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FORSCHEN
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Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Osteooncology and Bone Health



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- **Versionen 2002–2024:**

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Bisphosphonates in Metastatic Breast Cancer

	Oxford		
	LoE	GR	AGO
▪ Therapy of hypercalcemia	1a	A	++
▪ Reduction of skeletal events / complications	1a	A	++
▪ Reduction of bone pain	1a	A	++
▪ Increasing bone pain-free survival	1a	A	++
▪ Treatment beyond osseous progression	5	D	++
▪ Use of bone resorption marker for therapy monitoring	5	D	-
▪ Bisphosphonates alone for pain control	5	D	-

Meta-analyses and Reviews (metastatic breast cancer)

1. Coleman R, Hadji P, Body JJ et al. Bone health in cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2020; 31(12):1650-1663. doi: 10.1016/j.annonc.2020.07.019.
2. O'Carrigan B, Wong MH, Willson ML et al. Bisphosphonates and other bone agents for breast cancer. Cochrane Database Syst Rev. 2017 Oct 30;10:CD003474. doi: 10.1002/14651858.CD003474.pub4.
3. Van Poznak C, Somerfield MR, Barlow WE et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017
4. Tesfamariam Y, Jakob T, Wöckel A et al. Adjuvant bisphosphonates or RANK-ligand inhibitors for patients with breast cancer and bone metastases: A systematic review and network meta-analysis. Crit Rev Oncol Hematol. 2019;137:1-8.

Results of Phase III trials (metastatic breast cancer)

1. Body JJ, Diel IJ, Lichinitser MR et al. Intravenous ibandronate reduces the incidence of skeletal complications in patients with breast cancer and bone metastases. Ann Oncol 14:1399-1405,2003
2. Diel IJ, Body JJ, Lichinitser MR et al. Improved quality of life for long-term treatment with the bisphosphonate ibandronate in patients with metastatic bone disease due to breast cancer. Eur J Cancer 40:1704-1712, 2004
3. Body JJ, Diel IJ, Lichinitser M et al. Oral ibandronate reduces the risk of skeletal complications in breast cancer patients with with


- metastatic bone disease; results from two randomized, placebo-controlled phase III studies. Br J Cancer 90:1133-1137., 2004
4. Tripathy D, Lichinitser M, Lazarev A et al. Oral ibandronate for the treatment of metastatic bone disease in breast cancer: efficacy and safety results from a randomized, double-blind, placebo-controlled trial. Ann Oncol 15:743-750, 2004
 5. Rosen LS, Gordon D, Kaminski M et al. . Long-term efficacy and safety of zoledronic acid compared with pamidronate disodium in the treatment of skeletal complications in patients with advanced multiple myeloma or breast cancer. Cancer 98:1735-1744, 2003
 6. Rosen LS, Gordon DH, Dugan W et al. Zoledronic acid is superior to pamidronate for the treatment of bone metastases in breast carcinoma patients with at least one osteolytic lesion. Cancer 100:36-43, 2004

Clinical relevance of bone resorption marker

1. Van Poznak C, Somerfield MR, Barlow WE et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017

Bisphosphonates for bone pain control

1. Van Poznak C, Somerfield MR, Barlow W. et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017

		Denosumab in Metastatic Breast Cancer		
		Oxford		
		LoE	GR	AGO
 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> ▪ Therapy of hypercalcemia ▪ Reduction of skeletal events / complications ▪ Reduction of bone pain ▪ Increasing bone pain-free survival ▪ Treatment beyond progression <ul style="list-style-type: none"> ▪ Progression while on bisphosphonates ▪ Use of bone resorption markers for therapy monitoring ▪ Denosumab alone for pain control 	1a 1a 1a 1b 5 4 5 5	A A A A D C D D	++ ++ ++ ++ ++ +/- - -

Denosumab - Therapy of bone metastases and skeletal related complications

1. Stopeck AT, Lipton A, Body JJ et al. Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study, J Clin Oncol 28:5132-5139, 2010
2. Lipton A, Steger GG, Figueroa J, et al. Extended efficacy and safety of denosumab in breast cancer patients with bone metastases not receiving prior bisphosphonate therapy. Clin Cancer Res 14:6690–6699, 2008
3. Lipton A, Steger GG, Figueroa J, et al. Randomized active-controlled phase II study of denosumab efficacy and safety in patients with breast cancer-related bone metastases. J Clin Oncol 25:4431–4437, 2007
4. O'Carrigan B, Wong MH, Willson ML et al. Bisphosphonates and other bone agents for breast cancer. Cochrane Database Syst Rev. 2017 Oct 30;10:CD003474. doi: 10.1002/14651858.CD003474.pub4.
5. Tesfamariam Y, Jakob T, Wöckel A et al. Adjuvant bisphosphonates or RANK-ligand inhibitors for patients with breast cancer and bone metastases: A systematic review and network meta-analysis. Crit Rev Oncol Hematol. 2019;137:1-8.

Progression under bisphosphonates

1. Fizazi, K, Lipton, A, Mariette X, et al. Randomized phase II trial of denosumab in patients with **bone** metastases from prostate cancer, breast cancer, or other neoplasms after intravenous bisphosphonates. J Clin Oncol 27:1564-71, 2009
2. Mjelstad A, Zakariasson G, Valachis A et al. Optimizing antiresorptive treatment in patients with bone metastases: time to initiation,


switching strategies, and treatment duration. Support Care Cancer. 2019;27(10):3859-3867. doi: 10.1007/s00520-019-04676-6.

Clinical relevance of bone resorption marker

1. Van Poznak C, Somerfield MR, Barlow WE et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017

Bisphosphonates for bone pain control

1. Van Poznak C, Somerfield MR, Barlow WE et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017



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Skeletal Metastases Treatment with Radionuclids

Oxford		
LoE	GR	AGO
1b	B	+
2b	B	+
1b	B	+
1b	B	+
2b	B	+
2b	C	+
1b	B	+

▪ **Tumor progression after standard treatment of multiple / disseminated metastases and intolerable bone pain**

- ¹⁸⁶Rhenium-hydroxyethyliden-diphosphonat
- ¹⁵³Samarium
- ⁸⁹Strontium
- ²²³Radium
- ¹⁷⁷Lu-EDTMP
- ¹⁸⁸Rhenium-HEDP

Cave: the potential benefits should be weighed against the risk of myelosuppression and pancytopenia

