The 65th ASH Annual Meeting Abstracts

# POSTER ABSTRACTS

## 613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

### Improvement in Survival of Patients with FLT3 Mutated Acute Myeloid Leukemia: Results from a Retrospective Canadian Cohort

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**Introduction:** FLT3 internal tandem duplication (ITD) mutations have been historically associated with inferior outcomes in patients with acute myeloid leukemia (AML) and an intermediate risk status as per the European LeukemiaNet (ELN) 2022 guidelines. In 2017, the US FDA granted approval to midostaurin for frontline treatment and a year later, gilteritinib for use in relapsed/refractory (R/R) AML. These agents began to be widely used in our provincial leukemia program in early 2018 as per the label indications. In this study, we compared clinical outcomes for patients with FLT3-ITD mutated AML before and after this change in British Columbia.

**Methods:** We identified patients in our program database diagnosed with FLT3-ITD mutated AML from January 1, 2010 to December 31, 2021. Only patients receiving intensive chemotherapy with cytarabine and anthracycline were included. Patients were divided into two eras: 2010-2017 (era 1) and 2018-2021 (era 2). The two eras were compared in terms of patient characteristics, genetics, rate of complete remission (CR) and CR with incomplete count recovery (CRi), receipt of allogeneic stem cell transplant (alloSCT) and the overall and relapse free survival (OS and RFS). OS was calculated from diagnosis to death from any cause and was not censored at the time of alloSCT. RFS was calculated from CR/CRi to relapse. Patients without an event during the study period were censored at the time of last follow-up. Categorical variables were compared using Chi-square and Fisher exact tests and continuous variable were compared using paired T tests. Kaplan-Meier survival method and log rank test were used to estimate and compare survival. Uni- and multivariate analyses were performed in a Cox proportional regression model and alloSCT was considered as a time dependent covariate.

**Results:** 169 patients were included (era 1=101, era 2=68). The median duration of follow up of the entire cohort was 17 months (range 0.5-148.6 months) and follow-up of surviving patients (n=70) was longer in era 1 vs. era 2 (median 88 months vs. 32 months, p<0.001). The median age of the entire cohort was 60 years (range 26-79 years) and it was comparable in both eras. Most patients had normal cytogenetics (era 1: 76%; era 2: 69%). NPM1 was mutated in 69/101 (68%) and 38/68 (56%) patients in eras 1 and 2 respectively. Due to lack of genetic data for era 1, we did not risk stratify based on the recent ELN classification. The rate of CR/CRi was 58/101 (57%) vs. 40/68 (59%) after induction chemotherapy and 78/101 (77%) vs. 58/67 (87%) (p=0.09) at any time in eras 1 and 2 respectively. AlloSCT was performed in 58% and 72% of patients in the two cohorts. Midostaurin was used in 82% and gilteritinib was used in 26% of era 2 patients in the second era. OS was significantly longer in era 2 (median OS 73 months vs. 11 months, HR (death) 6.2, p=0.012) (Figure). The 2-year OS rate was higher in era 2 (57%) than in era 1 (39%). In patients achieving CR/CRi, median RFS was longer in era 2 (51 vs. 16 months, p=0.43), although this was not statistically significant. In univariate Cox regression analysis the following factors were associated with improved OS: use of midostaurin (HR 0.487, 95% CI 0.304-0.779, p=0.003), diagnosis in era 2 (HR 0.583, 95% CI 0.38-0.895, p=0.014) and receipt of alloSCT (HR 0.346,) 95% CI 0.219-0.545, p<0.001). Other parameters including age, sex, NPM1 status and cytogenetics were not significant. In multivariate analysis including era, midostaurin and alloSCT, only the receipt of alloSCT was associated with

significantly improved OS (HR 0.362, 95% CI 0.229 - 0.572, p<0.001) whereas use of midostaurin (HR=0.465, CI 0.207-1.042, p=0.063) and era (HR 1.12, 95% CI 0.538-2.34, p=0.76) were not significant.

**Conclusions:** Our results show thatOS for patients with FLT3-ITD AML has improved in patients diagnosed in a more recent treatment era. Patients diagnosed after 2018 were more frequently treated with AlloSCT and FLT3-inhibitors, which may have resulted in improvements in OS. Our findings support the assignment of FLT3-ITD AML to theintermediate risk category as per the current ELN guidelines. A limitation of this study is the differences in follow-up time between eras, which may influence the event rate between the groups.

