Guidelines Breast
Version 2018.1D

Osteoonkologie und Knochengesundheit

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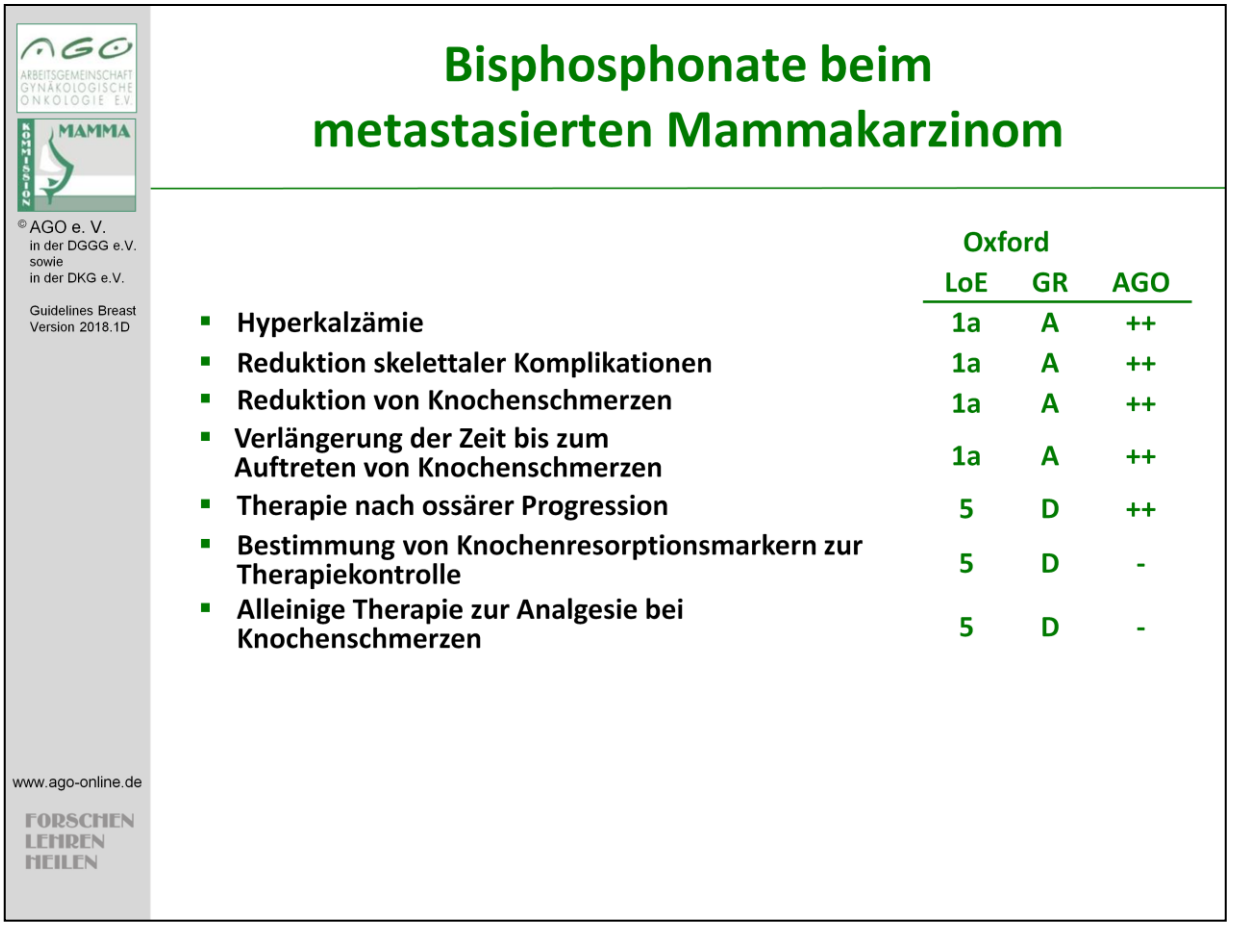
- **Versionen 2002–2017:**
  Bischoff / Böhme / Brunnert / Dall / Diel / Fehm / Fersis / Friedrich/ Friedrichs / Hanf / Huober / Jackisch / Janni / Liedtke / Lux / Maas / Nitz / Oberhoff / Schaller / Scharl / Schütz / Seegenschmiedt / Solomayer / Souchon
- **Version 2018:**
  Fehm / Solomayer



Metaanalysen and Reviews (metastatic breast cancer)

1. Coleman R, Body JJ, Aapro M, et al. ESMO Guidelines Working Group Bone health in cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol 2014,25 Suppl 3:iii124-37.
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

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

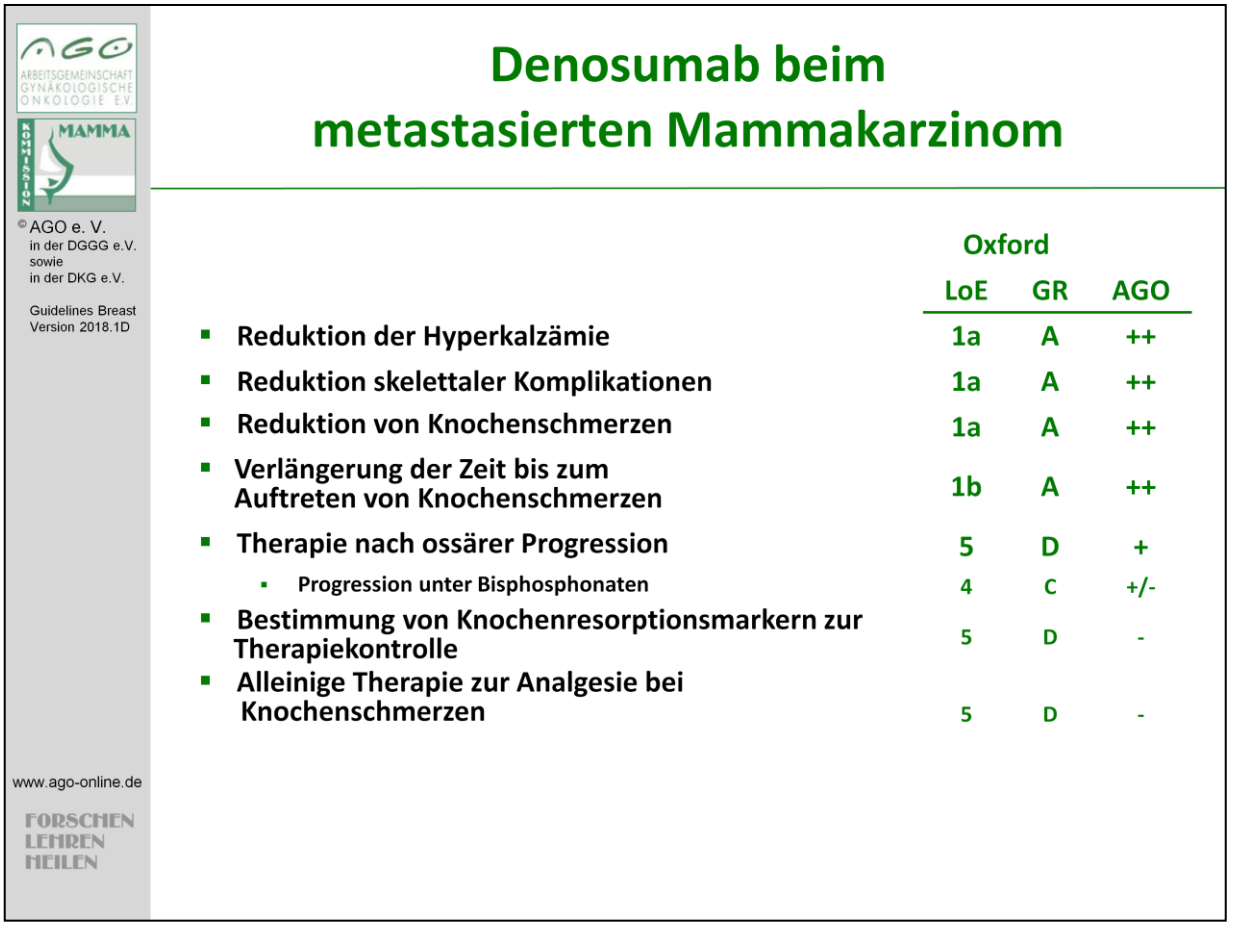
4. Tripathy D, Lichinitser M, Lazarev A et al. Oral ibandronate for the treatment of metastatic bone disease in breast cancer: efficacy and safety results from a randomized, double-blind, placebo-controlled trial. Ann Oncol 15:743-750, 2004
5. Rosen LS, Gordon D, Kaminski M et al. . Long-term efficacy and safety of zoledronic acid compared with pamidonate 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 - Therapy of bone metastases and skeletal related complications

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

1. 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
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 Oncol *25:*4431–4437*,* 2007
3. 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.

