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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Preliminary Results from a Phase 1b Dose De-Escalation Stage of Abnl-Marro 001: An International MDS/MPN Working Group Study

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Background:
Myelodysplastic/Myeloproliferative neoplasms (MDS/MPN) represent a group of rare hematologic malignancies, distinguished by their concurrent dysplastic and proliferative features. Patients with these neoplasms have an increased risk of acute leukemia transformation and often present with extramedullary and constitutional symptoms. The only approved therapies for MDS/MPNs are hydroxyurea, decitabine (oral decitabine/cedazuridine and parenteral decitabine) or azacitidine (parenteral) for pts with CMML. Given the rarity and the heterogeneity of MDS/MPNs, prospective studies focusing specifically on MDS/MPN have been uncommon, and refining treatment strategies has been difficult. ***ABNL-MARRO*** (**A** **B**asket study of **N**ove **l** therapy for untreated **M**DS/MPN **a**nd **R**elapsed/ **R**efractory **O**verlap Syndromes) is an international cooperative effort that leverages the expertise of the MDS/MPN International Working Group (IWG) and provides a framework for collaborative studies around the world to advance treatment of MDS/MPN and to explore clinical and pathologic markers of disease severity, prognosis, and treatment response (Moyo TK et.al *BMC Cancer*. 2022).
Methods:
ABNL-MARRO 001 (AM-001) is an open-label, phase 1b/2 study testing the treatment combination of ASTX727 (days 1-5), a fixed dose oral combination pill containing 35 mg of the DNMTi decitabine (DEC) and 100 mg of the cytidine deaminase inhibitor cedazuridine (CED), together with a series of active agents in myeloid disease (see Figure 1a) for MDS/MPN. In arm A, ASTX727 is combined with itacitinib 300 mg (days 1-28), a selective JAK1 inhibitor in newly diagnosed and relapsed/refractory (R/R) pts. Here we report results from the 3+3 dose de-escalation phase 1b portion used to determine the recommended

Phase 2 dose (RP2D) in arm A. Dose-limiting toxicities (DLTs) were assessed in cycle 1. Disease response was assessed by the MDS/MPN IWG response criteria (Savona et.al., *Blood.* 2015).

Results:

Seven patients were enrolled with a median age 75 (range 32-82) years with newly diagnosed (4 pts) or R/R (3 pts) MDS/MPN. Three patients had CMML, 2 had MDS/MPN-U, and 2 had refractory MDS/MPN RST. One patient was not DLT evaluable given severe disease-induced cytopenia, and was not included in the assessment (patient 4 in Figure 1b). The majority of pts experienced a treatment-emergent adverse event (TEAE) of any grade; the most common (≥30% of pts) were thrombocytopenia (50%), neutropenia (30%), and constipation (30%); 50% of pts experienced a Grade ≥3 TEAE; the most common was neutropenia (30%). No DLTs were reported, and these AEs were consistent with what has been reported in the use of ASTX727 (Savona et al. *Blood.* 2022). One patient achieved a CR, and two additional patients had the best overall response of optimal marrow response after receiving 6 cycles of treatment. All patients are alive with a median follow-up of 12 months (range 6-17 months). The clinical responses and time-on-treatment of all pts in phase 1b are summarized in Figure 1b.

Summary/Conclusion:

Based on the preliminary results of the phase 1b study, the dosing schedule of 35 mg DEC / 100 mg CED daily for 5 days in combination with itacitinib 300 mg daily for 28 days was selected as the RP2D as it balanced clinical efficacy with an acceptable and manageable safety profile. This regimen and dose are being utilized in a 28-day cycle in the ongoing global, multi-center phase 2 study (NCT04061421).

