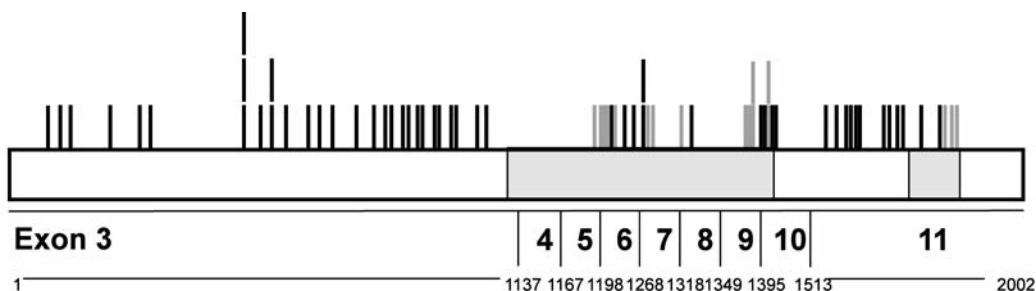


TET2 mutations in secondary acute myeloid leukemias: a French retrospective study

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Online Supplementary Figure S1. Location of TET2 mutations. Frameshifts, nonsense mutations, insertions or mutations of splice sites are indicated as black bars. Missense mutations are indicated as gray bars.

Online Supplementary Table S1. Description of *TET2* mutations and of clinical, cytogenetic and molecular characteristics of *TET2* mutated patients. MRC: myelodysplasia-related changes; TR: therapy-related; *WT1 mutation or SNP at exon 7/9. nd: not done; na: not available; IC: intensive chemotherapy; CR: complete remission; OS: overall survival in months.

| N. pts | WHO 2008 | FAB | Karyotype | <i>TET2</i> mutation position | NPM1 | FLT3IT DD835 | N- or KRAS | CKIT D816V | WT1 ex7/9 | IC | RC | OS | Outcome |
|--------|----------|-----|---|-------------------------------|------|--------------|------------|------------|-----------|----|----|------|---------|
| 1 | MRC | M5 | 46, XX | Q1834FS | no | no | no | no | no | 0 | na | na | na |
| 2 | MRC | M1 | 46,XX, inv(3)(q21q26) | C1633FS/Q891X | yes | yes | no | no | no | 1 | 1 | 1.5 | dead |
| 3 | MRC | M2 | 46, XY | S1898F | nd | nd | nd | nd | nd | 1 | 1 | 17.0 | alive |
| 4 | MRC | M2 | 47, XY, +8 | Y1751X Splice site ex 8 | no | no | no | no | yes* | na | na | 14.7 | dead |
| 5 | MRC | M5 | 46, XY | Q943X | no | yes | no | no | no | 0 | na | 4.1 | dead |
| 6 | MRC | M6 | ≥3 anomalies | G908FS | no | no | no | no | no | na | na | 17.5 | dead |
| 7 | MRC | M2 | 47,XY,+8[4]/46,XY[16] | L446FS | no | no | no | no | no | na | na | 6.5 | dead |
| 8 | MRC | M2 | ≥3 anomalies | H1382R | no | no | no | no | yes* | 1 | 1 | 11.9 | dead |
| 9 | MRC | M2 | 46,XX,del(5)(q13q33) | V1056FS | no | no | no | no | yes* | 0 | na | 12.1 | dead |
| 10 | MRC | M2 | 48,XY,+8,+8 | S254FS/L1418P | no | no | no | no | no | 0 | na | 1.5 | dead |
| 11 | MRC | M4 | 46, XX | Q1068FS | no | no | yes | no | yes | 1 | 1 | 12.6 | dead |
| 12 | TR | M1 | 46, XX | E157FS/P1655FS | yes | yes | no | no | yes* | 1 | 1 | 0.4 | dead |
| 13 | MRC | M5 | 46, XY | C1211Y/G1869V | yes | no | no | no | yes* | 1 | 1 | 5.7 | dead |
| 14 | MRC | M2 | 46, XY | C470FS/R1404X | no | no | no | no | no | 1 | 0 | 26.1 | dead |
| 15 | MRC | M2 | 46, XY | E1851FS/P1759FS | no | no | no | no | yes | 1 | 1 | 2.5 | dead |
| 16 | MRC | M4 | 46, XX | I331FS/R1216X | no | no | no | no | no | 1 | 0 | 60.2 | dead |
| 17 | MRC | M2 | 46,XX,add(6)(p22)[12] /46,XX[8] | C1271FS | no | no | no | no | no | na | na | na | na |
| 18 | MRC | M2 | 46, XY | Q876X/I1444FS | no | yes | no | no | no | 0 | 0 | 0.0 | dead |
| 19 | MRC | M2 | 46, XY | D115FS/S1798X | no | no | no | no | no | 1 | 0 | 36.9 | dead |
| 20 | MRC | M2 | ≥3 anomalies | E1879K | nd | no | nd | nd | nd | 1 | 1 | 4.3 | dead |
| 21 | MRC | M5 | 46, XY | S696FS /Q1526FS | no | no | yes | no | no | 1 | 1 | 0.3 | dead |
| 22 | MRC | M2 | 47,XY,+8[9]/46,XY[1] | Q916X/L1244FS | no | no | yes | no | no | 1 | 0 | 1.8 | dead |
| 23 | MRC | M2 | 46, XY | N595FS | no | no | yes | no | no | 1 | 0 | 25.5 | dead |
| 24 | TR | M2 | 46, XY | D1384N | no | yes | no | no | no | 1 | 0 | 9.8 | dead |
| 25 | MRC | M4 | 46, XY | Y1255FS/A1443FS | yes | no | yes | no | no | 1 | 0 | 5.6 | dead |
| 26 | MRC | M2 | 45,XY,inv(3)(q21q26),-7 | R550X | no | no | yes | no | yes | 1 | 0 | 14.3 | dead |
| 27 | MRC | M5 | 46, XY | Y1421X | no | no | no | no | yes* | 1 | 0 | 12.0 | dead |
| 28 | MRC | M1 | ≥3 anomalies | S1203R | no | yes | yes | no | no | 1 | 0 | 42.2 | alive |
| 29 | MRC | M1 | 46,XY,del(7)(q21q31) | Q909X/G1192V | no | no | no | yes | no | 1 | 1 | 12.0 | dead |
| 30 | TR | M7 | ≥3 anomalies | C171X | nd | no | nd | nd | nd | 1 | 1 | 1.2 | dead |
| 31 | MRC | M4 | 46, XX | M1333FS | nd | no | nd | nd | nd | 1 | 1 | 4.5 | dead |
| 32 | MRC | M0 | 46,XY,del(7)(q31q35), del(11)(p11p13)[10] /46,XY[5] | K568FS | no | no | nd | nd | nd | 1 | 1 | 1.8 | dead |
| 33 | MRC | M5 | 45,XY,-7[22] / 46,XY[2] | Q917X/Q1687X | no | no | no | no | no | 1 | 1 | 8.5 | dead |
| 34 | MRC | M4 | 49,XXY,+8,+11 | S1292G | no | no | no | no | no | 0 | na | 3.9 | dead |
| 35 | MRC | M2 | ≥3 anomalies | Q947X | no | no | yes | no | yes* | 0 | na | 0.3 | dead |
| 36 | MRC | M2 | 46, XY | Q720X/Q740X | no | no | no | no | yes* | 1 | 0 | 8.9 | dead |
| 37 | MRC | M4 | ≥3 anomalies | Q618X | no | no | no | no | no | 1 | 1 | 7.3 | dead |
| 38 | MRC | M5 | 46, XX | Ins R1215/C1271X | no | no | no | no | no | 1 | 0 | 40.2 | dead |
| 39 | MRC | M4 | 46, XX | H1868FS | yes | yes | no | no | no | 0 | na | na | na |
| 40 | MRC | M5 | ≥3 anomalies | Q659FS /T1566FS | yes | no | no | no | no | 1 | 1 | 33.5 | alive |
| 41 | MRC | M5 | 47,XX,+8[2]/46,XX[25] | Q1274P | yes | no | no | no | no | na | na | 0.1 | dead |
| 42 | MRC | M4 | 46, XY | L446FS | yes | yes | no | no | no | 1 | 0 | 0.4 | dead |
| 43 | MRC | M1 | 45,XY,-7 | Q324X | no | no | no | no | no | 0 | na | 0.5 | dead |
| 44 | MRC | M5 | ≥3 anomalies | Q744X/Ins L1421 | no | no | no | no | no | na | na | na | na |
| 45 | MRC | M5 | 46, XY | Splice site ex 5 | no | no | yes | no | yes* | 0 | na | 0.0 | dead |
| 46 | MRC | M5 | 46, XY | D1384H | no | no | no | no | no | 0 | na | 15.0 | alive |
| 47 | MRC | M4 | 46, XY | Q1702X | no | yes | no | no | no | 1 | 1 | 68.9 | alive |
| 48 | TR | M1 | 51,XY,+mar1X4, +mar2[6]/46,XY[17] | H1817FS | no | no | no | no | no | 0 | na | na | na |
| 49 | MRC | M2 | 46, XY | L446X/R550X | no | no | no | no | no | 0 | na | na | na |

