EDITORIAL

Selling ourselves short

Aprikian, Fleshner, Langleben and Hames have carried out a provocative analysis comparing the cost per month of survival benefit with maximal androgen blockade compared to systemic interventions for advanced breast and colon cancer. The study showed that the survival benefit of MAB using a non-steroidal anti-androgen was about 50% of the cost of vinorelbine for lung cancer, 10% of the cost of irenotecan for colon cancer, and 10% of the cost of trastuzumab for breast cancer.

Good health care is expensive. Much of what we do is directed towards relieving pain and suffering, rather than extending life. Measures which extend life should be taken seriously, (not withstanding that this extended life needs to have quality to be worthwhile). Even a modest survival benefit, adjusted for quality of life effects, may be of great importance to the individual patient.

This benefit has been discounted with respect to MAB. The question of MAB vs monotherapy, the single most studied clinical question in Urology (27 prospective randomized blinded trials at last count), has been answered about as definitively as its been possible to do in a rapidly changing field where a minor survival benefit is anticipated. The answer from multiple systemic overviews and meta-analyses, is that MAB offers a minor survival benefit. This can be characterized as a 10% reduction in the risk of death at 5 years, or a 3 month survival benefit in metastatic disease. Quality of life effects of MAB compared to monotherapy are minor.

And yet, the pundits have rejected this benefit. A landmark, and in my view, opinion shifting article from Hopkins, entitled "Complete androgen blockade for prostate cancer: What went wrong?[1] concludes as follows:

> **"The data strongly indicate that the most compelling explanation for the occasionally positive trials is that the overall complete androgen blockade effect size is indeed minimal, and, *IN OUR OPINION*, of negligible clinical significance."**

The acknowledgement that the authors are simply giving a personal opinion is welcome, but doesn't excuse it.

Aprikian et al document the survival benefits with the systemic therapies used at such great expense in lung, colon, and breast cancer: 2 to 5 months, essentially the same benefit as for MAB, so lightly discounted by Laufer et al. In most cases, the side effects of these therapies are considerably more severe.

We've sold the survival benefit of MAB short. Undoubtedly, the benefits of MAB are confined to some subsets of patients; some patients may benefit a great deal, while others may not benefit at all. The benefit in non-metastatic disease is unknown, but may be more substantial (in duration) than in metastatic disease. The benefit may be greater when anti-androgens are stopped on progression, (the randomized studies were initiated in the pre-PSA, pre-anti-androgen withdrawal era, invoked anti-androgen until death, and used flutamide or nilutamide) and may be greater with the newer anti-androgen (bicalutamide). Aprikian et al have demonstrated that the cost is acceptable compared to other standard interventions for cancer. This is an important contribution to the literature. We should embrace the modest survival benefit of MAB and offer it to appropriate patients.

Stothers has produced a superb summary of the role of nitrous oxide in patients with overactive bladders. The nitrous oxide pathway has gone from an obscure gaseous mechanism involved in erectile function, to a fundamental physiologic system implicated in a host of pathophysiologic pathways, including bladder dysfunction and neoplastic transformation. It behooves all urologists interested in mechanisms of disease to be familiar with this area, and this article is a very clear summary of the field.

1. Laufer M, Denmeade SR, et al *J Urol* July 2000;164:3-9.

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