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Aligning the Goals of Industry and Publicly Funded Clinical Trials with the Goals of Patients

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Drug Development Landscape - Disclosures

- The great progress that has been made in the treatment of cancer is, in part, the result of partnerships between the pharmaceutical industry and public entities
- While Industry and Academia share many of the same goals, there are differences
- Patient engagement and interests may be prioritized differently in industry vs public sponsored trials
- I am a practicing breast medical oncologist, have led both industry and public sponsored trials, and have treated many patients with these agents and have no other disclosures

What should patients expect?

- Access to treatment that will give them the best chance for survival (patients evaluate risk vs benefit variably)
- Best quality of life possible
- High quality care delivered safely and efficiently
- Affordable healthcare

What does Pharma want?

- Efficient clinical trials that generate high-quality data
- Rapid accrual to their trials
- FDA approval of their drugs

- Their drugs and products to be used as indicated, for the greatest number of patients

Goals of Therapeutic Clinical Trials

Industry Sponsor

- Drug Registration
  - Often based on survival
  - Driven by regulatory requirements
- Label Extension
- Expand Market Share
- Create Shareholder Value

Public Sponsor

- Optimize Treatment
  - Survival and Quality of Life
  - Reflective of patient goals
  - Strategies not addressed by industry
  - Optimal drugs and dosing schedules
- Label Extension
- Create New Knowledge
- Improve Public Health

Adapted from Rich Schilsky

Industry vs Federally Funded Interventional Cancer Trials

- 8,128 Industry Trials; 1,498 Federally funded trials – US based, 2008-2022

- Federally funded trials were more commonly:

  - Prevention trials
  - Screening trials
  - Early phase trials
  - Multi-modality – combining with biologic agents, radiation, and/or surgery
  - Dose de-escalation trials
  - Rare cancer trials
  - Pediatric oncology trials

Unger https://ascopubs.org/doi/abs/10.1200/JCO.2025.43.16_suppl.11095

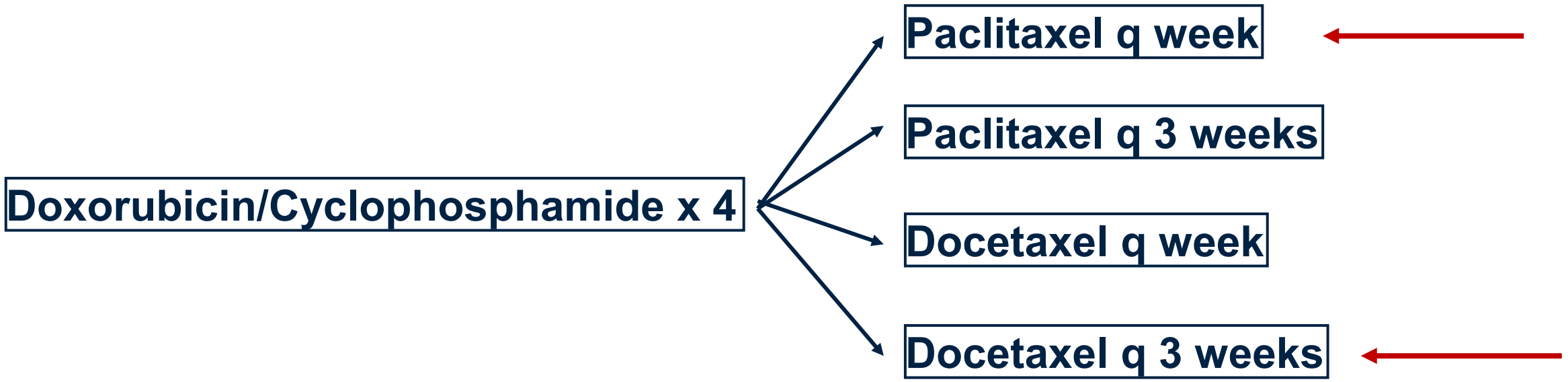
2 Scenarios in the treatment of breast cancer patients

- The development of ”same in class” taxanes
  - Goals of SIC – better efficacy and/or less toxicity
  - Paclitaxel – original taxane, off patent, low cost
  - Docetaxel – on patent, high cost

  - For early stage HER2 negative breast cancer
  - For early stage HER2 positive breast cancer
  - For metastatic breast cancer

- The use of the bone modifying agent zolendronic acid for patients with metastatic breast cancer and bone metastases

