**Supplemental Figure legends**

**Supplemental Figure 1S.** Electropherograms of nine non-synonymous changes identified by RNA-seq and validated by direct Sanger sequencing. Trios of traces (diagnosis, hematological remission and relapse) are provided for each mutation. Since the analyzed Ph+ ALL patient achieved a hematological remission, but not a molecular remission, the collected and analyzed sample labeled as "remission" maintained a residual level of Bcr-Abl transcript. This would explain the dynamics of some mutations during progression (e.g.: a clone with *TMEM46* G59D mutation was still found at remission and disappeared at relapse; a clone with *MVP* P620S mutation was still found at remission and again it disappeared at relapse; a clone with *CTSZ* R183Q mutation was firstly found at remission and thereafter maintained at relapse). The star sign indicates the mutated allele.

**Supplemental Figure 2S.** Distribution of the 4,334 and 3,651 primary ALL and relapse isoforms with at least one putative AS event. An average of 1.5 and 1.3 putative AS per isoform was estimated, with 73% and 81% of observed primary ALL and relapse alternatively spliced isoforms that resulted from one putative AS event only.

**Supplemental Figure 3S.** Number of putative AS events per class of exon skipping.

**Supplemental Figure 4S.** Results from GeneGo Pathway Map showing the "Metaphase checkpoint" (p value = $3.94E^{-10}$). Genes with thermometers are from list of up-regulated genes and the level of thermometer is proportional to the fold change.

**Supplemental Figure 5S.** Results from GeneGo Pathway Map showing the "Signal transduction PKA signaling" (p value = $2.60E^{-07}$). Genes with thermometers are from list of down-regulated genes and the level of thermometer is proportional to the fold change.

**Supplemental Figure 6S.** Gene expression levels of *AURORA Kinase B* and *SURVIVIN* in 8 matched diagnosis-relapse BCR-ABL1 positive ALL samples measured by quantitative RT-PCR analysis.