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The Economic Impact of 5-HT$_3$ Receptor Antagonists

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JONES AND COLLEAGUES present data on the budgetary impact of the 5-HT$_3$ receptor antagonists [1]. However, their model makes no attempt to quantify the financial and resource benefits of using the 5-HT$_3$ receptor antagonists in terms of their enhanced efficacy and tolerability (i.e. the costs associated with caring for a patient experiencing emesis or the side-effects of conventional antiemetics). In this regard it is of particular interest that Jones *et al.* suggest that the use of the 5-HT$_3$ receptor antagonists is not justified over the delayed emesis period. They have ignored data in the literature that report good efficacy for oral ondansetron over this period [2–4], and show that it is superior to placebo and metoclopramide following cisplatin [5] and non-cisplatin [6] chemotherapy, respectively. Clearly, the role of the 5-HT$_3$ receptor antagonists over this period needs to be further defined; in particular, to quantify the additional benefits resulting from their enhanced tolerability and impact on patients' quality of life [7, 8]. Conventional antiemetics have a significant propensity for side-effects, e.g. extrapyramidal reactions and sedation which are associated with impaired quality of life. The lack of such side-effects with ondansetron enables patients to carry out normal daily activities at home or work.

The cost effectiveness of 5-HT$_3$ receptor antagonists in clinical practice can only be fully evaluated from a broader perspective. Limiting the scope of evaluation to drug acquisition costs ignores the financial consequences of treatment failure and side-effects.

Table 1. GM-CSF-related side-effects in 59 testicular cancer patients treated with intensified PEI chemotherapy

Side-effects	Number of patients		
	5 μg/kg	10 μg/kg	Total
Anaphylactic type reaction (bronchospasm, myalgia, fever, skin reaction)	2	3	5 (8.4%)
Fever (without infection)	0	3	3 (5.1%)
Cutaneous reaction alone	1	1	2 (3.4%)

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Ductal Carcinoma *in situ*

Melvin J. Silverstein

DR LAWRENCE [1] correctly states that our 7-year actuarial recurrence rate following tumourectomy and radiation for patients with ductal carcinoma *in situ* (DCIS) is 10%. Since half the treatment failures were invasive, he assumes that the "risk of invasive cancer in DCIS patients treated with tumourectomy and radiation is 5%" at 7 years. Since he does not have the raw data and does not know the timing or the type (invasive or non-invasive) of each recurrence, this 5% figure may or may not be true. He then goes on to compare this 5% invasive recurrence rate in our treated DCIS patients with a number that he claims represents the general population's chances of developing invasive breast cancer, a figure of 12–15%. He then concludes that the treated DCIS patient has a lower risk of developing invasive breast cancer than women in the general population: 5 vs. 12–15%. He goes on to say that "mastectomy is more prophylactic to prevent invasive cancer than therapeutic for DCIS". Then using 5 vs. 12–15%, he says "based on statistical risk, all women over 60 should be recommended for mastectomy".

The risk of developing invasive breast cancer quoted by The American Cancer Society is 11% [2] not 12–15%. More importantly, this is the cumulative risk if the patient lives to the age of 110. It is not the risk over the next 7 years (which is extremely small) and thus it cannot be compared with the 7-year actuarial recurrence risk stated in our paper.

What Dr. Lawrence has done is to compare the short-term risk of local recurrence in an irradiated DCIS patient with the long-term, life-time risk of any woman developing invasive

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breast cancer, an unfair comparison, an apple with an orange. Any conclusion based on this comparison is erroneous.

In addition, Dr. Lawrence's suggests that mastectomy is our first choice for the treatment of DCIS. Nothing could be further from the truth. In the late 1970s, The Breast Center was the first group in Los Angeles aggressively espousing breast conservation therapy as an equivalent treatment, in terms of survival, for favourable breast carcinomas when compared with mastectomy. In quality of life terms, it is better than mastectomy. To us, mastectomy is a last resort, not the treatment of choice. Currently, almost 70% of our patients with breast cancer are treated with breast conservation. In our paper, we stated that "excision and radiation was the appropriate choice for patients interested in preserving their breasts, who met the clinical criteria used in the study, and who were willing to assume a small, but not absolutely quantifiable risk of local recurrence" (most patients). For those patients who are absolutely unwilling to assume any increased risk, no matter how small (a very small percentage of patients), we suggest mastectomy. This is a far cry from a general recommendation of mastectomy for all patients with DCIS and it should not be misconstrued to mean that. When Dr. Lawrence uses his statistics to say that (bilateral) mastectomy should be considered for all women over 60, he isn't serious (we hope). We think he's questioning why any mastectomies at all are done for patients with this low grade disease [3]. Dr. Lawrence is a great believer in breast preservation and so are we!

Since we wrote the referenced paper [4], we have become even more conservative. Impressed by the serial subgross work of Holland *et al.* [5] showing that most DCIS lesions are larger than expected but unifocal, we have begun treating selected DCIS patients with true quadrantectomy and plastic surgical repair of the breast. When clear margins are achieved no radiation therapy is given.

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Corrections

Breast Cancer Working Conference—The 6th EORTC Breast Cancer Working Conference (*European Journal of Cancer* Vol. 29A, No. 4, p. 648) will be held in Amsterdam on 6–9 September 1994, not 1993 as previously stated.

Steroid Receptor Enhancement by Natural Interferon-β in Advanced Breast Cancer by G. Sica *et al.* In this article published in Vol. 29A, No. 3, pp. 329–333, the column headings of the table below were unfortunately misprinted.

Table 3. Side-effects recorded during treatment

Side-effect		Number of patients (% of cases) Group A	Group B
		22	23
Fever	<38°C	3 (13.64)	8 (34.78)
	>38°C	1 (4.54)	1 (4.35)
Shiver	Grade I	3 (13.64)	2 (8.69)
Asthenia	Grade I	3 (13.64)	2 (8.69)
	Grade II	1 (4.54)	2 (8.69)
Arthralgia	Grade I	1 (4.76)	1 (4.35)
Leukopenia	Grade I	1 (4.54)	1 (4.35)
	Grade II	1 (4.54)	1 (4.35)
Somnolence	Grade II	0	1 (4.35)
Itching	Grade II	0	1 (4.35)
Hypertension	Grade II	1 (4.54)	0
Transaminases	Grade I	0	1 (4.35)
	Grade II	0	1 (4.35)
	Grade IV	0	1 (4.35)
γ-GT	Grade I	0	2 (8.69)
	Grade IV	0	1 (4.35)
Lactate dehydrogenase	Grade III	0	1 (4.35)
Alkaline phosphatase	Grade I	2 (9.09)	2 (8.69)

*Treated with IFN-β for at least 2 weeks.