

補助療法での検討

HER 2 陽性乳がんは再発高危険群であり、治癒が望める補助療法での有用性が検討されている。主として化学療法との併用であるが、NSABP B-31 では AC (ADM 60 mg/CPA 600 mg) × 4 cycle を標準として、Pacl × 4 cycle あるいは、これに Pacl × 4 → Trastuzumab を加える検証を行っている。また、NCCTG 9831 は、AC (60/600) を標準として Pacl weekly あるいは Pacl + Trastuzumab の臨床試験を行っている。

エビデンスの質：なし

推奨の強さ：現時点では推奨されない。

おわりに

乳がんの薬物療法は新規薬剤の開発に伴い大規模な第III相試験が行われている。これらの臨床試験結果が発表されるとここに述べた内容が大幅に変更になるか、あるいは現時点で不明であることが明白になる可能性も高い。平成 13 年（2001 年）における標準的治療であることを明記しておく。

略字

ADM: doxorubicin, EPI: epirubicin, CPA: cyclophosphamide, 5-FU: 5-fluorouracil, MTX: methotrexate, Doc: docetaxel, Pacl: paclitaxel, q3wks: every 3 weeks, q4wks: every 4 weeks, po: per oral, iv: intravenous infusion, JCOG: Japan Clinical Oncology Group, TAM: tamoxifen, Ral: Raloxifene, MPA: medroxyprogesterone acetate, MA: megestrol acetate, Anas: Anastrozole, Letr: Letrozole, Exam: Examestane

文 献

- 1) Canadian Medical Association: The Canadian Task Force on the periodic health examination. *Can Med Assoc J* 121: 193, 1979.
- 2) Evidence-based medicine Working Group: Evidence-based Medicine, A new approach to teaching the practice of medicine. *JAMA* 268: 2420-2425, 1992.
- 3) Fields K, et al: Breast Cancer. Decision Making in Oncology—Evidence-Based Management. Djulbegovic B, Sullivan DM eds, Churchill Livingstone, London, 1999, pp 253-265.
- 4) 名郷直樹: EBM 実践ワークブック. 南江堂, 東京, 1999.
- 5) Biesecker BB, et al: Genetic counseling for families with inherited susceptibility to breast and ovarian cancer. *JAMA* 269: 1970-1973, 1993.
- 6) Wooster R, et al: Identification of the breast cancer susceptibility gene BRCA 2. *Nature* 378: 789-792, 1995.
- 7) Fisher B, et al: Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 90: 1371-1388, 1998.
- 8) Delmas PD, et al: Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. *N Engl J Med* 337: 1641-1647, 1997.
- 9) Goldhirsch A, et al: Meeting Highlights: International Consensus Panel on the Treatment of Primary Breast Cancer. *J Natl Cancer Inst* 90: 1601-1608, 1998.
- 10) Early Breast Cancer Trialist's Collaborative Group: Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy. 133 randomized trials involving 31000 recurrences and 24000 deaths among 75000 women. *Lancet* 339: 71-85, 1992.
- 11) Early Breast Cancer Trialist's Collaborative Group: Polychemotherapy for early breast cancer: an overview of the randomized trials. *Lancet* 352: 930-942, 1998.
- 12) Bonadonna G, et al: Combination chemotherapy as an adjuvant treatment in operable breast cancer. *N Engl J Med* 294: 405-410, 1976.
- 13) Fisher B, et al: Sequential methotrexate and fluorouracil for the treatment of node-negative breast cancer patients with estrogen receptor-negative tumors: eight-year results from national surgical adjuvant breast and bowel project (NSABP) B-13 and first report of findings from NSABP B-19 comparing methotrexate and fluorouracil with conventional cyclophosphamide, methotrexate and fluorouracil. *J Clin Oncol* 14: 1982-1992, 1996.
- 14) Fisher B, et al: Tamoxifen and chemotherapy for lymph node-negative, estrogen receptor-positive breast cancer. *J Natl Cancer Inst* 89: 1673-1682, 1997.
- 15) Yamauchi H, et al: When is a tumor marker ready for prime time? A case study of c-erb-B 2 as a predictive factor in breast cancer.

