MLB-01-003: Open Label Phase 2 Study of BBP-418 in Patients with Limb Girdle Muscular Dystrophy Type 2I

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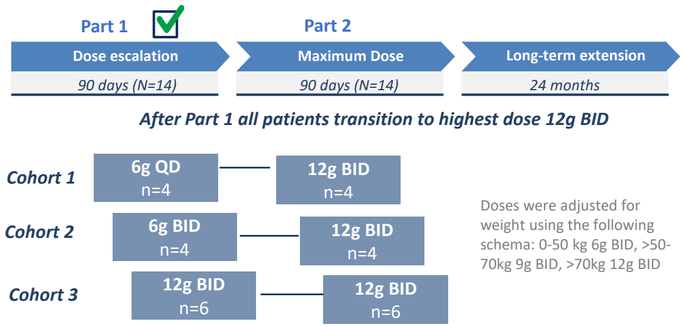
Introduction

Introduction: Limb Girdle Muscular Dystrophy (LGMD) Type 2I, also called LGMDR9 FKRP-related, is caused by bi-allelic loss-of-function of the fukutin-related protein (FKRP) gene which results in hypoglycosylation of alpha-dystroglycan (αDG). BBP-418 (Ribitol) is an investigational drug being evaluated as an orally administered substrate supplementation intended to saturate the FKRP enzyme driving increased glycosylation of αDG, thus ameliorating the root cause of disease in LGMD2I.

Objectives: The MLB-01-003 Phase 2 study is intended to explore the safety and tolerability, feasibility and usefulness of selected clinical efficacy and pharmacodynamic (PD) assessments in 14 patients with LGMD2I receiving ascending doses of BBP-418.

Trial Design



Doses were adjusted for weight using the following schema: 0-50 kg 6g BID, >50-70kg 9g BID, >70kg 12g BID

KEY ENDPOINTS

- NSAD
- 10-meter walk test / 100-meter walk
- FVC
- PUL2.0
- Ratio of glycosylated αDG to total αDG
- Creatine Kinase

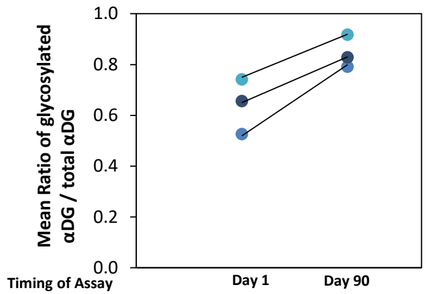
KEY INCLUSION CRITERIA

- Age between 12-55 at enrollment
- Genetically confirmed LGMD2I
- Body weight >30kg
- Able to complete 10MWT ≤12 seconds unaided (moderate disease) or unable to (severe disease)

Biomarker data – αDG and CK

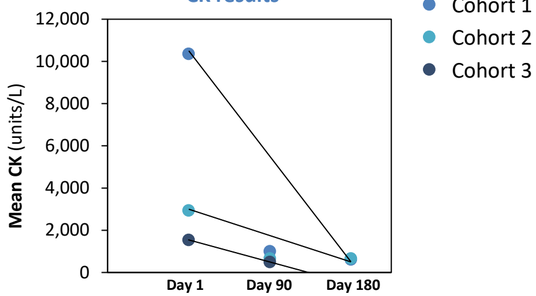
Patients showed increases in glycosylated αDG and statistically significant decreases in creatine kinase from baseline assessment after treatment with BBP-418

αDG results[1]



Cohort	# pts	Average α-DG change day 90 from baseline
1 (6g QD)	N=4	0.28 (+65%)
2 (6g BID)	N=2[2]	0.18 (+24%)
3 (12g BID)	N=4	0.17 (+31%)

CK results[3,4]