Statement: 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

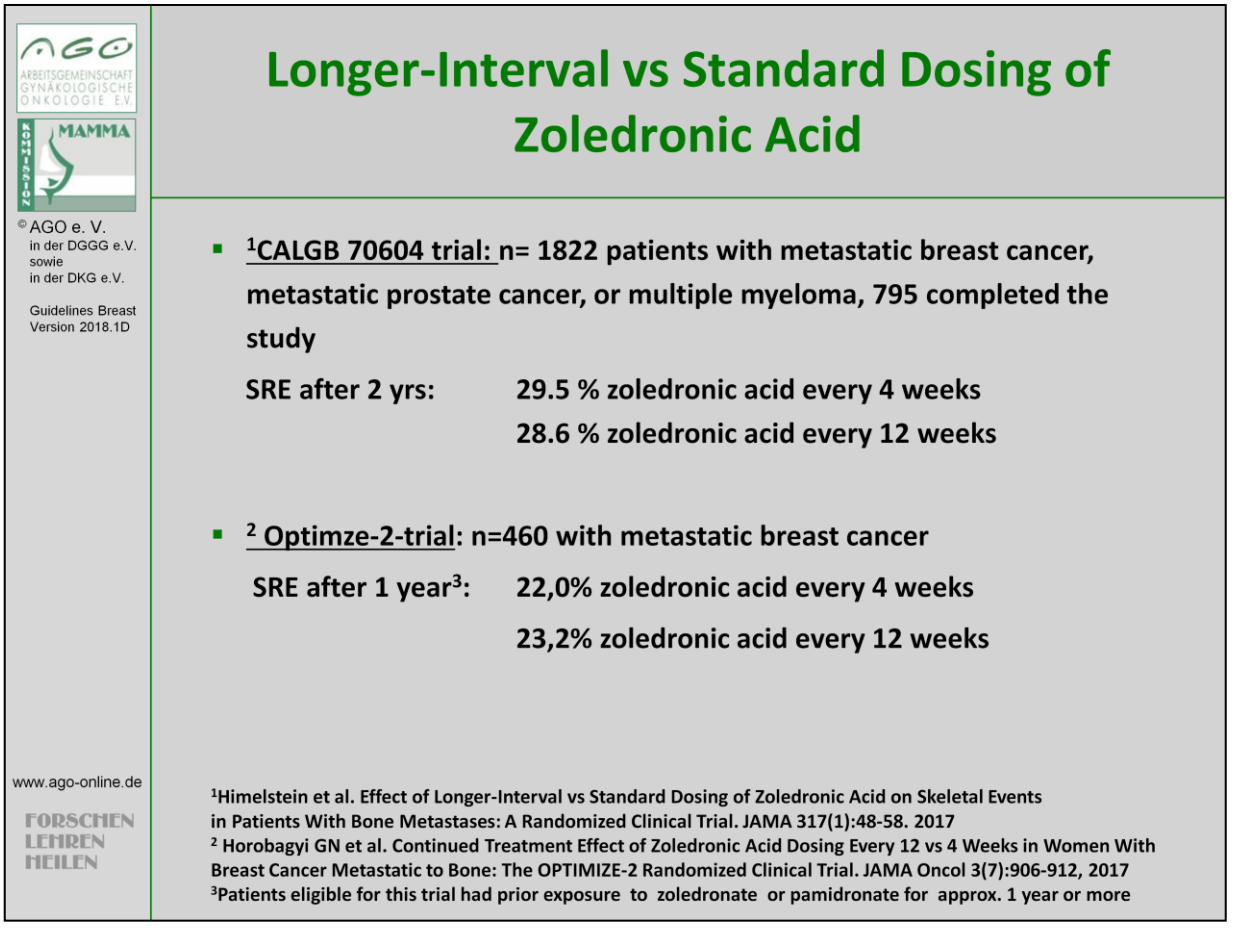
Clinical relevance of bone resorption marker

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



1. Himelstein 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

Bisphosphonate und Denosumab für die Therapie von Knochenmetastasen

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	Oxford		
	LoE	GR	AGO
▪ Clodronat p.o. 1600 mg täglich	1a	A	++
▪ Clodronat i.v. 1500 mg q3w / q4w	1a	A	++
▪ Pamidronat i.v. 90 mg q3w / q4w	1a	A	++
▪ Ibandronat i.v. 6 mg q3w / q4w	1a	A	++
▪ Ibandronat p.o. 50 mg täglich	1a	A	++
▪ Zoledronat i.v. 4 mg			
▪ q4w	1a	A	+
▪ q12w	1a	A	++
▪ Denosumab 120 mg s.c. q4w	1a	A	++
▪ Denosumab 120 mg s.c. q12w	4	C	-
▪ Andere Dosierungen oder Schemata, wie z.B. aus den Studien zur adjuvanten Situation oder Osteoporosetherapie	5	D	--

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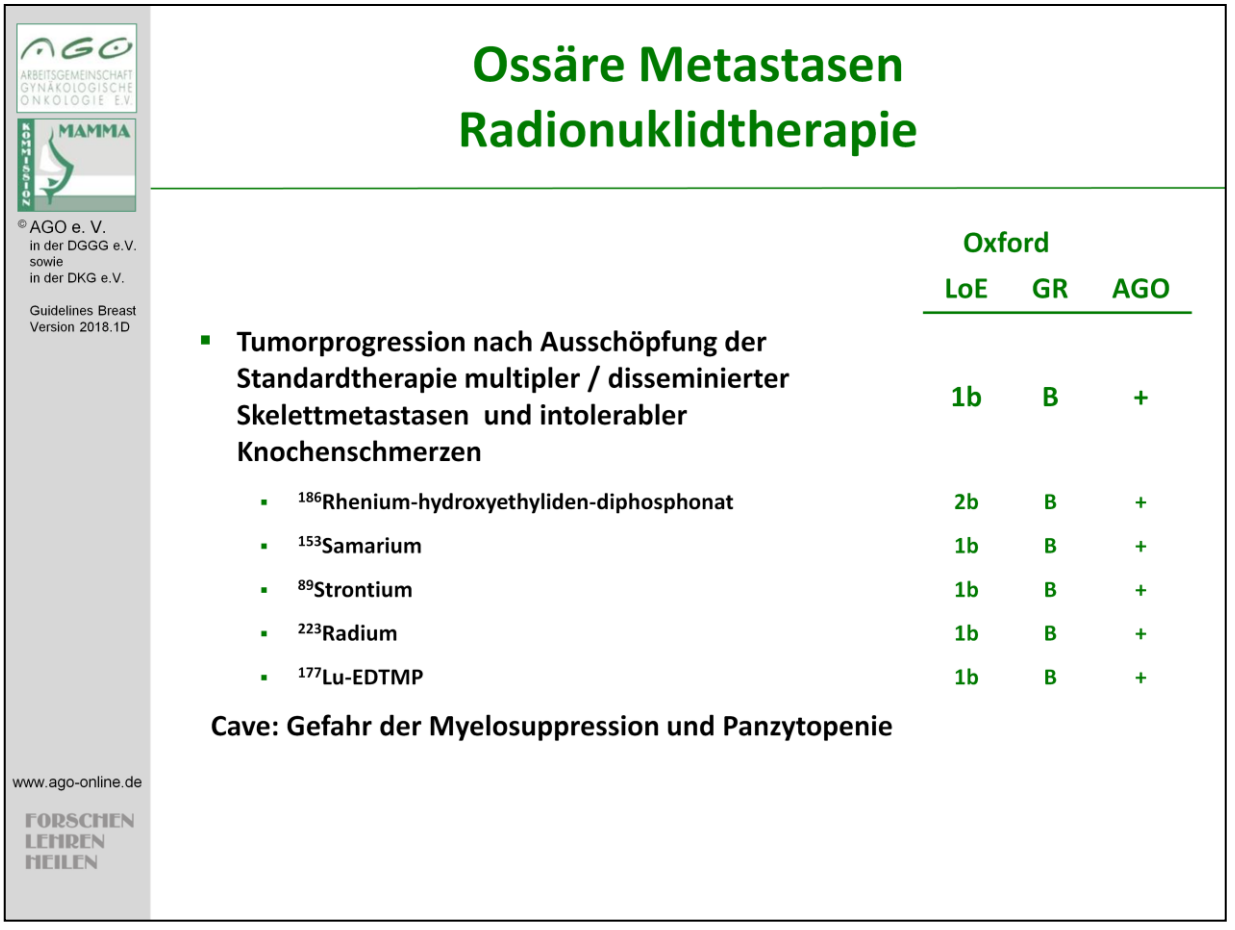
FORSCHEN
LEHREN
HEILEN

