



VITAL BREAST CANCER DRUGS HIGHLIGHT FUNDING ETHICS

The ongoing reluctance to proclaim two breast cancer drugs proven to slow early disease progression and save lives for specific indications has frustrated State medical oncologists anxious to thrash out a speedy solution, especially in the Western Cape.

They are in urgent talks with resource-constrained Western Cape and national pharmaceutical coding committees, whom they say have quibbled for years, citing drug cost inequities, cost inefficiencies and data paucity on 'life years'. Widely known as the most prevalent cancer in women nationally, the only available caseload data (National Cancer Registry, 1999) put annual breast cancer diagnoses in South Africa at 6 000, with the lifetime risk for women at 1 in 27.

Texanes, a class of drugs which show overall survival benefits of about 5% and proven non-recurrence benefits in early-stage diagnosis, would cost the country about R120 million annually (based on an estimate of 2 000 early-stage public sector patients). Trastuzumab (Herceptin) on the other hand, boasts a 50% decrease in relapse and a one-third improvement in survival in a potentially curable setting, making it a highly attractive clinical option. Used together, they can be highly effective.

However there is one snag: trastuzumab would cost about R200 million per annum to theoretically cure just 30 women (based on 600 eligible public sector patients), raising the cost bar to what coding committee members regard as impossible heights.

Professor Paul Ruff, head of medical oncology at Wits University/Johannesburg General Hospital, who made these calculations 'for illustrative purposes only' told *Izindaba* that it 'basically comes down to a money issue'. He said texanes were available

on public sector hospital codes in Gauteng and KwaZulu-Natal but in very few, if any, other provinces. He confirmed that there was no uniform national drug committee proclamation on either drug.

Western Cape oncologists are now engaging more fully with their own committee, which has displayed what some of them earlier regarded as a fatal lack of urgency.

Professor Justus Apffelstaedt, head of the multidisciplinary breast clinic at Tygerberg Hospital, estimates, based on First-World data, that the lack of wider availability of texanes alone costs 'too many' lives annually in his province.

Apffelstaedt, whose Tygerberg clinic treats about 350 new cases of breast cancer a year, said texanes increased absolute survival rates in the USA by 2 - 4% (in populations that generally reported far earlier for treatment than was usual in South Africa).

SA breast cancer treatment 'suboptimal'

He claimed texanes would push up the survival rate in the Western Cape by 'at least double these percentages', translating to a 'significant number' of lives a year (based on 1 000 new breast cancer cases per year). 'With texanes, breast cancer patients will recover more often and earlier,' he asserted, adding that its non-availability was particularly frustrating when it was being used in equivalent public sector facilities elsewhere.

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'What's excruciating is that the pharmaceutical coding committee has had motivations from us four times in as many years and turned them down on ludicrous grounds. We can see they don't have a clue about oncology and what's needed'. Apffelstaedt said that for the typical public sector patient presenting with low-key pre-metastatic breast cancer, texanes presented a 14.7% better chance of them being alive in 10 years' time than with the currently available CMF-like chemotherapy.

Texanes and trastuzumab are on the WHO guidelines for breast cancer treatment and are internationally considered highly appropriate clinical therapies.

A senior specialist in clinical and radiation oncology, who did not wish to be named for fear of damaging the 'very constructive relationship' with the drug committees, said there were 'massive' studies in texanes and trastuzumab for curative therapy.

'Sure, I don't jump up and down about the texanes metanalysis where the overall post-metastatic survival benefit is about 5%, but trastuzumab with its 50% decrease in relapse and so far a one-third improvement in survival in a potentially curable setting, is worth going for!'

'The drug committee keeps asking us for qualities (quality-of-life year measurements). I've had several individual (pre-metastatic) applications turned down in the last year.'

Many medical oncologists want to use trastuzumab with texanes in a curative setting, especially where other chemotherapy is contraindicated. One charged: 'We have almost no lines of treatment here for breast cancer. In the private sector you give one and then another, or a 'top dressing'. Their team had 'bust a gut' to obtain approval for the drugs, to no avail.



'I think that in the next 3 - 4 months (from August), we'll have data on taxanes for every condition, so it can be a definite yes or no,' he said.

Drug manufacturer Roche had promised the local public sector oncologists a 'special price' from overseas several years ago, but this never materialised.

