Initial experience using intravenous BPM31510 for treatment of pediatric patients with CoQ10 deficiency

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I. Abstract

Introduction: Primary CoQ10 deficiency (PCQD) is a multisystem primary mitochondrial disease treated with oral CoQ10 replacement therapy with varying results likely related to lack of standardized formulations, limited gastrointestinal (GI) absorption, as well as low tissue uptake and blood brain barrier penetrance. BPM31510 is a novel formulation of intravenously administered drug-lipid conjugated ubidecarenone that addresses the challenges of delivering CoQ10 into tissues (including brain) and bypasses inconsistent GI tract absorption.

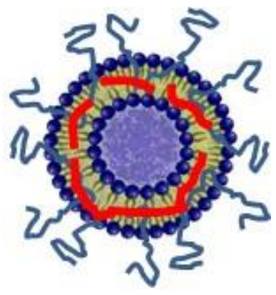
Methods: Four patients with PCQD have been treated with BPM31510 under named-patient and compassionate use requests a 9-year-old [c.812G>A; p.Arg271His; c.1821C>A; p.Tyr607Ter] and a 16 year old [c.1042C>T; p.Arg348* homozygous] in Germany, a 10 year-old in the US [1q42.13 28kb deletion (c.1390 C>T; p.Arg464Trp], and a 17-year old (c.811C>T, p.Arg271Cys; c.911C>T, p.Ala304Val) in Italy. In the two German patients, treatment with 30 mg/kg of OTC CoQ10 supplements had minimal benefit with variable plasma levels. The US patient received 50 mg/kg/day of OTC CoQ10 supplements with minimal, unsustained benefit. The 17-year-old patient in Italy received 30 mg/kg/day of OTC CoQ10 supplements, and 520 mg/day of idebenone for recurrent stroke-like episodes, with no benefit.

Results: The German patients were treated ≥9 months with improvements on the Scale for the Assessment and Rating of Ataxia (SARA), the Friedreich's Ataxia Rating Scale Activities of Daily Living, 9-Hole Peg Test, and patient- and/or caregiver-reported global impression of change and Goal Attainment scales (particularly writing speed). The US patient received a 6-month treatment course and showed markedly improved MM-COAST (Mitochondrial Myopathy Composite Assessment Tool) composite score across muscle strength, fatigue, balance, dexterity and exercise intolerance tests performed 18 weeks after the baseline assessments. These results aligned with improved patient reported outcomes (PedsQL, Lansky Performance scale, PediCat and the Modified Fatigue Impact Scale) and enhanced muscle CrCest MRI measurement of in vivo muscle mitochondrial function. The patient in Italy was studied with multiple functional scale assessments and showed improvement of 2 points in the SARA scale after 17 weeks of treatment and didn't present any additional stroke-like episodes. Across all patients, parents, schoolteachers, and/or parents of peers have reported substantial clinical improvement in all 4 patients. Routine clinical biochemical and hematologic measurements indicated no safety concerns. None of the patients reported any adverse events from the BPM31510 infusions.

Conclusion: This preliminary evidence in 4 patients thus far suggests that BPM31510 can be safely administered, is well tolerated, and may have a substantial effect on PCQD disease progression.

II. BPM31510

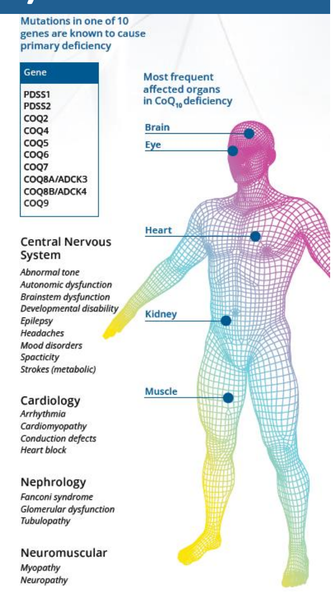
- Proprietary & **stable** formulation
- Contains oxidized (active) CoQ10 (red lines in image)
- High **bioactivity due to presentation of CoQ10 to the cell in the right orientation**
- Lipid nanoparticle suspension
- Enrichment in **mitochondria**