Online Supplementary Table S2. Comparison of clinical and biological characteristics of patients with MRC-AML versus TR-AML.

| | MRC | TR | |
|---|----------------|----------------|--------|
| Number | 201 | 46 | |
| Age (years) | 64 [57-74] | 61 [54-72] | 0.160 |
| Sex ratio M/F | 2.0 | 0.6 | <0.001 |
| <i>TET2</i> (%) | 2.3 | 8.7 | 0.035 |
| Hemogram | | | |
| Hb (g/dL) | 9.1 [7.9-10.0] | 8.9 [7.7-10.0] | 0.0352 |
| MCV (fl) | 96 [89-101] | 96 [89-101] | 0.264 |
| Leukocytes (10 ⁹ /L) | 7.2 [2.9-22.5] | 23 [4.9-72] | 0.004 |
| Platelets (10 ⁹ /L) | 98 [35-120] | 69 [24-83] | 0.134 |
| Peripheral blasts (%) | 33 [7-52] | 49 [22-71] | 0.001 |
| Bone marrow blasts (%) | 49 [32-65] | 61 [44-78] | 0.003 |
| Multilineage dysplasia (%) | 69 | 44 | 0.002 |
| Karyotype | | | |
| Normal (%) | 31 | 15 | 0.033 |
| Monosoma (%) | 26 | 30 | 0.321 |
| ≥ 3 anomalies (%) | 37 | 43 | 0.430 |
| Recurrent anomalies (%) | 7.5 | 22 | 0.003 |
| Molecular abnormalities | | | |
| <i>NPM1</i> (%) | 10 | 17 | 0.393 |
| <i>FLT3</i> -ITD or <i>FLT3</i> -D835 (%) | 9 | 25 | 0.005 |
| <i>NK-RAS</i> (%) | 15 | 17 | 0.856 |
| <i>WT1</i> exon 7 or 9 (%) | 28 | 25 | 0.759 |
| Complete remission rate (%) | 55 | 61 | 0.356 |
| Overall survival (months) | 11 | 5.5 | <0.001 |