Drug committee member replies

A senior member of their province's pharmaceutical coding committee and member of the national tertiary and quaternary Essential Drugs List (EDL) committee, who also asked not to be named for fear of 'creating an unhelpful climate', said the issue was 'complex'.

Reporting the issue in 'an emotive way' belied the complex health economics, 'unconvincing' quality-of-life data and the ethical considerations of formulating a consistent and equitable drug policy in a resource-poor setting. He did add, however, 'they've been slow to ask and we've been slow to respond', admitting that the provincial committee had been 'somewhat obstructive because we're trying to develop a (uniform) national policy on how we look at oncology'.

From a brutal cost point of view, the dilemma for funding breast cancer drugs centres on relative and absolute risk; in other words, does one proclaim drug therapies for saving *and/or* prolonging lives and, if so, what is the quality of the lives so prolonged?

The committee member said he hoped this would be rectified nationally for taxanes before the year's end, but ruled out trastuzumab as 'just too expensive'.

'I think that in the next 3 - 4 months (from August), we'll have data on taxanes for every condition, so it can be a definite yes or no,' he said. He claimed the taxanes data were inconclusive, mainly because most studies were in populations with advanced metastatic disease.

Professor Bettina Taylor, Head of Health Policy at Medscheme Health Risk Solutions and a member of UCT's Research Ethics Committee, said confrontation between clinical policy makers and treating doctors was 'not unexpected, given the different perspectives'. The policy makers often cited the huge price tags for drugs as unjustified by the extra months of life they might offer and, perhaps more importantly, other lives lost as a result of limitations of the health care system. The 'lost opportunity' costs of allocating additional funds to expensive new drugs had to be considered, she said, citing a potentially 'more effective' reduction of breast cancer deaths by channelling the same funds towards improving surgery waiting lists.

Listing chemotherapeutic agents on provincial and national drug lists provided them with Prescribed Minimum Benefit (PMB) status – a vital factor in the ongoing debate. Such listing would impact negatively on the affordability of such options and further deepen the inequity of the existing PMB package.

She added that, given the link between public and private sector drug policy, it was 'somewhat unfortunate' that the representatives of the private funding industry had to date, to the best of her knowledge, not been consulted in the collation of the EDL.

Private medical schemes currently paid for taxanes and trastuzumab, but access within lower contribution options tended to be limited to keep the scheme affordable.

Oncologists 'suddenly got louder'

The *Izindaba* drug committee source said medical oncology had 'generally been very quiet', but in the last year became very vocal, 'motivating us more, probably because of international clinician peer pressure'.

Because of the overlap between the national and local coding processes,

'we thought it useful to let the national process run its course. There's so much emotionality it's worthwhile having a team effect, even if it is slower.'

He explained his 'lack of data' rationale thus: 'We're caught up in an ethical dilemma because the clinical trial scenario is moving but there's been no declaration on the cost-effectiveness of the backbone therapy'.

The majority of biological plausibility studies of new agents were conducted in metastatic disease before being tested in a primary setting. 'With breast cancer if you catch it early and give chemo you can aim for cure, that's the gold standard. Then if patients present late and there's a metastatic disorder and you're not curing, they're going to die, but it will take a long time,' he said.

He said the mantra of oncologists was that 'some therapy must be offered'. 'However we have to ask, how much longer do they live?'

While taxanes had shown biological plausibility in many cancers, the only data his committee had on taxanes were for metastatic ovarian carcinoma. 'We ask for quality-of-life data that make for cost efficiency, but we're caught up in this scenario that the drugs are internationally recognisable and our guys (clinicians) are embarrassed'.

Now that the matter had 'come to a head, we're going to sit down and try and find a mechanism for moving forward'. It would be 'inequitable to put carcinoma on a pedestal', when other diseases deserved to be judged on the same criteria. 'Nor can we accept slightly immature data on breast cancer,' he added.

In the UK the National Institute of Clinical Excellence paid out the

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equivalent of between R435 000 and R580 000 for one quality-adjusted life-year. 'In resource-poor settings we just don't have the same value. It sounds terrible, but what is the value of a life? We're the ones who have to divvy out the money!'

Ruff said about 40% of breast cancers occurred in Gauteng, 25% in the Western Cape, with KwaZulu-Natal and the Free State together totalling about 30%. The remaining 5% occurred in provinces with little or no appropriate health care infrastructure.

'We don't really know what we're doing because the cancer data are so bad in this country,' he cautioned.

Chris Bateman