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Letters to the Editor

In reply to Vergier *et al*: Fluorescence *in situ* hybridization, a diagnostic aid in ambiguous melanocytic tumors: European study of 113 cases

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To the Editor: The study by Vergier *et al*[1] on the impact of FISH as a diagnostic aid in ambiguous melanocytic tumors contains logical and factual errors. By comparison with outcome they found that the sensitivity and specificity of histopathological review were 95 and 52%, and the sensitivity and specificity of FISH were 43 and 80%. They also state that 'by considering cases as truly malignant only if histopathological diagnosis was 'favor malignant' and FISH positive, the diagnosis was optimized, especially by increasing specificity (76% instead of 52% for expert diagnosis alone), and also by improving sensitivity compared with FISH alone (90 *vs* 43% for FISH result alone)'. However, it is impossible to increase both the sensitivity and the specificity by combining two binary tests. From their Table 2 one can deduce that if truly malignant is defined as double positives (ie, histopathological review favors malignant and FISH is positive) the sensitivity would be 43% (9 out of 21) and not 90% as stated by the authors. Sequential testing as proposed by the authors shifts the threshold in favor of either sensitivity or specificity but not in favor of both, ie, it does not improve the diagnostic accuracy. Thus, their statement that 'the histopathological diagnosis combined with FISH data improves the accuracy of diagnosis' is factually wrong. In the light of the fact that of 21 cases with metastases 20 were favored malignant by histopathological review and only 9 of these were positive by FISH the statement that 'the value of FISH test is to add a reproducible demonstration of malignancy to the histopathological diagnosis, especially in doubtful/ambiguous melanocytic tumors', is also factually wrong.

Disclosure/conflict of interest
The author declares no conflict of interest.

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Reference

1 Vergier B, Prochazkova-Carlotti M, de la Fouchardiere A, *et al*. Fluorescence *in situ* hybridization, a diagnostic aid in ambiguous melanocytic tumors: European study of 113 cases. Mod Pathol 2011;24:613–623.

Response to Harald Kittler

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To the Editor: As Harald Kittler stated,[1] it is impossible to increase both the sensitivity and the specificity of a diagnosis strategy based on two binary tests by combining them, in comparison to considering them alone. In our study[2] combining the results of a histopathological review and a FISH test for the diagnosis of ambiguous melanocytic tumors, we considered a case as positive if both histopathological review and FISH were positive, and a case as negative if both histopathological review and FISH test were negative, omitting to consider as negative also the cases that were negative for one of the two tests.

Therefore we recalculated the test performance (Table 1) from the initial individual results (Table 2). Our conclusion is still that the specificity of the combined tests was increased (89%), compared with histopathological review alone (52%) and FISH test alone (80%). The positive predictive value of the combined tests tended to be increased (57%), compared with FISH alone (39%) and