

Docetaxel and Paclitaxel in Breast Cancer

comparing the cost-effectiveness of different taxane regimens

SUMMARY

Breast cancer is the most common cancer in New Zealand women, and the second most common cause of death from cancer. Chemotherapy given after surgery reduces the risk of recurrence and death from regionally invasive breast cancer. The taxanes docetaxel and paclitaxel have been a key component of chemotherapy regimens since the late 1990s, usually given after anthracycline-based chemotherapy. Most guidelines do not specify which taxane is preferred as traditionally they have been considered similarly effective, although with different side-effects and costs. However, refinements in taxane regimens in recent years and dramatic changes in costs have changed the balance of effects, side-effects, costs, and cost-effectiveness between different taxane regimens. Re-evaluation is now appropriate to help guide funding decisions for taxanes. This pamphlet compares the cost-effectiveness of the two most commonly used taxane regimens: weekly paclitaxel and 3-weekly docetaxel.

We evaluated two taxane regimens, part of chemotherapy for early regional breast cancer

These were:

- Weekly paclitaxel
- 3-weekly docetaxel

These two regimens were compared to each other, and also to 3-weekly paclitaxel, the previous standard taxane regimen (now largely superseded). The taxanes were given sequentially with an anthracycline-based regimen.

We used a simulation model to estimate cost-effectiveness using NZ data

For each comparison, the model estimates how much health benefit is gained (in quality-adjusted life-years or QALYs) and how much it costs the health system until the end of life. These are combined into a single Incremental Cost-Effectiveness Ratio or ICER.

Health gain is through survival benefit

The main health gain from taxanes is through improved survival from breast cancer, but the model also takes into account health losses from the major side-effects of taxanes: febrile neutropenia and peripheral neuropathy. Compared with standard 3-weekly paclitaxel, the mean health gain per patient was greater with weekly paclitaxel at 0.51 QALYs than for 3-weekly docetaxel at 0.20 QALYs. Incremental costs (over and above standard 3-weekly paclitaxel) were also greater with weekly paclitaxel at NZ\$ 12,284 per patient than for 3-weekly docetaxel at NZ\$ 4,021. Moving from 3-weekly docetaxel to weekly paclitaxel would thus add 0.30 QALYs, but at an additional cost of NZ\$ 8,263 per patient.

Which is the most cost-effective?

Using a cost-effectiveness threshold of NZ\$ 45,000 per QALY (as per international guidance), both weekly paclitaxel and 3-weekly docetaxel are cost-effective compared to standard 3-weekly paclitaxel (ICERs of NZ\$ 23,900 per QALY and NZ\$ 19,400 per QALY respectively). Moving from 3-weekly docetaxel to weekly paclitaxel is still cost-effective at an ICER of NZ\$ 27,100 per QALY gained.

Our bottom line

Our model estimated, based on study data, a higher survival benefit for weekly paclitaxel than for 3-weekly docetaxel, although there remains uncertainty about this. If this assumption holds true and Government is willing to pay at least NZ\$ 27,000 per QALY, then weekly paclitaxel is the optimal choice because it achieves a greater health gain. If the two regimens are assumed to have equal effectiveness, then 3-weekly docetaxel is the optimal choice.

IN MORE DETAIL

Basics of Taxanes in Breast Cancer

The taxanes docetaxel and paclitaxel are now a standard part of chemotherapy regimens after surgery in women with early breast cancer. They improve survival when used sequentially with anthracycline-based chemotherapy regimens, compared to anthracycline-based regimens alone. Traditionally docetaxel and paclitaxel have been considered to be similarly effective. Guidelines do not usually specify which taxane is preferred, and decisions are usually based on costs and side-effect profiles. However, taxane regimens have been refined in recent years resulting in different costs and better outcomes. In particular, weekly paclitaxel has been shown to be superior to the previous standard 3-weekly paclitaxel. Additionally, the acquisition cost of docetaxel in New Zealand fell by 80% in 2011. Weekly paclitaxel and 3-weekly docetaxel are now the two most commonly used taxane regimens in breast cancer, but the cost-effectiveness of these two regimens have not been directly compared.

Two Taxane Regimens

The two taxane regimens we evaluated were:

	Regimen	Usage in NZ	Dose and Cycle	Impact on breast cancer survival in our model ^a
1	Weekly Paclitaxel	Common	12 cycles of weekly paclitaxel at dose of 80 mg/m ²	Reduces mortality from breast cancer by 27%
2	3-weekly Docetaxel	Common	4 cycles of 3-weekly docetaxel at dose of 100 mg/m ²	Reduces mortality from breast cancer by 13%

^a Survival benefit from the E1199 study adjusted from all causes of death to death from breast cancer (Sparano et al. NEJM 2008; 358 (16): 1663-71).