Breast Adjuvant Trial E1199
Eastern Cooperative Oncology Group (ECOG)

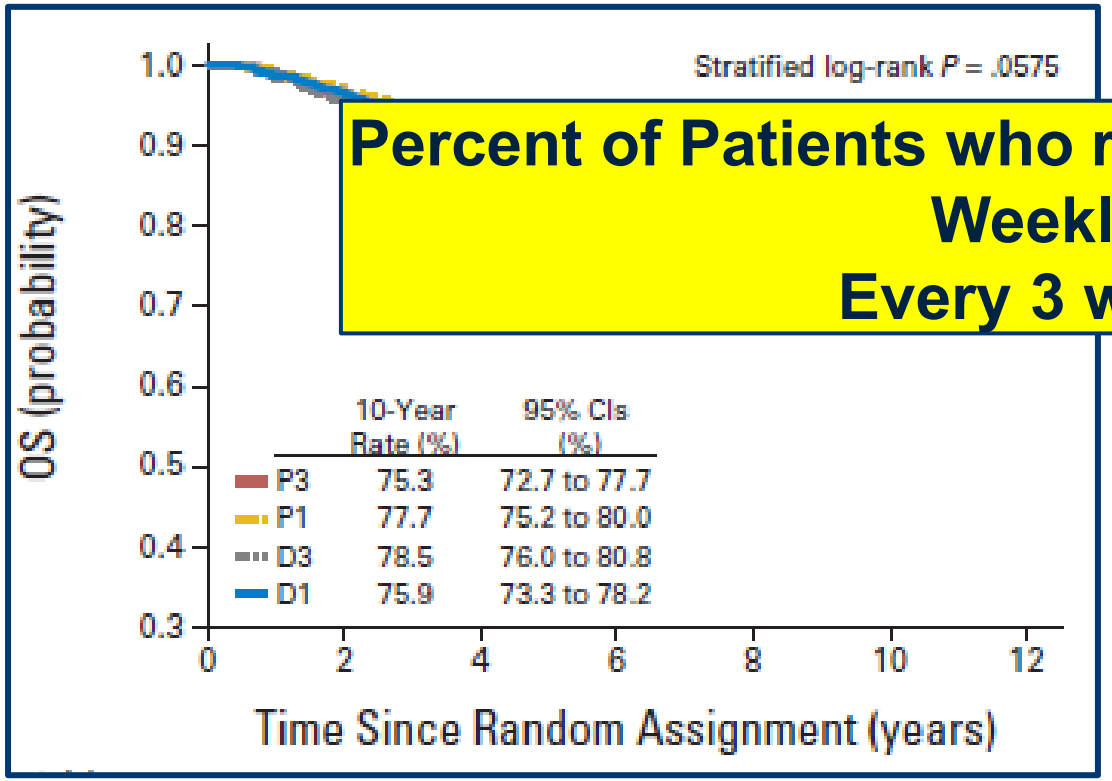


4950 patients randomized

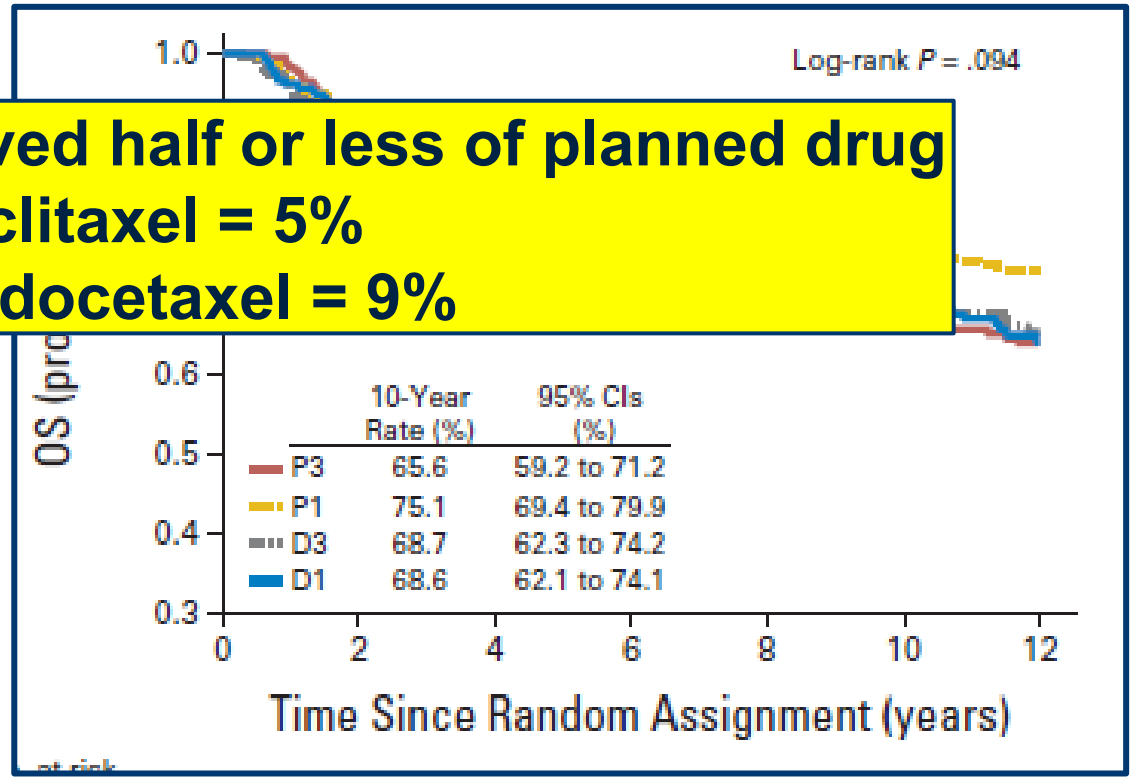
Sparano J Clin Oncol 2025; DOI: 10.1200/JCO.2015.60.9271

Breast Adjuvant Trial E1199
Eastern Cooperative Oncology Group (ECOG)

Percent of Patients who received half or less of planned drug
