M-STAR, an Ongoing Phase 3 Study in Participants with Multiple System Atrophy–Baseline Characteristics

Jose-Alberto Palma Carazo[1], Lila Brady[2], Aaron Ellenbogen[3], Roy Freeman[4], Günter Höglinger[5], Gil L'Italien[2], Horacio Kaufmann[1], Anthony Lang[6], Phillip Low[7], Wassilios Meissner[8], Huw Morris[9], Susan Perlman[10], Werner Poewe[11], Jeremy Schmahmann[12], Wolfgang Singer[7], Steven Vernino[13], Gregor Wenning[11], Victoria Wirtz[2], Irfan Qureshi[2] for the M-STAR Study Investigators

1. Dysautonomia Center, New York University School of Medicine 2. Biohaven Pharmaceuticals 3. QUEST Research Institute 4. Center for Autonomic and Peripheral Nerve Disorders, Beth Israel Deaconess Medical Center 5. Department of Neurology, Hannover Medical University 6. The Edmond J Safra Program in Parkinson's disease University Health Network and the Department of Medicine, University of Toronto 7. Department of Neurology, Mayo Clinic 8. University of Bordeaux CRMR Atrophie Multisystématisée CHU Bordeaux 9. Institute of Neurology, UCL Queen Square 10. Department of Neurology, University of California, Los Angeles 11. Department of Neurology, Medical University of Innsbruck 12. Ataxia Unit, Department of Neurology, Massachusetts General Hospital 13. Department of Neurology and Neurotherapeutics, UT Southwestern Medical Center

Objective

To describe baseline characteristics of participants randomized in the ongoing M-STAR phase 3 study evaluating the disease modifying effect of verdiperstat on multiple system atrophy (MSA).

Background

MSA is a rare, adult-onset, rapidly progressive, and fatal neurodegenerative disease with no disease modifying treatment available. Verdiperstat (previously BHV-3241/AZD3241) is a first-in-class, oral, potent, selective, brain-permeable, irreversible myeloperoxidase (MPO) inhibitor. In phase 2 studies in Parkinson's disease (PD) and MSA, treatment with verdiperstat was generally safe and well tolerated. Verdiperstat decreased MPO activity in plasma, providing evidence of target engagement; reduced translocator protein binding on brain PET imaging in PD, providing proof of mechanism (decreased microglial activation/neuroinflammation)[1]; and demonstrated favorable trends on clinical efficacy measures (Unified MSA Rating Scale [UMSARS]) at 12 weeks[2].

Methods

M-STAR is a randomized, double-blind, placebo-controlled, parallel group study. Ambulatory participants, 40–80 years of age, with possible or probable MSA[3], including MSA-P or MSA-C, are randomized to 48 weeks of treatment with verdiperstat 600 mg twice daily or placebo. The primary efficacy endpoint is change from baseline to Week 48 in verdiperstat- vs. placebo-treated participants on a score derived from the UMSARS, optimized (based on health authority guidance) to assess clinically meaningful change in ability to function.

Results

Between July 2019 and July 2020, M-STAR enrolled 336 participants at 48 sites across 6 countries. Baseline characteristics are presented (Figs. 1–7, Tables 1–5).The sex breakdown of participants is almost even (Fig. 3), 97% are not Hispanic or Latino (Fig. 4), and most are white (Fig. 5). Participants are close to evenly split between Parkinsonian and Cerebellar subtypes of MSA, with slightly more MSA-C, and the breakdown is similar to that in peer trials[4–6] (Table 2). 67% are diagnosed with probable MSA (Table 4). M-STAR participants have slightly higher baseline UMSARS scores compared to peer trials except for the Epigallocatechin Gallate (EGCG) trial that also had almost all participants diagnosed with probable MSA (Table 5).

Conclusion

Baseline characteristics of M-STAR participants provide key information about the enrolled population, including MSA diagnostic classifications and clinician- and patient-reported disease severities, which is significant for MSA clinical trials and therapeutic development.

Baseline Demographic Characteristics

Figure 1. 6 Study Countries: U.S.A., Italy, Germany, France, Austria, and the U.K.

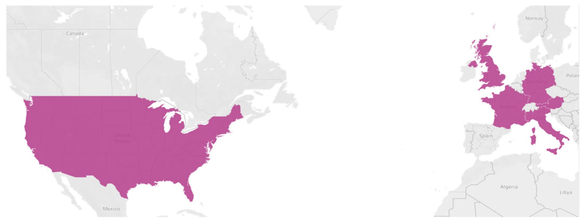


Table 1. Age and Weight Characteristics

	Age	Weight (kg)
Mean	62	79
Standard Deviation	7	19
Median	61	78
Min, Max	43, 80	44, 237