Reviews / Overview

1. Hoskin PJ: Radioisotopes for metastatic bone pain. Lancet Oncol 6(6):353-4, 2005
2. Bauman G, Chrette M, Reid R, Sathya J. Radiopharmaceuticals for the palliation of painful bone metastasis-a systemic review. Radioth Oncol 75: 258-70, 2005
3. Roque i Figuls M, Martinez-Zapata MJ, Scott-Brown M et al. Radioisotopes for metastatic bone pain (Cochrane Review). In: The Cochrane Library 2011, Issue 7. John Wiley & Sons, Ltd. Art. No.: CD003347. DOI: 10.1002/14651858.CD003347.pub2

¹⁸⁶Rhenium (¹⁸⁶Re-HEDP)

1. de Klerk JM, van het Schip AD, Zonnenberg BA et al. Phase 1 study of rhenium-186-HEDP in patients with bone metastases originating from breast cancer. J Nucl Med 137:244-49, 1996
2. Han SH, Zonneberg BA, de Klerk JM et al. ¹⁸⁶Re-etidronate in breast cancer patients with metastatic bone pain. J Nucl Med 40:639-42, 1999
3. Kolesnikov-Gauthier H, Carpentier P, Depreux P et al. Evaluation of toxicity and efficacy of ¹⁸⁶Re-hydroxyethylidene diphosphonate in patients with painful bone metastases of prostate or breast cancer. J Nucl Med 41:1689-94, 2004
4. Limouris GS, Shukla SK, Condi-Paphiti A et al. Palliative therapy using rhenium-186-HEDP in painful breast osseous metastases. Anticancer Res 17:1767-72, 1997

¹⁵³Samarium (¹⁵³Sm-EDTMP)

1. Anderson PM, Wiseman GA, Dispenzieri A et al. High-dose samarium-153 ethylene diamine tetramethylene phosphonate: low toxicity of skeletal irradiation in patients with osteosarcoma and bone metastases. *J Clin Oncol* 20:189-96, 2002
2. Serafini AN. Systemic metabolic radiotherapy with samarium-153 EDTMP for the treatment of painful bone metastasis. *Q J Nucl Med*. 45:91-9, 2001
3. Kolesnikov-Gauthier H, Lemoine N, Tresch-Bruneel E et al. Efficacy and safety of ¹⁵³Sm-EDTMP as treatment of painful bone metastasis: a large single-center study. *Support Care Cancer*. 2017 Sep 17. doi: 10.1007/s00520-017-3885-3

⁸⁹Strontium (⁸⁹Sr-Chlorid)

1. Baziotis N, Yakoumakis E, Zissimopoulos A et al. Strontium-89 chloride in the treatment of bone metastases from breast cancer. *Oncology* 55:377-81, 1998
2. Fuster D, Herranz D, Vidal-Sicart S et al. Usefulness of strontium-89 for bone pain palliation in metastatic breast cancer patients. *Nucl Med Commun* 21:623-26, 2002
3. Kasalicky J, Krajska V. The effect of repeated strontium-89 chloride therapy on bone pain palliation in patients with skeletal cancer metastases. *Eur J Nucl Med* 25:1362-67, 1998
4. Sciuto R, Festa A, Pasqualoni R et al. Metastatic bone pain palliation with ⁸⁹Sr and ¹⁸⁶Re-HEDP in breast cancer patients. *Breast Cancer Res Treat* 66:101-19, 2001

²²³Ra-dichloride:

1. Pandit-Taskar N, Larson SM, Carrasquillo JA. Bone-seeking radiopharmaceuticals for treatment of osseous metastases, Part 1: α therapy with ²²³Ra-dichloride. *J Nucl Med* 55(2):268-74, 2015
2. Rugo HS, Van Poznak CH, Neven P et al. Radium-223 in women with hormone receptor-positive bone-metastatic breast cancer receiving endocrine therapy: pooled analysis of two international, phase 2, randomized, double-blind, placebo-controlled trials. *Breast Cancer Res Treat* 2023 Dec 20. Doi: 10.1007/s10549-023-07147-z.

¹⁷⁷Lu (Lutetium)-EDTMP

1. Agarwal KK, Singla S, Arora G, Bal C. (¹⁷⁷)Lu-EDTMP for palliation of pain from bone metastases in patients with prostate and breast cancer: a phase II study. *Eur J Nucl Med Mol Imaging*. 42(1):79-88,2015

2. Sharma S, Singh B, Koul A et al. Comparative Therapeutic Efficacy of ^{153}Sm -EDTMP and ^{177}Lu -EDTMP for Bone Pain Palliation in Patients with Skeletal Metastases: Patients' Pain Score Analysis and Personalized Dosimetry. *Front Med (Lausanne)*. 2017 May 1;4:46. doi: 0.3389/fmed.2017.00046. eCollection 2017.

Breast Cancer-Related Bone Metastases. J Clin Onc 2007; 25 (28): 4431-4437

Non-randomized studies:

1. Addison CL, Bouganim N, Hilton J et al. A phase II, multicentre trial evaluating the efficacy of de-escalated bisphosphonate therapy in metastatic breast cancer patients at low-risk of skeletal-related events. Breast Cancer Res Treat 2014; 144: 615-624

Systematic reviews:

1. Awan AA, Hutton B, Hilton J et al., De-escalation of bone-modifying agents in patients with bone metastases from breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat. 2019;176(3):507-517.

	Oxford		
	LoE	GR	AGO
▪ Clodronate PO 1600 mg daily	1a	A	++
▪ Clodronate IV 1500 mg q3w / q4w	1a	A	++
▪ Pamidronate IV 90 mg			
▪ q3w / q4w	1a	A	++
▪ q12w	2b	B	+/-
▪ Ibandronate IV 6 mg q3w / q4w	1a	A	++
▪ Ibandronate PO 50 mg daily	1a	A	++
▪ Zoledronate IV 4 mg			
▪ q4w	1a	A	+
▪ q12w	1a	A	++
▪ Denosumab 120 mg SC			
▪ q4w	1a	A	++
▪ q12w	1b	B	+/-
▪ Other dosing or schedules, e.g. from adjuvant trials or therapy of osteoporosis	5	D	-
▪ Planned sequential therapy with multiple agents	2b	B	+/-

Reviews / Guidelines:

1. O'Carrigan B, Wong MH, Willson ML et al. Bisphosphonates and other bone agents for breast cancer. Cochrane Database Syst Rev. 2017;10:CD003474. doi: 10.1002/14651858.CD003474.pub4.
2. Van Poznak C, Somerfield MR, Barlow WE et al. Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. J Clin Oncol 35(35):3978-3986, 2017
3. Ibrahim MF, Mazzarello S, Shorr R et al. Should de-escalation of bone-targeting agents be standard of care for patients with bone metastases from breast cancer? A systematic review and meta-analysis. Ann Oncol. 26(11):2205-13, 2015
4. Awan AA, Hutton B, Hilton J et al., De-escalation of bone-modifying agents in patients with bone metastases from breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat. 2019;176(3):507-517.
5. Shapiro CL, Moriarty JP, Dusetzina S et al. Cost-Effectiveness Analysis of Monthly Zoledronic Acid, Zoledronic Acid Every 3 Months, and Monthly Denosumab in Women With Breast Cancer and Skeletal Metastases: CALGB 70604 (Alliance). J Clin Oncol. 2017; 35(35):3949-3955.