- J Clin Oncol* 19: 2334-2356, 2001.
- 16) Early Breast Cancer Trialist'Collaborative Group: Analysis of overview results. Presented at the fifth meeting of Early Breast Cancer Trialist'Collaborative Group, Oxford, United Kingdom, September 21-23, 2000 (abstract).
 - 17) National Institutes of Health Consensus Statement on the adjuvant therapy of breast cancer. Available at: <http://adp.od.nih.gov/consensus/cons/114/114-statement.htm>
 - 18) Wood W, et al: Dose and dose intensity trial of adjuvant chemotherapy for stage II, node-positive breast carcinoma. *N Engl J Med* 330: 1253-1259, 1994.
 - 19) Thor AD, et al: ErbB-2, p 53, and efficacy of adjuvant therapy in lymph node-positive breast cancer. *J Natl Cancer Inst* 90: 1346-1360, 1998.
 - 20) Budman D, et al: Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. *J Natl Cancer Inst* 90: 1205-1211, 1994.
 - 21) Fisher B, et al: Increased intensification and total dose of cyclophosphamide in a doxorubicin-cyclophosphamide regimen for the treatment of the primary breast cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-22. *J Clin Oncol* 15: 1858-1869, 1997.
 - 22) Fisher B, et al: Further evaluation of intensified and increased total dose of cyclophosphamide in a doxorubicin-cyclophosphamide regimen for the treatment of the primary breast cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-25. *J Clin Oncol* 17: 3374-3388, 1999.
 - 23) Henderson IC, et al: Improved disease-free and overall survival from the addition of sequential paclitaxel but not from the escalation of doxorubicin dose level in the adjuvant chemotherapy of patients with node-positive primary breast cancer. *Proc ASCO* 17: 101 a, 1998.
 - 24) Levine MN, et al: Randomized trial of intensive cyclophosphamide, Epirubicin, and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer. *J Clin Oncol* 16: 2651-2658, 1998.
 - 25) Coombes RC, et al: Adjuvant cyclophosphamide, methotrexate and fluorouracil versus fluorouracil, epirubicin, and cyclophosphamide chemotherapy in premenopausal women with axillary node-positive operable breast cancer: results of a randomized trial. *J Clin Oncol* 14: 35-45, 1996.
 - 26) Bonneterre J, et al: Results of a randomized trial of adjuvant chemotherapy with FEC 50 vs FEC 100 in high risk node-positive breast cancer patients. *Proc ASCO* 17(abstr 473): 124 a, 1998.
 - 27) Adachi I, et al: Randomized comparison of sequential endocrine and chemotherapy versus combined chemoendocrine therapy in patients with advanced breast cancer. *Chemotherapy Challenges for Future* (Kimura K, Carter SK&Griswold ed). 5: 276-287, 1990.
 - 28) 神田和弘・他: 再発・進行乳がんに対する5-FU, Adriamycin, Cyclophosphamide (FAC療法)の効果. *癌と化学療法* 8: 749-755, 1981.
 - 29) 富永 健・他: 共同研究による Epirubicin の乳がんに対する phase II study. *癌と化学療法* 13: 2187-2192, 1986.
 - 30) Fumoleau P, et al: Better outcome of premenopausal node-positive (N+) breast cancer patients (pts) treated with 6 cycle vs 3 cycle of adjuvant chemotherapy: Eight year follow-up results of FASG 01. *Proc ASCO* 18(abstr 252): 67 a, 1999.
 - 31) Bonadonna G, et al: Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer. The results of 20 years of follow-up. *N Engl J Med* 332: 901-926, 1995.
 - 32) 野村雍夫・他: 原発進行・再発乳がんに対する Cyclophosphamide, Methotrexate, 5-Fluorouracil (CMF)併用療法の臨床的検討. *癌と化学療法* 21: 194-1956, 1994.
 - 33) Engelsman E, et al: "Classical" CMF versus a 3-weekly intravenous CMF schedule in postmenopausal patients with advanced breast cancer. *Eur J Cancer* 27: 966-970, 1991.
 - 34) Abe O: The role of chemoendocrine agents in postoperative adjuvant therapy for breast cancer: meta-analysis of the 1st collaborative studies of postoperative adjuvant chemotherapy for breast cancer (ACETBC). *Breast Cancer* 1: 1-9, 1994.
 - 35) Morimoto T, et al: Postoperative adjuvant randomized trial comparing chemoendocrine therapy for patients with stage II breast cancer: 5-year results from the Nishinihon cooperative study group of adjuvant chemoendocrine therapy for breast cancer (ACETBC) of Japan. *Eur J Cancer* 32: 235-242, 1996.
 - 36) Toi M, et al: Role of Thymidine phosphorylase for predicting the prognosis and therapeutic effect of 5'-DFUR-5-fluorouridine, A