1. Templeton AJ 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)
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. 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
5. 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
6. Himelstein 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
7. 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



Reviews / Overview

1. Hoskin PJ: Radioisotopes for metastatic bone pain. Lancet Oncol 6(6):353-4, 2005
2. Bauman G, Chrrette M, Reid R, Sathya J. Radiopharmaceuticals for the palliation of painful bone metastasis-a systemic review. Radioth Oncol 75: 258-70, 2005
3. Roque M, Martinez MJ, Alonso-Coello P et al. Radioisotopes for metastatic bone pain (Cochrane Review). In: The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd. (Cochrane Database Syst Rev 2003:CD003347), 2004

^{186}Rhenium (^{186}Re-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

^{153}Samarium (^{153}Sm-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

^{89}Strontium (^{89}Sr-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 89-Sr and 186-Re-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

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 153Sm-EDTMP and 177Lu-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.

Knochenmetastasen in der Wirbelsäule

Operationsindikatoren

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

- **Spinales Kompressionssyndrom**
  - **Mit progredienter neurologischer Symptomatik**
  - **Mit pathologischen Frakturen**
- **Instabilität der Wirbelkörper**
- **Läsionen in vorbestrahlten Teilen der Wirbelsäule**

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. Loblaw DA, Laperriere NJ. Emergency treatment of malignant extradural spinal cord compression: an evidence-based guideline. J Clin Oncol 16:1613-24, 1998
5. Walker MP, Yaszemski MJ, Kim CW et al. Metastatic disease of the spine: evaluation and treatment. Clin Orthop 2003;415 Suppl:S165-75
6. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, http://leitlinienprogrammonkologie.de/Supportive-Therapie.95.0.html (Zugriff am 13.01.2018)

Knochenmetastasen – Spinales Kompressionssyndrom / Paraplegie

	Oxford		
	LoE	GR	AGO
▪ Operation zur Dekompression, Reduktion der Tumormasse und Stabilisierung (< 24 h) sowie Bestrahlung der Wirbelsäule (RT)	2b	C	++
▪ Bestrahlung der WS (< 24 h) +/- Steroide	3b	C	++
▪ Sofortiger Therapiebeginn	1c	D	++

Patienten in Studien mit unterschiedlichen Tumorentitäten!

1. 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
2. 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
3. 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
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, Veninga T, Stalpers LJ, et al. Outcome after radiotherapy alone for metastatic spinal cord compression in patients with oligometastases. J Clin Oncol 25:50-6 , 2007
6. Regine WF, Tibbs PA, Young A, et al. Metastatic spinal cord compression: a randomized trial of direct decompressive surgical resection plus radiotherapy vs. radiotherapy alone. Int J Radiat Oncol Biol Phys 2003:57(Suppl.):S125. abstract #3
7. Loblaw DA, Laperriere NJ. Emergency treatment of malignant extradural spinal cord compression: an evidence-based guideline. J Clin Oncol 16:1613-24, 1998
8. Regine WF, Tibbs PA, Young A et al. Metastatic spinal cord compression: a randomized

trial of direct decompressive surgical resection plus radiotherapy vs. radiotherapy alone. Int J Radiat Oncol Biol Phys 2003:57(Suppl.):S125. abstract #3

9. Galasko CS, Norris HE, Crank S. Spinal instability secondary to metastatic cancer. J Bone Joint Surg Am 82: 570–594, 2000
10. Walker MP, Yaszemski MJ, Kim CW et al. Metastatic disease of the spine: evaluation and treatment. Clin Orthop 2003;415 Suppl: S 165–175
11. Helweg-Larsen S, Sorensen PS, Kreiner S. Prognostic factors in metastatic spinal cord compression: a prospective study using multivariate analysis of variables influencing survival and gait function in 153 patients. Int J Radiat Oncol Biol Phys 46: 1163–1169, 2000
12. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, http://leitlinienprogrammonkologie.de/Supportive-Therapie.95.0.html (Zugriff am 13.01.2018)

Knochenmetastasen: Operationstechniken

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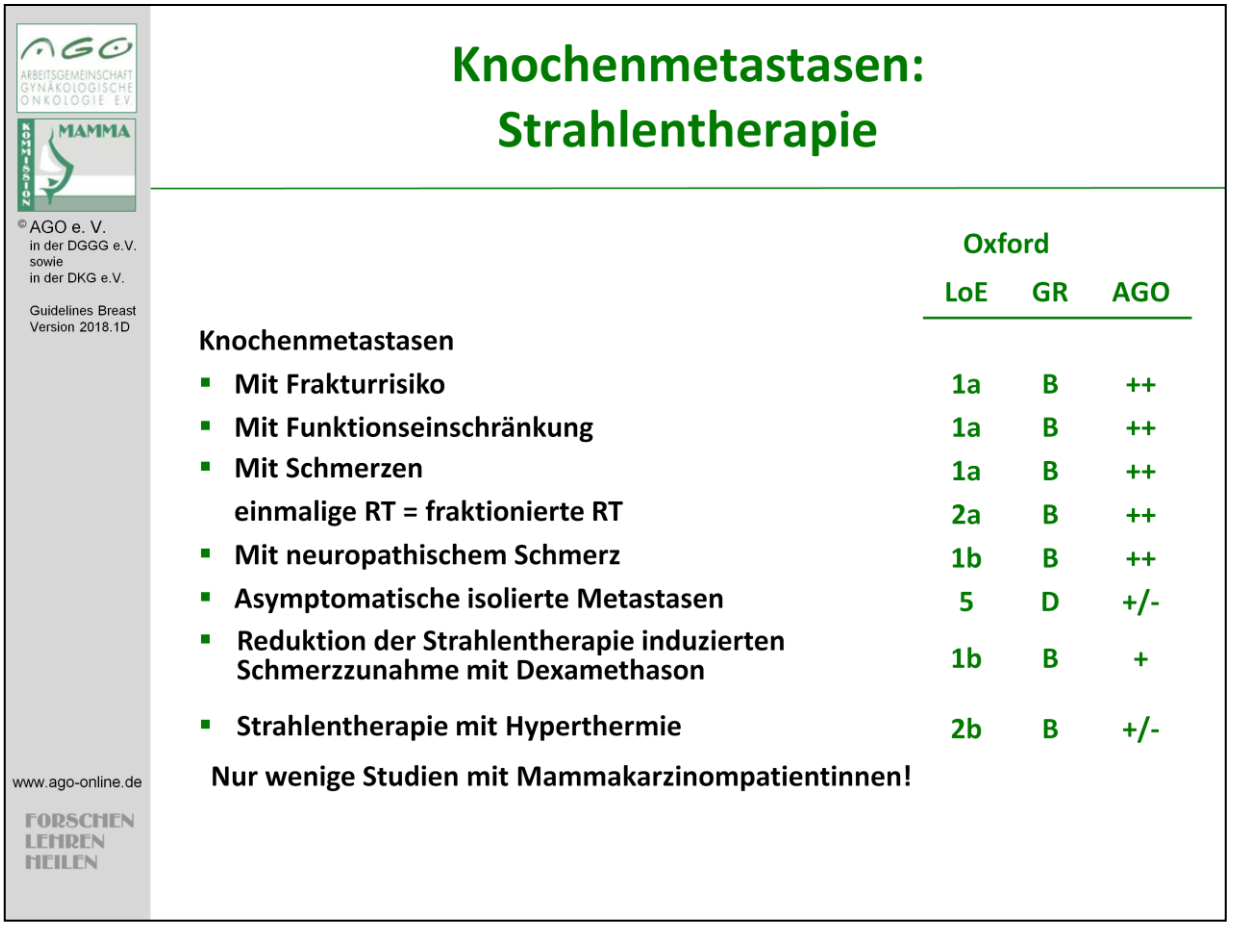
Wirbelsäule und Extremitäten

