Supplementary Table 1. MRONJ frequency according to regimen of antiresorptive agents in patients with osteoporosis*

Reference	Year	Regimen	Numbers	Observation	Control	Any BPs	Oral BPs	Oral_Exp	ZA	ZA_Exp	DMB	DMB_ Exp	Study Design	Notes
Amigues C et al. [1]	2023	BPs (ZA/RIS/ALE) ZA 5mg q1y	2,233,436 (RIS) 2,432,373 (ALE) 614,932 (ZA)	10 yrs (2011-2020)			ALE 5.1 /100,000 p-y RIS 2.0 /100,000 p-y	ALE 69±54 mo (TTO) RIS 68±40 mo (TTO)	9.6 /100,000 p-y	49±22 mo (TTO)			Retrospective cohort study	French National Pharmacovigilance Database (BNPV)
Wang Q et al. [2]	2023	ZA 5mg q1y ALE 70mg q1w or 10mg qd	1,035 (ZA) 828 (ALE)	1-3 yrs			0 (ALE)	N/A	0	N/A			Meta-analysis	8 eligible trials
Liu FC et al. [3]	2023	DMB, BPs	3,665 (BPs) 3,665 (DMB)	8 yrs		249 /100,000 p-y		N/A			147 /100,000 p-y	N/A	Retrospective cohort study	The cumulative incidence rates of ONJ in both groups were similar for the first and second years of drug use (p=0.062), but significantly different from the third year onwards (p=0.022).
Everts-Graber J et al. [4]	2022	DMB, BPs	3,068	4 yrs		45 /100,000 p-y		3.3 yrs (2.1-5.6)			283 /100,000 p-y (including prev BP users) 943 /100,000 p-y if DMB only patients	2.9 yrs (2.2-4.7)	Retrospective cohort study	Osteoporosis register of the Swiss Society of Rheumatology 5 BP□ and 12 DMB□ related ONJ cases were found. Nine of the 12 patients who developed ONJ under DMB had undergone prior therapy with BPs,

* Studies were included if they enrolled ≥2,000 patients (≥1,000 for Korean data) with an adequate follow-up period, or if they utilized the Korean National Health Insurance Service database. Only studies that did not combine cancer and osteoporosis patients, and that clearly reported the incidence or prevalence of MRONJ, were selected.

													yielding a rate ratio of 6.3 (95% confidence interval [CI] 2.1 to 22.8), p < 0.001.
Rhee Y et al. [5]	2022	DMB	1,266 (DMB),	6 yrs							0	350.0± 71.4 days	Prospective observational study	Korean data
Kim SH et al. [6]	2021	BPs new user (ALE, RIS, IBA, ZA, PAM), non-BP user	164,926 (BP new user - ALE 40,250 - RIS 38,189 - IBA PO 3,983 - IBA IV 4,978 - ZA 274 - PAM 1,776 - BP switch 75,476) 164,926 (non-BP user)	4 yrs	6.94 /100,000 p-y (non-BP user)	20.85 /100,000 p-y (BP new user)	0.08% (31/40250, ALE) 0.05% (20/38189, RIS) 0.08% (3/3983, IBA) 0.14% (109/75,476, BP switch)	N/A	0% (0/274, ZA) 0.04% (2/4978, IBA) 0.06% (1/1776, PAM)	N/A			Retrospective cohort study	Korean data (KNHIS) - Higher risk for ONJ in patients receiving higher cumulative doses of BP - Independent risk factors: old age, diabetes, hypertension, rheumatoid arthritis, and dental factors such as tooth extraction and periodontal disease
Park JH et al. [7]	2021	BPs (PAM,ALE,IBA ,RIS,ZA)	74,491 (RIS 40,606, ALE 23,209, IBA 9,129, PAM 812, ZA 735)	upto 12 yrs (2004-2015)		total 45.06 /100,000 p-y 25.75 /100,000 p-y (ddd<365) 53.43 /100,000 p-y (365-730) 65.85 /100,000 p-y (730-1094) 63.70 /100,000 p-y (1,095-1,459) 75.78 /100,000 p-y (>1,460)							Retrospective cohort study	Korean data (NHIS-HEALS) - A gradual, but not sudden, dose-dependent increase in ONJ risk with BP exposure
Veszelyne Kotan E et al. [8]	2019	BPs (ALE,CLO,IBA ,PAM,RIS,ZA)	222,477	5 yrs (2010-2014)			0.08% (140/170411)	N/A	0.13% (67/51,225)	N/A			Retrospective registry-based study	Hungarian National Healthcare Services Center's database