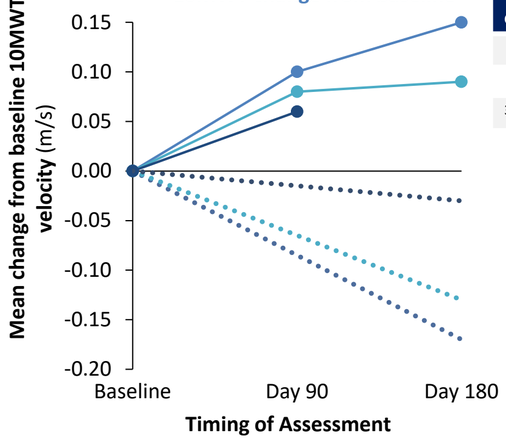


Cohort	# pts	Average % CK change day 90 from baseline	Average % CK change day 180 from baseline
1 (6g QD)	N=4	-68%	-77%
2 (6g BID)	N=4	-75%	-78%
3 (12g BID)	N=4	-67%	NA

Functional data – 10MWT

Patients showed increases in velocity in 10MWT after treatment with BBP-418

10MWT change from baseline

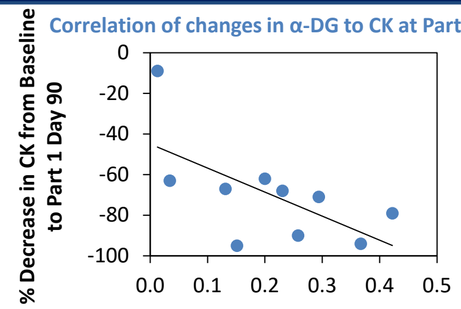


Cohort	# pts	Baseline	Part 1 Day 90	Part 2 Day 180
		Average 10MWT Velocity (m/sec) (Change from baseline)		
1 (6g QD)	N=3[5]	2.72	2.82 (+0.10)	2.87 (+0.15)
2 (6g BID)	N=4	1.48	1.56 (+0.08)	1.57 (+0.09)
3 (12g BID)	N=3[5]	1.06	1.12 (+0.06)	NA

Natural history declines from baseline were measured from the MLB-01-001 Lead-in Natural history study for the same group of patients over six months and compared to velocities after 90 and 180 days of treatment

Correlations in biomarkers

Correlation of changes in α-DG to CK at Part 1 Day 90[1,2]



Safety and tolerability

- 58 adverse events (AEs) were recorded with 8 possibly or probably related to BBP-418 treatment
- The 8 possibly/probably related AEs include: diarrhea (3x grade 1, 1x grade 2), nausea (2x grade 1), stomachache (1x grade 2), and dyspepsia (1x grade 1)
- No discontinuations or interruptions in therapy
- 1 severe adverse event recorded unrelated to the treatment

Conclusions

Phase 2 Study of BBP-418 in LGMD2I patients revealed:

- No treatment-related SAEs or dose limiting toxicities
- Increases in glycosylated αDG were measured across all cohorts with an average increase of +0.21 at day 90
- Declines were noted for creatine kinase, a key marker of muscle breakdown, of 70% at day 90 to 77% at day 180
- Small increases in velocity in the 10MWT were measured at 0.08 m/sec at day 90 for all cohorts and 0.12 m/sec at day 180 for cohorts 1 and 2
- Velocity increases on treatment compare favorably to natural history data where the same patients declined by an average of 0.12 m/sec over 6-months in the 10MWT

Additional biomarker and clinical data is anticipated in Q2/3 2022; Ph3 trial plans in development

[1]Ratios are normalized against healthy control samples; normalization technique under development and subject to change
[2]Values excluded where signal intensities were below reliable quantification threshold
[3]Cohort 1 Day 1 CK draws taken after functional assessments; all other draws done prior to functional assessment
[4]CK change from baseline as part 1 day 90 is statistically significant with P < 0.05
[5]Includes ambulatory patients only defined by ability to complete the 10MWT ≤12 seconds

Interim, "top-line," and preliminary data presented, announced, or published from time to time may change as more data become available, as additional analyses are conducted, or as audit and verification procedures are performed on such preliminary data. Rodriguez H, Hutchaleelaha A , Kelley K and D Sproule are employees of ML BioSolutions Inc and BridgeBio Pharm, Inc. and may own stock and/or stock options. ML Bio Solutions, Inc. and BridgeBio Pharma, Inc., funded and participated in the research for this study and provided writing support for this poster.

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