Oxford LoE: 3b **GR: C** **AGO: +**

- **Marknagelung**
- **Plattenosteosynthesen**
- **Verbundosteosynthesen (Osteosynthese und Einbringen von PMMA)**
- **Wirbelkörperersatz durch Titanspacer**
- **Tumorendoprothesen**
- **Vertebroplastie / Kyphoplastie +/- Thermoablation des Tumors**
- **Kypho-IORT* (nur in Studien)**
- **Resektion einzelner Knochenmetastasen in der oligometastatischen Situation (Sternum, Rippen, Wirbelkörper)**

*Studienteilnahme empfohlen

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
2. 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
3. Ali SM, Harvey HA, Lipton A: Metastatic breast cancer: overview of treatment. Clin Orthop Rel Res 2003;1 (415S) (Suppl): 132–137
4. Fourney DR, Gokaslan ZL: Thoracolumbar spine: surgical treatment of metastatic disease. Curr Opin Orthop 14 (3): 144–152, 2013
5. Fourney DR, Schomer DF, Nader R et al: Percutaneous and kyphoplasty for painful vertebral body fractures in cancer patients. J Neurosurg 98 (Suppl): 21–30, 2003
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
7. Berenson J1, Pflugmacher R, Jarzem P et al. Cancer Patient Fracture Evaluation (CAFE) Investigators. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. Lancet Oncol 12(3):225-35, 2011
8. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, http://leitlinienprogrammonkologie.de/Supportive-Therapie.95.0.html (Zugriff am 13.01.2018)



1. 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
2. Souchon R, Wenz F, Sedlmayer F, Budach W 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
3. Hartsell WF, Scott C, Bruner DW et al. Phase III randomised trial of 8 Gy in 1 fraction vs. 30 Gy in 10 fractions for palliation of painful bone metastases: preliminary results of RTOG 97-14. Int J Radiat Oncol Biol Phys 2003:57(Suppl.):S124. abstract #1
4. McDonald R, Ding K, Brundage M et al. Effect of Radiotherapy on Painful Bone Metastases: A Secondary Analysis of the NCIC Clinical Trials Group Symptom Control Trial SC.23. JAMA Oncol 3(7):953-959, 2017
5. Lutz S, Berk L, Chang E et al. American Society for Radiation Oncology (ASTRO) Palliative radiotherapy for bone metastases: an ASTRO evidence-based guideline. Int J Radiat Oncol Biol Phys 79(4):965-976, 2011
6. Hoskin PJ, Yarnold JR, Roos DR et al . Second Workshop on Palliative Radiotherapy and Symptom Control: Radiotherapy for bone metastases. Clin Oncol (R Coll Radiol) 13:88-90, 2001
7. McQuay HJ, Collins SL, Carroll D, Moore RA. Radiotherapy for the palliation of painful bone metastases. Cochrane Database Syst Rev 2000;2:CD001793

8. Wu J, Bezjak A, Chow E et al. A consensus development approach to define national research priorities in bone metastases: proceedings from NCIC CTG workshop. Clin Oncol (R Coll Radiol) 15: 496–499, 2003
9. Chow E, Harris K,Fan G, Tsao M, Sze WM. Palliative radiotherapy trials for bone metastases: a systematic review. J Clin Oncol 25:1423-36, 2007
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11. Chi MS, Yang KL, Chang YC et al. Comparing the Effectiveness of Combined External Beam Radiation and Hyperthermia Versus External Beam Radiation Alone in Treating Patients With Painful Bony Metastases: A Phase 3 Prospective, Randomized, Controlled Trial. Int J Radiat Oncol Biol Phys 100(1):78-87, 2018
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Knochenmetastasen: Schmerztherapie nach Vorbestrahlung

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	Oxford		
	LoE	GR	AGO
Rekurrenter Knochenschmerz in vorbestrahlten Arealen des Skeletts			
▪ Einmalige RT *	3b	C	++
▪ Fraktionierte RT *	3b	C	+
▪ Radionuklidtherapie	3b	C	+
▪ MR-gesteuerter hochfokussierter Ultraschall	1b	B	+
▪ Radiofrequenzablation	4	C	+
▪ Kryoablation	4	C	+

* Dosis und Fraktionierung hängt von der Lokalisation, vom Intervall zur letzten Strahlentherapie sowie von Dosis und Fraktionierung der ersten Strahlentherapie ab.

Recurrent bone pain in pre-irradiated parts of the skeleton

1. 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
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. Galasko CS, Norris HE, Crank S. Spinal instability secondary to metastatic cancer. J Bone Joint Surg Am 82:570-594, 2000
4. Haddad P, Wong R, Wilson P et al. Factors influencing the use of single versus multiple fractions of palliative radiotherapy for bone metastases: a 5-year review and comparison to a survey. Int J Radiat Oncol Biol Phys 2003:57(Suppl.):S278. abstract #1029
5. Van der Linden Y, Lok J, Steenland E et al. Re-irradiation of painful bone metastases: a further analysis of the Dutch Bone Metastasis Study. Int J Radiat Oncol Biol Phys 2003:57(Suppl.):S222. abstract #163
6. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL,

http://leitlinienprogrammonkologie.de/Supportive-Therapie.95.0.html (Zugriff am 18.01.2018)

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, Gaudin A, Hakime A, Tselikas L, Teriitehau C, Baudin E, Auperin A, de Baere T. Thermal ablation techniques: a curative treatment of bone metastases in selected patients? Eur Radiol 24(8):1971-80, 2014
2. Hegg RM, Kurup AN, Schmit GD, Weisbrod AJ, Atwell TD, Olivier KR, Moynihan TJ, Callstrom MR. Cryoablation of sternal metastases for pain palliation and local tumor control. J Vasc Interv Radiol 25(11):1665-70, 2014