- intermediate form of Capecitabine, in early breast cancer patients; findings from a randomized controlled trial. *Proc ASCO* 31 a: abstr 120, 2001.
- 37) Lohrish C, et al: Optimal adjuvant cytotoxic therapy for breast cancer. Educational Book of American Society of Clinical Oncology, 2001, pp 61-70.
 - 38) Early Breast Cancer Trialist's Collaborative Group: Tamoxifen for early breast cancer: an overview of the randomized trials. *Lancet* 351: 1451-1467, 1998.
 - 39) Fisher B, et al: Chemotherapy with or without tamoxifen for patients with ER negative breast cancer and negative nodes: Results from NSABP B 23. *Proc ASCO* 19(abstr 277): 72 a, 2000.
 - 40) Early Breast Cancer Trialist's Collaborative Group: Ovarian ablation in early breast cancer: an over view of the randomized trials. *Lancet* 348: 1189-1196, 1996.
 - 41) Scottish Cancer Trials Breast Group and ICRF Breast Unit: Adjuvant ovarian ablation versus CMF chemotherapy in premenopausal women with pathological stage II breast carcinoma: The Scottish trial. *Lancet* 341: 1293-1298, 1993.
 - 42) Kaufmann M, et al: Goserelin, a depot gonadotropin-releasing hormone against in the treatment of premenopausal patients with metastatic breast cancer. *J Clin Oncol* 7: 1113-1119, 1989.
 - 43) Boccard F, et al: Ovarian ablation versus goserelin with or without Tamoxifen in pre-perimenopausal patients with advanced breast cancer: results of multicentric Italian study. *Ann Oncol* 5: 337-342, 1994.
 - 44) Boccard F, et al: Cyclophosphamide, methotrexate, and fluorouracil versus tamoxifen plus ovarian suppression as adjuvant treatment of estrogen receptor-positive pre-/perimenopausal breast cancer patients: Results of the Italian Breast Cancer Adjuvant Study Group 02 Randomized Trial. *J Clin Oncol* 18: 2718-2727, 2000.
 - 45) Taylor CW, et al: Multicenter randomized clinical trial of goserelin versus surgical ovariectomy in premenopausal patients with receptor-positive metastatic breast cancer: An intergroup study. *J Clin Oncol* 16: 994-999, 1998.
 - 46) Davidson N, et al: Effect of chemohormonal therapy in pre-menopausal, node (+), receptor (+) breast cancer: Eastern cooperative oncology group phase III intergroup trial. *Proc ASCO* 18: 67 a, 1999.
 - 47) Jakesz R, et al: Comparison of adjuvant therapy with Tamoxifen and goserelin vs. CMF in premenopausal stage I and II hormone-responsive breast cancer patients: Four year results of Austrian Breast Cancer Study Group (ABCSG) Trial 5. *Proc ASCO* 18: 67 a, 1999.
 - 48) Ejlertsen B, et al: Comparable effect of ovarian ablation versus CMF chemotherapy in premenopausal hormone receptor positive breast cancer patients. *Proc ASCO* 18(abstr 248): 66 a, 1999.
 - 49) Roche HH, et al: Complete hormonal blockade versus chemotherapy in premenopausal early-stage breast cancer patients with positive hormone-receptor and 1-3 node-positive tumor: Results of the FASG 06 trial. *Proc ASCO* 19(abstr 279): 72 a, 2000.
 - 50) Jonat W for the Zoladex Early Breast Cancer Re Association: Zoladex vs CMF as adjuvant therapy in pre-/perimenopausal early breast cancer: Preliminary efficacy-QOL, and BMD results from the ZEBRA study. *Breast Cancer Res Tret* 64: 13, 2000.
 - 51) Rutqvist LE: Zoladex and tamoxifen as adjuvant therapy in premenopausal breast cancer: A randomized trial by the Cancer Research Campaign (CRC) Breast Cancer Trial Group, the Stockholm Breast Cancer Trial Group, The South-East Sweden Breast Cancer Group and the Gruppo Intersdisciplinare Valtazione Interventi in Oncologia. *Proc ASCO* 18(abstr 251): 67 a, 1999.
 - 52) Davidson N: Hormonal ablation, in: NIH Consensus Development Conference on Adjuvant Therapy for Breast Cancer. Bethesda, MD, National Institutes of Health, 2000, pp 63-66.
 - 53) Fisher B, et al: Postoperative chemotherapy and Tamoxifen compared with Tamoxifen alone in the treatment of positive-node breast cancer patients aged 50 years and older with tumors responsive to Tamoxifen: Results from the National Surgical Adjuvant Breast and Bowel Project B-16. *J Clin Oncol* 8: 1005-1018, 1990.
 - 54) International Breast Cancer Study Group: Effectiveness of adjuvant chemotherapy in combination with Tamoxifen for node-positive postmenopausal breast cancer patients. *J Clin Oncol* 15: 1385-1394, 1997.
 - 55) Fisher B, et al: The worth of chemotherapy and Tamoxifen over TAM alone in node-negative patients with estrogen-receptor

