Reply to "Rare coincident *NPM1* and *RUNX1* mutations in intermediate risk acute myeloid leukemia display similar patterns to single mutated cases". Haematologica 2014;99(2):e20-21.

We appreciate the efforts of Fasan *et al.*[1] to further investigate the relationship between *NPM1* and *RUNX1* mutations in *de novo*, intermediate-risk acute myeloid leukemia and confirm the rare co-occurrence of these two mutations in their cohort. We would like to clarify that we did not report that all four *RUNX1* mutations in the *NPM1*-mutated cases of our study "were located outside the TAD or RHD domain", as stated by Fasan *et al.*[1] Rather, we reported that two of the four *RUNX1* mutations (those in Patients 1 and 2; see paragraph 2 of our paper) were located in the transactivation domain (TAD).[2] Thus, we must emphasize that the *RUNX1* mutations in our *NPM1*-mutated cases were in-frame and located outside of the Runt Homology Domain (RHD), not outside of all functional domains of *RUNX1*. Interestingly, four of the *RUNX1* mutations identified by Fasan *et al*. in their *NPM1*-mutated cases (c.877C>T, c.984C>G, c. 890 C>T, and c. 977T>C) were also in-frame and located outside of the RHD. One caveat is that c.877C>T and c.984C>G result in premature stop codons; a phenomenon we did not see among the *RUNX1* mutations in the *NPM1*-mutated cases of our cohort.

We would also like to clarify that we did not report that all four *RUNX1* mutations in the *NPM1*-mutated cases of our study "were also present in the germline", as stated by Fasan *et al*.[1] in paragraph 1 of their letter. Instead, we reported in paragraph 3 that "germline material was screened in those *RUNX1*-mutated/*NPM1*-mutated patients for whom buccal cells were available (UPN 1-3)".[2] Germline material was not available for Patient 4 of our study and thus germline *RUNX1* mutation status of this patient is unknown.

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2. Mendler JH, Maharry K, Becker H, Eisfeld AK, Senter L, Mrózek K et al. In rare acute myeloid leukemia patients harboring both RUNX1 and NPM1 mutations, RUNX1 mutations are unusual in structure and present in the germline. Haematologica. 2013;98(8): e92-4.

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