, and further injections were planned in most (at least 81%) of these patients.

The additional value of our study is the presentation of data from 2 types of outpatient clinics: osteoporosis treatment centres (Type I centres) and small orthopaedic, rheumatological, or family doctor outpatient centres (Type II centres). Such data provide further perspective regarding osteoporosis management and treatment in Poland. For example, more patients were enrolled from Type I centres than from Type II centres, suggesting that specialists prescribe denosumab more frequently than general practitioners [20]. Conversely, a study in neighbouring countries reported that internists and rheumatologist prescribed denosumab with similar frequency; however, the authors did not compare the characteristic of patients enrolled in the different study centres [17].

While gender and age were similar across the different centre types in our study, socioeconomic characteristics differed slightly. Compared with patients enrolled at Type II centres, those enrolled at Type I centres had a higher educational level, were more likely to live at home alone or with family, and were more likely to have laboratory assessments to diagnose osteoporosis. In addition, clinical risk factors for osteoporosis, including prior fractures, occurred more frequently in patients from Type I centres. Women enrolled at Type I centres were more likely to have received prior PMO therapy and calcium supplements. This indicates that Type I treatment centres offer a more extensive treatment approach for osteoporosis. However, these data should be interpreted with caution due to the small sample sizes.

Concerning initiation of the study treatment, the percentage of patients starting with denosumab due to contraindications to, or failure of, other osteoporosis therapies was much higher in Type I centres. In addition, patients enrolled at Type I centres were more likely to complete the 12-month follow-up.

There are few published data to compare our observations with others. However, the differences we observed between patients managed in different treatments centres suggest that patients with more severe symptoms of osteoporosis, and/or more comorbidities, are referred to specialist osteoporotic centres that have access to more extensive diagnostics.

In this article we presented detailed sociodemographic and disease-related characteristics of patients who had routinely implemented denosumab therapy. Most of them continued denosumab for at least 12 months, and their BMD T-scores increased.

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Contribution statement

Amgen (Europe) GmbH designed the study in cooperation with the authors. T.B., E.W., and M.R.B. were involved in data collection. All authors participated in data interpretation, critically revised the manuscript versions and accepted the final version before submission.

Conflict of interest

E.M.S. received speaker honorarium from Amgen; T.B. received speaker honorarium from Amgen, IBSA; M.R.B. received speaker honorarium from Amgen, Apotex, Lilly, Merck, MSD, Polpharma, Roche, Sanfarm, Servier, Teva, Unipharm, and Zentiva and received fees and/or travel grants from Amgen, MSD, Polpharma, Roche, Servier, and Zentiva; K.D. and K.P.K. are Amgen employees; E.S. has received speaker honorarium from Amgen, SunFarm, LekAM, Biofarm, and MSD and received fees and/or travel grants Amgen, Berlin-Chemie, and Merck; E.W. declared no conflict of interests.

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