**Disclosures Stubbins:** *AbbVie:* Consultancy, Honoraria; *Jazz Pharmaceuticals:* Honoraria; *Pfizer:* Honoraria. **Chung:** *Takeda:* Consultancy, Honoraria; *Astella Pharma:* Honoraria; *Novartis:* Honoraria; *Paladin:* Honoraria. **Song:** *Forus:* Honoraria; *Novartis:* Honoraria; *BMS:* Honoraria; *Sanofi:* Honoraria; *Janssen:* Honoraria; *GSK:* Honoraria; *Amgen:* Honoraria; *Gilead:* Honoraria. **White:** *Novartis:* Honoraria. **Toze:** *AbbVie:* Honoraria, Research Funding; *Beigene:* Honoraria; *Janssen:* Honoraria; *Astra-Zeneca:* Research Funding. **Hay:** *Novartis:* Honoraria; *Kite/Gilead:* Honoraria; *Janssen:* Research Funding; *BMS:* Honoraria. **Sanford:** *Astellas:* Honoraria; *AbbVie:* Honoraria.

| Patient Characteristics | | 2010-2017 N=101 | 2018-2023 N=68 | P |
|---|---|---|---|---|
| Female gender n (%) | | 56 (55%) | 34 (50%) | 0.531 |
| Median age (range) | | 60 years (26-29) | 61.5 (28-73) | 0.632 |
| <60 years n (%) | | 49 (48.5%) | 38 (47%) | |
| Ethnicity | White | 48 (47.5%) | 41 (60.2%) | |
| | Black | 1 (0.9%) | 0 | |
| | South-east Asian/Chinese | 9 (8.9%) | 4 (5.8%) | |
| | Others (Asian Indians, Japanese, Hispanic, Middle-eastern/Arab Eastern European) | 8 (7.9%) | 14 (20.5%) | |
| | Ethnicity not known | 35 (34.6%) | 9 (13.2%) | |
| Cytogenetic Risk Category (%) | Normal | 77 (76.2%) | 47 (69.1%) | 0.107 |
| | Other Intermediate | 19 (18.8%) | 10 (14.7%) | |
| | Adverse | 4 (3.9%) | 9 (13.2%) | |
| | Missing | 1 (0.9%) | 2 (2.9%) | |
| NPM1mut n (%) | | 69 (68.3%) | 38 (55.8%) | 0.107 |
| Response To Intensive Induction therapy | CR/CRi rate n (%) | 58 (57.4%) | 40 (58.8%) | 0.454 |
| | Refractory Disease n (%) | 43 (42.5%) | 27 (39.7%) | |
| | Unknown status n (%) | 0 | 1 (1.4%) | |
| Midostaurin use in Induction/Consolidation (%) | | 0 | 56 (82.3%) | <0.001 |
| Gilteritinib use (%) | | 1 (0.9%) | 18 (26.4%) | <0.001 |
| Sorafenib | | 7 (6.9%) | 6 (8.8%) | 0.770 |
| AlloSCT n (%) | | 59 (58.4%) | 49 (72%) | 0.075 |
| Conditioning | Reduced intensity | 10 (9.9%) | 11 (16.1%) | 0.626 |
| | Myeloablative | 49 (48.5%) | 38 (55.8%) | |
| Donor | Matched related | 23 (22.7%) | 11 (16%) | 0.204 |
| | Unrelated | 31 (30.6%) | 35 (51.4%) | |
| | Haploidentical | 2 (1.9%) | 2 (2.9%) | |
| | Cord | 3 (2.9%) | 1 (1.4%) | |

Table: Patient Characteristics by Era of Diagnosis
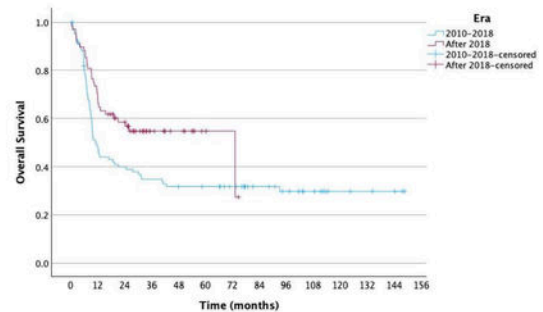


Figure: Overall Survival by Era of Diagnosis (n=169)

**Figure 1**

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