n=329 for weight

Figure 2. Number of Randomized Participants in Each Age Group

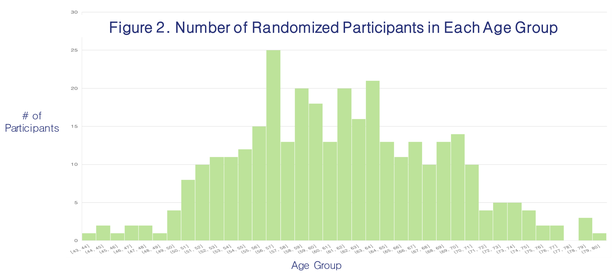


Figure 3. Breakdown by Sex: 49.4% of Participants Are Female

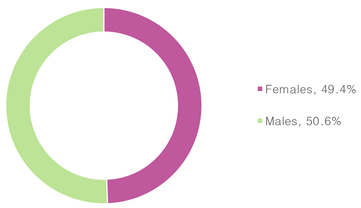


Figure 4. Breakdown by Ethnicity: 3.0% of Participants Are Hispanic or Latino

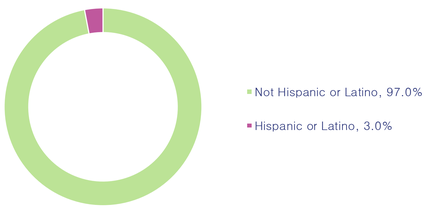
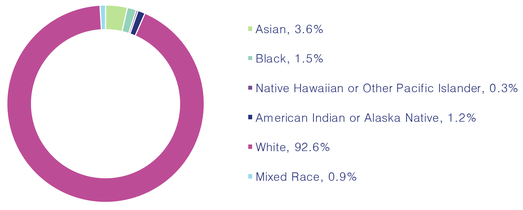


Figure 5. Breakdown by Race: 92.6% of Participants Are White



References:

1. Jucaite, A, et al., Brain. 2015 Sep;138(Pt9):2687-700.
2. Mullen, J, et al. Poster at International MSA Congress. Mar 2018.
3. Gilman, S, et al. Neurology. 2008 Aug26;71(9):670-6.
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Acknowledgements:

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Trial Registration:

ClinicalTrials.gov Identifier: NCT03952806.
EudraCT Number: 2019-001100-38

Baseline Disease Characteristics

Table 2. MSA Subtype (Parkinsonian vs. Cerebellar) Breakdown in the M-STAR Study vs. Other MSA Studies – Epigallocatechin Gallate (EGCG)[4] and Rifampicin[5]

	Verdiperstat	EGCG		Rifampicin	
	Treatment + Placebo (n=336)	Treatment (n=47)	Placebo (n=45)	Treatment (n=50)	Placebo (n=50)
MSA-P	46%	53%	53%	38%	44%
MSA-C	54%	47%	47%	62%	56%

Note: Rasagiline study only enrolled participants with MSA-P

Table 3. Clinical Global Impression of Severity (CGI-S) and Patient Global Impression of Severity (PGI-S) in the M-STAR study

	CGI-S	PGI-S
Mean	3.98	2.96
Standard Deviation	0.86	0.69
Median	4	3

n=334 for CGI-S and PGI-S. CGI-S Scale: 1 (normal) – 7 (among the most extremely ill) PGI-S Scale: 1 (normal) – 4 (severely ill)

Table 4. MSA Subtype Breakdown in the M-STAR Study vs. Other MSA Studies – Epigallocatechin Gallate (EGCG),[4] Rifampicin,[5] and Rasagiline[6]

	Verdiperstat	EGCG		Rifampicin		Rasagiline	
	Treatment + Placebo (n=336)	Treatment (n=47)	Placebo (n=45)	Treatment (n=50)	Placebo (n=50)	Treatment (n=84)	Placebo (n=90)
Probable MSA	67%	98%	96%	38%	44%	55%	39%
Possible MSA	33%	2%	4%	62%	56%	45%	61%

Table 5. Mean and (SD) or [range] for UMSARS Scores: Part I and Part II. M-STAR compared to other MSA studies

	Verdiperstat	EGCG		Rifampicin		Rasagiline	
	Treatment + Placebo (n=334)	Treatment (n=47)	Placebo (n=45)	Treatment (n=50)	Placebo (n=50)	Treatment (n=84)	Placebo (n=90)
UMSARS Part I	20.2 (5.7)	N/A	N/A	13.1 (3.8)*	12.1 (3.4)*	17.7 (4.5)	16.8 (5.5)
UMSARS Part II	19.9 (6.4)	23 [18-25]	22 [16-27]	16.6 (4.6)	15.2 (4.8)	20.5 (5.3)	19.6 (4.9)

*Question 11 omitted. UMSARS Part I: 0 (normal) – 48 (most affected). UMSARS Part II: 0 (normal) – 56 (most affected) UMSARS Part I + II: 0 (normal) – 104 (most affected)

Figure 6. UMSARS Scores Part I

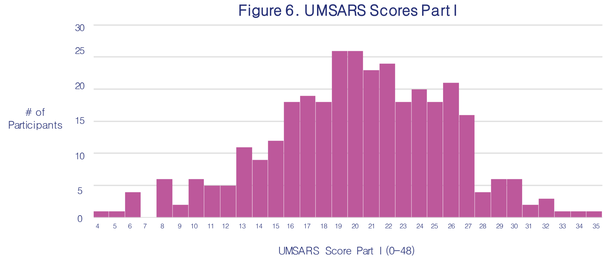
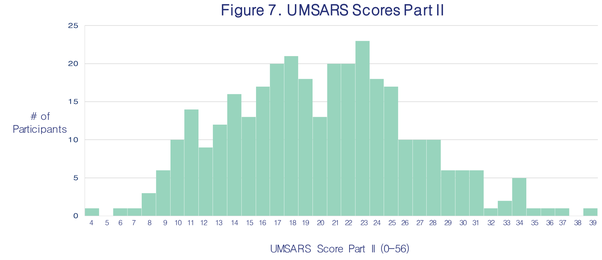


Figure 7. UMSARS Scores Part II



Preliminary data
N=336 unless otherwise noted