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Blood 142 (2023) 4249–4250

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Comparison between Dasatinib-Blinatumomab Vs Ponatinib-Blinatumomab Chemo-Free Strategy for Newly Diagnosed Ph+ Acute Lymphoblastic Leukemia Patients. Preliminary Results of the Gimema ALLL2820 Trial

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Introduction. The outcome of Philadelphia positive acute lymphoblastic leukemia (Ph+ ALL) has dramatically improved in the last decade, due with the introduction in the clinical practice of tyrosine kinase inhibitors (TKIs). A further improvement has been obtained with the use of blinatumomab as a consolidation strategy in newly diagnosed patients. We previously designed an induction/consolidation chemotherapy-free frontline trial with dasatinib followed by blinatumomab (GIMEMA LAL2116, D-ALBA); the preliminary results showed that after 2 cycles of blinatumomab (primary endpoint), molecular responses were achieved in 60% of cases and that, with a median follow-up of 18 months, overall survival (OS) and disease (DFS) were 95% and 88% (Foà et al, NEJM 2020). An updated follow-up at 53 months (Foà et al, under revision and ASH 2023) confirmed the favorable long-term outcomes with OS and DFS of 75.8% and 80.7%, respectively. A total of 9 relapses occurred. The median time to relapse was 4.4 months (1.9-25.8); 4 were at the central nervous system (CNS). To further improve the outcome of these patients, we designed a phase III trial (GIMEMA ALL2820) in which in the experimental arm dasatinib was substituted with ponatinib, followed - in the consolidation phase - by at least 2 cycles of blinatumomab. The trial is currently enrolling.
Aims. To compare the efficacy of the combination of ponatinib followed by blinatumomab with that reported with dasatinib followed by blinatumomab for the management of newly diagnosed adult Ph+ ALL patients.
Patients and Methods. From September 2021 to July 2023, 74 patients have been enrolled in the experimental arm, based on ponatinib followed by at least 2 cycles of blinatumomab; the induction period has been reduced from 85 to 70 days and the dose of ponatinib was either 45 mg or 30 mg, according to patient's age. A dose reduction to 30 mg was foreseen by day 28 of induction, regardless of age, to avoid unacceptable toxicities. Furthermore, CNS prophylaxis was strengthened with a total of

15 medicated lumbar punctures and triple intrathecal therapy (methotrexate, aracytin and steroids) was administered. Finally, transplant allocation was not left to investigator's choice, but it was established according to biological features (minimal residual disease and presence of the *IKZF1* ^{plus} genotype).

Results. Median age was 57 years (range 20-80), with 31% of patients being older than 65 years; 51% were males, the median white blood count (WBC) was 12 x10 ^{9}/l (1-207 x10 ^{9}/l). The p190 fusion protein was detected in 75.6% of cases, the p210 in 21.6% and p190/p210 in 2.7%. The *IKZF1* ^{plus} genotype was detected in 33% of cases. The median follow-up is 6.1 months (0 - 20.3). Of the 74 patients enrolled, 16 were still receiving induction treatment and have therefore been excluded from the present analysis, and 40 have received ≥2 cycles of blinatumomab. Regarding the induction phase, 55 of 58 patients (95%) achieved a complete hematologic remission (CHR), while 3 patients (5%) died in induction (a 77-year-old woman for unknown causes, a 68-year-old man for an intestinal occlusion and a 52-year-old man due to pneumonia). A molecular response (including both MRD negative and positive non-quantifiable (PNQ) cases) was obtained in 21/55 cases (38.2%). By the end of the consolidation phase, of the 40 evaluable patients 25 (62.5%). achieved a molecular response. So far, a single patient has relapsed (WBC at onset 121 x10 ^{9}/l and a *IKZF1* ^{plus} genotype) after 3 months from CHR: at relapse, this case harbored a T3151 mutation (Sanger sequencing and digital droplet PCR at diagnosis were wild type). At recurrence, CD19 expression was maintained.

Conclusions. The preliminary analysis of the GIMEMA ALL2820 trial proved the feasibility of this ponatinib-blinatumomab induction consolidation strategy for newly diagnosed Ph+ ALL of all ages, with a 95% CHR rate. Molecular responses at the end of induction are slightly superior in the current trial (38.2% vs 29% in the D-ALBA study), whereas they are virtually equivalent after 2 cycles of blinatumomab (62.5% vs 60% in in the D-ALBA). So far, the benefit of the current protocol appears to rely on a lower relapse rate, with only 1 relapse being observed to date, while in the same time period 3 relapses were documented with the dasatinib-blinatumomab combination. Further details will be provided.

Disclosures Chiaretti: *Amgen:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *Gilead:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees. **Luppi:** *Sanofi:* Membership on an entity's Board of Directors or advisory committees; *Gilead Sci:* Membership on an entity's Board of Directors or advisory committees, Other: Travel Grant; *Jazz Pharma:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Grifols:* Membership on an entity's Board of Directors or advisory committees; *Daiichi-Sankyo:* Membership on an entity's Board of Directors or advisory committees; *MSD:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees. **Borlenghi:** *Amgen, Incyte:* Other: travel grants; *AbbVie, BMS:* Consultancy. **Vetro:** *ABBVIE:* Honoraria; *BMS:* Honoraria; *Jazz Pharmaceuticals:* Honoraria. **Rambaldi:** *Abbvie:* Honoraria.

https://doi.org/10.1182/blood-2023-189632