Weekly paclitaxel = 5%
Every 3 week docetaxel = 9%



All Patients



Patients with Triple Negative Breast Cancer

Sparano J Clin Oncol 2015; DOI: 10.1200/JCO.2015.60.9271

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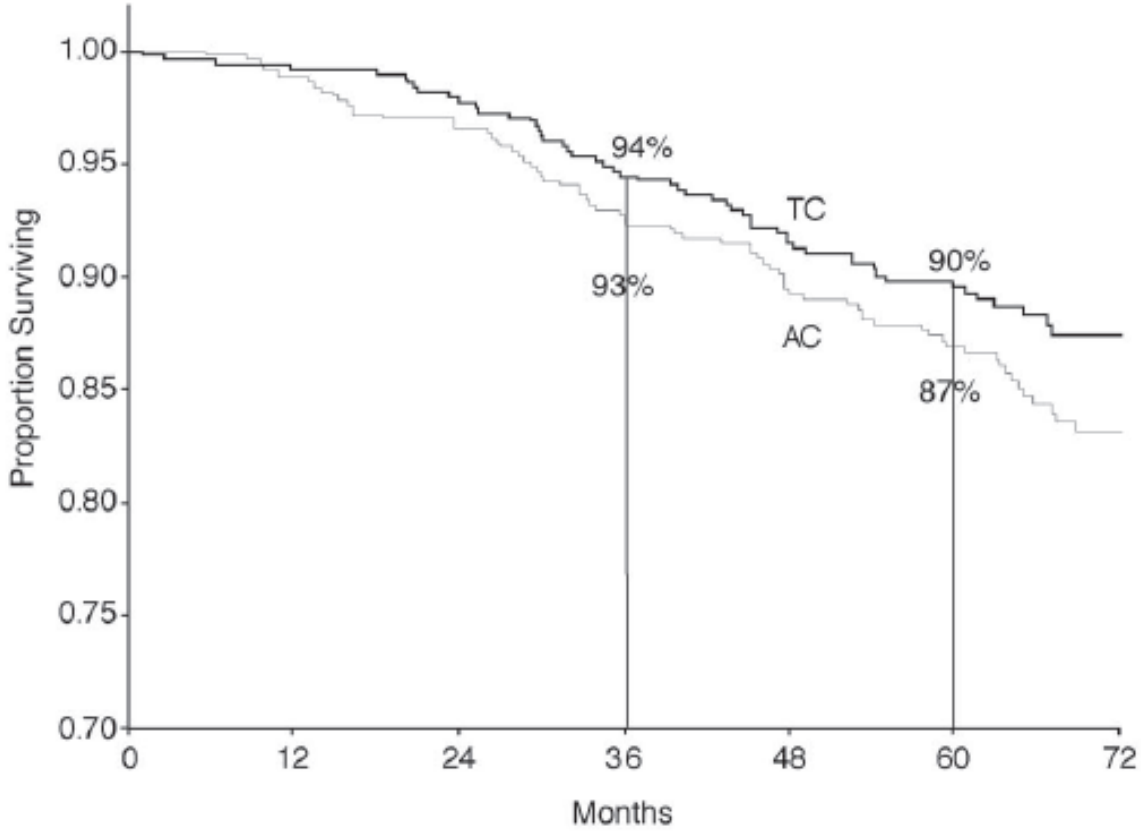
Doxorubicin/Cyclophosphamide vs Docetaxel/Cyclophosphamide