Zoledronic acid:

1. Himmelstein AL, Foster JC, Khatcheressian JL et al. Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in

- Patients With Bone Metastases: A Randomized Clinical Trial. JAMA 317(1):48-58, 2017
2. Hortobagyi GN, Van Poznak C, Harker WG et al. Continued Treatment Effect of Zoledronic Acid Dosing Every 12 vs 4 Weeks in Women With Breast Cancer Metastatic to Bone: The OPTIMIZE-2 Randomized Clinical Trial. JAMA Oncol 3(7):906-912, 2017
 3. Amadori D, Aglietta M, Alessi B et al. Efficacy and safety of 12-weekly versus 4-weekly zoledronic acid for prolonged treatment of patients with bone metastases from breast cancer (ZOOM): a phase 3, open-label, randomised, non-inferiority trial. Lancet Oncol 14(7):663-70, 2013
 4. Santini D, Galvano A, Pantano F et al. How do skeletal morbidity rate and special toxicities affect 12-week versus 4-week schedule zoledronic acid efficacy? A systematic review and a meta-analysis of randomized trials. Crit Rev Oncol Hematol. 2019;142:68-75.

Pamidronate:

1. Amir E, Freedman O, Carlsson L et al. Randomized Feasibility Study of De-escalated (Every 12 wk) Versus Standard (Every 3 to 4 wk) Intravenous Pamidronate in Women With Low-risk Bone Metastases From Breast Cancer. Am J Clin Oncol 2013; 36: 436-442
2. Addison CL, Bouganim N, Hilton J et al. A phase II, multicentre trial evaluating the efficacy of de-escalated bisphosphonate therapy in metastatic breast cancer patients at low-risk of skeletal-related events. Breast Cancer Res Treat 2014; 144: 615-624

Denosumab & bisphosphonates:


1. Clemons M, Ong M, Stober C et al. A randomised trial of 4- versus 12-weekly administration of bone-targeted agents in patients with bone metastases from breast or castration-resistant prostate cancer. Eur J Cancer 2021; 142: 132-140
2. Lipton A, Steger GG, Figueroa J et al. Randomized Active-Controlled Phase II Study of Denosumab Efficacy and Safety in Patients With Breast Cancer-Related Bone Metastases. J Clin Onc 2007; 25 (28): 4431-4437
3. Clemons M, Liu M, Stober C, Pond G, et al.; REaCT investigators. Two-year results of a randomised trial comparing 4- versus 12-weekly bone-targeted agent use in patients with bone metastases from breast or castration-resistant prostate cancer. J Bone Oncol. 2021 Sep 2;30:100388. doi: 10.1016/j.jbo.2021.100388. PMID: 34567960; PMCID: PMC8449269.

Denosumab:


1. Templeton AJ, Stalder L, Bernhard J et al. Prevention of symptomatic skeletal events with denosumab administered every 4 weeks versus every 12 weeks: A noninferiority phase III trial (SAKK 96/12, REDUSE). J Clin Oncol 32:5s, 2014 (suppl; abstr TPS5095)

Sequential therapy with different BTAs:

1. Srivastava A, Noguera-Gonzales GM, Geng Y et al. Prevalence of medication related osteonecrosis of the jaw in patients treated with sequential antiresorptive drugs: systematic review and meta-analysis. Support Care Cancer. 2020. doi: 10.1007/s00520-020-05882-3.



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Metastatic Bone Disease of the Spine


Indications for surgery

Oxford LoE: 2b
GR: C
AGO: ++

- **Spinal cord compression**
 - With progressive neurological symptoms
 - With pathological fractures
- **Instability of the spine**
- **Lesions in pre-irradiated parts of the spine**

1. Wood TJ, Racano A, Yeung H et al. Surgical management of bone metastases: quality of evidence and systematic review. *Ann Surg Oncol* 21(13):4081-9, 2014
2. Ju DG, Yurter A, Gokaslan ZL et al. Diagnosis and surgical management of breast cancer metastatic to the spine. *World J Clin Oncol* 10;5(3):263-71, 2014
3. Rades D, Veninga T, Stalpers LJ et al. Prognostic factors predicting functional outcomes, recurrence-free survival, and overall survival after radiotherapy for metastatic spinal cord compression in breast cancer patients. *Int J Radiat Oncol Biol Phys* 64(1):182-8, 2006
4. Walker MP, Yaszemski MJ, Kim CW et al. Metastatic disease of the spine: evaluation and treatment. *Clin Orthop* 2003;415 Suppl:S165-75
5. Guideline Program Oncology (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive care of oncological patients – Version 1.3 – 2020 AWMF-Register Nr.: 032/054OL. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf
6. Ahangar P, Aziz M, Rosenzweig DH et al. Advances in personalized treatment of metastatic spine disease. *Ann Transl Med.* 2019;7(10):223. Review.
7. Conti A, Acker G, Kluge A et al., Decision Making in Patients With Metastatic Spine. The Role of Minimally Invasive Treatment Modalities. *Front Oncol.* 2019;19;9:915.

8. Schoenfeld AJ, Le HV, Marjoua Y et al. Assessing the utility of a clinical prediction score regarding 30-day morbidity and mortality following metastatic spinal surgery: the New England Spinal Metastasis Score (NESMS). *Spine J.* 2016;16(4):482-90, doi: 10.1016/j.spinee.2015.09.043
9. Rothrock RJ, Barzilai O, Reiner AS et al. Survival Trends After Surgery for Spinal Metastatic Tumors: 20-Year Cancer Center Experience. *Neurosurgery* 2020;nyaa380, doi: 10.1093/neuros/nyaa380.