- (ER) positive invasive breast cancer (BC); first results from NSABP B-20. *Proc ASCO* 16: 1 a, 1997.
- 56) Fisher B, et al: Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: Findings from national surgical adjuvant breast and bowel project B-18. *J Clin Oncol* 15: 2483-2493, 1997.
- 57) Mauriac L, et al: Effects of primary chemotherapy in conservative treatment of breast cancer patients with operable tumors larger than 3 cm. *Ann Oncol* 2: 347-354, 1991.
- 58) Hortobagyi GN: Treatment of breast cancer. *N Engl J Med* 339: 974-984, 1998.
- 59) Fossali R, et al: Cytotoxic and hormonal treatment for metastatic breast cancer: A systemic review of published randomized trials involving 31,510 women. *J Clin Oncol* 16: 3439-3460, 1998.
- 60) Greenberg PAC, et al: Long-term follow-up of patients with complete remission following combination chemotherapy for metastatic breast cancer. *J Clin Oncol* 14: 2197-2202, 1996.
- 61) Paterson AHG, et al: Effect of chemotherapy on survival in metastatic breast cancer. *Breast Cancer Res Treat* 1: 357-363, 1982.
- 62) Smalley RV, et al: Combination versus sequential five-drug chemotherapy on metastatic carcinoma of the breast. *Cancer Res* 36: 3911-3916, 1976.
- 63) Hoogstraten B, et al: Combination chemotherapy and adriamycin in patients with advanced breast cancer. *Cancer* 38: 13-20, 1976.
- 64) Lena MD, et al: Combined chemotherapy-radiotherapy approach in locally advanced breast cancer. *Cancer Chemother Pharmacol* 1: 53-59, 1978.
- 65) Cooper RG: Combination chemotherapy in hormone resistant breast cancer. *Proc Am Assoc Cancer Res* 10: 15, 1969.
- 66) Tranum BL, et al: Adriamycin combinations in advanced breast cancer. A Southwest Oncology Group Study. *Cancer* 49: 835-839, 1982.
- 67) Segaloff A, et al: An evaluation of the effect of vincristine added to cyclophosphamide, 5-fluorouracil, methotrexate, and prednisone in advanced breast cancer. *Breast Cancer Res Treat* 5: 311-319, 1985.
- 68) Tormey DC, et al: Comparison of induction chemotherapies for metastatic breast cancer. An Eastern Cooperative Oncology Group Trial. *Cancer* 50: 1235-1244, 1982.
- 69) Henderson IC, et al: Principles in the management of metastatic disease, in Henderson IC, Harris Jr (eds): *Breast Disease* (2nd ed). Lippincott, New York, 1990, pp 547-677.
- 70) Tannock IF, et al: A randomized trial of two dose levels of cyclophosphamide, methotrexate and fluorouracil chemotherapy for patients with metastatic breast cancer. *J Clin Oncol* 6: 1377-1387, 1988.
- 71) Muss HB, et al: Combination chemotherapy in advanced breast cancer: a randomized trial comparing a three-vs a five-drug program. *Arch Intern Med* 137: 1711-1714, 1977.
- 72) Chlebowksi RT, et al: Significance of relapse after adjuvant treatment with combination chemotherapy or 5-fluorouracil alone in high-risk breast cancer. *Cancer Res* 41: 4399-4403, 1981.
- 73) Taguchi T: A phase II study of CPT-11 in advanced breast cancer. *Int J Oncol* 5: 404-405, 1994.
- 74) Von Hoff DD, et al: Risk factors for doxorubicin-induced congestive heart failure. *Ann Intern Med* 91: 710-717, 1979.
- 75) Nielsen D, et al: Epirubicin cardiotoxicity: A study of 135 patients with advanced breast cancer. *J Clin Oncol* 8: 1806-1810, 1990.
- 76) 田口鐵男・他: 進行・再発乳癌に対するepirubicinとdoxorubicinの比較臨床試験. 痢と化学療法 13: 3498-3507, 1986.
- 77) Peretz DJ, et al: A randomized comparison of single-agent doxorubicin and epirubicin as first-line cytotoxic therapy in advanced breast cancer. *J Clin Oncol* 9: 2148-2152, 1991.
- 78) Carmo-Pereira J, et al: A comparison of two doses of adriamycin in the primary chemotherapy of disseminated breast carcinoma. *Br J Cancer* 56: 471-473, 1987.
- 79) Lopez M, et al: 5-fluorouracil, adriamycin, cyclophosphamide (FAC) vs. 5-fluorouracil, epirubicin, cyclophosphamide (FEC) in metastatic breast cancer. 46: 1-5, 1989.
- 80) Focan C, et al: Dose-response relationship of epirubicin-based first-line chemotherapy for advanced breast cancer: A prospective randomized trial. *J Clin Oncol* 11: 1253-1263, 1993.
- 81) Tranum BL, et al: Adriamycin in combination for the treatment of the breast cancer; A southwest Oncology Group study. *Cancer* 41: 2078-2083, 1978.
- 82) Nemoto T, et al: Comparison of four-combination chemotherapy programs in metastatic