1,016 patients

One goal was to reduce cardiac toxicity risk from doxorubicin

Survival curves should go from 0-100

Funded by Pharma patent holder for Docetaxel
Authors received consulting and honoraria from Funder

Would paclitaxel have given survival outcomes at least equal and better quality of life?

Jones, JCO 2006; DOI: 10.1200/JCO.2006.06.5391

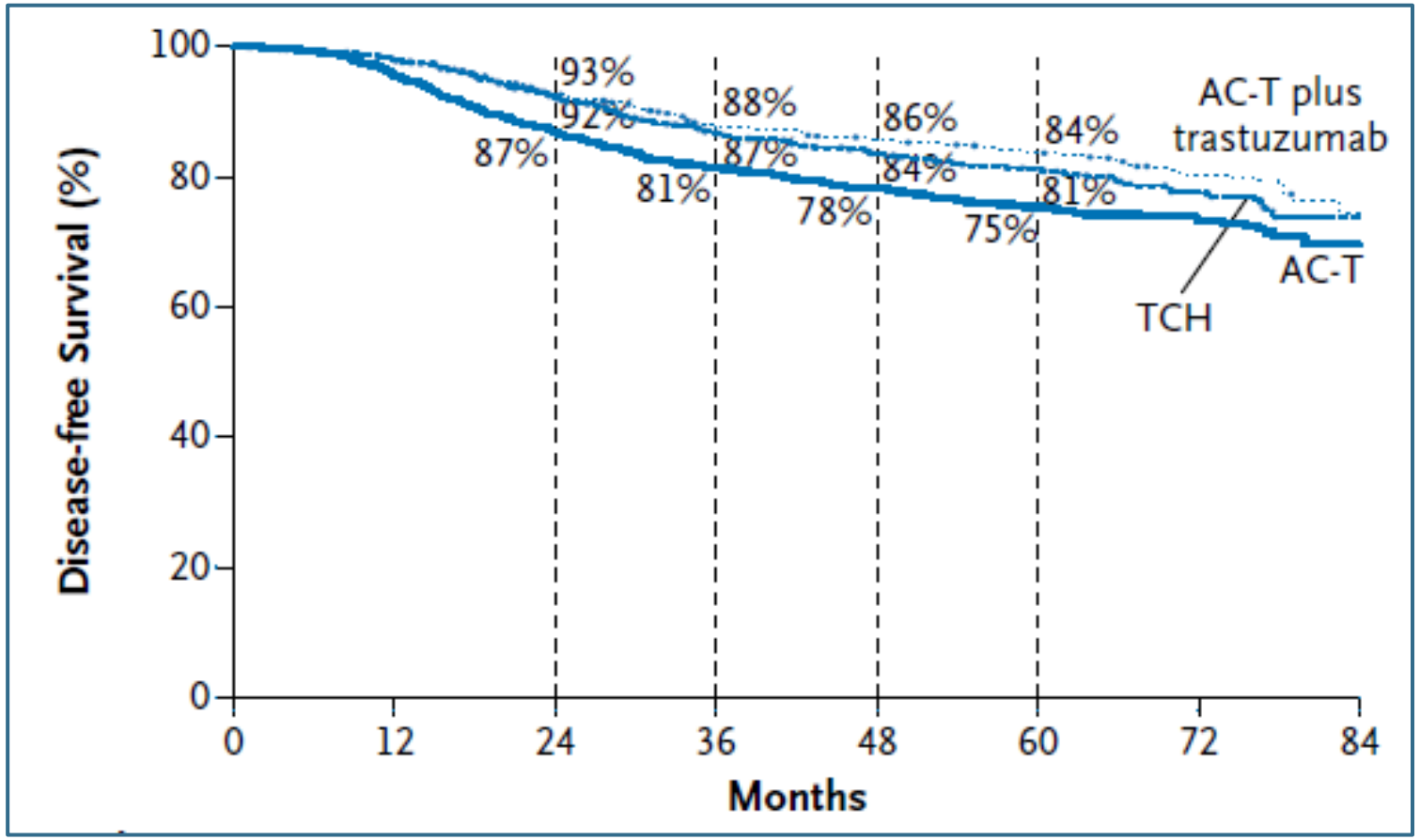
National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2025
Invasive Breast Cancer