These two regimens were compared to each other and also to 3-weekly paclitaxel (4 cycles of 175 mg/m²), the previous standard taxane regimen (now largely superseded). All taxane regimens were preceded by 4 cycles of an anthracycline-based regimen (doxorubicin 60 mg/m² plus cyclophosphamide 600 mg/m²).

Model

We began with the population of women aged ≥ 25 years diagnosed with regional breast cancer in New Zealand in 2011 and used a Markov model to follow this population through to death or 110 years. For each of the taxane regimens, we estimated:

- Health gain in quality-adjusted life-years or QALYs
- Health system costs in NZ\$ (including additional health costs from extra life)
- Cost-effectiveness of each regimen in Incremental Cost-Effectiveness Ratios or ICERs (with each regimen compared to 3-weekly paclitaxel and to each other)

The model included the following health states that had different costs and different quality of life attached to them:

- Diagnosis and treatment phase (maximum 6 months followed by remission unless a fatal event occurred)
- Febrile neutropenia (maximum 4 days followed by recovery unless the event was fatal)
- Neuropathy (maximum 3 months followed by recovery)
- Remission (maximum 19.5 years)
- Cure (20 years post diagnosis)
- Preterminal (maximum 11 months)
- Terminal (maximum 1 month)
- Death from breast cancer
- Death from other causes
- Death from febrile neutropenia

QALY or Quality-Adjusted Life-Year:

The remaining life expectancy, adjusted for quality of life. Think of one QALY as one year of life in perfect health.

Assumptions in the Model

Our model contains multiple assumptions. Some of these assumptions apply across all BODE³ evaluations, and are described in a range of protocols at the BODE³ website [here](#). Some assumptions are specific to this topic: please refer to the published journal article for more information: Webber-Foster R, Kvizhinadze G, Rivalland G, Blakely T. [Cost-effectiveness analysis of docetaxel versus paclitaxel in adjuvant treatment of regional breast cancer in New Zealand](#). *Pharmacoeconomics* 2014; 32:707–724.

For more detail please refer to Webber-Foster R, Kvizhinadze G, Rivalland G, Blakely T. [Cost-effectiveness analysis of docetaxel versus paclitaxel in adjuvant treatment of regional breast cancer in New Zealand](#). *Pharmacoeconomics* 2014; 32:707–724.

Some of our key assumptions include:

- We used a health system perspective and so did not include costs and consequences beyond the health system (such as productivity costs).
- We allowed for expected or background disease and limited the maximum amount of QALYs that could be gained with increasing age.
- We applied a 3% per annum discount rate to costs and QALYs gained.
- We included unrelated health system costs (average expected costs to the health system).
- Individuals alive 20 years after diagnosis were assumed cured of breast cancer.

ICER or Incremental Cost-Effectiveness Ratio:

The difference in costs between one intervention and its comparator, divided by the difference in health gain. An ICER tells you how much more (or less) cost-effective an intervention is compared to something else.

QALYs, Costs & Cost-Effectiveness

Compared with standard 3-weekly paclitaxel, the mean health gain per patient was greater with weekly paclitaxel at 0.51 QALYs than for 3-weekly docetaxel at 0.20 QALYs. Compared with standard 3-weekly paclitaxel, costs were also greater with weekly paclitaxel at NZ\$ 12,284 per patient than for 3-weekly docetaxel at NZ\$ 4,021. Moving from 3-weekly docetaxel to weekly paclitaxel would thus add 0.30 QALYs, but at an additional cost of NZ\$ 8,263 per patient.

The ICER for weekly paclitaxel compared to 3-weekly paclitaxel was NZ\$ 23,900 per QALY gained. The ICER for 3-weekly docetaxel compared to 3-weekly paclitaxel was lower, at NZ\$ 19,400 per QALY gained. Moving from 3-weekly docetaxel to weekly paclitaxel is still cost-effective at an ICER of NZ\$ 27,100 per QALY gained.