- breast cancer: comparison of multi drug therapy with cytoxin, 5-FU and predonine versus cytoxin and adriamycin, versus cytoxin, 5-FU and adriamycin, versus cytoxin, 5-FU and predonine alternating with cytoxin and adriamycin. *Cancer* 49: 1988-1993, 1982.
- 83) Huinink WWB, et al: A phase II trial with docetaxel in second line treatment with chemotherapy for advanced breast cancer. *Ann Oncol* 5: 527-532, 1994.
- 84) Chevallier B, et al: Docetaxel is a major cytotoxic drug for the treatment of advanced breast cancer: A phase II trial of the clinical screening cooperative group of the European organization for research and treatment of cancer. *J Clin Oncol* 13: 314-322, 1995.
- 85) Hudis C, et al: Phase II and pharmacologic study of docetaxel as initial chemotherapy for metastatic breast cancer. *J Clin Oncol* 14: 58-65, 1996.
- 86) Trudeau ME, et al: Docetaxel in patients with metastatic breast cancer: A phase II study of the National Cancer Institute of Canada-Clinical Trials Group. *J Clin Oncol* 14: 422-428, 1996.
- 87) Valero V, et al: Phase II trial of docetaxel: A new, highly effective antineoplastic agent in the management of patients with Anthracycline-resistant metastatic breast cancer. *J Clin Oncol* 13: 2886-2894, 1995.
- 88) Cortes JE, et al: Docetaxel. *J Clin Oncol* 13: 2643-2655, 1995.
- 89) Gianni L, et al: Paclitaxel efficacy in patients with advanced breast cancer resistant to anthracycline. *Semin Oncol* 21: 29-33, 1994.
- 90) Schiller JH, et al: A phase I trial of 3-hour infusions of paclitaxel with or without granulocyte colony-stimulating factor. *Semin Oncol* 21: 9-14, 1994.
- 91) Seidman AD, et al: Paclitaxel as second and subsequent therapy for metastatic breast cancer: Activity independent of prior anthracycline response. *J Clin Oncol* 13: 1152-1159, 1995.
- 92) Gianni L, et al: Paclitaxel in metastatic breast cancer: a trial of two dose by a 3-hour infusion in patients with disease recurrence after prior therapy with anthracyclines. *J Clin Oncol* 87: 1169-1175, 1995.
- 93) Geyer C, et al: A phase II trial of paclitaxel in patients with metastatic refractory carcinoma of the breast. *Proc ASCO* 15: abstr 92, 1996.
