Report

Improvement of quality control for steroid receptor measurements: analysis of distributions in more than 40000 primary breast cancers

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Summary

All French laboratories that routinely assay estradiol (ER) and progesterone (PR) receptors participate in the European EORTC quality control program based on twice-yearly analysis of 5 cytosolic preparations. This system has considerably reduced inter-laboratory variations, but does not cover all aspects of these assays. Analysis of receptor value distributions is also crucial to ensure that receptor measurements remain stable with time, independently of the laboratory and assay method. This study involved 83907 receptor assays carried out in the last 17 years by 17 laboratories belonging to the French Study Group on Tissue and Molecular Biopathology. The assays were based on radioligand binding (RLA) or immunoenzymology (EIA). For each laboratory, the medians and positivity rates were analysed according to two totally objective criteria, the patient’s age and the year of assay, and according to histological grade and histological type of the tumor in order to verify the correlations classically described. Age-related distributions varied little between laboratories, compared with data published by 7 European EORTC laboratories [1]. The results remained relatively stable with time in the RLA method for ER and PR, and in the EIA method for PR. Median ER-EIA data showed a marked increase between 1987 and 1989, mainly due to changes in the quality of Abbott reagents during this period. Otherwise, this analysis confirms previous pathophysiological observations.

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Introduction

Estradiol (ER) and progesterone (PR) receptor assays are routinely used for the choice of breast cancer treatment, given the poor prognosis of tumors that lack these receptors [2, 3] and, above all, the higher probability of a response to hormone therapy when they are present [4–6]. A cut-off value (10–20 fmol/mg protein) is commonly used to distinguish between ‘negative’ and ‘positive’ tumors. In addition, various publications have shown the value of quantitative assays in clinical studies [4, 5]. Since 1980 the EORTC Receptor Study Group has been providing recommendations for the standardization of ER and PR assays [7–13]. It has also set up quality controls for these assays [11] and more than 140 European laboratories now adhere to them. These quality controls, based on the analysis of cytosolic preparations distributed by a central coordinator (Professor Benraad, Nijmegen), have considerably reduced inter-laboratory variations. However, a number of steps are not covered by the quality control set-up, sampling protocols, cytosol preparation, data expression, and cut-off values. As

Figure 1. Distribution of ER-RLA according to age of the patients. Numbers in italics represent coefficients of variation (CV) between laboratories. (a) EORTC Receptor Study Group; (b) French Study Group on Tissue and Molecular Biopathology. (Figures 1–4, part a, are reprinted from: Eur J Cancer, Vol 31A, No 3, pp 411–417, 1995; Romain S, Lainé Bidron C, Martin PM, Magdelénat H on behalf of the EORTC receptor study group: Steroid receptor distribution in 47892 breast cancers. A collaborative study of 7 European laboratories: with kind permission from Elsevier Science Ltd, The Boulevard, Langford Lane, Kidlington OX5 1GB, UK.)