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# POSTER ABSTRACTS

## 613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

### Tyrosine Kinase Inhibitors with Intensive Chemotherapy in AML with t(9;22)(q34.1;q11.2)/ *BCR::ABL1*: Time to Reconsider Prognostic Risk? a Study from the Dataml Registry

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**Introduction**

*De novo* AML with t(9;22)(q34.1;q11.2)/ *BCR::ABL1* is now a distinct entity of the ICC and WHO 2022 classifications within the group of AML with defining genetic abnormalities. This entity is distinguished from cases with history of chronic myeloid leukemia (CML) and ≥ 20% blasts, which are classified as CML in myeloid blast phase (CML-BP), although the distinction between both entities could be challenging. In the 2022 ELN classification, AML with *BCR::ABL1* belong to the adverse risk group. However, this entity is very rare and generally excluded from clinical trials. Thus, there is little data on outcome especially since the era of BCR::ABL1 inhibitors (Orsmark-Pietras C *et al.*). In this study, we thought to describe treatments and outcome of patients (pts) with *de novo* AML with t(9;22)(q34.1;q11.2)/ *BCR::ABL1* in comparison with CML-BP and ELN 2017 intermediate (Int) or adverse (Adv) risk AML.

**Methods**

Inclusion criteria were: pts aged ≥ 18y, included in the DATAML registry between 2000 and 2021, with either *de novo BCR::ABL1* AML defined as no previous history of CML, no previous treatment with TKI and ≥ 20% blasts in bone marrow/blood or CML-BP defined as the occurrence of ≥ 20% blasts following the diagnosis of CML in chronic phase. Outcomes of pts with *de novo BCR::ABL1* AML were compared with those of CML-BP pts and AML with ELN 2017 Int (n=643) or Adv (n=863)

risk treated with intensive chemotherapy (IC) over the same period. A 50-gene NGS panel was retrospectively performed on available samples.

**Results**

We identified 20 pts with *de novo BCR::ABL1* AML among 5819 AML (0.3%). We only studied the 18 pts who received IC. Their main characteristics were: female to male ratio (55.6%), median age (54y), extramedullary disease (47%) including splenomegaly (35%); high WBC at diagnosis; isolated t(9;22) (67%); p210 isotype (78%), mutations in *ASXL1*, *RUNX1*, *NPM1*, *TET2*, *BCOR*, *BCORL1*, *DNMT3A*, *EZH2*, *IDH1*, *KDM6A*, *NF1*, *SMC1A*, *SRSF2*, *WT1*. Comparisons with the 24 pts CML-BP who were treated with IC are shown in the Table. The main differences between both groups was a higher WBC and the presence of *NPM1* mutation in *de novo* pts whereas *ABL1* mutations were found in CML-BP only. Induction chemotherapy was mainly cytarabine and daunorubicin (45-90 mg/m²) combined with imatinib (median dose 600 mg, range 400-800). Only 2 patients did not receive imatinib because the drug was not available in 2000-2003. Those 2 pts achieved complete remission (CR) but subsequently relapsed and died from progression. Overall, 17 pts (94.4%) achieved CR or CR with incomplete hematologic recovery (CRi) after one or two induction cycles, one pt failed and there was no early death. Consolidation was mainly high dose cytarabine with imatinib and 12 pts received an allogeneic hematopoietic cell transplantation (alloHCT) in first CR/CRi with myeloablative or reduced intensity conditioning in 7 and 5 pts, respectively. Five pts received maintenance therapy with imatinib (n=4) or nilotinib (n=1). Of note, 4 of the 5 CR/CRi pts who were not transplanted in CR1 did not relapse. With a median follow-up of 76.3 months, median RFS was not reached and 2y-RFS was 82.4% (95%CI, 55-94). Median OS was not reached and 2-y OS was 77.4% (95%CI, 50.3-90.9). Of note, there were 3 late deaths at 48, 60 and 84 months unrelated to AML (1 lung cancer, 1 pancreatic cancer, 1 infection).