Saag KG et al. [9]	2017	ALE 70mg q1w for 3yrs ALE 70mg q1w for 2yrs after RMO 210mg q1m for 1yr	2,014 (ALE) 2,040 (RMO)	2.7 yrs (median)		0.05% (1/2014, ALE for 3 yrs) 0.05% (1/2040, ALE for sequential)	2-3 yrs					RCT	ARCH study
Bone HG et al. [10]	2017	DMB	1,802 (BP)	10 yra	0 /100,000 p-y					7.2 /100,000 p-y	10 yrs	RCT	FREEDOM-ext
Cosman F et al. [11]	2016	RMO+DMB vs DMB	3,221	2 yrs	0					0.06% (RMO to DMB group)	2 yrs	RCT	DMB sequential after RMO
Lapi F et al. [12]	2013	Oral BPs	65,220	2.7 yrs		36.6 /100,000 p-y	N/A					Retrospective cohort study	BPs Effectiveness Safety Trade-off (BEST) database
Bone HG et al. [13]	2013	DMB	2,343 (DMB 10 yr)	6 yrs						0.18% (4/2243, 6 yrs) 0.09% (2/2206, 3 yrs)	6 vs. 3 yrs	RCT	DMB 6 yrs versus PMO 3 yrs+ DMB 3 yrs (FREEDOM-ext)
Malden N et al. [14]	2012	ALE 10mg qd or 70mg q1w	N/A	5 yrs		22 /100,000 drug p-y	4.7 yrs (4 mo-13yrs) (TTO)					Prospective case series	
Tennis P et al. [15]	2012	Oral BPs	31,244 (unexposed 28,476 IV 135 PO 8,468)	55,335 p-y	26 /100,000 p-y	15 /100,000 p-y	16,471 p-y	0	244 p-y			Retrospective cohort study	
Lo JC et al. [16]	2010	Oral BPs (ALE, IBA, RIS)	8,572	2.7 yrs		0.10% (9/8,572) >4 yrs: 0.21%, <4 yrs: 0.04% 28 /100,000 p-y	3.5 yrs (IQR, 2.5-4.7) 4.4 yrs (IQR, 3.8-4.9) (TTO)					Retrospective cohort study	Kaiser Permanente PROBE (Predicting Risk of Osteonecrosis with Bisphosphonate Exposure) study Survey (61.5% response)
Hong JW et al. [17]	2010	Oral BPs (ALE, IBA, RIS)	9,882-12,752	3 yrs		0.05-0.07%	43.1 mo (5-120) (TTO)					Retrospective cohort study	Korean data
Grbic JT et al. [18]	2010	ZA 5mg q1y	5,903 (ZA) 5,140 (Control)	1-3 yrs	0.02% (1/5140)			<1 /14,200 p-y	about 14,200 p-y			Systematic review	5 completed HORIZON trials

					0.017% (1/5,903)						
Cummings SR et al. [19]	2009	DMB	2,207 (DMB 7 yr)	3 yrs	0 /100,000 p-y			0 /100,000 p-y	3 yrs	RCT	FREEDOM
Grbic JT et al. [20]	2008	ZA 5mg q1y	3,889 (ZA) 3,876 (PBO)	3 yrs	<1/10,000 p-y 0.03% (1/3876)	<1 /10,000 p-y 0.03% (1/3,889)	1-3 yrs			RCT	HORIZON-PFT
Lyles KW et al. [21]	2007	ZA 5mg q1y	1,065 (ZA) 1,062 (PBO)	1.9 yrs (median)	0	0	N/A			RCT	HORIZON-RFT

(ALE: aledronate, BP: bisphosphonate, CLO: clodronate, ddd: defined daily dose, DMB: denosumab, Exp: duration of exposure, IBA: ibandronate, IQR: Interquartile range, IV: intravenous administration, mo: months, N/A: not available, ONJ: osteonecrosis of the jaw, PAM: pamidronate, PBO: placebo, PO: oral administration, p-y: per person-years, qd: once per day, q1m: once per month, q1w: once per week, q1y: once per year, RCT: randomized controlled trial, RIS: risedronate, RMO: romosozumab, TTO: time to onset, yr: year, ZA: zoledronic acid)

