Book report

A quiet revolution in the endocrine therapy of breast cancer

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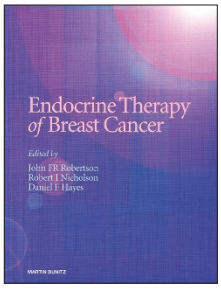

A new generation of physicians and scientists should obtain a copy of *Endocrine Therapy of Breast Cancer*. The book is a welcome addition to one's personal library or for purchase by a departmental library. The style and presentation are good with an excellent balance of clinical research and basic science. Although it is not stated, the prospective audience seems to be physicians-in-training, scientists engaged in cancer research and PhD students who need to learn about pioneering advances in targeted cancer therapeutics.

The book is divided into 15 chapters with two major sections covering the use of endocrine therapy in clinical practice and the biological aspects of endocrine therapy. The two clinical editors, Daniel Hayes and John Robertson open the first chapter with powerful statements: 1) "one of the greatest success stories in the history of cancer treatment has been the application of endocrine treatment for breast cancer" and 2) "it is fair to say that endocrine therapy can be considered the paradigm for molecular medicine as a whole with a considerable two-way interaction between the laboratory and the clinic." The editors have selected a distinguished medical oncologist, Gabriel Hortobagyi, to write the Forward because he witnessed the "quiet revolution" and saw how the knowledge about the oestrogen receptor, which at that time was a potential predictive test for endocrine ablative surgery, was transformed to become a successful target for therapeutics.

It is important to have a book that states where we are and where a future path will take us and the authors do a good job with this work. Robert Nicholson is an excellent scientific resource and provides an outstanding perspective to the current and future directions in endocrine research. Kathleen Pritchard, another author whose experience reaches back to the genesis of targeted endocrine therapy, writes an encyclopedic chapter on ovarian ablation. For a revised edition (and there should be revised editions in this pharmaceutically important area) I would like to see a separate chapter on a balanced argument about the endocrinology and efficacy of combination chemotherapy versus complete endocrine blockade in oestrogen receptor positive premenopausal patients. Perhaps a combined chapter from opposing camps would be fun!

The editors, for completeness, state the laboratory and clinical case for antiprogestins as rational therapy in breast cancer. A case for a role of progesterone or progestins in carcinogenesis can be made both in the laboratory and clinic but the development of an antiprogestin as a targeted breast cancer drug has "lost the plot". The response rate with antiprogestins has been extremely low and the concern I have is that at the 100 mg daily doses they also have oestrogenic actions [1]. Could the results with antiprogestins, at enormous doses, be a variation on "high dose" oestrogen therapy in breast cancer? This is not an unreasonable suggestion as we go back to the future and again consider oestrogen therapy after exhaustive antihormone treatment as stated in Chapter 4. There needs to be a rethink in subsequent editions about the need for antiprogestin chapters. Nevertheless, there is clearly a need to address the shortcomings of the concept today.

Finally, as a molecular pharmacologist, my evaluation of accuracy is often drawn to the formulae. The structure is the life or death of a targeted molecule. Unfortunately, the editors need to encourage the publisher to transpose formulae correctly, as incorrect structures can mislead in a reference work. Page 48 is a case in point with many formulae incorrectly copied (5 out of 10) and one investiga-

tional compound, SR16234, is not referenced in the text. This is not the only problem as the structure of anastrozole is incorrect on page 236.

Despite these minor shortcomings, the editors and authors provide a new generation with an excellent state-of-the-art book. The work truly reflects how much has been achieved in endocrine therapy in thirty years. The key to the successful advance with medicines targeted to the oestrogen receptor was the resurrection of the compound ICI 46,474, as tamoxifen, after it was abandoned in 1972. Although the story of the development of tamoxifen is not mentioned in the book it is documented elsewhere [2].

Although my clinical colleagues in the book trace the story back to George Beatson and a response in a single patient in 1896, I think that success for molecular targeting in cancer in modern times can be viewed quite simply. When asked how contraceptives worked, Gregory Pincus, the father of the oral contraceptive, replied, "no ovulation, no egg, no baby." By analogy, the evolution of the *Endocrine Therapy of Breast Cancer* could be summarized as – no target (oestrogen receptor), no drug (tamoxifen), no story.

Competing interests

None declared.

References

1. Jeng MH, Langan-Fahey SM,Jordan VC: **Estrogenic actions of RU486 in hormone-responsive MCF-7 human breast cancer cells.** *Endocrinology* 1993, **132:**2622-2630.
2. Jordan VC: **Tamoxifen: a most unlikely pioneering medicine.** *Nature Reviews Drug Discovery* 2003, **2:**205-213.

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