Dietary Management Outcomes During SynPheny-1, a Phase 2 Clinical Trial of a Live Biotherapeutic, SYNB1618, for the Management of Phenylketonuria

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Introduction

- Dietary intake of phenylalanine (Phe) has a major impact on blood Phe levels in PKU patients.
- Stability in dietary Phe intake is critical in clinical trials for accurate interpretation of an investigational drug's (IMP) effect.
- Dietary management during SynPheny-1 included a novel approach of using set menus to decrease diet variability by guiding the patient in their food choices in order to have a consistent Phe intake day-to-day. It also included close monitoring and support from a metabolic dietitian to help with menu compliance.
- The traditional method of using 3-day diet records is primarily used for diet recording and not for guiding dietary intake to help maintain a consistent nutrient intake.
- Interim data of 8 participants are presented.

Methods

Patient Screening

- Participants completed 5-day diet records noting their usual intake; these were reviewed with the dietitian for clarity and accuracy and analyzed for baseline Phe, protein and calorie intake with MetabolicPro.
- **Outcome**: Participants' intake goals for a stable diet were +/-10% of their baseline intake of Phe and protein for the duration of the study.

Menu Template

- 5 custom daily menus, plus a list of "free foods" were created for each participant based on baseline goals. Biomarker and tracer menus were created for those study particular days.
- Using a template, menus and "free foods" were provided to participants via an app or a workbook.

Diet Run-in, Treatment, and Follow-up

- Diet data entered in the app was uploaded to the online portal daily or patients recorded intake in the workbook daily; the dietitian checked in with the patient 3x/week.
- Participants' actual intake was obtained daily and analyzed in MetabolicPro; results were then entered in the study database.

SynPheny-1 Study Outline

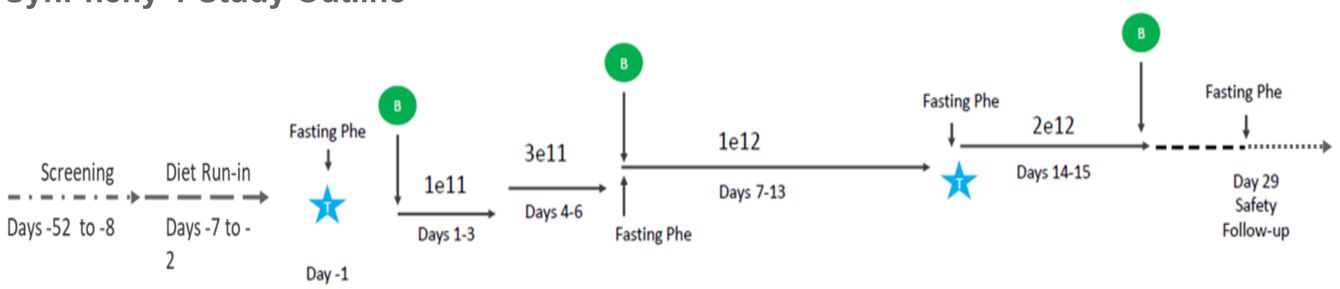


Figure 1: Participants reported their 5-day dietary intake during the screening period. They started using the customized daily menus 7 days prior to first dose of SYNB1618 and continued throughout the study until the follow-up visit 2 weeks after the last dose. The time on menus was 30 days total. ★=Tracer, B = Biomarker.

Results

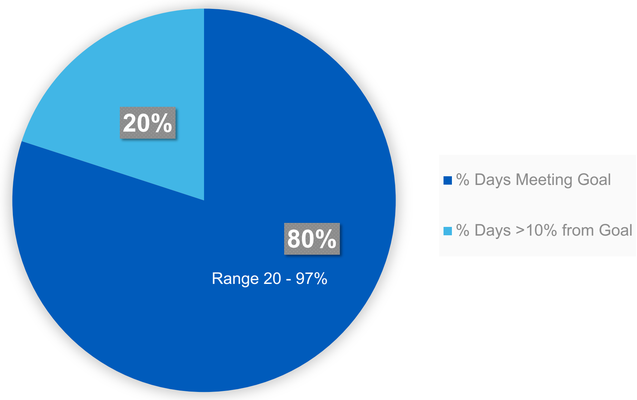
Participants' Experience:

- 4/8 participants used the app to access and log menu selection while 4/8 chose to use the paper version
- Participants over time desired more variety; study dietitians were available to make adjustments in real-time which enhanced ability to maintain the baseline goal
- All study dietitians reported satisfaction with real-time data reporting from the app output

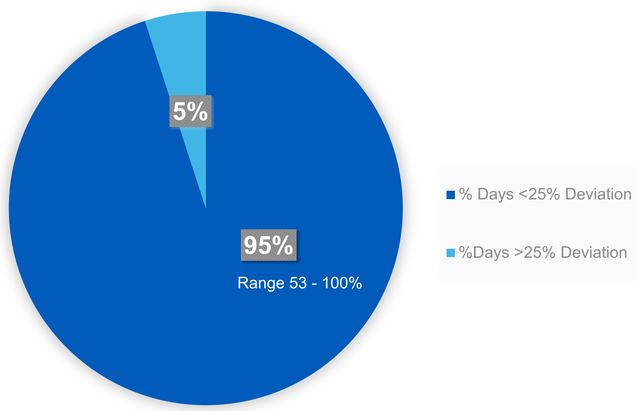
Diet Management:

- 7/8 participants had 10 or less baseline Phe deviations total during the study
- The median percent of baseline goal adherence was 80% of study days
- The median percent baseline adherence within +/- 25% of target intake was 95% of study days
- The median number of baseline goal adherence was 24 of 30 days (range 6-29days) during the 30 study days on menus
- The median percent deviation from baseline was 18% (range 12-36%) on days that deviations were present

Median Percent of Study Days Patients Maintained Baseline Phe Goal



Median Percent of Study Days Patients Maintained Phe Baseline Within 25%



Conclusions

- Tight baseline dietary Phe control was achieved using this method, despite study challenges including COVID restrictions, virtual management, and restricted travel to clinical research centers.
- Real-time compliance monitoring was possible with dietary support.
- Overall, this method was useful to control baseline Phe intake during a small Phase 2 clinical trial.

References and Funding

- U. S. Food and Drug Administration. Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research. (2018). Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development: Guidance for Industry. FDA-2018-15777
- MetabolicPro. www.metabolicpro.org.
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