III. Primary CoQ10 Deficiency (PCQD)

- Most patients present early in childhood; the earlier the presentation, the worse the prognosis
- Identification of patients has accelerated with the advent of next-gen sequencing (mito panel)
- The current standard of care is based on over-the-counter (OTC) oral CoQ10 supplementation

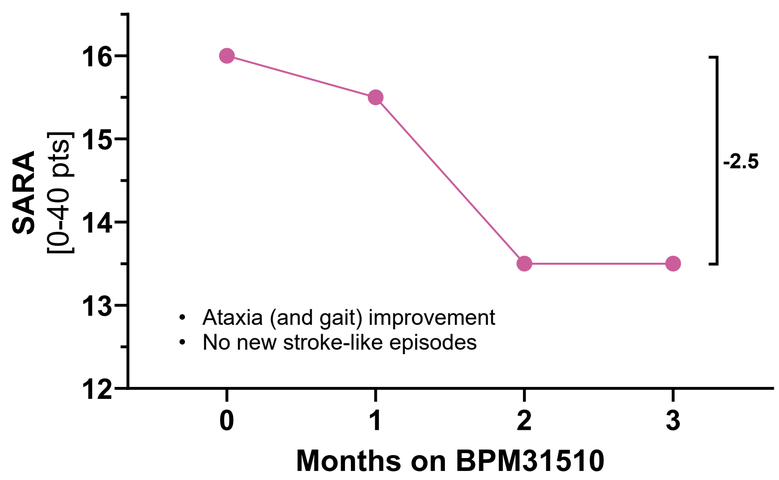
Coenzyme Q10 is a lipid-soluble molecule synthesized endogenously and plays a vital role in several essential cellular processes, including mitochondrial energy production, fatty acid beta-oxidation, pyrimidine biosynthesis, and antioxidant defense. Its biosynthesis is incompletely characterized and requires products of at least 12 known genes. The pathogenesis of PCQD is complex and related to the different functions of CoQ10. PCQD can affect any part of the body, but particularly the brain, muscle and kidney tissues. The common phenotypes are encephalomyopathy, severe infantile multisystemic disease, nephropathy, cerebellar ataxia and atrophy, and mitochondrial myopathy. The clinical trajectory of patients with PCQD is clearly progressive, serious and potentially life-threatening.



