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POSTER ABSTRACTS

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

A Phase II Study of Single Agent Aspacytarabine (BST-236) in Adults Unfit for Intensive Chemotherapy with Relapsed or Refractory Acute Myeloid Leukemia (R/R AML) or Higher Risk Myelodysplastic Syndromes (R/R HR MDS)

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Background-Common treatment approaches for R/R AML and to some extent HR MDS involve intensive chemotherapy regimens, typically combining high dose cytarabine with other drug(s), but these intensive regimens may not be suitable for unfit or elderly patients. To address this issue, a cytarabine prodrug called BST-236 has been developed, which delivers high doses of cytarabine while reducing systemic toxicity, making it a potential option for intensive chemotherapy in older and frail patients. This Phase II study aimed to assess the efficacy and tolerability of BST-236 in unfit patients with R/R AML or HR MDS previously treated with a non-intensive regimen.

Methods-This ongoing Phase 2 trial (NCT *04827719*) enrolled HR MDS and AML patients (pts) aged ≥ 75 years or with co-morbidities incompatible with intensive chemotherapy. MDS pts were refractory or had relapsed to azacytidine (AZA), and AML pts to AZA, low-dose cytarabine (LDAC) or AZA -venetoclax (VEN), given as a first line regimen. Each BST-236 induction and maintenance course consisted of 6 daily 1-hour intravenous infusions at a dose of 4.5 g/m ^{2}/d (containing 3 g/m ^{2}/d of cytarabine). After completing 1 induction cycle, patients with stable disease (SD) or partial response could undergo a second similar cycle, and patients who achieved complete remission (CR) could receive 2 to 4 maintenance cycles at the same schedule. Inclusion of 20 AML and 20 MDS pts was planned.

Results-From August 2021 to May 2023, 16 MDS and 20 AML pts from 9 centers were enrolled, with a median follow up of 3 months.

MDS: Median age was 74.8 years [IQR, 71.2-76.4] and ECOG was 0- 1 in all but 1 patient . All pts were previously treated with AZA and 4 (29%) had adverse R-IPSS karyotype. 14/16 were evaluable for response after 1 induction: 1 (7%) CR, 2 (14%) marrow CR, 7 (50%) SD. Hematological improvement was observed in 6 (43%) patients. Two serious treatment related adverse events (SAE) - febrile neutropenia and sepsis - occurred in 2 pts. Median duration of hospitalization for the induction cycle was 29.5 days [IQR 25.5-32.5] and 30-day mortality rate was 0%.

AML: Median age was 77.6 years [IQR, 73.8-79.4] and all pts had ECOG 0-1. Two pts were previously treated with AZA, 1 with LDAC, 17 with AZA-VEN and 8 (50%) had adverse ELN score. 17/ 20 pts were evaluable for response after 1 induction cycle

: 2 (12%) CR including 1 CR with negative MRD, 1 (6%) CRi, 10 (59%) SD. Three SAE- infections and hepatobiliary disorders- occurred in 2 pts. Median duration of hospitalization for the induction cycle was 26 days [IQR 23.2-30.8] and 30-day mortality rate was 10%.
Four MDS pts still need to be enrolled, and follow up is ongoing. An update will be presented at the meeting.
Conclusion- Response rates with BST-236, in this pretreated older frail R/R AML and MDS population, were modest. Toxicity, including myelosuppression, however appears lower than with conventional intensive chemotherapy, suggesting this treatment could be interesting earlier in the disease course.

Disclosures Cluzeau: *Jazz Pharma:* Consultancy, Speakers Bureau; *Abbvie:* Consultancy, Speakers Bureau; *Incyte:* Speakers Bureau; *Syros:* Speakers Bureau; *Keros:* Speakers Bureau; *BMS:* Consultancy, Speakers Bureau; *Servier:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau. **Papayannidis:** *Abbvie, Astellas, Servier, Menarini/Stemline, BMS, Pfizer, Amgen, Janssen, Incyte, Novartis:* Honoraria; *Pfizer, Astellas, Janssen, GSK, Blueprint, Jazz Pharmaceuticals, Abbvie, Novartis, Delbert Laboratoires:* Membership on an entity's Board of Directors or advisory committees. **Fenaux:** *Janssen:* Consultancy, Honoraria, Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding; *AbbVie:* Consultancy, Honoraria, Research Funding; *Jazz:* Consultancy, Honoraria, Research Funding; *Novartis:* Consultancy, Honoraria, Research Funding; *French MDS Group:* Honoraria.

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