Bisphosphonates

1. Schilcher, J., V. Koeppen, P. Aspenberg et al. Risk of atypical femoral fracture during and after bisphosphonate use. Acta Orthop 100-107, 2015
2. Body JJ. Breast Cancer: Bisphosphonate therapy for metastatic bone disease. Clin Cancer Res. 2006; 12(20 Suppl):6258s-6263s.
3. Coleman RE. Risks and benefits of bisphosphonates. Br J Cancer 98(11):1736-40., 2008
4. 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
5. Tralongo, P, Repetto, L, Di Mari, A, et al. Safety of long-term administration of bisphosphonates in elderly cancer patients. Oncology 67:11216, 2004
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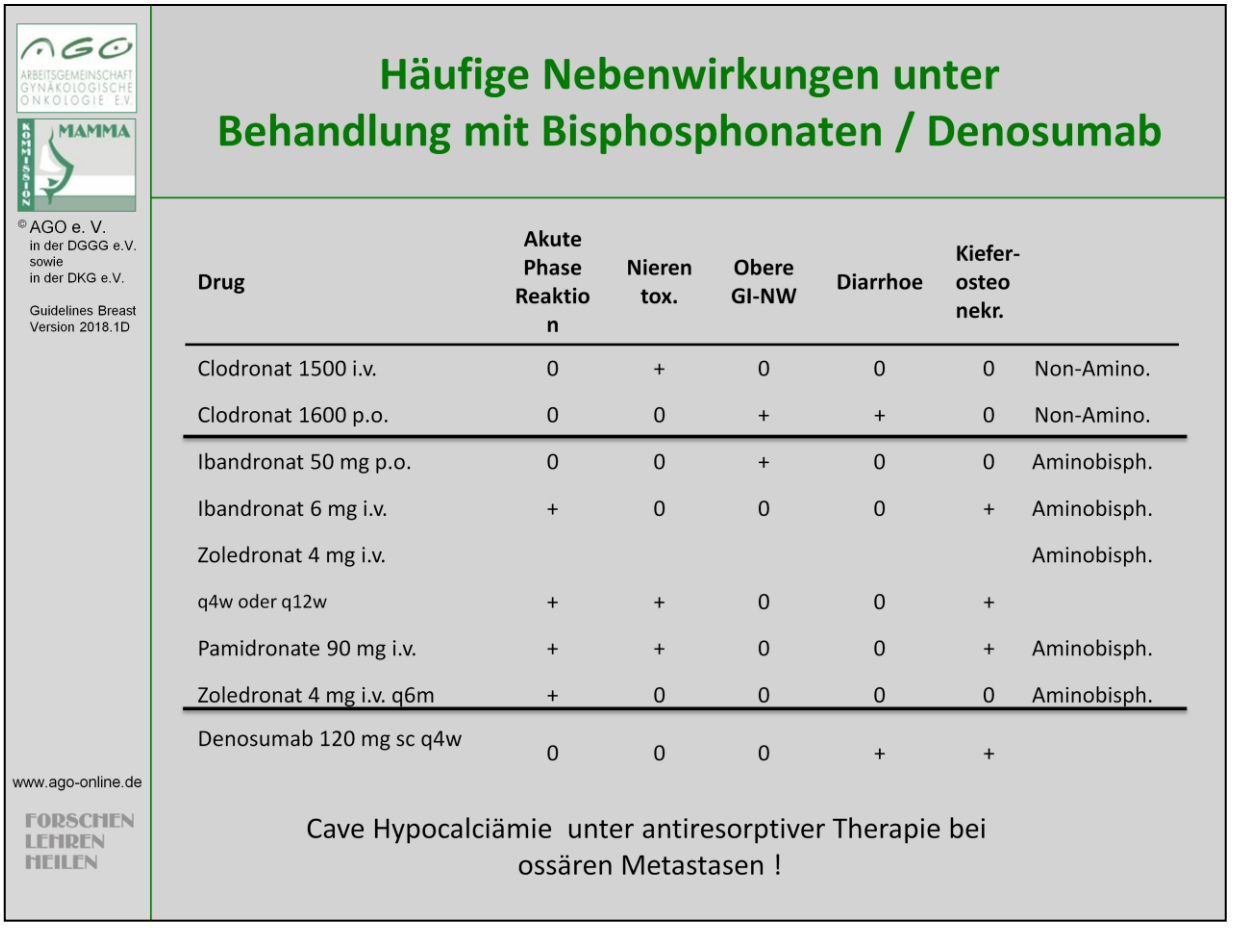

Häufige Nebenwirkungen unter Behandlung mit Bisphosphonaten / Denosumab

Drug	Akute Phase Reaktion	Nieren tox.	Obere GI-NW	Diarrhoe	Kiefer-osteo nekr.	
Clodronat 1500 i.v.	0	+	0	0	0	Non-Amino.
Clodronat 1600 p.o.	0	0	+	+	0	Non-Amino.
Ibandronat 50 mg p.o.	0	0	+	0	0	Aminobisph.
Ibandronat 6 mg i.v.	+	0	0	0	+	Aminobisph.
Zoledronat 4 mg i.v.						Aminobisph.
q4w oder q12w	+	+	0	0	+	
Pamidronate 90 mg i.v.	+	+	0	0	+	Aminobisph.
Zoledronat 4 mg i.v. q6m	+	0	0	0	0	Aminobisph.
Denosumab 120 mg sc q4w	0	0	0	+	+	

Cave Hypocalciämie unter antiresorptiver Therapie bei ossären Metastasen !

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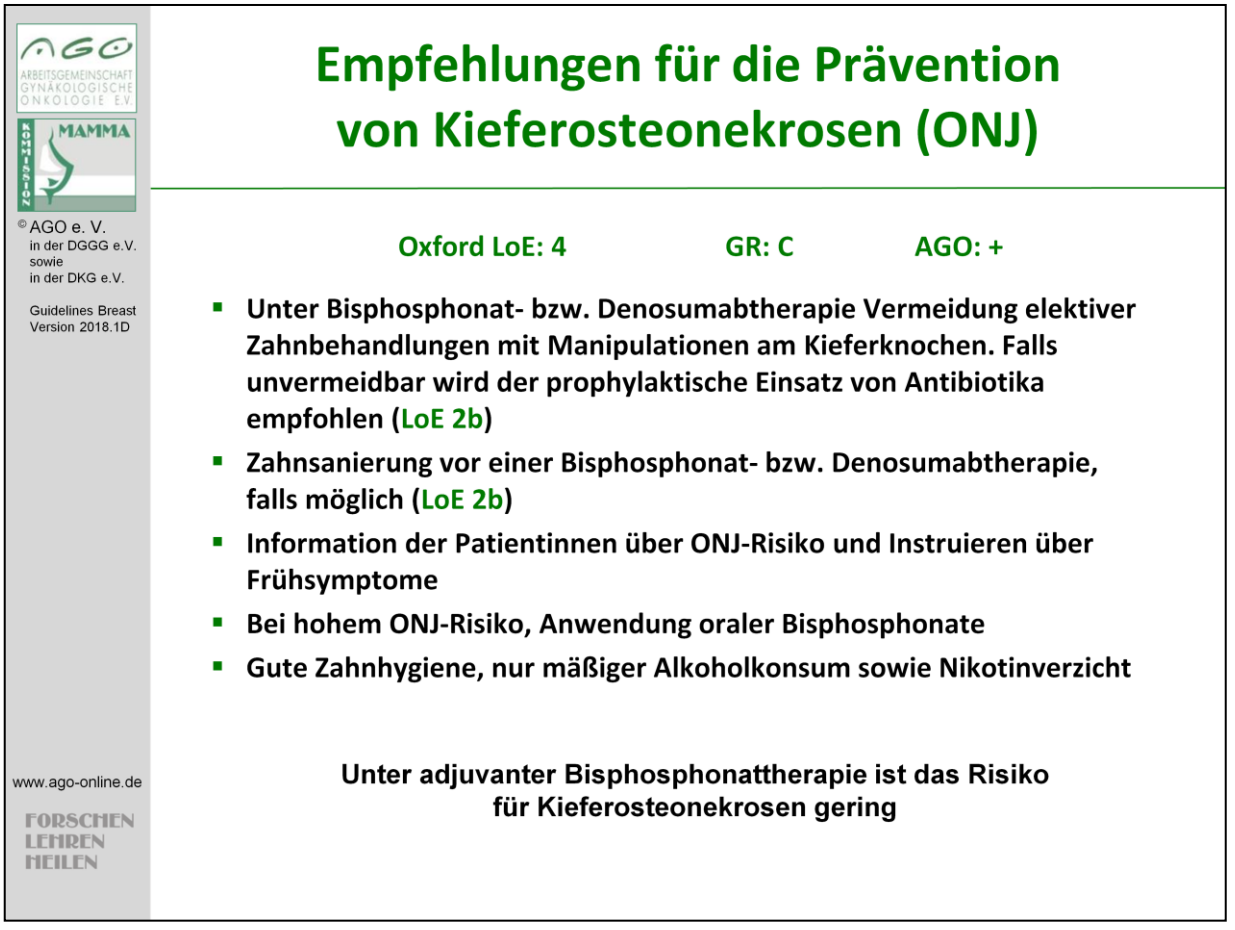

