A multicenter total therapy strategy for *de novo* adult Philadelphia chromosome positive acute lymphoblastic leukemia patients: final results of the GIMEMA LAL1509 protocol

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Supplemental Materials and Methods

CNS prophylaxis

CNS prophylaxis was mandatory: 5 medicated rachicenteses (intrathecal methotrexate, 12 mg, and intrathecal methylprednisolone, 20 mg) were carried out during induction (at diagnosis, day +22, +45, +57 and 85) and then every month for a total number of 12.

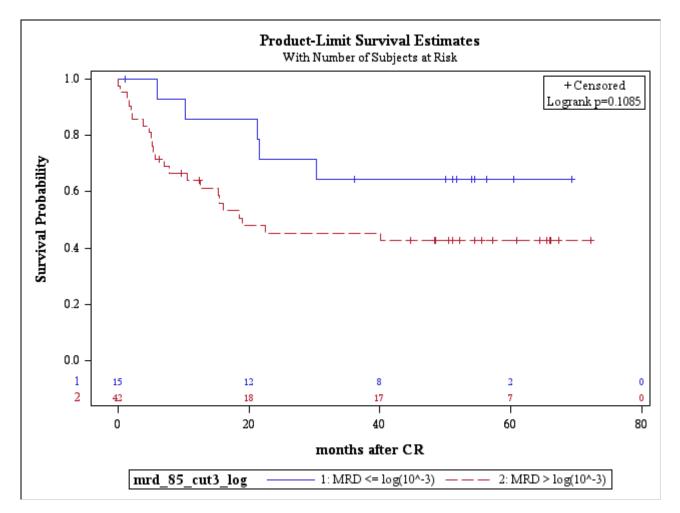
MRD monitoring after induction

For MRD monitoring, *BCR-ABL1* levels were normalized to the number of the *ABL1* control gene and expressed as *BCR-ABL1/ABL1*×100; the level of *BCR-ABL1* expression was then converted into a base 10 logarithmic scale. In determining the integrity of RNA, the criteria for excluding RNA samples was established as an ABL1 copy numbers <10000 for negative samples and <1000 for those positive and quantifiable. The number of BCR/ABL1 copies was normalised with respect to the number of ABL1 copies and expressed as the number of BCR-ABL1/ABL1 copies x 102.

After the induction phase, MRD was monitored every two months during the first 6 months for patients who received dasatinib only and every three months during the subsequent 6 months, then every four months during the second and third year, and every six months during the fourth and fifth year. For patients who underwent an allo-SCT, molecular testing was carried out every two months during the first year, then every four months during the second and third year and every six months during the fourth and fifth year. For patients who underwent chemotherapy with clofarabine-cyclophosphamide, MRD levels were tested after the first and second cycle, then every two months during the first year, then every four months during the second and third year and every six months during the fourth and fifth year.

Supplemental Table 1. Number and type of adverse events occurring during protocol

Type of disorder	Overall	Dasatinib induction	Dasatinib consolidation	Clopharabine- Endoxan	Dasatinib after Clopharabine- Endoxan	Allo- SCT	Dasatinib after allo- SCT
Hematological	124 (66%)	62	-	36	-	21	5
Gastrointestinal	12 (6%)	2	-	2	1	6	1
Hepato-biliary	3 (1.5%)	-	-	-	-	2	1
General	7 (3.7%)	-	-	1	-	6	-
Immune	2 (1%)	-	-	-	-	2	-
Infections	12 (6%)	2	-	3	-	7	-
Metabolic	1 (0.5%)	1	-	-	-	-	-
CNS	1 (0.5%)	1	-	-	-	-	-
Laboratory	18 (9.6%)	12	-	1	-	5	-
Renal/Urinary	2 (1%)	-	1	-	-	1	-
Respiratory	2 (1%)	-	-	-	-	2	-
Skin	4 (2.1%)	1	-	-	-	3	-



Additional supplemental figure. For revisors only. DFS according to MRD cut-off level of 10-3