Supplementary Materials

CML cases

Patient 1: A 33 year old male diagnosed with CML in 10/2007 started on 600mg imatinib. BM biopsy in 02/2008 showed 20-30% CD117(+)/CD34(+) blasts. BM karyotyping identified t(9;22)(q34;q11) in all cells and a 20% clone with an additional Ph (Figure 2A). D-FISH detected *BCR-ABL1* in most of the cells (Figure 2B), 61% had a missing signal from the non-rearranged *ABL1*, including 6% with a double Ph [Figure 2B(iii,iv)]. The genome loss at 9q34 was estimated by aCGH to be 2.6Mb, spanning the regions of *PKN3* and *NUP214* genes thus encompassing the entire *ABL1* (Figure 2C). Started on 100mg dasatinib with poor response and excess of BM blasts. Allo-HSCT performed in 08/2008. FISH in 10/2008 showed successful engraftment and lack of *BCR-ABL1* in the BM, confirmed in 10/2009.

Patient 2: A 37 year old male was diagnosed in 10/2001 with Ph-positive CML due to t(9;22)(q34;q11). After lack of response to interferon and HU, Glivec (600mg) commenced in 04/2002 achieving CCyR within 6 months. Three years later (04/2005) blast transformation was diagnosed and treated to heamatological remission, followed by sex-mismatch allo-BMT (05/2005). Molecular remission was not achieved post BMT and D-FISH (07/2005) showed host origin in 10% of the BM cells, all of which were *BCR-ABL1* positive with atypical signal pattern of 3F0R1G consistent with loss of the wild *ABL1* allele in cells with double Ph. G banding identified a large deletion of the long arm of chromosome 9 among other karyotype changes (Supplementary Table 1). Patient passed away in 12/2005.

Patient 3: A 25 years old female diagnosed with CML in 05/2004 with an atypical D-FISH pattern of 1F2R2G indicative of three way variant translocation t(9;22;16)(q34;q11;q13) leading to masked Ph (1). Failed to achieve CCyR on imatinib by 10/2004, when she progressed to lymphoid blast phase. Sibling allo-HSCT was performed and CCyR achieved in 11/2004. Due to rising counts dasatinib (70mg) was started in 03/2005. *BCR-ABL1* fusion signals were detected by D-FISH in 14% of the interphase BM cells, while aCGH revealed cryptic 2.1Mb deletion at 9q34.1, which include the entire non-rearranged *ABL1* (Supplementary Figure 1b). Achieved clinical and hematological remission on dasatinib (100mg) and HU but failed to reach CCyR. In 12/2005 a second lymphoid blast transformation with CNS involvement occurred and she passed away in 05/2006.

1. Virgili A, Brazma D, Reid AG, et al. FISH mapping of Philadelphia negative BCR/ABL1 positive CML. Mol Cytogenet 2008;1:1-13.