		Oxford		
		LoE	GR	AGO
 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> Decompression surgery, reduction of tumor volume, stabilization surgery (< 24 h) and irradiation of the spine 	2b	C	++
	<ul style="list-style-type: none"> Irradiation of the spine (< 24 h) <ul style="list-style-type: none"> Radiation therapy regimen (1 x 8-10 Gy vs. multiple fractions) depending on prognosis, performance status and patient's preference 	3b	C	++
	<ul style="list-style-type: none"> Immediate start of treatment 	1c	D	++
	<ul style="list-style-type: none"> Steroids (start at first symptoms) <ul style="list-style-type: none"> - Dexamethasone 16-24 mg/d, then reduction over 2 weeks 	2a	C	+
<p>Clinical trials have included patients with different tumor entities!</p>				

Recommendations and Clinical Practice Guidelines:

1. Loblaw DA, Mitera G, Ford M et al. A 2011 Updated Systematic Review and Clinical Practice Guideline for the Management of Malignant Extradural Spinal Cord Compression. *Int J Radiat Oncol Biol Phys.* 2012;84(2):312-7. doi: 10.1016/j.ijrobp.2012.01.014.
2. Souchon R, Feyer P, Thomssen C et al. Clinical recommendations of DEGRO and AGO on preferred standard palliative radiotherapy (RT) of bone and cerebral metastases, metastatic spinal cord compression, and leptomeningeal carcinomatosis in breast cancer. *Breast Care* 5:401-7, 2010
3. Souchon R, Wenz F, Sedlmayer F et al. DEGRO practice guidelines for palliative radiotherapy of metastatic breast cancer: Bone metastases and metastatic spinal cord compression (MSCC). *Strahlenther Onkol* 185:417-424, 2009
4. Groenen KHJ, van der Linden YM, Brouwer T et al. The Dutch national guideline on metastases and hematological malignancies localized within the spine; a multidisciplinary collaboration towards timely and proactive management. *Cancer Treat Rev* 2018;69:29-38. doi: 10.1016/j.ctrv.2018.05.013.
5. Guideline Program Oncology (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive care of oncological patients – Version 1.3 – 2020 AWMF-Register Nr.: 032/054OL. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf

Reviews:

1. Loblaw A, George KJ, Misra V. Surgical and Radiotherapeutic Management of Malignant Extradural Spinal Cord Compression. Clin Oncol (R Coll Radiol) 2020;32(11):745-752. doi: 10.1016/j.clon.2020.07.022.

Operative therapy:

1. Patchell RA, Tibbs PA, Regine WF et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet 2005 Aug 20-26;366(9486):643-8, doi: 10.1016/S0140-6736(05)66954-1.
2. Yang XG, Lun DX, Hu YC et al. Prognostic effect of factors involved in revised Tokuehashi score system for patients with spinal metastases: a systematic review and Meta-analysis. BMC Cancer 2018;18(1):1248. doi: 10.1186/s12885-018-5139-2.
3. Alpantaki K, Ioannidis A, Raptis K et al. Surgery for spinal metastatic tumors: Prognostication systems in clinical practice (Review). Mol Clin Oncol. 2020;12(5):399-402, doi: 10.3892/mco.2020.2008

Radiation therapy: Randomized studies:


1. Hoskin PJ, Hopkins K, Misra V et al. Effect of Single-Fraction vs Multifraction Radiotherapy on Ambulatory Status Among Patients With Spinal Canal Compression From Metastatic Cancer: The SCORAD Randomized Clinical Trial. JAMA 2019;322(21):2084-2094, doi: 10.1001/jama.2019.17913.
2. Rades D, Segedin B, Conde-Moreno AJ et al. Radiotherapy With 4 Gy x 5 Versus 3 Gy x 10 for Metastatic Epidural Spinal Cord Compression: Final Results of the SCORE-2 Trial (ARO 2009/01)
3. Thirion PG, Dunne MT, Kelly PJ et al. Non-inferiority randomised phase 3 trial comparing two radiation schedules (single vs. five fractions) in malignant spinal cord compression. Br J Cancer. 2020;122(9):1315-1323. doi: 10.1038/s41416-020-0768-z
4. Maranzano E, Bellavita R, Rossi R et al. Short-Course Versus Split-Course Radiotherapy in Metastatic Spinal Cord Compression: Results of a Phase III, Randomized, Multicenter Trial. J Clin Oncol. 2005;23(15):3358-65. doi: 10.1200/JCO.2005.08.193.
5. Maranzano E, Trippa F, Casale M et al. 8Gy single-dose radiotherapy is effective in metastatic spinal cord compression: results of a phase III randomized multicentre Italian trial. Radiother Oncol. 2009;93(2):174-9, doi: 10.1016/j.radonc.2009.05.012.

Radiation therapy: Non-randomized studies:

1. Rades D, Cacicedo J, Conde-Moreno AJ et al. Precision Radiation Therapy for Metastatic Spinal Cord Compression: Final Results of the PRE-MODE Trial. *Int J Radiat Oncol Biol Phys* 2020;106(4):780-789. doi: 10.1016/j.ijrobp.2019.11.401.
2. Rades D, Conde-Moreno AJ, Cacicedo J et al. 1x8 Gy versus 5x4 Gy for metastatic epidural spinal cord compression: a matched-pair study of three prognostic patient subgroups. *Radiat Oncol* 2018;13(1):21. doi: 10.1186/s13014-018-0968-3.
3. Rades D, Lange M, Veninga T et al. Final results of a prospective study comparing the local control of short-course and long-course radiotherapy for metastatic spinal cord compression. *Int J Radiat Oncol Biol Phys* 2011;79(2):524-30
4. Rades D, Karstens JH, Hoskin PJ, et al. Escalation of radiation dose beyond 30 Gy in 10 fractions for metastatic spinal cord compression. *Int J Radiat Oncol Biol Phys* 67:525-31, 2007
5. Rades D, Heidenreich E, Karstens JH. Final results of a prospective study of the prognostic value of the time to develop motor deficits before irradiation in metastatic spinal cord compression. *Int J Radiat Oncol Biol Phys* 53:975-9, 2002

Steroids: Systematic review:

1. Kumar A, Weber MH, Gokaslan Z et al. Metastatic Spinal Cord Compression and Steroid Treatment A Systematic Review. *Clin Spine Surg.* 2017;30(4):156-163. doi: 10.1097/BSD.0000000000000528.