HR-Positive, HER2-Negative	
Patients with HR-positive disease are recommended to receive adjuvant endocrine therapy ± CDK4/6 inhibitor therapy (see BINV-K).	
Preferred Regimens: **Preoperative or adjuvant setting:** • Dose-dense AC (doxorubicin/cyclophosphamide) followed or preceded by paclitaxel every 2 weeks[c] • Dose-dense AC (doxorubicin/cyclophosphamide) followed or preceded by weekly paclitaxel[c] • TC (docetaxel and cyclophosphamide) Adjuvant setting only: • If germline *BRCA1/2* mutations[d]: Olaparib	
Useful in Certain Circumstances: **Preoperative or adjuvant setting:** • Dose-dense AC (doxorubicin/cyclophosphamide) • AC (doxorubicin/cyclophosphamide) every 3 weeks (category 2B) • CMF (cyclophosphamide/methotrexate/fluorouracil) • AC followed by weekly paclitaxel[c]	**Other Recommended Regimens:** **Preoperative or adjuvant setting:** • AC followed by docetaxel every 3 weeks[c] • EC (epirubicin/cyclophosphamide) • TAC (docetaxel/doxorubicin/cyclophosphamide)

NCCN can only recommend guidelines supported by clinical trials

Chemotherapy for patients with HER2 positive breast cancer
AC-T vs AC-TH vs TCH



3222 patients

- **A = doxorubicin**
- **C = cyclophosphamide (in AC)**
- **T = docetaxel (in both regimens)**
- **C = carboplatin (in TCH)**
- **H = trastuzumab**

Funded by Pharma patent holders for Docetaxel and Trastuzumab

Would paclitaxel have given survival outcomes at least equal and better quality of life?

Slamon, N Engl J Med 2011;365:1273-83

Chemotherapy for patients with HER2 positive breast cancer
AC-T vs AC-TH vs TCH

Table 2. Therapeutic Index for Critical Clinical Events.*

Clinical Event	AC-T	AC-T plus Trastuzumab	TCH
		number of events	
Total events	201	146	149
Distant breast-cancer recurrence	188	124	144
Grade 3 or 4 congestive heart failure	7	21	4
Acute leukemia	6	1	1†

Would paclitaxel have given survival outcomes at least equal and better quality of life?

