Response to the Comments of K. Metze and R.L. Adam on the paper “c-erbB-2 expression and nuclear pleomorphism in canine mammary tumors”

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The following is our response to the comments of K. Metze and R.L. Adam (1).

The proto-oncogene c-erbB-2 is encoded in a tyrosine kinase receptor protein that has been described in different tumors and animals. Since the initial report by Slamon et al. (2), which showed an association between amplification of this gene and poor prognosis in breast cancer, several other studies have demonstrated overexpression of c-erbB-2 in about 10 to 20% of invasive breast carcinomas. The demonstration of a high percentage of c-erbB-2 overexpression in breast carcinomas suggests that it could represent an early event in breast carcinogenesis in humans (3-8) and dogs (9-11).

In our paper (12), we did not find any correlation between survival and c-erbB-2 expression or nuclear pleomorphism (P > 0.05), which is commented on by Metze and Adam (1). Really, the statistical method (Spearman rank correlation) is not the most adequate to evaluate the survival in this case as commented by Metze and Adam. However, the analysis by Kaplan-Meier plots as suggested would not be appropriate because of the small number of cases studied in our report.

Quantitative methods used in the evaluation or analysis of immunohistochemical and histological sections are very much discussed in the literature. Even imaging analysis methods do not seem to be standardized yet (13-17). The Hercept Test is the FDA-approved in vitro diagnostic test marketed by DAKO. It is a semi-quantitative immunohistochemical assay used to determine overexpression of HER-2 protein in breast cancer tissue, which considers percentage of marked cells and membrane staining intensity. There are criteria for interpretation of the staining results for Her-2/neu when the HercepTest is used, but the determination of staining intensity, percentage of complete membrane and cells staining is subjective. However, in a large number of studies the reproducibility of immunohistochemical analysis of cerbB-2 expression is satisfactory (18-22).

In conclusion, the main objective of our study was to demonstrate that spontaneous canine mammary tumors could be used as a model to study the mammary carcinogenic process. It is relevant to the study of human breast cancer, because we are using the same criteria and methods applied to breast cancer studies.

References

2. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ulrich


