ASH Annual Meeting - December 10, 2023

Final Results from Phase 1 Study of Briquilimab, an Anti-CD117 Monoclonal Antibody, in Combination with Low Dose Irradiation and Fludarabine Conditioning, Shows Durable Remissions in Older Adults with Acute Myeloid Leukemia in Complete Remission and Myelodysplastic Syndrome Undergoing Allogeneic Hematopoietic Cell Transplantation (AHCT)

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# **Conflict of Interest**

Gandhi - None

Muffly - Advisory Boards: Pfizer, Amgen, Jazz, Medexus, CTI Biopharma, Kite; Research Funding: Astellas, Jasper, Adaptive, Kite, BMS; Consulting: Astellas

Lee - Advisory Boards: Kadmon, Kite, Jazz; Research Funding: Incyte; Consulting: Fresenius

Scott- Advisory Boards: BMS, Alexion, Incyte, Taiho

Kwon, Youn, Yanagiba, Arulprakasam, Le, Pang - Employment: Jasper

Shizuru - Executive: Jasper; Advisory Boards: Shoreline

# Allogeneic HCT rates have significantly increased, especially in over 65 years old, in the U.S.





Includes Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, Myelodysplastic Syndromes/Myeloproliferative Neoplasms, Non-Hodgkin Lymphoma, Hodgkin Lymphoma

Briquilimab Inhibits CD117 (c-Kit; Stem Cell Factor Receptor) Signaling Leading to Transient Clearance of Hematopoietic Stem Cells (HSCs) from Their Bone Marrow Niche



Blockade of CD117 is <u>Synergistic</u> with Low Dose Radiation to Enhance Clearance of HSCs from the Niche and Enable HSC Engraftment in Immunocompetent Mouse Model



Chhabra et al. Sci Transl Med 2016; Pang et al. ASH 2019

# Study Design: Single-arm, Open Label, in MDS/AML Patients Not Eligible for Myeloablative Conditioning Regimens

### Key inclusion criteria:

- MDS or AML
- $\geq$ 60 years or HCT-Cl  $\geq$ 3
- HLA matched related or unrelated donor
- Exclude prior HCT

N = 32patients + HCT

### Experimental arm:

Briquilimab 0.6 mg/kg + Flu 30 mg/m<sup>2</sup> x 3 days + **TBI** 200-300 cGv

#### **Assessments:**

#### Primary endpoints:

- Safety and tolerability of briquilimab/TBI/Flu
- Briquilimab pharmacokinetics

#### Secondary endpoints:

- Engraftment and donor chimerism
- Relapse-free survival
- GVHD, Non-relapse mortality, and Overall Survival
- MRD clearance

#### Exploratory endpoints:

Depletion of HSPCs by briquilimab

# Treatment Schema: Outpatient Conditioning Regimen



- Real-time PK measurements and modeling were used to determine Flu start date
- TBI increased from 200 to 300 cGy after first 7 subjects to aid lymphoablation
- GVHD prophylaxis: Tacrolimus, Sirolimus, Mycophenolate Mofetil (Sandmaier et al, Lancet Haematology 2019)

## MDS & AML Patient Characteristics

Characteristic	All (N = 32)	AML in CR (N=13)	MDS (N = 16)	AML not in CR (N = 3)
Median age (range) - year	70 (62-79)	70 (62-79)	70 (63-77)	66 (66-69)
Sex - no. (%)				
Male	20 (62.5%)	8 (61.5%)	11 (68.8%)	1 (33.3%)
Female	12 (37.5%)	5 (38.5%)	5 (31.3%)	2 (66.7%)
Prior AML/MDS Therapy - no. (%)				
Untreated or growth factor supportive care only	3 (9.4%)	0 (0%)	3 (18.8%)	0 (0%)
One regimen only	16 (50.0%)	5 (38.5%)	11 (68.8%)	0 (0%)
Multiple regimens	10 (31.3%)	8 (61.5%)	2 (12.5%)	3 (100%)
Donor Type - no. (%)				
Matched related donor	7 (21.9%)	1 (7.7%)	6 (37.5%)	0 (0%)
Matched unrelated donor	21 (78.1%)	12 (92.3%)	10 (62.5%)	3 (100%)
TBI dose - no. (%)				
200 cGy	7 (21.9%)	3 (23.1%)	4 (25.0%)	0 (100%)
300 cGy	21 (78.1%)	10 (76.9%)	12 (75.0%)	3 (100%)

0.6 mg/kg IV Briquilimab PK: Consistent and Predictable Clearance



Briquilimab is an investigational agent and not approved for any indication.

## Safety and Tolerability

- No significant briquilimab infusion reactions
- No briquilimab-related SAEs
- No primary graft failure (one case of secondary graft failure)

TEAE within 30 Days Post-transplant by Severity Grade	Total (N=32)
Grade 1-2	11 (34.4%)
Grade 3	17 (53.1%)
Grade 4	4 (12.5%)*

\*Grade 4 TEAEs reported in 4 subjects: neutropenia, lymphopenia

## Briquilimab + 200-300 cGy TBI in All Patients Resulted in Neutropenia Followed by Neutrophil Engraftment by TD+26



# Median donor myeloid chimerism of 99% (range 96-100%) and median total chimerism of 95% (range 81-100%) at TD+90



# Final 1-year Efficacy Outcomes

At 1-year	AML in CR (n=13)	MDS (n=16)
Relapse/Progression	3 (23.1%)	5 (31.3%)
NRM	1 (7.7%)	1 (6.3%)
MRD Negative	8 (61.5%)	6 (37.5%)
Relapse Free Survival	9 (69.2%)	8 (50%)
Overall Survival	9 (69.2%)	8 (50%)

Rates of GVHD	All patients (n=32)
Acute GVHD (MAGIC) grade 2 grade 3-4	4 (12.5%) 1 (3.1%)
Chronic GVHD (NIH) mild moderate severe	8 (25.0%) 5 (15.6%) 0 (0%)

Measurable residual disease (MRD) was tested using cytogenetics, flow cytometry and next gen sequencing prior to and after HCT

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- MRD+ pre HCT to MRD- by 1 year post HCT occurred in
  - 7 of 10 subjects with AML
  - 6 of 14 subjects with MDS
- Median time to conversion from MRD+ to MRD negativity occurred at TD+28

## Final 1-year Efficacy Outcomes



## Summary of Phase 1 Trial Results

- Briquilimab at a dose of 0.6 mg/kg has predictable clearance and allows donor cell infusion at 9-14 days after briquilimab
- All patients engrafted with neutrophil recovery before Transplant Day +26
- Briquilimab/Flu/TBI is a novel conditioning regimen that appears safe, well-tolerated, permits full donor myeloid chimerism, and results in promising early MRD clearance
- These data are encouraging. The Sponsor, Jasper, is continuing to work with the transplant community on a path forward for briquilimab as a conditioning agent in stem cell transplantation.

## Acknowledgements

- Jasper Therapeutics and the Investigators would like to thank the patients and families for participating in this clinical trial (NCT#04429191).
- We would also like to thank the participating clinical sites, clinical staff, and collaborators