CR/CRi rate was significantly higher in pts with *de novo BCR::ABL1* AML(94.4%) compared with CML-BP (79.2%), AML with ELN 2017 Int (83.4%) or Adv (68.5%) risk (P<0.0001). RFS (median, CML-BP: 100.5 months, IQR 19.7-NR; ELN-Int: 20.6 months, IQR 7.2-115.3; ELN-Adv: 10.3 months, IQR 4.4-48.1; P<0.0001) and OS (median, CML-BP: 33.9 months, IQR 14.6-NR; ELN-Int: 26.9 months, IQR 10.3-117.3; ELN-Adv: 11.8 months, IQR 4.7-40.0; P<0.0001) were also significantly improved. 2-y OS was 77.4%, 57.0%, 53.7% and 33.4% in *de novo BCR::ABL1 AML*, CML-BP, AML with ELN2017 Int and Adv, respectively (P<0.0001) (Figure).

**Conclusion**

*De novo* AML with t(9;22)(q34.1;q11.2)/ *BCR::ABL1* is a very rare event in AML classifications (<1%) with particular features. Pts treated with IC and imatinib have a high rate of CR, very low incidence of relapse and a remarkable OS rate that do not support the ELN2022 risk classification . Pts may have prolonged RFS and OS without alloHCT. Further studies are needed to confirm these results and reclassify these AMLs in the intermediate or even favorable group of the ELN 2022 classification.

**Disclosures Dumas:** *Novartis:* Honoraria, Other: Research support for institution; *Servier:* Honoraria, Other: Research support for institution; *BMS:* Honoraria, Other: Research support for institution; *Abbvie:* Honoraria; *Astellas:* Honoraria, Other: Research support for institution; *Jazz pharmaceutical:* Honoraria; *Daiichi-Sankyo:* Honoraria, Other: Research support for institution; *Janssen:* Honoraria; *Roche:* Other: Research support for institution. **Tavitian:** *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Other: Webinar; *Servier:* Membership on an entity's Board of Directors or advisory committees. **Huguet:** *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Clinign:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Servier:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Incyte Corporation:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Forcade:** *Jazz:* Other: Travel support; *Sanofi:* Speakers Bureau; *GSK:* Speakers Bureau; *Gilead Sciences:* Other: Travel support, Speakers Bureau; *MSD:* Other: Travel support; *Astellas:* Speakers Bureau; *Alexion:* Other: Travel support, Speakers Bureau; *Novartis:* Consultancy, Other: Travel support, Speakers Bureau. **Pigneux:** *Gilead:* Honoraria; *Abbvie:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings; *Servier:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings, Research Funding; *Roche:* Research Funding; *BMS:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Astellas:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Jazz Pharmaceuticals:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria; *Pfizer:* Membership on an entity's Board of Directors or advisory committees. **Recher:** *Jazz Pharmaceuticals:* Other: Personal fees, Research Funding; *Novartis:* Other: Personal fees; *Astellas:* Other: Personal fees; *BMS:* Other: Personal fees, Research Funding; *Amgen:* Research Funding; *Abbvie:* Honoraria; *Servier:* Other: Personal fees; *MaatPharma:* Research Funding; *IQVIA:* Research Funding; *Takeda:* Other: Personal fees. **Bertoli:** *Servier:* Honoraria; *Abbvie:* Honoraria, Other: Travel; *Astellas:* Honoraria; *Novartis:* Honoraria; *BMS-Celgene:* Honoraria; *Jazz Pharmaceuticals:* Honoraria, Other: Travel.