- 94) Mamoune E, et al: 3-hour high-dose taxol infusion in advanced breast cancer: an NSABP phase II study. *Proc ASCO* 15: abstr 206, 1995.
- 95) Bishop J, et al: A randomized phase III study of Taxol vs CMFP in untreated patients with metastatic breast cancer. *Proc ASCO* 15: abstr 107, 1996.
- 96) 田口鐵男・他: RP 56976 (Docetaxel) の乳がんに対する前期第II相臨床試験. 癌と化学療法 21: 2453-2460, 1994.
- 97) Ando M, et al: Efficacy of Docetaxel 60 mg/m² in patients with metastatic breast cancer according to the status of Anthracycline resistance, *J Clin Oncol* 19: 336-342, 2001.
- 98) Jean-Marc A, et al: A phase III trial comparing docetaxel and doxorubicin (AT) vs doxorubicin and cyclophosphamide (AC) in first line metastatic breast cancer (MBC). *Proc ASCO* 18(abstr 485): 127 a, 1999.
- 99) Buzdar AU, et al: Prospective evaluation of paclitaxel versus combination chemotherapy with fluorouracil, doxorubicin, cyclophosphamide (FAC) as neoadjuvant therapy in patients with operable breast cancer. *J Clin Oncol* 17: 3412-3417, 1999.
- 100) Pouillart P, et al: Final results of a phase II randomized, parallel study of doxorubicin/cyclophosphamide (AC) and doxorubicin/paclitaxel (AT) as neoadjuvant treatment of local-regional breast cancer. *Proc ASCO* 18(abstr 275): 73 a, 1999.
- 101) Hainsworth JD, et al: Phase I trial of Docetaxel administered by weekly infusion in patients with advanced refractory cancer. *J Clin Oncol* 16: 2164-2168, 1998.
- 102) Winer E, et al: Failure of higher dose paclitaxel to improve outcome in patients with metastatic breast cancer: results of CALGB 9342. *Proc ASCO* 17(abstr 388): 101 a, 1998.
- 103) Loeffler TM: Is there a place for "Dose-Dense" weekly schedules of Taxoids? *Semin Oncol* 12: 32-34, 1998.
- 104) 木村盛彦・他: 進行・再発乳癌に対するPaclitaxel Weekly投与の臨床経験. 癌と化学療法 27: 1703-1798, 2000.
- 105) Osborne CK: Tamoxifen in the treatment of breast cancer. *N Engl J Med* 339: 1609-1618, 1998.
- 106) Howell A, et al: New endocrine therapies for breast cancer. *Eur J Cancer* 32: 576-588, 1996.
- 107) Buzdar AU, et al: Anastrozole versus megestrol acetate in the treatment of postmenopausal women with advanced breast carcinoma. *Cancer* 83: 1142-1152, 1998.
- 108) Jonat W, et al: A randomized trial comparing

