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.