Slamon, N Engl J Med 2011;365:1273-83

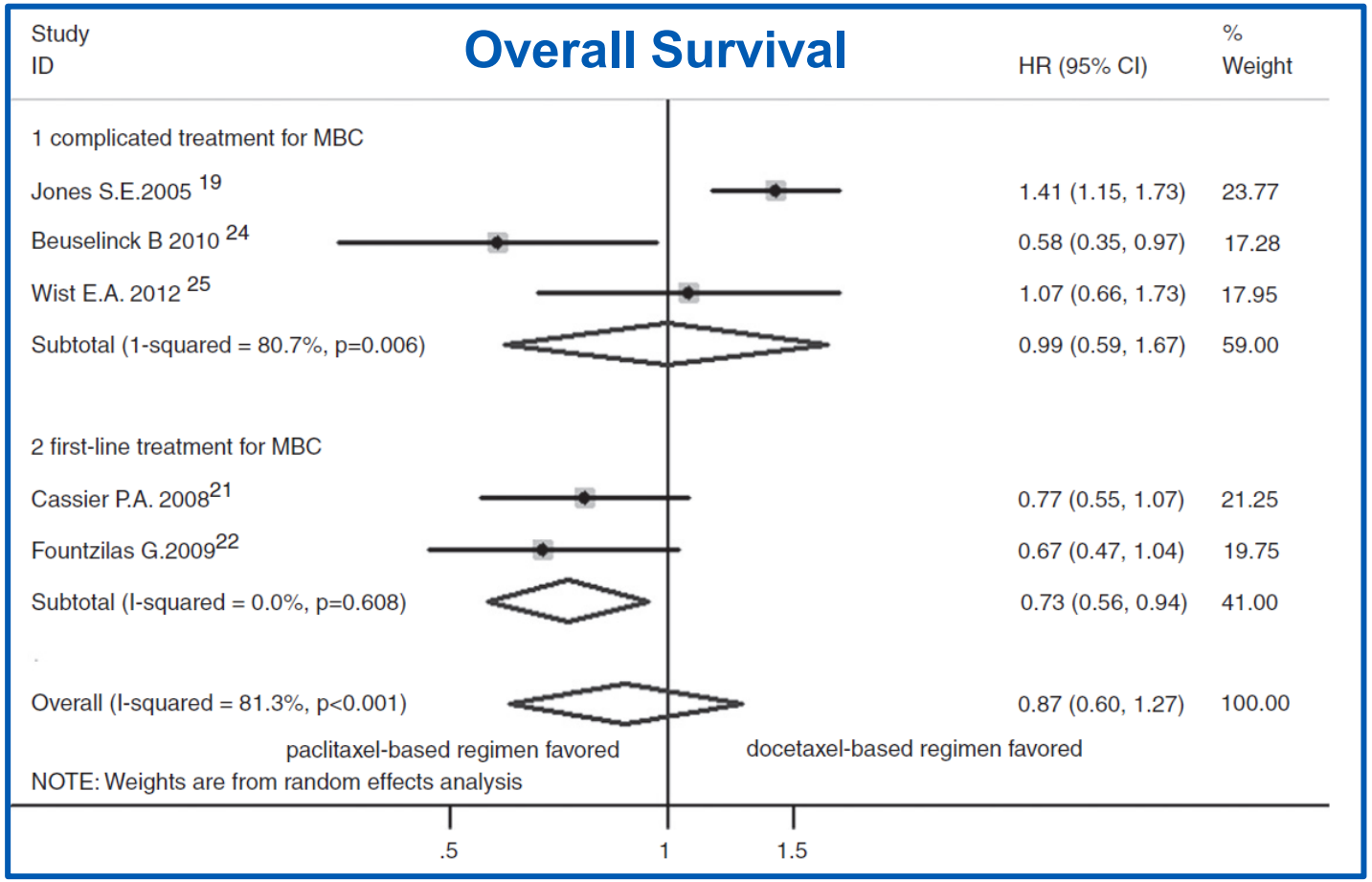
National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2025
Invasive Breast Cancer

HR-positive or negative and HER2-Positive
Patients with HR-positive disease are recommended to receive adjuvant endocrine therapy ± CDK4/6 inhibitor therapy (see BINV-K).
Preferred Regimens: Preoperative or adjuvant setting: • Paclitaxel + trastuzumab[f] (For very low risk disease – funded by patent holder for trastuzumab) • TCH (docetaxel/carboplatin/trastuzumab) • TCHP (docetaxel/carboplatin/trastuzumab/pertuzumab)

NCCN can only recommend guidelines supported by clinical trials

Paclitaxel-based vs Docetaxel-based regimens in Metastatic Breast Cancer: Systemic Review and Meta-analysis



Toxicity significantly less with paclitaxel

Neutropenia and fever
Anemia
Thrombocytopenia
Mucositis
Diarrhea
Fatigue

No toxicity significantly less with docetaxel

Qi, doi:10.1185/03007995.2012.756393

Taxanes, Survival and Quality of Life

- Would patients with early stage HER2 negative breast cancer have equal survival and better quality of life if they received:
  - Paclitaxel/Cyclophosphamide rather than Docetaxel/Cyclophosphamide
  - But there are no studies to support this approach

- Would patients with early stage HER2 positive breast cancer have equal survival and better quality of life if they received:
  - TCHP – paclitaxel/carboplatin/trastuzumab/pertuzumab rather than docetaxel/carbo/trastuzumab/pertuzumab
  - But there are no studies to support this approach

“Me-Too” Drugs Compared in Randomized Trials

“These results suggest a need for regulatory bodies to incentivize within-class RCTs. Such evidence would help determine whether next-in-class drugs provide meaningful advances in cancer care. This is particularly important given that me-too drugs have not led to price competition in oncology and many are approved through single-group trials or studies using suboptimal controls.”