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Adjuvante osteoprotektive Therapie zur Verbesserung des Überlebens

Guidelines Breast
Version 2018.1D

	Oxford		
	LoE	GR	AGO
▪ **Clodronate (oral)**			
▪ Postmenopausale Patientinnen	1a	A	+
▪ Prämenopausale Patientinnen	1a	B	+/-
▪ **Aminobisphosphonate (iv oder oral)**			
▪ Postmenopausale Patientinnen	1a	A	+
▪ Prämenopausale Patientinnen	1a	B	+/-
▪ **Denosumab (60 mg s.c. q6mo)**			
▪ Postmenopausale Patientinnen	1b[a]	B	+/-

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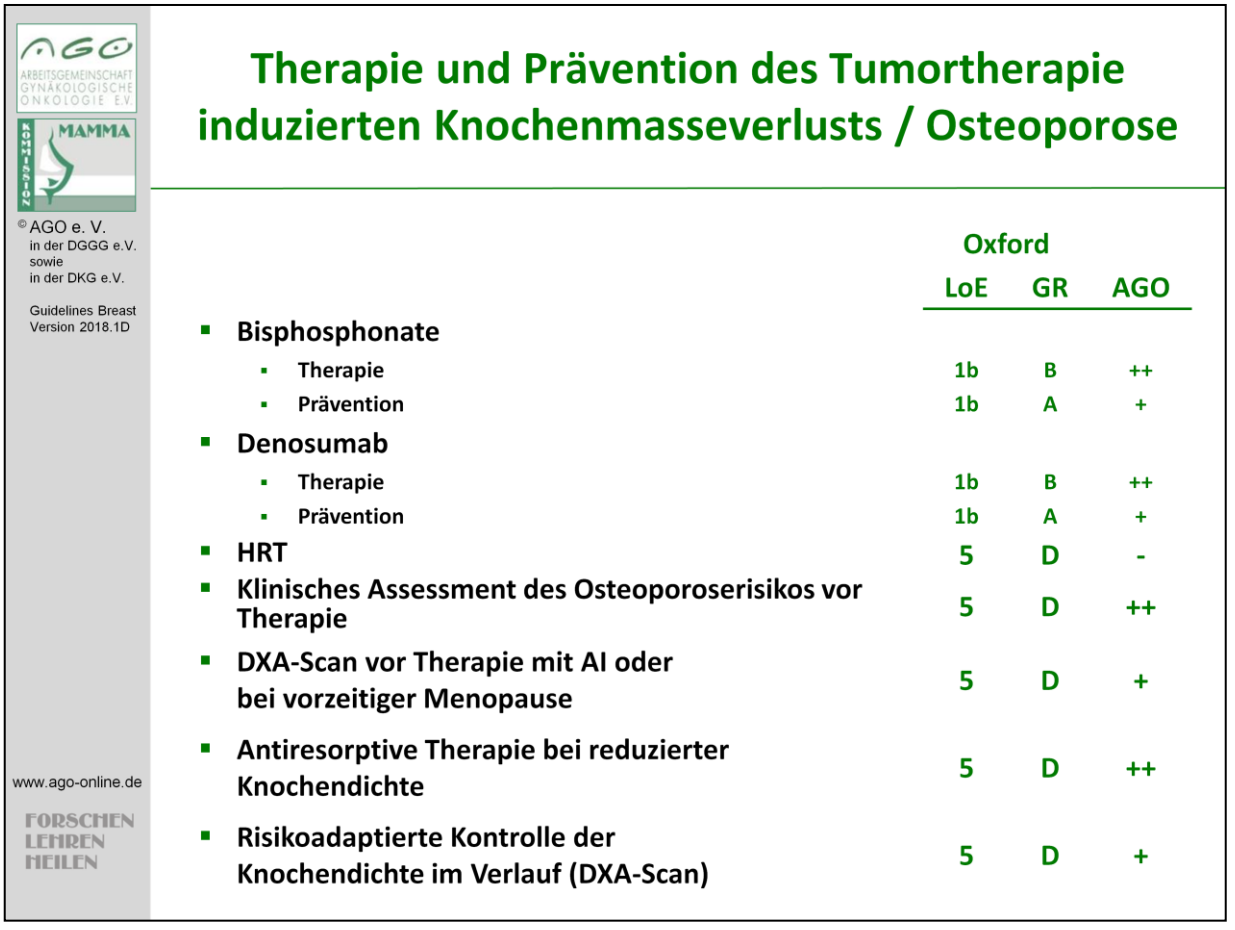

Therapie und Prävention des Tumortherapie induzierten Knochenmasseverlusts / Osteoporose

	Oxford		
	LoE	GR	AGO
▪ **Bisphosphonate**			
▪ Therapie	1b	B	++
▪ Prävention	1b	A	+
▪ **Denosumab**			
▪ Therapie	1b	B	++
▪ Prävention	1b	A	+
▪ **HRT**	5	D	-
▪ **Klinisches Assessment des Osteoporoserisikos vor Therapie**	5	D	++
▪ **DXA-Scan vor Therapie mit AI oder bei vorzeitiger Menopause**	5	D	+
▪ **Antiresorptive Therapie bei reduzierter Knochendichte**	5	D	++
▪ **Risikoadaptierte Kontrolle der Knochendichte im Verlauf (DXA-Scan)**	5	D	+