Disclosures Kishtagari: *Servier Pharmaceuticals:* Consultancy; *Geron Corporation:* Honoraria; *CTI BioPharma Corp., a Sobi company:* Consultancy, Honoraria, Speakers Bureau. **Padron:** *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Research Funding; *CTI:* Membership on an entity's Board of Directors or advisory committees; *Pharmaessentia:* Membership on an entity's Board of Directors or advisory committees; *Gillead:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Research Funding; *Kura:* Research Funding. **Cluzeau:** *BMS:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *Abbvie:* Consultancy, Speakers Bureau; *Jazz Pharma:* Consultancy, Speakers Bureau; *Syros:* Speakers Bureau; *Keros:* Speakers Bureau; *Servier:* Consultancy, Speakers Bureau; *Incyte:* Speakers Bureau. **Diez-Campelo:** *BMS/Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Advisory board fees; *Gilead Sciences:* Other: Travel expense reimbursement; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *GSK:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Moyo:** *Kite Pharmaceuticals:* Consultancy. **Braun:** *AstraZeneca:* Research Funding; *Blueprint Medicines:* Consultancy, Research Funding; *Gilead Sciences:* Research Funding; *Novartis:* Consultancy; *Oryzon Genomics:* Other: Institutional PI (FRIDA trial). **Patnaik:** *StemLine:* Research Funding; *Kura Oncology:* Research Funding; *CTI Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees. **Durivage:** *Theradex Systems, Inc.:* Current Employment. **Medeghri:** *Theradex Systems, Inc.:* Current Employment. **Anderson:** *Theradex Systems, Inc.:* Current Employment. **Platzbecker:** *Fibrogen:* Research Funding; *AbbVie:* Consultancy; *Roche:* Research Funding; *Curis:* Consultancy, Research Funding; *Celgene:* Honoraria; *Novartis:* Consultancy, Honoraria, Research Funding; *Silence Therapeutics:* Consultancy, Honoraria, Research Funding; *Amgen:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: travel support; medical writing support, Research Funding; *MDS Foundation:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy, Honoraria, Research Funding; *BeiGene:* Research Funding; *BMS:* Research Funding; *Geron:* Consultancy, Research Funding; *Janssen Biotech:* Consultancy, Research Funding; *Merck:* Research Funding; *Jazz:* Consultancy, Honoraria, Research Funding; *Syros:* Consultancy, Honoraria, Research Funding; *Servier:* Consultancy, Honoraria, Research Funding. **Fenaux:** *Jazz:* Consultancy, Honoraria, Research Funding; *Janssen:* Consultancy, Honoraria, Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding; *French MDS Group:* Honoraria; *Novartis:* Consultancy, Honoraria, Research Funding; *AbbVie:* Consultancy, Honoraria, Research Funding. **Santini:** *BMS, Abbvie, Geron, Gilead, CTI, Otsuka, servier, janssen, Syros:* Membership on an entity's Board of Directors or advisory committees. **Savona:** *AbbVie Inc.:* Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees; *CTI BioPharma Corp.:* Membership on an entity's Board of Directors or advisory committees; *Forma Therapeutics Inc.:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Geron Corporation:* Membership on an entity's Board of Directors or advisory committees; *Karyopharm Therapeutics Inc.:* Consultancy, Current equity holder in publicly-traded company, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Ryvu Therapeutics:* Consultancy, Current equity holder in publicly-traded company, Membership on an entity's Board of Directors or advisory committees; *Sierra Oncology, Inc.:* Membership on an entity's Board of Directors or advisory committees; *Taiho:* Membership on an entity's Board of Directors or advisory committees; *Takeda Pharmaceutical Company:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *TG Therapeutics, Inc.:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Boehringer Ingelheim:* Patents & Royalties; *ALX Oncology:* Research Funding; *Astex Pharmaceuticals:* Research Funding; *Incyte Corporation:* Research Funding.

Figure 1a

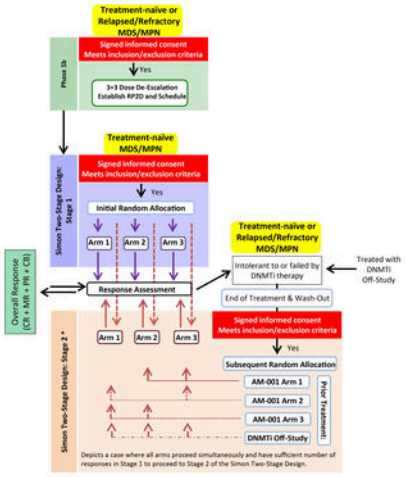

Figure 1b

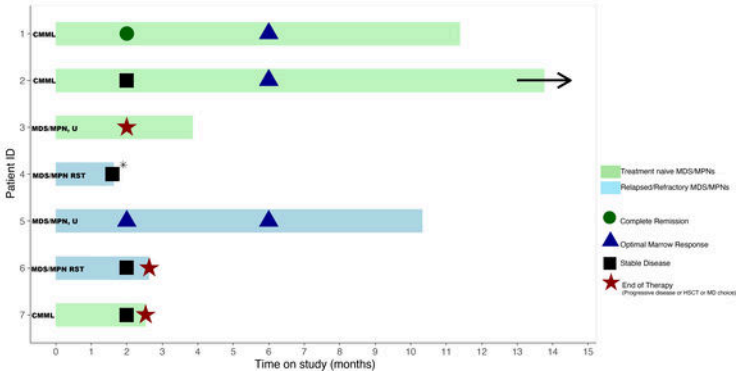

Figure 1

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