Supplementary Table 2. MRONJ frequency according to regimen of antiresorptive agents in patients with bone metastasis or multiple myeloma[†]

Disease	Reference	Year	Regimen	Numbers	Observation	PBO	Oral BPs	Oral_Exp	ZA	ZA_Exp	DMB	DMB_Exp	Study Design	Notes
Various cancer	Chiho Moon et al. [22]	2024	DMB 120mg/q4wks	1,278	9 yrs (2014-2023)						2.66% (34/1278)	6.91±8.41 dose		Korean data
Various cancer	Amigues C et al. [23]	2023	ZA 4mg/q1mo	41,924	10 yrs (2011-2020)				1,300 /100,000 p-y	27±22 mo (TTO)			Retrospective cohort study	French National Pharmacovigilance Database (BNPV)
BM	Ng TL et al. [24]	2021	IV BPs, DMB	1,077 (IV BPs) 948 (DMB)	N/A				1.6-4% (<2 yrs IV BPs) 3.8-18% (>2 yrs IV BPs)	N/A	1.9% (< 2yrs) 6.9% (> 2yrs)	N/A	Systematic review	
Solid cancer	Ehrenstein V et al. [25]	2021	ZA, DMB, or ZA to DMB	1,340 (DMB) 1,352 (ZA) 408 (ZA to DMB)	5 yrs				1.4% 100 /100,000 p-y	12.9 mo	5.7% 300 /100,000 p-y	19.8 mo	Retrospective cohort study	6.6% in ZA to DMB group
BC	Coleman R et al. [26]	2020	DMB 120mg/q4wks for 6mo and q/3mo 4.5yrs	2,256 (DMB) 2,253 (PBO)	5 yrs	0.2%					5.40%	35.8 mo	RCT	
Solid cancers	Coleman R et al. [26]	2020	DMB	2,256 (DMB) 2,253 (PBO)	5 yrs	0.2%					5%	N/A	RCT	
MM	Raje N et al. [27]	2018	ZA, DMB	859 (DMB) 859 (ZA)	50 mo				4%	17.6 mo	3%	13.6 mo	RCT	No significant difference
BC,PC, MM	Himelstein AL et al. [28]	2017	ZA q4wks or q12wks	1,822 (each 911)	2 yrs				2.0% (q4wks) 1.0% (q12wks)	N/A			RCT	CALGB cohort
BC	Coleman R et al. [29]	2014	ZA 4mg/q3-4wks for 6mo, /q3mo for 2yrs, /q6mo for 2.5yrs	1,681 (ZA) 1,678 (PBO)	Control 84.0mo (63-92.2, median) ZA 84.0mo (69.7-93.2, median)	0%			1.7% (26/1,681)	median 18 dose (11-19)			RCT	AZURE TRIAL

[†] Studies were included if they enrolled ≥2,000 patients (≥1,000 for Korean data or randomized controlled trials) with an adequate follow-up period. In addition, only studies in which treatment regimens could be clearly verified and in which patients with metastasis or cancer treatment–induced bone loss (CTIBL) were not mixed with osteoporosis patients were selected.