A Note on Cost-Effectiveness Thresholds and Willingness-To-Pay

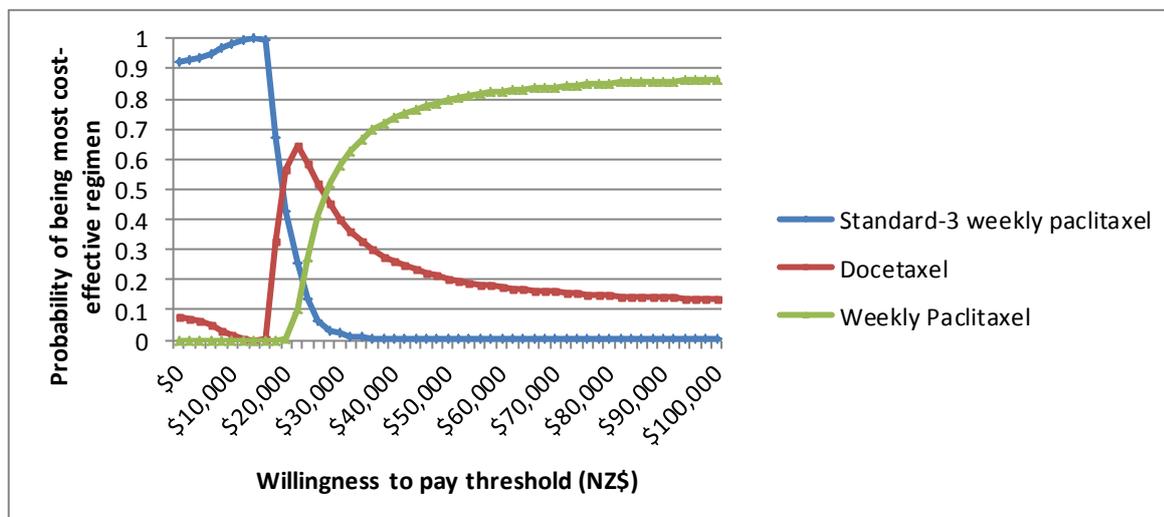
There is no consensus on a cost-effectiveness threshold in NZ. Our statements on cost-effectiveness stem from World Health Organization guidance, which is based on Gross Domestic Product (GDP) per capita. In NZ, GDP per capita is approximately NZ\$ 45,000. If the ICER for an intervention is less than NZ\$ 45,000 per QALY, we deem it cost-effective. However, our evaluations also make allowance for other thresholds, as shown below. It should also be noted that policy decisions are made on multiple considerations, and cost-effectiveness is only one of these.

Cost-effectiveness Threshold or Willingness-To-Pay:

Society's willingness to pay for an extra unit of health gain e.g. a QALY. If the ICER for an intervention is less than the threshold, the government can view it as cost-effective and may fund it. If ICER is greater than the threshold, it is not deemed to be cost-effective and the government may not fund it.

Which Taxane Regimen is Optimal?

There is always uncertainty around the estimates of cost-effectiveness. There is also variation in how much the government is willing to pay to gain 1 QALY. The graph below is a cost-effectiveness acceptability curve which takes both these factors into account. At different levels of willingness-to-pay, it shows the probability of each regimen being the most cost-effective of the three.



The graph shows that if government is willing to pay:

- Up to NZ\$ 20,000 per QALY gained: standard 3-weekly paclitaxel is the optimal choice
- Between NZ\$ 20,000 and NZ\$ 27,000 per QALY gained: 3-weekly docetaxel is the optimal choice
- Above NZ\$ 27,000 per QALY gained: weekly paclitaxel is the optimal choice

Costs, QALYs & Cost-Effectiveness in Different Populations

Age	Half the health gain and a little less costly for patients ≥ 65 years, overall less cost-effective compared to patients < 65 years for all comparisons.
Deprivation	No major differences between least deprived and most deprived.
Ethnicity	No major differences between Māori and non-Māori

Uncertainty in our Results

There is unavoidable uncertainty present in the values we put into our models, and thus uncertainty in estimates of costs, health gains, and cost-effectiveness. The greatest uncertainty is around the relative breast cancer survival benefit from 3-weekly docetaxel and weekly paclitaxel.

Changing Some Inputs and Assumptions

The results of the evaluation are sensitive to different inputs and assumptions. For example:

What if 3-weekly docetaxel and weekly paclitaxel had equal effectiveness?	The ICER for weekly paclitaxel compared with 3-weekly docetaxel increases to over NZ\$ 130,000 per QALY. Weekly paclitaxel becomes cost-ineffective versus docetaxel.
What if we ignore background disease as people age?	Health gains and cost-effectiveness for all comparisons improve by about 25%.
What if we discounted at different rates?	At a discount rate of 0%, cost-effectiveness improves by 13 to 20% for all comparisons. A discount rate of 6% worsens cost-effectiveness by about 13 to 20%.

Our Bottom Line

- 1 Both weekly paclitaxel and 3-weekly docetaxel are likely to be cost-effective compared with standard 3-weekly paclitaxel.
- 2 If the government is willing to pay at least NZ\$ 27,000 per QALY, weekly paclitaxel is the optimal choice because of the greater health gain.
- 3 Our model estimated, based on study data, that weekly paclitaxel provides a greater survival benefit than 3-weekly docetaxel, although there is uncertainty about this. If the two regimens were assumed to have equal effectiveness, weekly paclitaxel becomes cost-ineffective compared to docetaxel.