- two doses of the new selective aromatase inhibitor anastrozole (Arimedex) with MA in postmenopausal patients with advanced breast cancer. *Eur J Cancer* 32: 404-412, 1996.
- 109) Dombernowsky P, et al: Letrozole, a new oral aromatase inhibitor for advanced breast cancer: Double-blind randomized trial showing a dose effect and improved efficacy and tolerability compared with MA. *J Clin Oncol* 16: 453-461, 1998.
- 110) Gershonich M, et al: Letrozole, a new oral aromatase inhibitor: Randomized trial comparing 2.5 mg daily, 0.5 mg daily and aminoglutethimide in postmenopausal women with advanced breast cancer. *Ann Oncol* 9: 639-645, 1998.
- 111) Kaufmann M, et al: Examestane is superior to MA after tamoxifen failure in postmenopausal women with advanced breast cancer: Results of a phase III randomized double-blind trial. *J Clin Oncol* 18: 1399-1411, 2000.
- 112) Thurlimann B, et al: Examestane in postmenopausal pretreated advanced breast cancer: a multicenter phase II study in patients aminoglutethimide (AG) failure. *Proc Eur Soc Med Oncol* 5: abstr 144, 1994.
- 113) Buzdar A, et al: Anastrozole (Arimedex) versus Tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women—combined analysis from two identically designed multicenter trial. *Proc ASCO* 19: (abstr 609 D), 2000.
- 114) Koyama H, et al: A randomized controlled cooperative study of oral medroxyprogesterone acetate 1200 and 600 mg in patients with advanced or recurrent breast cancer. *Oncology* 56: 283-290, 1999.
- 115) Tominaga T, et al: Comparison of chemotherapy with or without medroxyprogesterone acetate for advanced or recurrent breast cancer. *Eur J Cancer* 34: 959-964, 1994.
- 116) Kangas L, et al: A new triphenylethylene compound, FC-1157 a: II, Antitumor effects. *Cancer Chemother Pharmacol* 17: 109-114, 1986.
- 117) Pyrjonen S, et al: Comparison of tamoxifen and tamoxifen in postmenopausal patients with advanced breast cancer: A randomized double blind-The "Nordic" phase III study. *Br J Cancer* 76: 270-277, 1997.
- 118) Nomura Y, et al: Clinical evaluation of NK 622 in advanced or recurrent breast cancer: A comparative study by a double blind method with tamoxifen. *Jpn J Cancer Chemother* 20: 247-258, 1993.
- 119) Gershonich M, et al: High dose toremifene vs tamoxifen in postmenopausal advanced breast cancer. *Oncology* 11: 29-36, 1997.
- 120) Holli K, et al: Safety and efficacy results of a randomized trial comparing adjuvant toremifene and tamoxifen in postmenopausal patients with node-positive breast cancer. *J Clin Oncol* 18: 3487-3494, 2000.
- 121) Stadtmauer EA, et al: Chemotherapy compared with autologous stem cell transplantation in the management of responding metastatic breast cancer. PBT-1. *Proc ASCO* 18: 1a, 1999.
- 122) Peters WP, et al: Preliminary results of a randomized comparison of two doses of combination alkylating agents as consolidation after CAF in patients with primary breast cancer involving ten or more axillary lymph nodes. *Proc ASCO* 18: 1a, 1999.
- 123) Bergh J: Results from a randomized adjuvant breast cancer study with high dose chemotherapy with CTCb supported by autologous bone marrow stem cells versus dose escalated and tailored FEC therapy. *Proc ASCO* 18: 2a, 1999.
- 124) Takashima S, et al: A phase II study of high-dose epirubicin (EPI) plus cyclophosphamide (CPA) with G-CSF for breast cancer patients with visceral metastases or hormone-independent tumors: A trial of the Japan Clinical Oncology Group. *Jpn J Clin Oncol* 27: 325-330, 1997.
- 125) Tokuda Y, et al: Randomized phase III study of high-dose chemotherapy (HDC) with autologous stem cell support as consolidation in high-risk postoperable breast cancer. Japan Clinical Oncology Group (JCOG 9208). *Proc ASCO* 20(abstr 148): 38a, 2001.
- 126) The American Society of Clinical Oncology: American Society of Clinical Oncology recommendation for the use of hematopoietic colony-stimulating factors: Evidenced-based, clinical practice guidelines. *J Clin Oncol* 12: 2471-2508, 1994.
- 127) Hughes WT, et al: 1997 Guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever. *Clin Infect Dis* 25: 551-573, 1997.
- 128) Sutherland CM, et al: Long-term survival and prognostic factors in patients with regional breast (skin, muscle, and/or chest wall attachment). *Cancer* 55: 1389-1387, 1985.

