

Afssaps Market control of MUC-1/CA 15-3 in vitro medical devices in vitro (2006/2007)

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The dosing of MUC-1, in practice, is used in the monitoring of patients with breast cancer in order to detect relapses and to evaluate the effectiveness of the treatment of advanced forms. It cannot be used to screen for breast cancer in the general population. On the other hand, if the level is high at the time of the diagnostic assessment of breast cancer, it makes it possible to correct stage classification and the therapeutic strategy which results from this.

Following analytical problems revealed by national quality monitoring operations and by European Oncochek monitoring concerning dosings of MUC-1/CA 15-3 in which results from the same sample were 'normalized' or were raised depending on the kits used, Afssaps carried out a control of the devices on the market.

The objective of this control was to evaluate the diagnostic performances of these devices in regard to a panel of one hundred and twenty samples divided into three groups: group 1 "without relapse", group 2 "with recent proven metastasis" and metastatic group 3 "over-expression of MUC-1". In addition, the information leaflets were examined taking into consideration the essential requirements of European directive 98/79/CE.

The 15 devices present on the market at the time of control were evaluated according to a protocol worked out by an expert group and addressed beforehand to the manufacturers. The results came up with two devices giving at least 1 false-positive among the 35 negative samples of group 1 and one device giving 1 false negative among the 39 positive samples of group 3. It seems that a better adjustment of the threshold value should, for a first analysis, avoid these false-positives and negatives.

In addition, the study carried out on samples of group 2, for which no criteria of evaluation had been fixed by the experts insofar as these are patients presenting recent metastases, show differences in clinical sensitivity according to the product. Indeed, nine devices present a value higher than the threshold announced in the information leaflet for all of the samples of group 2. On the other hand, 5 devices did not detect this rise in MUC-1 for the totality of the samples of this group.

Lastly, various nonconformities with directive 98/79/CE were raised in the information leaflets of the devices.

The results were addressed to the manufacturers in October 2006, and corrective measures were taken by the manufacturers in liaison with Afssaps.

In order to harmonize the results of various assays (current and future), Afssaps has set out the following recommendations:

- Threshold value: the determination of the threshold value must be obtained by ROC curve using a panel of patients with breast cancer whose clinical files are correctly documented. The groups should be made up on the one hand of at least 100 patients without relapse for at least 2 years and if possible for a longer duration after primary treatment and on the other hand of at least 100 patients with proven metastases. The concentrations of MUC-1/CA 15-3 of the panel used should be distributed between 10 and 500 U/ml and the area under the ROC curve should be close to 0,90.
- Upper limit of normality: The statistical distribution of the concentrations obtained from subjects without breast cancer can be indicated even if these assays are not used to screen the general population. This limit should correspond to at least the 95th percentile of this distribution.
- Hook Effect: the experts point out the possibility of a hook effect for this type of assay. The information leaflet should report this type of data clearly, if necessary.
- Decimals: taking into account the physiopathological variations of MUC-1, it is not necessary for the biologist to report results with decimals.
- Device: taking into account the dispersion of the concentrations of MUC-1 according to the technique used, the biologist should specify the device used.