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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Five-Year Follow up Results of Phase II Clinical Trial Evaluating Ruxolitinib (RUX) and Azacitidine (AZA) Combination Therapy in Patients (pts) with Myelodysplastic Syndrome/Myeloproliferative Neoplasms (MDS/MPNs)

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Introduction:
MDS/MPN represent a distinct category of Philadelphia chromosome negative myeloid neoplasms that share pathological and morphological characteristics with both MDS and MPN. Very few prospective studies have been conducted in pts with MDS/MPN, with currently available data showing a median overall survival (OS) of less than two years in this challenging subset. We conducted a phase 2 clinical trial evaluating the combination of JAK-inhibitor RUX with demethylating agent AZA in pts with MDS/MPN. The interim analyses (Assi *et al*, AJH 2018) showed objective responses in 57% pts and a median duration of response (DOR) of 8 months (mos). Herein we report the long-term follow up of a larger cohort of pts treated on this prospective ongoing clinical trial.
Methods:
We conducted an open label single-arm phase 2 clinical trial (NCT01787487) at the MD Anderson Cancer Center, Houston, evaluating the use of RUX-AZA in newly diagnosed or previously treated MDS/ MPN. Adults aged ≥ 18 years with MDS/MPN categorized as Intermediate 1-2 or High-risk by Dynamic International Prognosis Scoring System (DIPSS) (Passamonti *et al*, Blood 2010) were included. Pts previously exposed to RUX and/or AZA were excluded. RUX 5-20mg twice daily (per RUX label depending upon platelet counts at initiation) was given in 28-day cycles, and AZA 25mg/m2 (SQ or IV) Days 1- 5 was added starting cycle 4. Cycles were repeated every 4-6 weeks depending on count recovery. Response assessment was carried out using the 2015 International Consortium Proposal of response MDS/MPN criteria (Savona M *et al*, Blood 2015) and best objective response was tabulated. Progression free survival (PFS) included treatment change because of disease progression or inadequate response, transformation to acute myeloid leukemia (AML) or death and calculated from the time of therapy initiation.
Results:
From May 2013 to August 2022, 52 pts with a median age of 68 years (range, 39-82 years) were treated on trial. The data cutoff was July 15, 2023 (**Table 1).** 32 pts (61%) were males, and 9 (75%) pts were white. 50 pts (96%) had ECOG PS<2. Baseline median bone marrow (BM) blasts were 4.5% (range 0-19%), with 19 (37%) carrying *JAK2* mutations, and 16 (31%) with an abnormal karyotype. Intermideate-2 DIPSS was the most prevalent risk category, seen in 23 (44%) pts. At least one cytopenia was present in 32 (61%) pts, and three (6%) pts had bicytopenia. 24 of 49 (49%) had palpable splenomegaly, and 3 pts had undergone prior splenectomy. After a median follow up of 60 months (mos) (95% CI: 50.0-71.3) from therapy initiation, 18 (35%) pts are alive, and 1 pt is on active trial therapy. Objective responses per the MDS/MPN international consensus response criteria were observed in 28 (54%) pts and included clinical improvement in 14 (50%) pts, partial marrow response in 12 (43%) pts, optimal marrow response and cytogenetic complete remission in 1 (4%) pt each. The DOR in the 28 pts with objective response to therapy (censored for death in pts who died without evidence of progression) was 35 mos (95% CI: NE-73.5). The median OS in this group of responders was 36.4 mos (95% CI: NE-77.2). Five of these pts died without confirmed disease progression at the time of death. For the full cohort the median PFS was 13.4 mos (95% CI: 7.9-18.8) and median OS was 31.8

mos (95% CI: 18.5-44.9 **) (Figure 1).** Transformation to AML occurred in 12 (23%) pts, with the median time to transformation being 13.2 mos (range 2.9-71.3) and all of them have died at the time of last follow-up. 8 (15%) pts underwent allogenic stem cell transplant (ASCT) as subsequent therapy following treatment with AZA-RUX amongst whom 6 (75%) had shown objective responses prior to transplant. For the pts who underwent ASCT, median PFS from the initiation of AZA-RUX was 40.8 months and median OS was not reached.

Conclusion:

Long term follow up from this phase II prospective clinical trial demonstrates durable disease responses with the RUX-AZA combination in MDS/MPN, with the responses translating into improved survival outcomes.

Disclosures Senapati: *Kite Pharma:* Other: Advisory Board. **Pemmaraju:** *ClearView Healthcare Partners:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Imedex:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Protagonist Therapeutics, Inc.:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *EUSA Pharma:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Curio Science:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Dan's House of Hope:* Membership on an entity's Board of Directors or advisory committees; *CareDx:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Harborside Press:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Dava Oncology:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; 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Parameters		N (%), [range]
[redacted]	[redacted]	[redacted]
Gender	Males	32 (62)
[redacted]	[redacted]	[redacted]
Performance Status	ECOG PS<2	50 (96)
[redacted]	[redacted]	[redacted]
Baseline blood and BM	Hb (g/dl) WBC (10^9/L) Platelet (10^9/L) LDH (IU) BM blasts (%)	9.8 [6.1-14.4] 21.7 [2.2 - 123.2] 169 [53-1429] 758 [203-3615] 4.5 [0-19]
[redacted]	[redacted]	[redacted]
Cytogenetics	Diploid Complex Other abnormal karyotypes del 5q del 7q +8 inv 3	36 (69) 4 (8) 12 (23) 1 1 2 1
[redacted]	[redacted]	[redacted]
DIPSS	Low Int-1 Int-2 High	0 (0) 12 (23) 23 (44) 17 (33)
[redacted]		

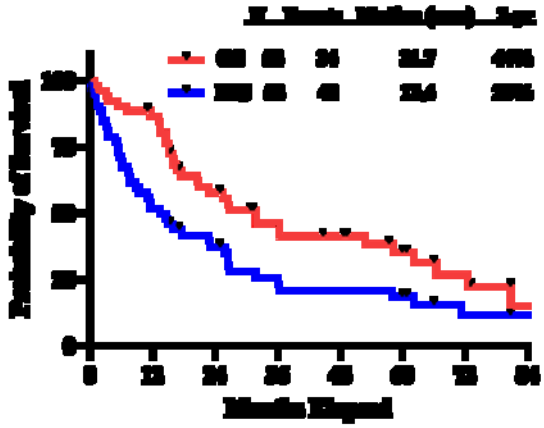

Figure 1

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