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Surgery for Bone Metastases Technical Aspects

Spine and limbs

Oxford LoE: 3b


GR: C

AGO: +

- **Marrow splints**
- **Plate osteosynthesis**
- **Compound osteosynthesis (replacement by PMMA and osteosynthesis)**
- **Vertebral replacement by titanspacer**
- **Tumor-Endoprosthesis**
- **Vertebroplasty / Kyphoplasty +/- thermoablation of the tumor**
- **Kypho-IORT (in studies only)**
- **Resection of involved bone in oligometastatic disease (sternum, ribs, vertebrae)**

1. Ju DG, Yurter A, Gokaslan ZL et al. Diagnosis and surgical management of breast cancer metastatic to the spine. World J Clin Oncol 10;5(3):263-71, 2014
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6. Walker MP, Yaszemski MJ, Kim CW et al. Metastatic disease of the spine. Evaluation and treatment. Clin Orthop Rel Res (415S) (Suppl): 165–175, 2003
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8. Guideline Program Oncology (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive care of oncological patients – Version 1.3 – 2020 AWMF-Register Nr.: 032/054OL. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf

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		Metastatic Bone Disease		
		Recurrent Bone Pain after RT		
		Oxford		
		LoE	GR	AGO
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	▪ Single dose RT *	1b	B	++
	▪ Fractionated RT *	1b	B	++
	▪ Radionuclide therapy	2b	B	+
	▪ Magnetic resonance-guided focused ultrasound	1b	B	+
	▪ Radiofrequency ablation	4	C	+
	▪ Cryoablation	4	C	+
* Dose and fractionation depending on location, interval from first radiotherapy (RT), and dose and fractionation of first RT				

Recurrent bone pain in pre-irradiated parts of the skeleton

1. Chow E, Guideline Program Oncology (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive care of oncological patients – Version 1.3 – 2020 AWMF-Register Nr.: 032/054OL. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf
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bone metastases. Radiother Oncol. 2022 Aug;173:240-253.

Magnetic resonance-guided focused ultrasound

1. Hurwitz MD, Ghanouni P, Kanaev SV, et al. Magnetic resonance-guided focused ultrasound for patients with painful bone metastases: phase III trial results. J Natl Cancer Inst 2014; 106.

Cryoablation / Radiofrequency ablation

1. Dechamps F, Farouil G, Ternes N et al.: Thermal ablation techniques: a curative treatment of bone metastases in selected patients? Eur Radiol 24(8):1971-80, 2014
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Side-Effects and Toxicity: Bisphosphonates (BP) and Denosumab (Dmab)	
	LoE
▪ Renal function deterioration due to IV-aminobisphosphonates	1b
▪ Osteonecrosis of the jaw (ONJ) mostly under IV-BP and Dmab therapy (1.4 – 2.8% / 1.3 – 3.2%)	1b
▪ Association with (simultaneous) anti-angiogenetic therapies	3b
▪ Severe hypocalcemia (Dmab > BPs)	1b
▪ Acute Phase Reaction (IV Amino-BPs, Dmab) 10–30%	1b
▪ Gastrointestinal side effects (oral BPs) 2–10%	1b
▪ Atypical femur fractures (absolute risk of 11 per 10,000 person years of BP use)	2b
▪ Increased fracture risk after discontinuation of Dmab	3b
▪ Extremely rare: Uveitis / Scleritis under BP treatment	4



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Bisphosphonates


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9. Clark EM, Durup D: Inflammatory eye reactions with bisphosphonates and other osteoporosis medications: What are the risks? Ther Adv Musculoskelet Dis 7:11-16, 2015.

Denosumab

1. Stopeck AT et al. Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study, *J Clin Oncol* 28:5132-5139, 2010
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Sequential therapy

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		Oxford			
		LoE	GR	AGO	
 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	Metastatic bone disease: Radiotherapy (RT)				
	Indications for radiotherapy for bone metastases				
	▪	Instability (risk of fracture)	1a	B	++
	▪	Impairment of mobility	1a	B	++
	▪	Localized pain	1a	B	++
	▪	Neurologic symptoms	1a	B	++
	▪	After surgery	2b	B	++
	▪	Omission of radiotherapy in case of R0-resection without fracture or cortical arrosion	4	C	+
	▪	Oligometastases without above mentioned criteria	2b	B	+/-
		Reduction of radiation-induced pain flare-up by dexamethasone	1b	B	+
	Radiotherapy in combination with hyperthermia	2b	B	+/-	
Limited number of breast cancer-specific trials!					

1. Alcorn S, Cortes AA, Bradfield S et al.. External Beam Radiation Therapy for Palliation of Symptomatic Bone Metastases: An ASTRO Clinical Practice Guideline. Pract Radiat Oncol. 2024 Sep-Oct;14(5):377-397.
2. Guckenberger M, Andratschke N, Belka C et al.. ESTRO clinical practice guideline: Stereotactic body radiotherapy for spine metastases. Radiother Oncol. 2024 Jan:190:109966.
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4. Oldenburger E, Brown S, Willmann J et al. ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases. Radiother Oncol. 2022 Aug:173:240-253.
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8. Konsultationsfassung S3-Leitlinie Supportive Therapie bei onkologischen PatientInnen Version 2.01 – September 2024 AWMF-
Registernummer: 032-054OL

	<h2 style="color: green;">Radiotherapy for bone metastases: Technique and fractionation</h2>
<p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> ▪ Performance status, symptoms, overall prognosis/life expectancy, mechanical stability and infiltration of the epidural space/spinal cord compression should be considered. ▪ For patients with uncomplicated painful bone metastases, single fraction radiotherapy with 8 Gy has comparable overall pain response rates compared to fractionated radiotherapy (i.e. 5x4 or 10x3 Gy). ▪ However, 1x8 Gy is associated with higher rates of re-treatment and potentially increased rates of pathological fracture and metastatic spinal cord compression during the course of disease. Thus, 1x8 Gy may preferentially be used in patients with a limited life expectancy. ▪ Stereotactic body radiotherapy with higher doses (e.g. 2x12 Gy, 3x9-10 Gy, 5x7 Gy, 10x4.85 Gy) potentially delivers higher complete and more durable pain response rates and is associated with higher local control. Thus, it should be considered in patients with uncomplicated bone metastases and a favorable prognosis. Pre-treatment MRT is recommended to assess epidural disease and for spinal cord contouring.