Olivier, JAMA Internal Medicine 2025; doi:10.1001/jamainternmed.2025.2892

Zolendronic Acid in the Treatment of Bone Metastases

- Used in women with osteoporosis to improve bone density and reduce the risk of fractures
  - Administered once or twice per year
- Breast cancer, prostate cancer, lung cancer, and multiple myeloma have high rates of bone involvement
- The bone involvement can cause pain, bone weakening and fractures
- Bisphosphonates strengthen bone and reduce the likelihood of fractures
- Original studies administered zolendronic acid every 3 or 4 weeks indefinitely

Efficacy and Safety of Zoledronic Acid in Patients with Breast Cancer Metastatic to Bone: A Multicenter Clinical Trial

GIACOMO CARTENÌ,[a] ROBERTO BORDONARO,[b] FRANCESCO GIOTTA,[c] VITO LORUSSO,[c] SIMONA SCALONE,[d] VINCENZA VINACCIA,[c] ROBERTA RONDENA,[c] DINO AMADORI[f]

Administered every 3 or 4 weeks

The Oncologist 2006;11:841–848

Zoledronic Acid Versus Placebo in the Treatment of Skeletal Metastases in Patients With Lung Cancer and Other Solid Tumors: A Phase III, Double-Blind, Randomized Trial—The Zoledronic Acid Lung Cancer and Other Solid Tumors Study Group

By Lee S. Rosen, David Gordon, Simon Tchekmedyian, Ronald Yanagihara, Vera Hirsh, M. Krzakowski, M. Pawlicki, Paul de Souza, Ming Zheng, Gladys Urbanowitz, Dirk Reitsma, and John J. Seaman

Administered every 3 weeks

J Clin Oncology 12:3150, 2003

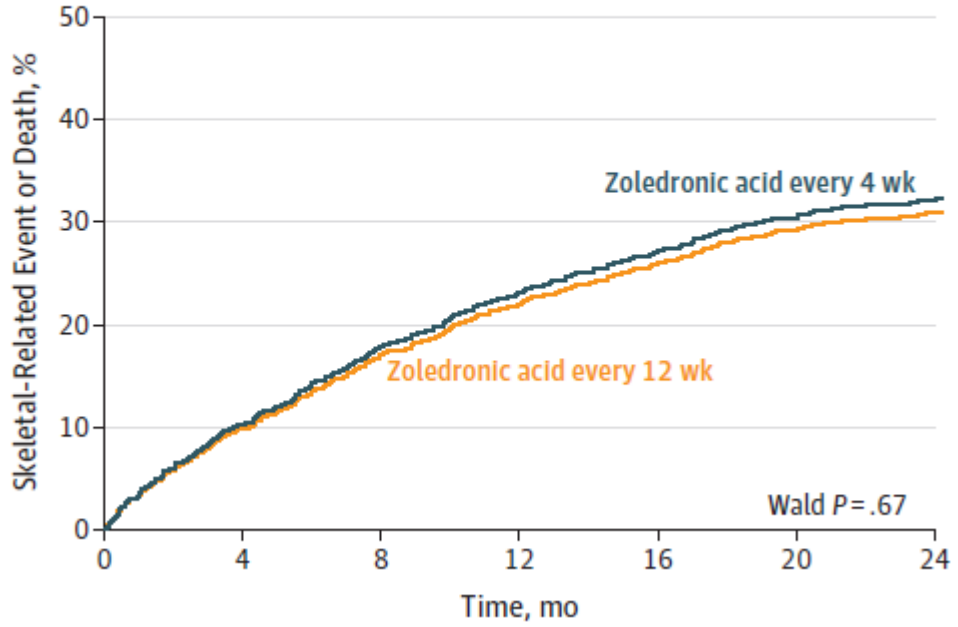
Funded by Pharma Patent Holder

JAMA | Original Investigation

Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in Patients With Bone Metastases

A Randomized Clinical Trial

Figure 2. Cause-Specific Cumulative Incidence of Skeletal-Related Events



- **>1800 patients randomized**
- **Osteonecrosis of the jaw**
  - 2% in 4 wk group
  - 1% in 12 wk group
- **Worsening renal function**
  - 20% in 4 wk group
  - 16% in 12 wk group

Funded by NCI Cooperative Group Alliance

Zolendronic Acid – every 4 wks vs every 12 wks

Advantages of every 12 wks

- Equally effective at reducing incidence of fractures
- 1/3 of the number of infusion room visits
- Maybe a reduction in complications – osteonecrosis and renal effects
- Less costly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