

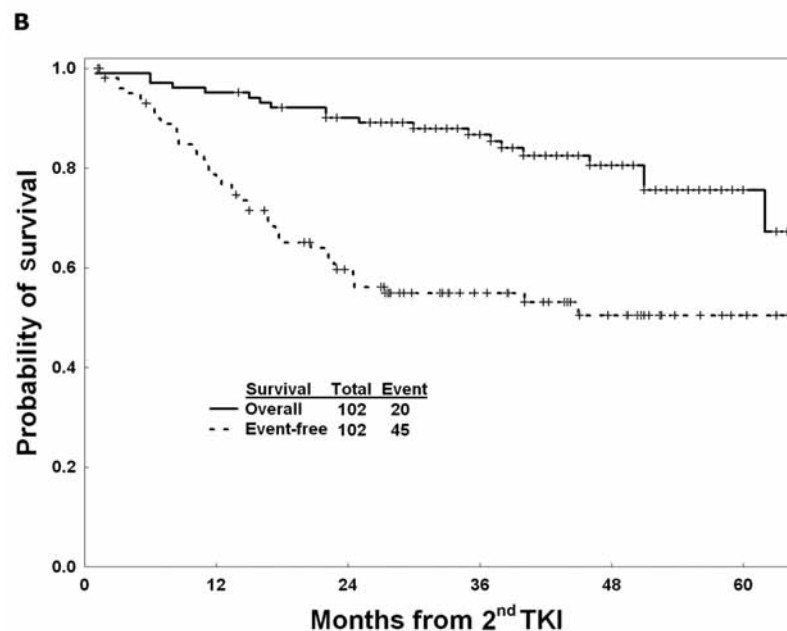
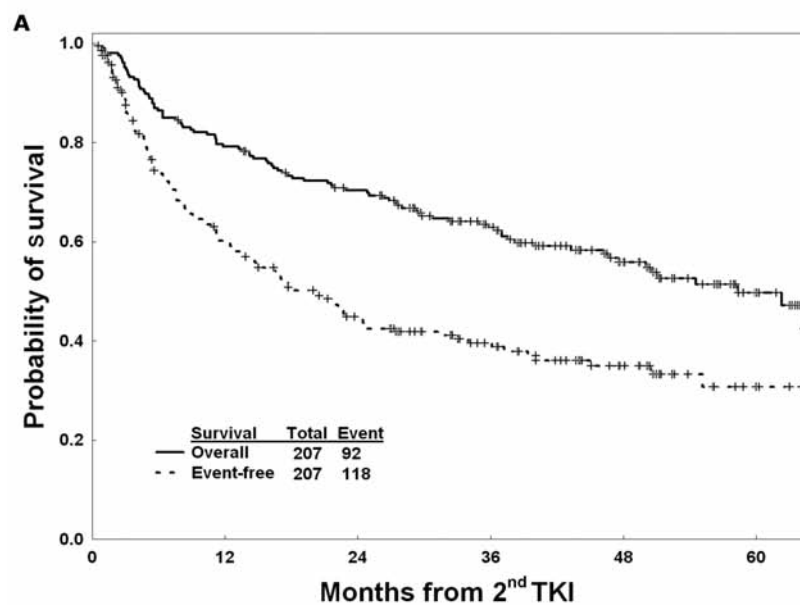
# Outcome of patients with chronic myeloid leukemia with multiple ABL1 kinase domain mutations receiving tyrosine kinase inhibitor therapy

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Online Supplementary Figure S1. Event-free survival and overall survival for the whole cohort of patients (A) and for patients with CML-CP (B).



Online Supplementary Table S1. Response to tyrosine kinase inhibitor therapy of patients with more than one BCR-ABL1 mutation. Of note, in 5 of 6 evaluable patients (patients 2, 3, 4, 5, 6, and 7), therapy with second generation TKI (2<sup>nd</sup> TKI) resulted in the elimination of one of the mutations present after imatinib failure. In 4 of those 5 cases (3, 4, 5, and 6) the remaining mutation was the one with the highest IC50 for the TKI used in each patient, suggesting that resistance and, therefore, a poor prognosis in patients with more than one mutation may be primarily driven by the presence of a less sensitive mutation to 2<sup>nd</sup> generation TKI.

| Pt No | CML phase          | Age (yr) | Imatinib Duration (mos) | Imatinib Best response | Reason off Imatinib   | Mutation prior to 2 <sup>nd</sup> TKI | 2 <sup>nd</sup> TKI | Duration 2 <sup>nd</sup> TKI (mos) | Best response 2 <sup>nd</sup> TKI | Mutation on 2 <sup>nd</sup> TKI | Response Duration (mos) | Reason Off 2 <sup>nd</sup> TKI | 3 <sup>rd</sup> TKI | Best response 3 <sup>rd</sup> TKI |
|-------|--------------------|----------|-------------------------|------------------------|-----------------------|---------------------------------------|---------------------|------------------------------------|-----------------------------------|---------------------------------|-------------------------|--------------------------------|---------------------|-----------------------------------|
| 1     | 2 <sup>nd</sup> CP | 67       | 44                      | CCyR                   | Resistance            | M351T, E255V                          | Nilotinib           | 5                                  | CHR                               | Not available                   | 3+                      | Pt's choice                    | Imatinib            | NA                                |
| 2     | CP                 | 84       | 77                      | CHR                    | Resistance & Toxicity | M351T, F359V                          | Bosutinib           | 24                                 | mCyR                              | M351T, F359V                    | 8                       | Resist                         | Nilotinib           | CHR                               |
| 3     | CP                 | 56       | 22                      | mCyR                   | Resistance            | M351T, F317L                          | Dasatinib           | 11                                 | None                              | F317L                           | -                       | Resist                         | Bosutinib           | Resist                            |
| 4     | CP                 | 54       | 37                      | PCyR                   | Progression (CE)      | M351T, G250E                          | Nilotinib           | 34                                 | CCyR                              | G250E                           | 6                       | Resist                         | Bosutinib           | CCyR                              |
| 5     | CP                 | 61       | 48                      | CHR                    | Resistance            | G250E, Y253H                          | Dasatinib           | 17                                 | CCyR                              | Y253H                           | 1+                      | Toxicity                       | INNO-406            | Resist                            |
| 6     | CP                 | 54       | 54                      | CHR                    | Resistance            | M351T, T315I                          | Dasatinib           | 2                                  | None                              | T315I                           | -                       | Resist                         | MK0457              | Resist                            |
| 7     | CP                 | 26       | 14                      | CHR                    | Progression (CE)      | E255K, E459K                          | Bosutinib           | 2                                  | None                              | None                            | -                       | Resist                         | Nilotinib           | Resist                            |