1. Alcorn S, Cortes AA, Bradfield S et al.. External Beam Radiation Therapy for Palliation of Symptomatic Bone Metastases: An ASTRO Clinical Practice Guideline. Pract Radiat Oncol. 2024 Sep-Oct;14(5):377-397.
2. Guckenberger M, Andratschke N, Belka C et al.. ESTRO clinical practice guideline: Stereotactic body radiotherapy for spine metastases. Radiother Oncol. 2024 Jan;190:109966.
3. Van der Velden J, Willmann J, Spalek M et al. ESTRO ACROP guidelines for external beam radiotherapy of patients with uncomplicated bone metastases. Radiother Oncol. 2022 Aug;173:197-206.
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Prophylactic Radiation Therapy versus Standard of Care for Patients with High-Risk Asymptomatic Bone Metastases

A multicenter randomized controlled Phase II clinical trial

- **Cohort:** 78 adult patients (24% breast) with high-risk bone metastases (n = 122), stratified by histology and planned SOC (systemic therapy or observation), randomly assigned in a 1:1 ratio to receive RT to asymptomatic bone metastases or SOC alone.
- **Definition of High risk:** Bone met. ≥2 cm; Involvement of hip/shoulder/sacroiliac joint or long bones (1/3-2/3 of the cortical thickness), involvement of junctional spine (C7-T1/T12-L1/L5-S1) and/or posterior involvement
- **Results:** 1 year: RT vs. SOC: SRE in one of 62 bone metastases (1.6%) vs. 14 of 49 bone metastases (29%) ($P < .001$) with significantly fewer patients hospitalized for SRE in the RT arm compared with the SOC arm (0 v 4, $P = .045$); median follow-up of 2.5 years: OS was significantly longer in the RT arm (hazard ratio [HR], 0.49; 95% CI, 0.27 to 0.89; $P = .018$)

1. Gillespie EF, Yang JC, Mathis NJ, et al. Prophylactic Radiation Therapy Versus Standard of Care for Patients With High-Risk Asymptomatic Bone Metastases: A Multicenter, Randomized Phase II Clinical Trial. *J Clin Oncol.* 2024;42(1):38-46. doi:10.1200/JCO.23.00753

 Common Side Effects during Treatment with Bisphosphonates / Denosumab						
Drug	Acute phase-reaction	Kidney Tox.	Upper GI-tract	Diarrhea	ONJ	
Clodronate 1500 IV	0	+	0	0	0	Non-Amino.
Clodronate 1600 PO	0	0	+	+	0	Non-Amino.
Ibandronate 50 mg PO	0	0	+	0	0	Aminobisph.
Ibandronate 6 mg IV	+	0	0	0	+	Aminobisph.
Zoledronate 4 mg IV (q4w or q12w)	+	+	0	0	+	Aminobisph.
Pamidronate 90 mg IV	+	+	0	0	+	Aminobisph.
Zoledronate 4 mg IV q6m	+	0	0	0	0	Aminobisph.
Denosumab 120 mg SC q4w	+	0	0	+	+	

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Cave: Hypocalcemia under antiresorptive therapy in pts with bone metastases!

Bisphosphonates

- Schilcher, J., V. Koeppen, P. Aspenberg et al. Risk of atypical femoral fracture during and after bisphosphonate use. Acta Orthop 100-107, 2015
- Body JJ. Breast Cancer: Bisphosphonate therapy for metastatic bone disease. Clin Cancer Res. 2006; 12(20 Suppl):6258s-6263s.
- Coleman RE. Risks and benefits of bisphosphonates. Br J Cancer 98(11):1736-40., 2008
- Dunstan CR, Felsenberg D, Seibel MJ. Therapy insight: the risks and benefits of bisphosphonates for the treatment of tumor-induced bone disease. Nat Clin Pract Oncol 4(1):42-55, 2007
- Tralongo, P, Repetto, L, Di Mari, A, et al. Safety of long-term administration of bisphosphonates in elderly cancer patients. Oncology 67:11216, 2004
- Chang, JT, Green, L, Beitz, J. Renal failure with the use of zoledronic acid. N Engl J Med 349(17):1676-9, 2003
- Hillner BE, Ingle JN, Chlebowski RT et al. American Society of Clinical Oncology: American Society of Clinical Oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer. J Clin Oncol 21(21):4042-57, 2003
- Aapro M, Abrahamsson PA, Body JJ et al. Guidance on the use of bisphosphonates in solid tumours: recommendations of an international expert panel. Ann Oncol 19(3):420-32, 2008
- Clark EM, Durup D: Inflammatory eye reactions with bisphosphonates and other osteoporosis medications: What are the risks? Ther Adv Musculoskelet Dis 7:11-16, 2015

Denosumab

1. Stopeck AT et al. Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study, J Clin Oncol 28:5132-5139, 2010
2. Taylor KH, Middlefell LS, and Mizen KD, "Osteonecrosis of the Jaws Induced by Anti-RANK Ligand Therapy," Br J Oral Maxillofac Surg 48(3):221-3, 2010



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Recommendations for Prevention of Osteonecrosis of the Jaw (ONJ)

Oxford LoE: 2a GR: A AGO: ++

- **During bisphosphonate or denosumab treatment, avoid any elective dental procedures involving jaw bone manipulations during treatment with bisphosphonates or denosumab**
- **Optimize dental status before start of bisphosphonate or denosumab treatment**
- **Inform patients about ONJ risk and educate about early symptom reporting**
- **In case of high risk for ONJ, use oral bisphosphonate**
- **Recommend good oral hygiene, limiting alcohol intake and quit smoking**
- **Under adjuvant bisphosphonate therapy, ONJ is rare (< 1%)**

AGSMO patientenbezogener Laufzettel
<https://www.onkosupport.de/asors/content/e4125/e4405>

1. Izzotti A, Menini M, Pulliero A et al. Bisphosphonates-associated osteonecrosis of the jaw: the role of gene-environment interaction. J Prev Med Hyg 54(3): 138-145, 2013
2. Fehm T, Felsenberg D, Krimmel M et al. Bisphosphonate-associated osteonecrosis of the jaw in breast cancer patients: recommendations for prevention and treatment. Breast 18(4):213-7, 2009
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7. Yarom N, Shapiro CL, Peterson DE et al Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline.

J Clin Oncol. 2019; 37(25):2270-2290. doi: 10.1200/JCO.19.01186.