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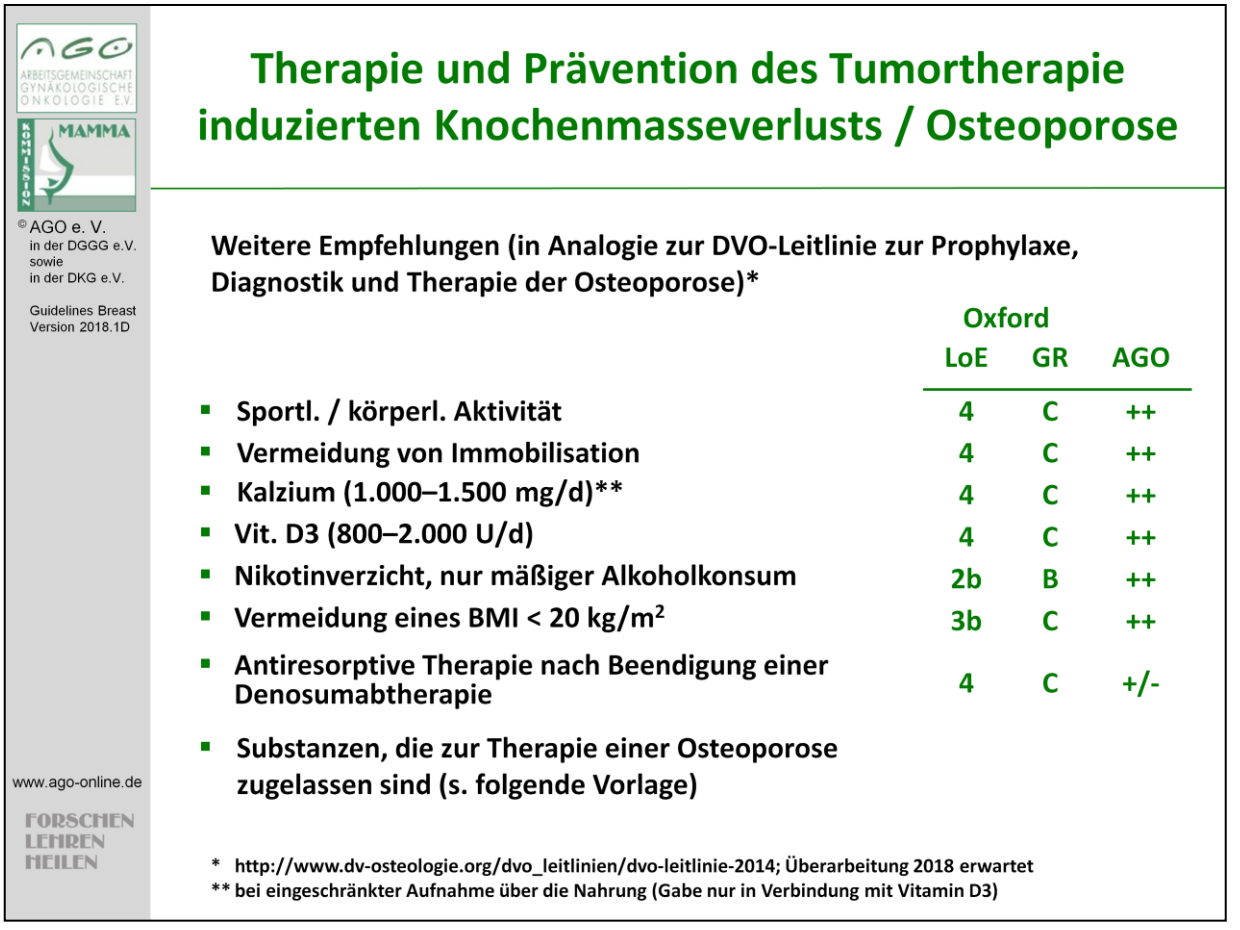

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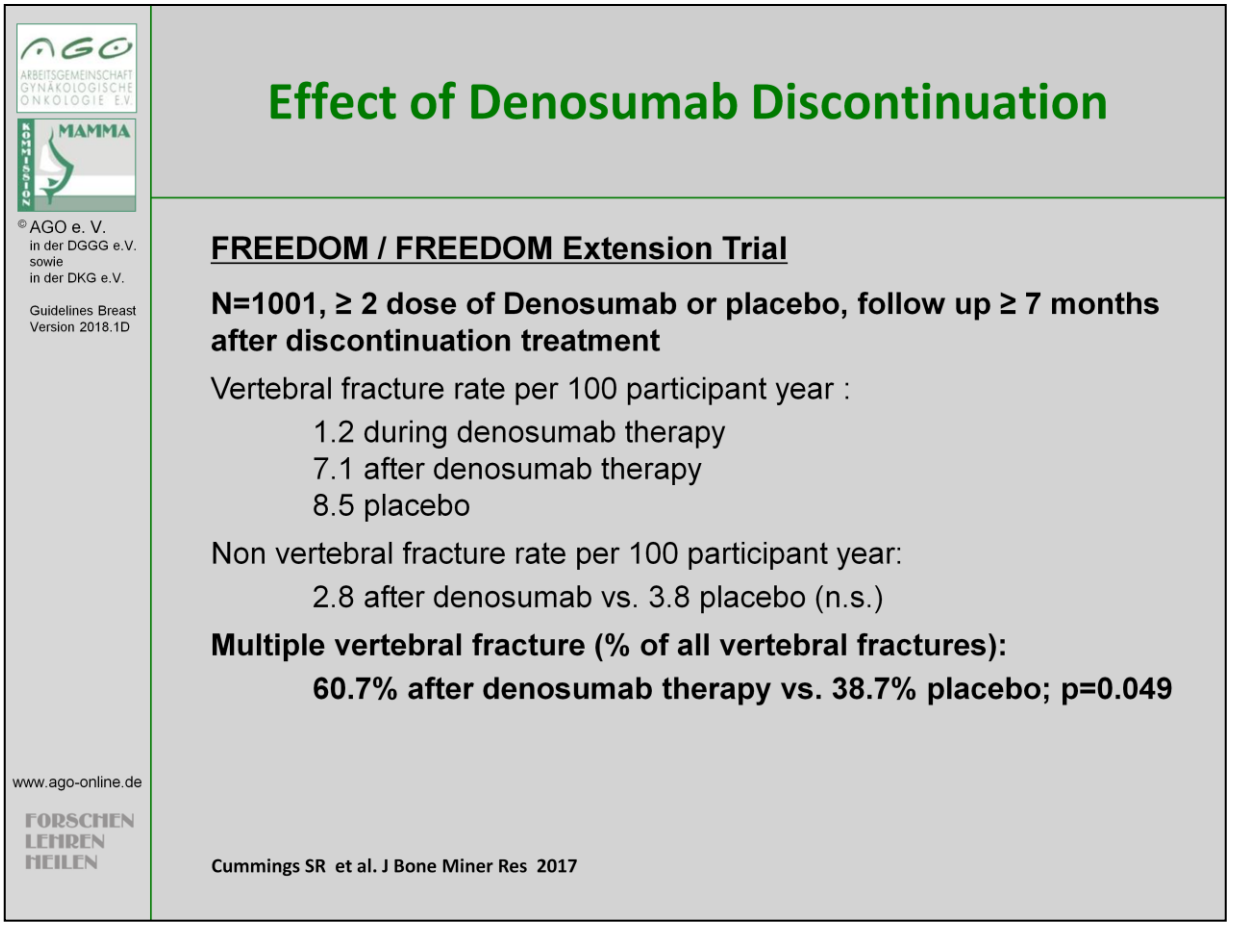

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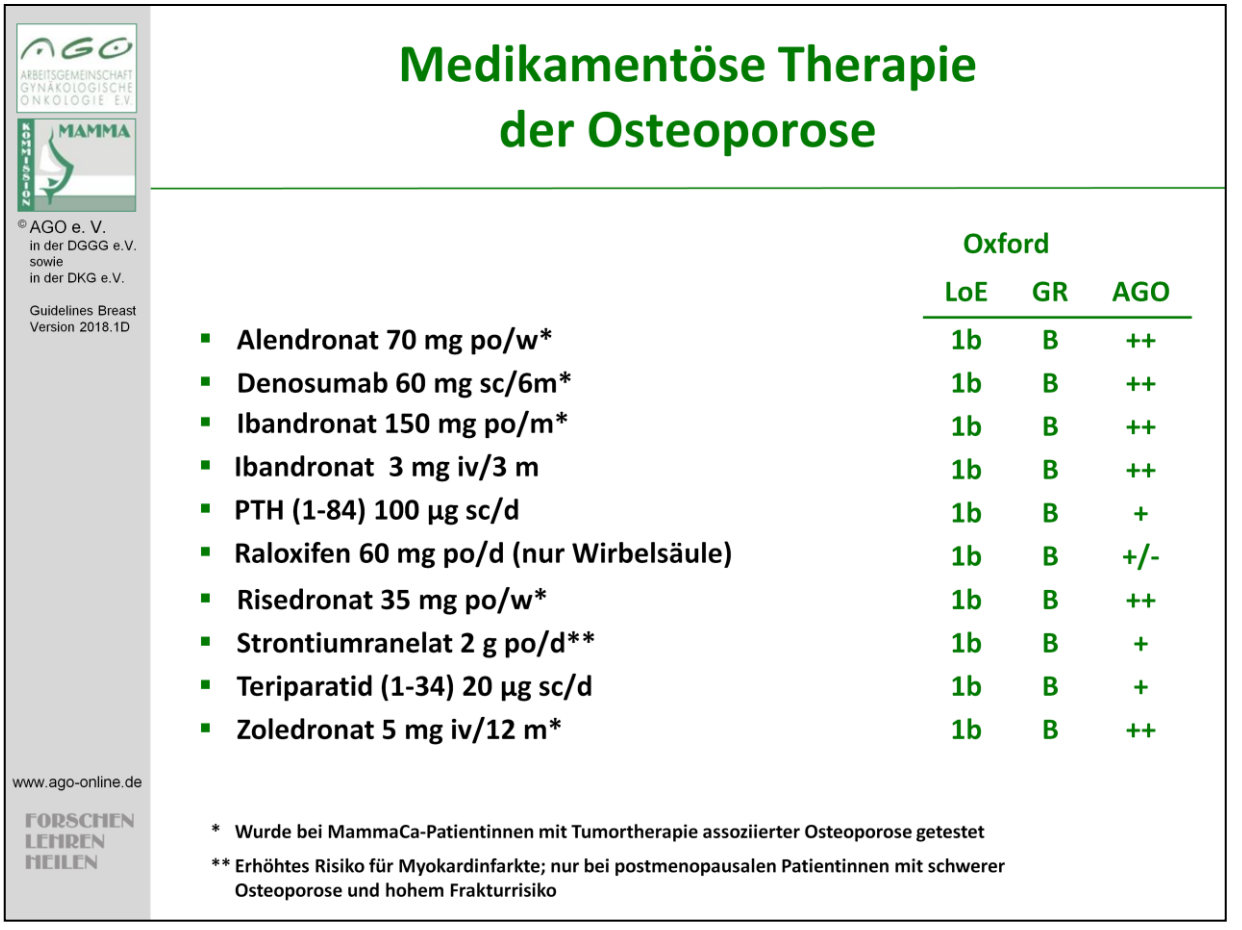