IV. Patient Demographics

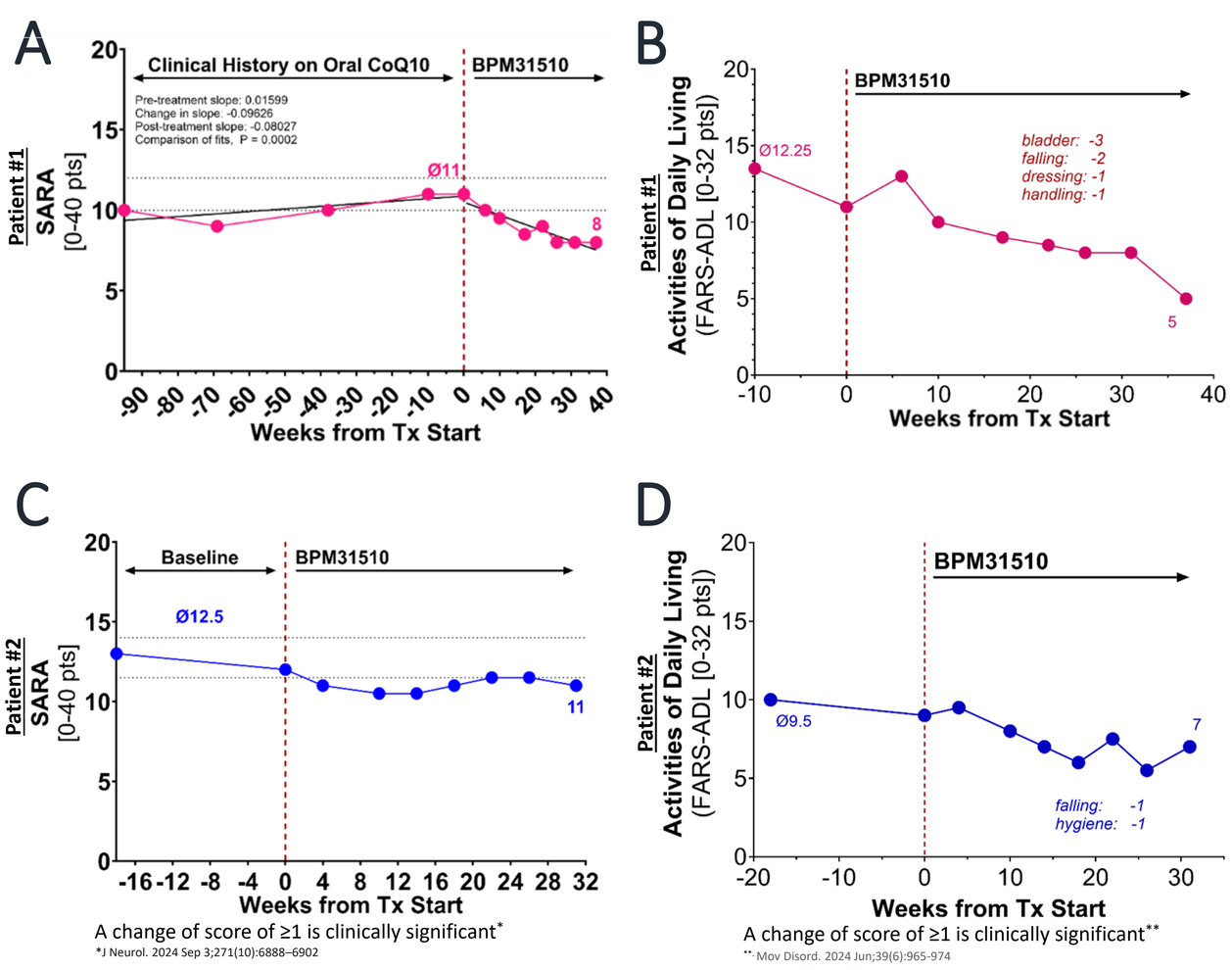
Patient details	Country	Tx Start	Mutation
9-year-old Female	Germany (#1)	10/19/2024	***COQ8A*** (c.812G>A; p.Arg271His; c.1821C>A; p.Tyr607Ter)
17-year-old Male	Germany (#2)	11/26/2024	***COQ8A*** (c.1042C>T; p.Arg348* homozygous)
10-year-old Female	USA	2/7/2025	***COQ8A*** (1q42.13 28kb deletion; c.1390 C>T; p.Arg464Trp)
16-year-old Female	Italy	7/24/2025	***COQ8A*** (c.811C>T, p.Arg271Cys; c.911C>T, p.Ala304Val)

V. SARA Score Improvement After Treatment in Italian Patient



SARA scores (Scale for the assessment and rating of ataxia) indicate an improvement in ataxia symptoms. Additionally, patient has had no stroke-like episodes since starting treatment. Previously patient had experienced these episodes every 2-3 months.