Table

| | *De novo*, N=18 | CML-BP, N=24 | *P* |
|---|---|---|---|
| **Age, median (range)** | 54.1 (22.4-71.2) | 52.3 (29.3-66.8) | 0.77 |
| **Gender** | | | |
| Female | 8 (44.4) | 11 (45.8) | 0.93 |
| Male | 10 (55.6) | 13 (54.2) | |
| **EMD - N, (%)** | 8 (47.1) | 13 (56.5) | 0.55 |
| Splenomegaly | 6 (35.3) | 11 (47.8) | 0.43 |
| Hepatomegaly | 4 (23.5) | 4 (17.4) | 0.70 |
| Adenopathies | 2 (11.8) | 3 (13.0) | 1 |
| CNS | 0 | 1 (4.3) | 1 |
| **WBC, $10^9$/L – median (IQR)** | 91.5 (20.8-143.0) | 32.9 (6.3-74.9) | 0.08 |
| **ACA – N, %** | 3 (33.3) | 11 (45.8) | 0.41 |
| **Isotype – N, %** | | | |
| p190 | 2 (11.1) | 2 (8.3) | 1 |
| p210 | 14 (77.8) | 18 (75.0) | |
| **Mutations – N, %** | | | |
| *ASXL1* | 4/14 (28.6) | 3/14 (21.4) | 1 |
| *RUNX1* | 4/14 (28.6) | 3/13 (23.1) | 0.22 |
| *NPM1* | 3/14 (21.4) | 0/14 | 0.48 |
| *TET2* | 2/14 (14.3) | 0/13 | |
| *BCOR* | 2/14 (14.3) | 1/13 (7.7) | 1 |
| *BCORL1* | 1/14 (7.1) | 0/13 | |
| *DNMT3A* | 1/14 (7.1) | 0/14 | |
| *EZH2* | 1/14 (7.1) | 0/13 | |
| *IDH1* | 1/14 (7.1) | 0/14 | |
| *KDM6A* | 1/14 (7.1) | 0/13 | |
| *MPL* | 1/14 (7.1) | 0/13 | |
| *NF1* | 1/14 (7.1) | 0/13 | |
| *SMC1A* | 1/14 (7.1) | 0/13 | |
| *SRSF2* | 1/14 (7.1) | 0/13 | |
| *WT1* | 1/14 (7.1) | 2/13 (15.4) | 0.60 |
| **BCR::ABL1 inhibitors – N, %** | | | 0.001 |
| No TKI | 2 (11.1) | 4 (16.7) | |
| Imatinib | 16 (88.9) | 8 (33.3) | |
| Nilotinib | 0 | 1 (4.2) | |
| Dasatinib | 0 | 7 (29.2) | |
| Ponatinib | 0 | 4 (16.7) | |
| **Anthracyclins – N, %** | | | 0.56 |
| Daunorubicin 45 mg/m² x 3d | 3 (16.7) | 3 (12.5) | |
| Daunorubicin 60 mg/m² x 3d | 6 (33.3) | 14 (58.3) | |
| Daunorubicin 90 mg/m² x 3d | 6 (33.3) | 4 (16.7) | |
| Idarubicin 8 mg/m² x 5d | 1 (5.6) | 1 (4.2) | |
| Other | 2 (11.1) | 2 (8.3) | |
| **AlloHCT, – N, %** | 12 (66.7) | 15 (62.5) | 0.78 |

Figure

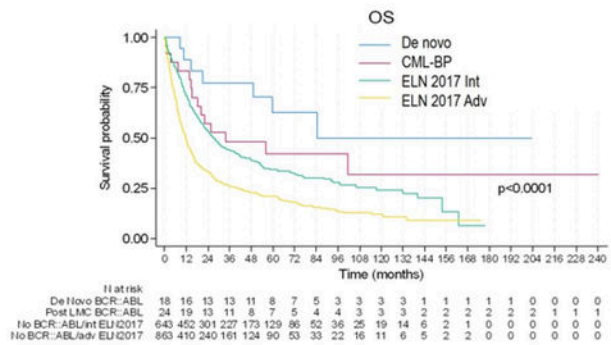


**Figure 1**

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