

# Ponatinib as targeted therapy for FGFR1 fusions associated with the 8p11 myeloproliferative syndrome

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**Online Supplementary Table S1.** Clinical and sample details from 5 cases with FGFR1 fusion genes.

| Sample ID | Sample type | Fusion gene          | Translocation    | Sex | Age (year) | Diagnosis |
|-----------|-------------|----------------------|------------------|-----|------------|-----------|
| F1        | PB          | <i>BCR-FGFR1</i>     | t(8;22)(p11;q11) | F   | 74         | EMS       |
| F2        | PB          | <i>FGFR1OP-FGFR1</i> | t(6;8)q27;p11)   | F   | 54         | EMS       |
| F3        | PB          | <i>ZMYM2-FGFR1</i>   | t(8;13)(p11;q11) | M   | 61         | EMS       |
| F4        | PB          | <i>BCR-FGFR1</i>     | t(8;22)(p11;q11) | F   | 52         | EMS-LBC   |
| F5        | PB          | <i>ZMYM2-FGFR1</i>   | t(8;13)(p11;q12) | M   | 50         | EMS       |

EMS: 8p11 myeloproliferative syndrome; LBC: lymphoid blast crisis, PB: peripheral blood.

**Online Supplementary Table S2.** Total colony counts from 5 samples with FGFR1 translocations and 8 control PB samples from healthy individuals. For cases 1, 4 and 5, after counting, colonies from Day 14 cultures were plucked for FISH analysis; the total number of colonies analyzed by FISH and the number *FGFR1*-fusion positive is given in brackets.

| Sample ID | Day 7 colony counts |       |        |        | Day 14 colony counts<br>( <i>FGFR1</i> fusion positive by FISH/total analysed by FISH) |                |               |               |
|-----------|---------------------|-------|--------|--------|--|----------------|---------------|---------------|
|           | 0 nM                | 20 nM | 100 nM | 500 nM | 0 nM   | 20 nM          | 100 nM        | 500 nM        |
| NPB1      | 39                  | 45    | 11     | 4      | 48   | 59             | 3             | 3             |
| NPB2      | 10                  | 7     | 5      | 3      | 43   | 19             | 11            | 4             |
| NPB3      | 22                  | 32    | 10     | 5      | 20   | 23             | 14            | 4             |
| NPB4      | 22                  | 25    | 12     | 5      | 25   | 34             | 19            | 10            |
| NPB5      | 72                  | 53    | 72     | 50     | 228  | 153            | 201           | 81            |
| NPB6      | 64                  | 63    | 63     | 24     | 117  | 147            | 153           | 42            |
| NPB7      | 28                  | 41    | 32     | 12     | 41   | 90             | 57            | 19            |
| NPB8      | 52                  | 19    | 12     | 4      | 183  | 105            | 58            | 30            |
| F1        | 60                  | 82    | 50     | 22     | 132  | 110            | 66            | 53<br>(32/32) |
| F2        | 33                  | 0     | 0      | 0      | 165  | 1              | 0             | 0             |
| F3        | 146                 | 77    | 52     | 4      | 164  | 81             | 60            | 15            |
| F4        | 54                  | 55    | 35     | 7      | 68   | 60             | 35            | 19<br>(30/30) |
| F5        | 388                 | 239   | 73     | 7      | 283<br>(76/103)  | 154<br>(24/52) | 77<br>(22/38) | 12<br>(5/8)   |

**Online Supplementary Table S3.** The total colony counts at each ponatinib concentration and proportion *ZMYM2-FGFR1* (Z-F) positive by FISH for case F5 allowed an estimate of the Z-F positive and negative colonies to be made showing that Z-F positive colony numbers fell at lower concentrations of ponatinib than Z-F negative colonies.

|  | 0 nM            | 20 nM            | 100 nM         | 500 nM        |
|--|-----------------|------------------|----------------|---------------|
| Total colony counts                                      | 283             | 154              | 77             | 12            |
| Proportion <i>ZMYM2-FGFR1</i> FISH positive (N)          | 0.73<br>(N=103) | 0.46 *<br>(N=52) | 0.58<br>(N=38) | 0.63<br>(N=8) |
| Calculated size of Z-F positive fraction of colony count | 207             | 71               | 45             | 9             |
| Calculated size of Z-F negative fraction of colony count | 76              | 83               | 32             | 3             |

\* $\chi^2, P > 0.001$ .