Working Group on Tumor Marker Criteria (WGTMC)

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Dear Sir,

During the ISOBM meeting in Quebec, September 1987, the working group on tumor marker criteria was founded. Its main assignment is to draw up general rules to help the interpretation of tumor marker concentrations in blood. All members have been consulted and the subjoined rules are a compilation of their comments. The WGTMC has drafted minimal demands for the establishment of reference values. It has also indicated the conditions for correct interpretations of marker alterations. We conclude by mentioning some general opinions.

A. To establish reference values one should use:

age-matched healthy controls;

international staging criteria; i.e., FIGO, TNM or Dukes' classifications.

B. For diagnostic purposes:

The reference value should be gathered from age-matched controls with appropriate benign disease of the same organ(s) and/or comparable tissue.

The adjoining histochemical report should be referred to.

The interpretation of changes in tumor marker levels should depend on whether or not anticancer therapy is administered.

A. If no therapy is given:

At least a linear increase in three consecutive samples (i.e. two time intervals) on a long scale should be registered to establish a recurrence. Usual intervals could be 3 months but are clinically determined. After a first increase, next samples should be taken after 2–4 weeks, irrespective of the absolute level (i.e., levels might be within the reference limit).

B. Changes in marker levels during therapy:

Increase in marker levels during therapy. Progressive disease is defined by an increase in the marker level of at least 25%. Sampling should be repeated within 2–4 weeks for additional evidence. 'Spiking' after the start of therapy should be excluded. The sampling interval during therapy may depend on the type of tumor and should be related to clinical follow-up.

Decrease in marker levels during therapy. With the concept that tumor load is related to the changes in serum tumor marker levels partial remission should be defined as a decrease of at least 50% in the marker level. Sampling should be performed before the start of chemotherapy courses.

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General opinions: A complete remission cannot be determined by marker levels, but if tumor marker levels are elevated the clinical decision of complete remission based on conventional methods should be considered incorrect unless an explanation for the presence of the elevated level is given.

The WGTMC also paid attention to the (apparent) half-life of tumor markers. The rate of decrease of tumor marker levels cannot be used as proof of a pathologic complete remission. The absence of an exponential decrease, however, is an ominous sign. The WGTMC would like to add to these statements that the phenomenon of the mixed response to anticancer therapy can be a pitfall in the interpretation of results. This aspect indeed needs further attention.

We hope that the WGTMC has set a number of criteria that will enable researchers and clinicians to compare and apply their results in a more fruitful way in the future.

For the working group of tumor marker criteria,

Dr. J.M.G. Bonfrer, Secretary

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