VI. Ataxia Evaluations Indicating Treatment Efficacy in the 2 German Patients



A change of score of ≥1 is clinically significant*

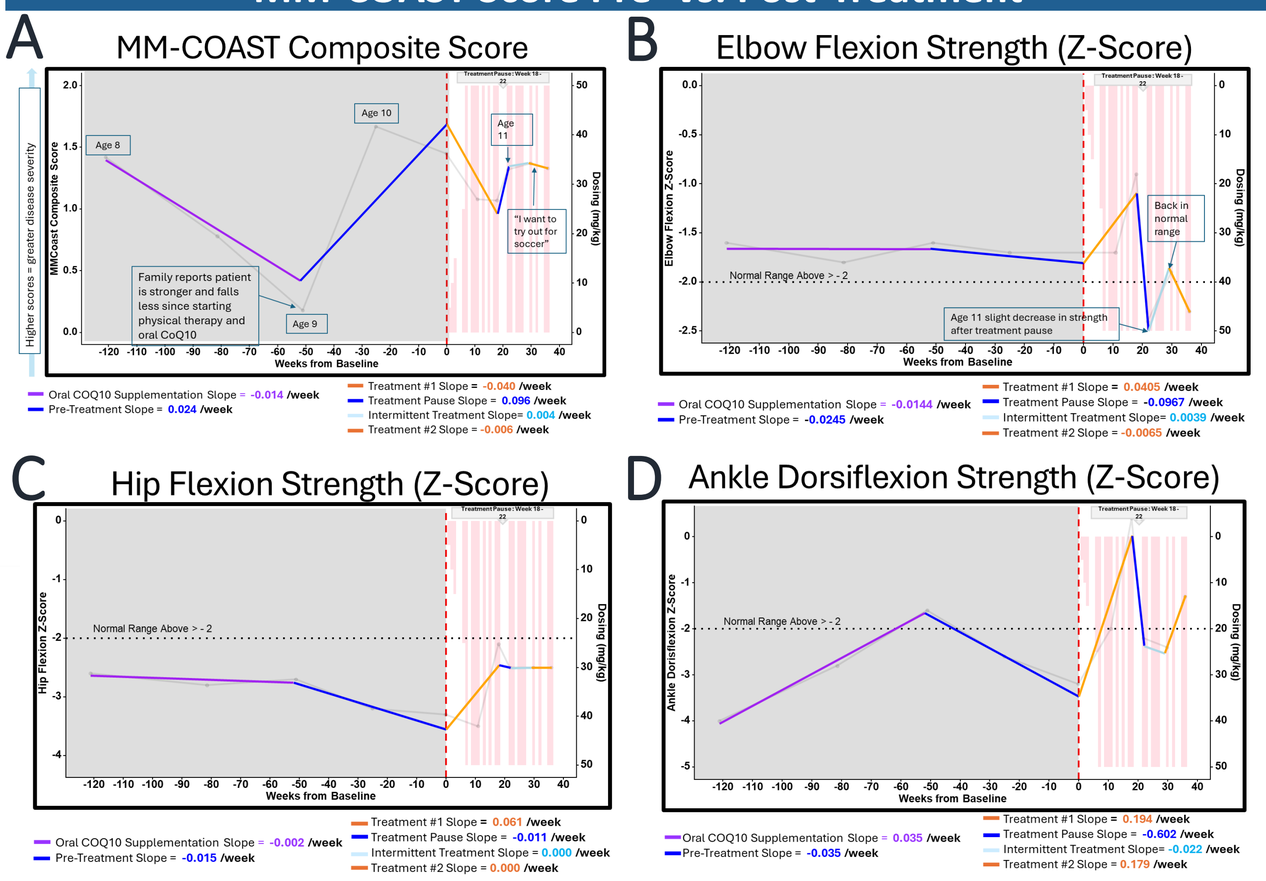
*J Neurol. 2024 Sep 3;271(10):6888–6902

A change of score of ≥1 is clinically significant**

**Mov Disord. 2024 Jun;39(6):965-974

SARA scores (Scale for the assessment and rating of ataxia) for A) P#1 and C) P#2, and FARS-ADL scores (Friedreich Ataxia Rating Scale-Activities of Daily Living) for B) P#1 and D) P#2 indicate an improvement in ataxia symptoms.

VII. US Patient Improvements in Dynamometry and Overall MM-COAST Score Pre- vs. Post-Treatment



Graphs showing **post treatment** improvements in **A)** MM-COAST composite score and of age-adjusted z-score showing improvement in strength (components of MM-COAST) of B) elbow flexors, C) hip flexors, and D) ankle dorsiflexors measured by hand-held dynamometry. Z-scores ≤ -2 S.D. are considered abnormal. This improvement regressed at the last data point following a 1-month unplanned treatment pause.

Spline regression analysis (blue line) demonstrates the pre-treatment and post-treatment MM-COAST trajectories. Vertical red line indicates initiation of treatment. Vertical yellow columns represent administered weekly doses up to a max dose of 50 mg/kg. Gaps in between the yellow columns indicate missed doses.

CONCLUSIONS – Preliminary Evidence of Potential Therapeutic Signal

- **BPM31510 weekly IV treatment has been well tolerated with no drug related clinically significant adverse events.**
- **All four patients have demonstrated improvements in ataxia and motility by SARA score (ataxia) or MM-COAST objective assessments (dynamometry)**
- **Noticeable improvements were observed as early as 4 weeks after treatment initiation and sustained past 20 weeks.**
- **Parents, teachers, and/or parents of peers have reported substantial improvement in day-to-day activities for all 4 patients.**

This preliminary evidence suggests that BPM31510 may have a substantial effect in patients with PCQD, warranting further investigation.

BPM31510 is an investigational drug whose safety and efficacy have not been established by the FDA.