BC	Barrett-Lee P et al. [30]	2014	ZA 4mg/q3-4wks IBA 50mg/qd po	697 (ZA) 704 (IBA PO)	ZA: median 91 wks IBA: median 92 wks		0.71%, (5/704) (IBA)	N/A	1.29% (9/697)	N/A			RCT	ZICE trial
MM	Jackson GH et al. [31]	2014	ZA 4mg/q3-4wks CLO 1600mg/qd po	981 (ZA) 979 (CLO PO)	Median 5.9 yrs		0.5% (CLO)	N/A	3.7%	N/A			RCT	MRC Myeloma IX trial
Solid cancers	Henr y D et al. [32]	2014	ZA, DMB	800 (DMB) 797 (ZA)	3 yrs				1.10%	N/A	0.80%	N/A	RCT	No significant difference
MM, BC, PC, solid tumors (except breast and prostate)	Peddi P et al. [33]	2013	DMB 0.1, 0.3, 1.0, 3.0mg/kg (one dose) / PAM 90mg (one dose) DMB 120mg q4w / ZA 4mg q4w	2,846 (ZA) 2,885 (DMB)	34-41mo				1.3% (37/2,846)	N/A	1.8% (52/2,885)	N/A	Systematic review	
Solid cancers, MM	Saad F et al. [34]	2012	ZA 4mg q4wks Dmab 120mg q4wks	5,723	34-41mo				1.30%	median 14 mo (TTO)	1.80%	median 14 mo (TTO)	RCT	Data merged from 3 trials
BC	Coleman R et al. [35]	2011	ZA 4mg/q3-4wks for 6mo and q3mo for 2 yrs and q6mo for 2.5 yrs	1,665 (ZA) 1,675 (PBO)	3 yrs	0%			0.7% (11/1665)	median 746 days (238-1029) (TTO)			RCT	AZURE: BIG 01-04
BC	Coleman RE et al. [36]	2011	ZA 4mg/q3-4wks for 6mo and q3mo for 2yrs and q6mo	1,681 (ZA) 1,678 (PBO)	5 yrs (53.5-60.9 mo)	0%			1.1% (17/1681)	N/A			RCT	
PC	Fizazi K et al. [37]	2011	ZA, DMB	950 (DMB) 951 (ZA)	24-42 mo				1%	17.1 mo	2%	20.7 mo	RCT	No significant difference
BC	Stopeck AT et al. [38]	2010	ZA 4mg q4wks DMB 120mg q4wks	1,013 (ZA) 1,020 (DMB)	median 17mo				1.4% (14/1,013)	N/A	2.0% (20/1,020)	N/A	RCT	
MM	Morgan GJ et al. [39]	2010	ZA 4mg q3-4wks CLO 1600mg qd po	981 (ZA) 979 (CLO PO)	median 3.7 yrs (2.9-4.7)		0.3% (3/979) (CLO) Intensive pathway <1% (2/556) Non-Intensive pathway <1% (1/423)	N/A	3.5% (35/983) Intensive pathway 4% (21/555) Non-Intensive pathway 3% (14/428)	N/A			RCT	

BC,MM	Hoff AO et al. [40]	2008	iv BPs (ZA, PAM)	3,994	8 yrs	1.2% (BC) 2.4% (MM)	BC - PAM 2.49 yrs (1.73-3.24) - ZA 1.38 yrs (0.3-1.60) - both sequentially 3.33 yrs (1.28-5.51) MM - PAM 1.59 yrs (0.25-2.72) - ZA 1.26 yrs (0.57-3.10) - both sequentially 4.18 yrs (2.18-5.35)	Case series
MM, PC, BC	Estilo CL et al. [41]	2008	iv BPs	4,835		0.72% (28/4,835)	28.8 mo (0.9-100.8) (TTO)	Case series

(BC: breast cancer, BM: bone metastasis, BP: bisphosphonate, CLO: clodronate, DMB: denosumab, Exp: duration of exposure, IBA: ibandronate, IV: intravenous administration, MM: multiple myeloma, mo: months, N/A: not available, PAM: pamidronate, PBO: placebo, PC: prostate cancer, PO: oral administration, p-y: per person-years, RCT: randomized controlled trial, RIS: risedronate, TTO: time to onset, yr: year, ZA: zoledronic acid)

Supplementary Table 3. MRONJ frequency according to regimen of antiresorptive agents in patients with CTIBL[‡]