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<u>Raloxifen</u>

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<u>Strontium renalate</u>

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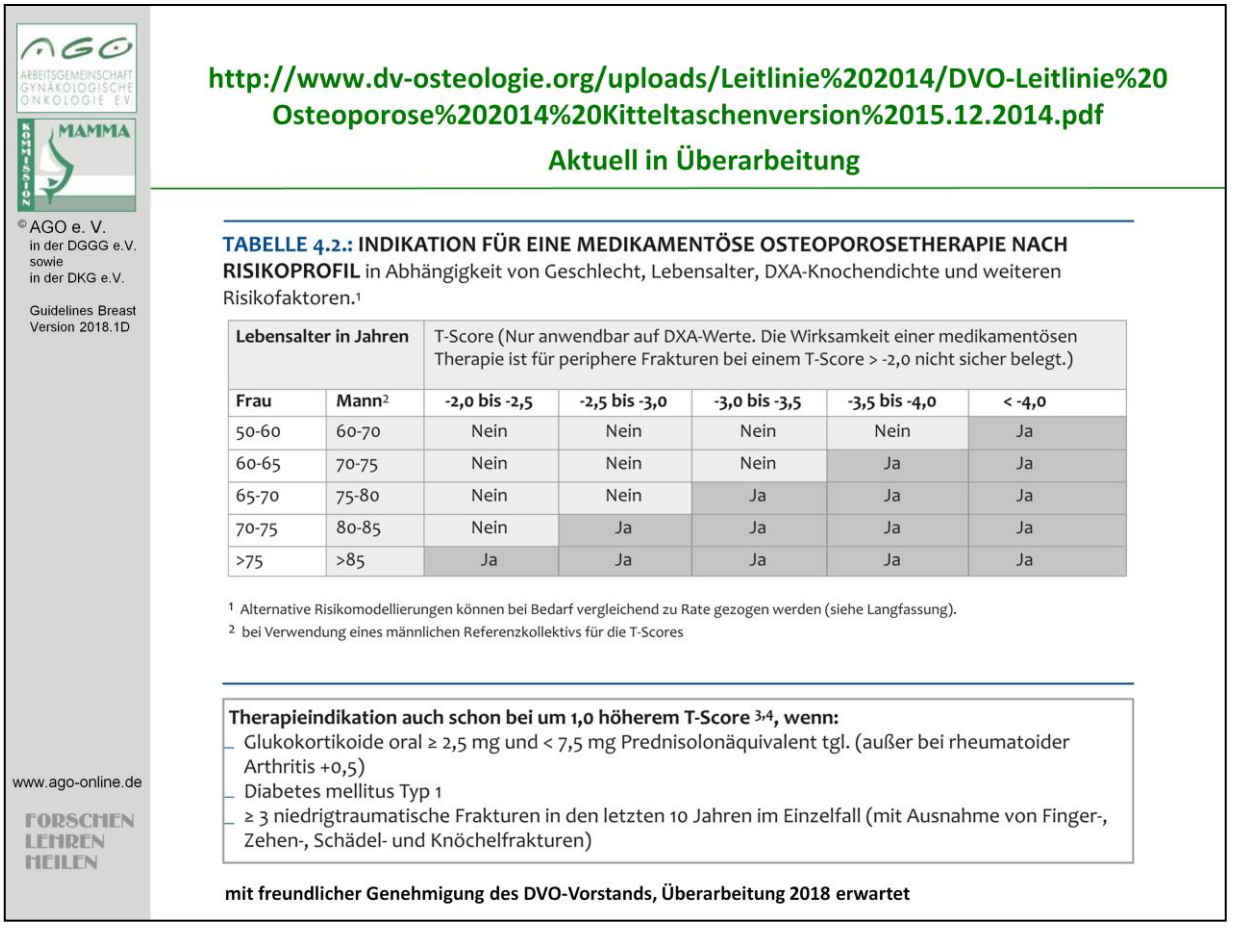

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Aktuell in Überarbeitung

TABELLE 4.2.: INDIKATION FÜR EINE MEDIKAMENTÖSE OSTEOPOROSETHERAPIE NACH RISIKOPROFIL in Abhängigkeit von Geschlecht, Lebensalter, DXA-Knochendichte und weiteren Risikofaktoren.[1]

Lebensalter in Jahren		T-Score (Nur anwendbar auf DXA-Werte. Die Wirksamkeit einer medikamentösen Therapie ist für periphere Frakturen bei einem T-Score > -2,0 nicht sicher belegt.)				
Frau	**Mann[2]**	**-2,0 bis -2,5**	**-2,5 bis -3,0**	**-3,0 bis -3,5**	**-3,5 bis -4,0**	**< -4,0**
50-60	60-70	Nein	Nein	Nein	Nein	Ja
60-65	70-75	Nein	Nein	Nein	Ja	Ja
65-70	75-80	Nein	Nein	Ja	Ja	Ja
70-75	80-85	Nein	Ja	Ja	Ja	Ja
>75	>85	Ja	Ja	Ja	Ja	Ja

[1] Alternative Risikomodellierungen können bei Bedarf vergleichend zu Rate gezogen werden (siehe Langfassung).
[2] bei Verwendung eines männlichen Referenzkollektivs für die T-Scores

Therapieindikation auch schon bei um 1,0 höherem T-Score [3,4], wenn:
- Glukokortikoide oral ≥ 2,5 mg und < 7,5 mg Prednisolonäquivalent tgl. (außer bei rheumatoider Arthritis +0,5)
- Diabetes mellitus Typ 1
- ≥ 3 niedrigtraumatische Frakturen in den letzten 10 Jahren im Einzelfall (mit Ausnahme von Finger-, Zehen-, Schädel- und Knöchelfrakturen)

mit freundlicher Genehmigung des DVO-Vorstands, Überarbeitung 2018 erwartet

1. German guidelines for the treatment of osteoporosis by the DVO: http://www.dv-osteologie.org/uploads/Leitlinie%202014/DVO-Leitlinie%20Osteoporose%202014%20Kurzfassung%20und%20Langfassung%2018.%2009.%202014.pdf
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