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9. <https://www.onkosupport.de/asors/content/e4125/e4405>

		Oxford		
		LoE	GR	AGO
■ Aminobisphosphonate (IV or oral)				
■ Postmenopausal patients or premenopausal patients under ovarian suppression*		1a	A	+
■ Clodronate (oral)				
■ Postmenopausal patients*		1a	A	+
■ Premenopausal patients		1a	B	+/-
■ Denosumab (6 x 120 mg/3–4w + 14 x 120 mg/3m)				
■ Stage II and III postmenopausal patients		1b	B	-
■ Denosumab (60 mg SC q6m)				
■ Postmenopausal patients undergoing AI therapy		1b	B	+/-

* independent of the intrinsic subtype



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Clodronate

1. Ben-Aharon I, Vidal L, Rizel S et al. Bisphosphonates in the adjuvant setting of breast cancer therapy--effect on survival: a systematic review and meta-analysis. PLoS One. 2013 Aug 26;8(8):e70044. doi: 10.1371/journal.pone.0070044. eCollection 2013. Review.
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Adjuvant Aminobisphosphonates

1. Ben-Aharon I, Vidal L, Rizel S et al. Bisphosphonates in the adjuvant setting of breast cancer therapy--effect on survival: a systematic review and meta-analysis. PLoS One. 2013 Aug 26;8(8):e70044. doi: 10.1371/journal.pone.0070044. eCollection 2013. Review.
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Denosumab


1. Gnant M, Pfeiler G, Steger GG, Austrian Breast and Colorectal Cancer Study Group. Adjuvant denosumab in postmenopausal patients with hormone receptor-positive breast cancer (ABCSG-18): disease-free survival results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2019 Mar;20(3):339-351.
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3. Coleman R, Finkelstein DM, Barrios C et al. Adjuvant denosumab in early breast cancer (D-CARE): an international, multicentre, randomised, controlled, phase 3 trial. *Lancet Oncol.* 2020 21(1):60-72.

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1. Dhesy-Thind S, Fletcher GG, Blanchette PS et al. Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: A Cancer Care Ontario and American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 35(18):2062-2081, 2017
2. Eisen A, Somerfield MR, Accordino MK, et al. Use of adjuvant bisphosphonates and other bone-modifying agents in breast cancer: ASCO-OH (CCO) guideline update. *J Clin Oncol* 2022; 40: 787-800.



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Dosage of Adjuvant Bisphosphonates for Improvement of Survival*

- **Non-Aminobisphosphonates:**
 - Clodronate PO 1600 mg/d (Bonefos / Clodronic acid)
 - Clodronate PO 1040 mg/d (Ostac / Clodronic acid)

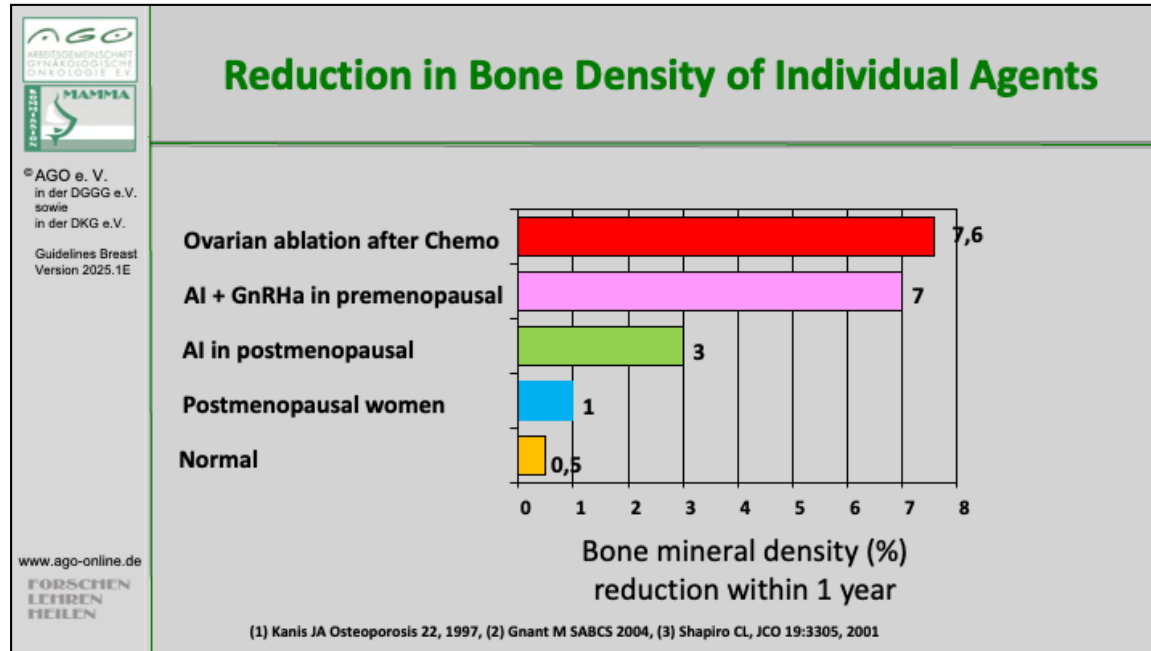
- **Aminobisphosphonates:**
 - Zoledronate IV 4 mg/6 m (Zometa / Zoledronic acid)
 - Ibandronate PO 50 mg/d (Bondronat / Ibandronic acid)
 - Pamidronate PO (orally not available in most countries)
 - Risedronate PO 35 mg/w* (Actonel / Risedronic acid)
 - Alendronate PO 70 mg/w (Fosamax / Alendronic acid)
 - Optimal duration yet to be defined; in adjuvant studies duration of BP treatment varied from 2–5 years

*Utilisation of the NHS Predict Tool to estimate the effect of bisphosphonate use on overall survival,
<https://breast.predict.nhs.uk/tool>