- 129) Overgaard M, et al: Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. *N Engl J Med* 337: 949-955, 1997.
- 130) Ragaz J, et al: Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 337: 956-962, 1997.
- 131) Sundraesan N, et al: Surgical treatment of brain metastasis. *Cancer* 55: 1382-1388, 1985.
- 132) 大川智彦・他: 転移性脳腫瘍に対する放射線治療の臨床的検討. 癌の臨床 34: 11139-1146, 1988.
- 133) Kida Y, et al: Radiotherapy of the metastatic brain tumors with gamma-knife. *Acta Neurochir* 63: 89-94, 1995.
- 134) Singer FR, et al: Treatment of hypercalcemia of malignancy with intravenous etidronate. A controlled multicenter study. *Arch Intern Med* 151: 471-476, 1991.
- 135) O'Rourke NP, et al: Effective treatment of malignant hypercalcemia with a single infusion of clodronate. *Bone* 9: 123-130, 1993.
- 136) Body JJ, et al: Treatment of tumor-induced hypercalcemia with the bisphosphonate pamidronate: Dose-response relationship and influence of the tumour type. *Ann Oncol* 5: 359-363, 1994.
- 137) Theriault RL, et al: Pamidronate reduces skeletal morbidity in women with advanced breast cancer and lytic bone lesions: A randomized, placebo-controlled trial. *J Clin Oncol* 17: 846-854, 1999.
- 138) Bloomfield DJ: Should bisphosphonates be part of the standard therapy of patients with multiple myeloma or bone metastases from other cancers? An evidence-based review. *J Clin Oncol* 16: 1218-1225, 1998.
- 139) Diel JJ, et al: Reduction in new metastasis in breast cancer with adjuvant clodronate treatment. *N Engl J Med* 339: 357-363, 1998.
- 140) Body JJ, et al: Current use of bisphosphonates in oncology. *J Clin Oncol* 16: 3890-3899, 1998.
- 141) Hortobagyi GN, et al: Efficacy of pamidronate in reducing skeletal complications in patients with breast cancer and lytic bone metastasis. *N Engl J Med* 335: 1785-1791, 1996.
- 142) 立石昭夫: 骨転移がんの診断と治療. 癌と化学療法 23: 1262-1268, 1996.
- 143) Cobleigh MA, et al: Multinational study of the efficacy and safety of humanized anti-HER 2 monoclonal antibody in women who have HER 2-overexpressing metastatic breast cancer that has progressed after chemotherapy. *J Clin Oncol* 17: 2639-2648, 1997.
- 144) Tokuda Y, et al: Dose escalation and pharmacokinetic study of a humanized anti-HER 2 monoclonal antibody in patients with HER 2/neu-overexpressing metastatic breast cancer. *Br J Cancer* 81: 1419-1425, 1999.
- 145) Norton L, et al: Overall survival advantage to simultaneous chemotherapy plus the humanized anti-HER" monoclonal antibody Herceptin in HER 2-overexpressing metastatic breast cancer. *Proc ASCO* 18(abstr 483): 127 a, 1999.
- 146) Hudis C, et al: Characterization of cardiac dysfunction observed in the HERCEPTIN. *Breast Cancer Res Treat* 50: 232-235, 1998.