Disease	Reference	Year	Regimen	Numbers	Observation	Control	Any BPs	Oral BPs	Oral_Exp	ZA	ZA_Exp	DMB	DMB_Exp	Study Design	Notes
BC	Gralow JR et al. [42] Kizub DA et al. [43]	2020, 2021	ZA 4 mg q1m for 6mo, then q3mo CLO 1600 mg qd PO IBA 50 mg qd PO	2,231 (ZA) 2,235 (CLO PO) 1,552 (IBA PO)	3 yrs			0.36% (CLO), 0.77% (IBA)	57.1% (1276/2235) complete therapy (CLO) 60.8% (943/1552) complete therapy (IBA)	1.26%	63.2% (1,410/2,231) complete therapy			RCT	SWOG S0307 trial
BC	Vliek SB et al. [44]	2022	IBA po 50mg qd for 3 yrs	565 (ET+IBA) 551 (ET only)	3 yrs	0.18% (1/551)		1.94% (11/565)	N/A					RCT	TEAM-IIB trial
BC	Coleman R et al. [26]	2020	DMB 120 mg q4wks for 6 months, then q3mo for 5 yrs	2,256 (DMB) 2,253 (PBO)	6.5 yrs	0.18%						5.4%	30.5 months	RCT	
BC	Gnant M et al. [45]	2019	DMB (60 mg/q6mo)	1,711 (DMB) 1,709 (PBO)	5 yrs	0%						0%	N/A	RCT	
BC	O'Carrigan B et al. [46]	2017	ZA (6 studies), PO BPs (3 studies)	13,242 (9 studies)	1-7.5 yrs	0%	0.5% (35/7,047)	0.27%	N/A	1.34%	N/A	0%	N/A	Systematic review	CTIBL regimen 연구만 포함하여 계산
BC	Gnant M et al. [47]	2015	ZA 4mg q6mo for 3 yrs	900 (ZA) 903 (PBO)	median 94.4mo (0-114)	0%				0%	N/A			RCT	Austrian Breast and Colorectal Cancer Study Group trial 12 (ABCSG-12)
BC	Rathbone EJ et al. [48]	2013	ZA 4mg q1m for 6 mo, q3mo for 2 yrs, q6mo for 2.5 yrs	244 (ZA) 242 (PBO)	73.9 mo (60.7-84.2)	0%				2.10%	863 days (21-			RCT	AZURE trial

[‡] Studies were included if they enrolled ≥1,000 patients (≥500 for randomized controlled trials) with an adequate follow-up period. Similarly, only studies in which treatment regimens could be clearly verified and in which patients with metastasis or CTIBL were not mixed with osteoporosis patients were selected.

											2,767) (TTO)					
BC	Valachis A et al. [49]	2013	ZA 4mg q1m for 6mo, q3mo for 2 yrs and q6mo for 2.5yrs ZA 4mg q6mo (9 studies) ZA 4mg q3mo (4 studies) ZA 4mg q3wks (1 study)	4774 (ZA)	12-96 mo	0%					0.52% (25/4774)	4-10 times			Systematic review	
BC	Coleman R et al. [50]	2013	ZA 4mg q6mo for 5 yrs	532 (upfront) 533 (delayed)	5 yrs						0.44% (3/676)	N/A			RCT	ZO-FAST trial
PC	Smith MR et al. [51]	2009	DMB vs. placebo	734 (DMB) 734 (PBO)	2 yrs						0 /100,000 p-y	N/A	0 /100,000 p-y	N/A	RCT	
BC	Mauri D et al. [52]	2009	ZA 4mg q1m for 6mo, q3mo for 2 yrs and q6mo for 2.5yrs ZA 4mg q6mo (5 studies) ZA 4mg q3mo (2 studies) IBA po 150mg q1m RIS 35mg q1w CLO 1,600mg qd	10694 5312 (BP) vs 5382 (control) ZA (3987), CLO 669), PAM 460), RIS (171), IBA PO (25)	N/A	0.24% (1/5382)	0.24% (13 /5312)	0% (IBA) 0% (RIS) 0% (CLO)	2 yrs (IBA) 1-2 yrs (RIS) 2-3 yrs (CLO)		0.33% (13/3987)	4-10 times			Metaanalysis	Adjuvant use of BPs is relatively safe in adjuvant treatment of BC, even the risks are not entirely negligible.
BC	Gnant M et al. [53]	2009	ZA 4mg q6mo for 3 yrs	899 (ZA) 904 (PBO)	47.8 mo (median)	0% (0/904)					0%	n/a			RCT	ABCSG-12 trial

(BC: breast cancer, BP: bisphosphonate, CLO: clodronate, DMB: denosumab, ET: endocrine therapy, Exp: duration of exposure, IBA: ibandronate, mo: months, N/A: not available, PAM: pamidronate, PBO: placebo, PC: prostate cancer, PO: oral administration, qd: once per day, q1m: once per month, q1w: once per week, RCT: randomized controlled trial, RIS: risedronate, TTO: time to onset, yr: year, ZA: zoledronic acid)