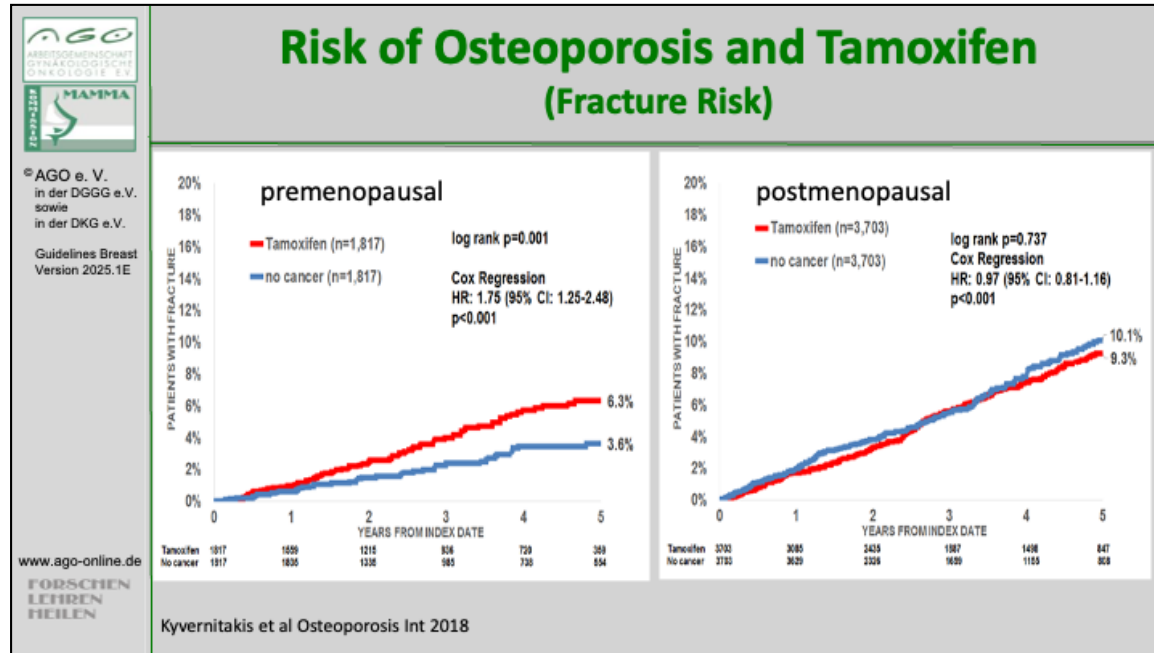
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SUCCESS A trial (Friedl et al., JAMA Oncol 2021; 7: 1149-1157)		
	2 y ZOL (n = 1.447) (4 mg IV every 3 mo for 2 y)	5 y ZOL (n = 1.540) (4 mg IV every 3 mo for 2 y + 4 mg IV every 6 mo for 3 y)
Survival	No differences for DFS, OS, DDFS	
Bone recurrences	n = 28	n = 25
Adverse Events		
Grade III/IV	n = 98 (5.1% of patients)	n = 159 (7.6% of patients)
SRE bone pain	3.7%	8.3%
Arthralgia	3.1%	5.1%
Fractures	n = 3	n = 14
ONJ	n = 5	n = 11


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		Oxford		
		LoE	GR	AGO
 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> ▪ Bisphosphonates <ul style="list-style-type: none"> ▪ Therapy ▪ Prevention (2–5 yrs) ▪ after discontinuation of Denosumab (1-2 years) ▪ Denosumab <ul style="list-style-type: none"> ▪ Therapy ▪ Prevention (up to max. 3 yrs) ▪ Hormone replacement therapy ▪ Vitamin K2 substitution ▪ Clinical risk assessment for osteoporosis at baseline according to DVO S3 – guidelines (as of 09/2023) ▪ Routine determination of 25-hydroxyvitamin D levels ▪ DXA-scan at baseline in pts with endocrine therapy and / or premature menopause ▪ Antiresorptive therapy according to DVO S3 – guidelines (as of 09/2023) ▪ Repeat DXA-scan based on risk 			
		1b	B	++
		1b	A	+
		3c	C	+
		1b	B	++
		1b	A	+/-
		5	D	-
		2b	B	-
				++
		3d	B	+/-
		5	D	+
				++
		5	D	+


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Vitamin K

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Therapy and Prevention of Tumor Therapy- Induced Bone Loss / Osteoporosis

Further recommendations (based on DVO-guidelines as of 09/2023)*

	Oxford		
	LoE	GR	AGO
▪ Physical activity	4	C	++
▪ Avoiding immobilisation	4	C	++
▪ Calcium (1000–1500 mg/d)**	4	C	++
▪ Vitamine D3 suppl. (800 U/d)	4	C	++
▪ Quit smoking, reduction of alcohol	2b	B	++
▪ Avoid BMI < 20 kg/m ²	3b	C	++
▪ Bisphosphonates after discontinuation of Denosumab (1-2 years)	3c	C	+
▪ Drugs approved for osteoporosis treatment in adults (see next slide)			

* <https://dv-osteologie.org/osteoporose-leitlinien>
** if nutritional supply is insufficient (in combination with Vit D3 only)

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Effect of Denosumab Discontinuation

FREEDOM / FREEDOM Extension Trial

n = 1001, ≥ 2 dose of Denosumab or placebo, follow up ≤ 7 months after discontinuation treatment

Vertebral fracture rate per 100 participant year:

- 1.2 during denosumab therapy
- 7.1 after denosumab therapy
- 8.5 placebo

Non vertebral fracture rate per 100 participant year:

- 2.8 after denosumab vs. 3.8 placebo (n.s.)

Multiple vertebral fracture (% of all vertebral fractures):

60.7% after denosumab therapy vs. 38.7% placebo; p = 0.049

Cummings SR et al. J Bone Miner Res 2017

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	Oxford		
	LoE	GR	AGO
▪ Alendronate 70 mg PO/w*	1b	B	++
▪ Zoledronate 5 mg IV/12m*	1b	B	++
▪ Ibandronate 150 mg PO/m*	1b	B	++
▪ Ibandronate 3 mg IV/3 m	1b	B	++
▪ Risedronate 35 mg PO/w*	1b	B	++
▪ Denosumab 60 mg SC/6m*	1b	B	++
▪ Raloxifene 60 mg PO/d (improves spine only)	1b	B	+/-
▪ Parathyroid hormone 100 µg SC/d	1b	B	+
▪ Strontium ranelate 2 g PO/d**	1b	B	+
▪ Teriparatide 20 µg SC/d	1b	B	+
▪ Romosozumab 210mg s.c./m for 12m***	1b	B	+

* Drugs tested in clinical studies with breast cancer patients and tumor therapy-induced osteoporosis
 ** Elevated risk of myocardial infarction (MI); only for to postmenopausal pts. with severe osteoporosis + high fracture risk
 *** Elevated risk of MI and CVI; only for postmenopausal. pts with severe osteoporosis + high fracture risk

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Indication for Osteoporosis Drug Therapy (as of 09/2023)

DVO Guideline Osteoporosis 2023

Short version including:

- Risk factor table for therapy threshold determination
- Tables for determining therapy thresholds (women, men)

<https://dv-osteologie.org/osteoporose-leitlinien>

1. <https://dv-osteologie.org/osteoporose-leitlinien>