Supplementary Table 4. MRONJ frequency according to regimen of antiresorptive agents in patients with nonmalignant bone disease[§]

Disease	Reference	Year	Regimen	Numbers	Observation	DMB	DMB_Exp	Study Design	Notes
GCTB	Jiang CY et al. [54]	2022	DMB 120 mg/q1w for 3 wks, 120 mg/q4-12wks afterwards	37	>5 yrs	13.50%	N/A	Retrospective cohort study	interval of DMB was changed frequently
GCTB	Raimondi A et al. [55]	2020	DMB 120 mg/q1w for 2 wks, 120 mg/q4wks afterwards	29	70 mo	13.8%	92.5 mo	Retrospecitve case series	
GCTB unresectable	Chawla S et al. [56]	2019	DMB 120mg/q1m	526	58.1 mo	3.23%	N/A	Phase 2 study	
GCTB	Rutkowski P et al. [57]	2018	DMB 120 mg/q1w for 2 wks, 120 mg/q4wks afterwards	138	23 mo	1.4% (2/138)	8 mo	Retrospective case series	
GCTB	Palmerini E et al. [58]	2017	DMB 120 mg/q1w for 3 wks, 120 mg/q4wks afterwards	97	10 yrs	6.0%	39.6 mo	Retrospective cohort study	5-year ONJ-free survival of 92%

(DMB: denosumab, Exp: duration of exposure, mo: months, N/A: not available, PBO: placebo, qd: once per day, q1m: once per month, q1w: once per week, yr: year)

[§] Considering the total number of available studies, all relevant studies were included except for case reports..

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Supplementary Table 5. Human studies of teriparatide administration for medication-related osteonecrosis of the jaw (MRONJ) treatment in the past 10 years.

Reference	Total Pt	Medical Condition	BP Route	Duration (Years)	Trigger Event	Stage	Surgical Tx	TPTD Duration (Months)	Outcome
Kwon et al. (2012)[6]	6	OP	Oral	3–8	NA	2 or 3	100%	1–3	Favorable
Narvarez et al. (2013)[7]	1	OP	NA	2.7	Spon	NS	None	8	Favorable
Yoshiga et al. (2013)[8]	2	NA	Oral	4.5	Spon	3	50%	3	Favorable
Kim et al. (2014)[9]	15	OP	Oral/IV	3	Ext/Imp/Spon	2 or 3	80%	6	Favorable
Kakehashi et al. (2015)[10]	10	NA	Oral	4.3	Ext/Perio	2 or 3	100%	4–24	Favorable
Yao et al. (2016)[11]	1	OP	Oral	2	Ext	3	100%	18	Favorable
Zushi et al. (2017)[12]	1	OP	Oral	6	Imp	3	100%	5	Favorable
Jung et al. (2017)[13]	6	OP	Oral	0.5–15	NA	2 or 3	100%	1–4	Favorable
Kim et al. (2019)[14]	1	OP	Oral	4	Imp	3	None	2	Favorable
Morishita et al. (2020)[15]	29	OP	Oral/IV	0.8–7.3	Ext/Perio	1–3	38%	0.3–26	Favorable
Ohbayashi et al. (2020)[16]	12	OP	Oral	1–10	NA	2 or 3	None	6	Favorable

Reference	Total Pt	Medical Condition	BP Route	Duration (Years)	Trigger Event	Stage	Surgical Tx	TPTD Duration (Months)	Outcome
Sim et al. (2020)[17]	34	OP/CA/MM	NA	NA	Ext/Imp/Spon	0–3	40%	2	Favorable
Yoshiga et al. (2021)[18]	15	OP	Oral	1-17	NA	2 or 3	none	NA	Favorable
Kim et al. (2024)[19]	29	OP	Oral/IV	NA	Ext/Perio/Imp/Spon	1-3	100%	3	Favorable
Choi et al. (2024)[20]	3	OP	Oral/IV	2-10	Ext/NA	2 or 3	100%	4-12	Favorable

(Pt: patient, BP: bisphosphonate, Tx: treatment, TPTD: teriparatide, OP: osteoporosis, CA: cancer, MM: multiple myeloma, IV: intravenous, NA: not available, Spon: spontaneous, Ext: extraction, Imp: implant, Perio: periodontitis)

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