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Comparative Effectiveness of Pegvaliase versus Standard Therapy for Phenylketonuria: Insights from a Longitudinal Analysis of Patient Blood Phenylalanine Levels

Phenylketonuria (PKU) is a metabolic disorder caused by a variant of the phenylalanine hydroxylase (*PAH*) gene

Reduces PAH enzyme activity

Causes accumulation of phenylalanine (Phe) leading to intellectual disability

If left untreated, PKU results in impaired executive function, as well as behavioral, psychiatric, and movement disorders

Elements of PKU treatment

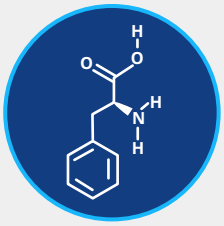
Phe-restricted diet

Pharmacotherapy

Medical nutrition therapy (MNT) to ensure protein intake

Sapropterin dihydrochloride (sapropterin; Kuvan®, BioMarin Pharmaceutical Inc., Novato, CA, USA)

A cofactor for PAH



Successful response to drug with ≥30% reduction in blood Phe levels

First clinically approved drug for PKU

Only 20% to 56% of patients with PKU respond to sapropterin

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Pegvaliase (Palynziq, BioMarin Pharmaceutical Inc.)

New drug approved for treatment of PKU in adults

Injectable formulation of pegylated Phe ammonia lyase enzyme

Drug converts Phe to ammonia and trans-cinnamic acid

Evidence for the efficacy of pegvaliase

Real-world evidence is limited but growing

Studies involving direct comparison with standard of care (MNT with or without sapropterin) are limited

Studies involving indirect comparison with standard of care are available

Phase 3 PRISM trials (PRISM-1 + PRISM-2)

Phenylketonuria Demographics, Outcomes and Safety Registry (PKUDOS)

Studies analyzing the primary efficacy endpoints (mean blood Phe level at year 1 and 2) found:

Pegvaliase is more effective than the standard of care (MNT with or without sapropterin) in lowering blood Phe in adults

Comparative advantage of pegvaliase over the standard of care may increase with time

Additional complementary analysis of findings from PRISM and PKUDOS

Inclusion criteria for analysis

Patients aged 16 years or above with PKU

Baseline blood Phe concentrations >600 µmol/L

Outcome measures

Percentage of patients achieving blood Phe levels

- ≤600 µmol/L
- ≤360 µmol/L
- ≤120 µmol/L

Treatment groups

- Pegvaliase (n = 183)
- Sapropterin + MNT (n = 82)
- MNT (n = 67)

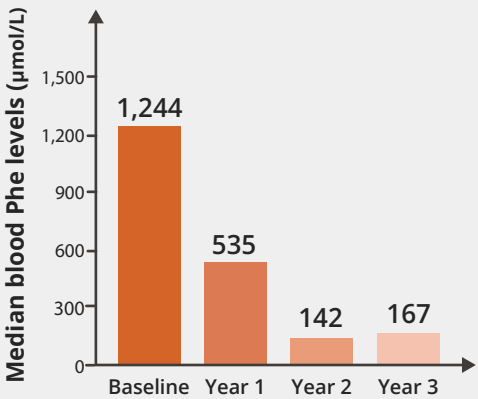
Analysis of follow-up data from year 1, 2, and 3 revealed:

Median blood Phe concentrations were lower in the pegvaliase group than in the sapropterin + MNT and MNT groups

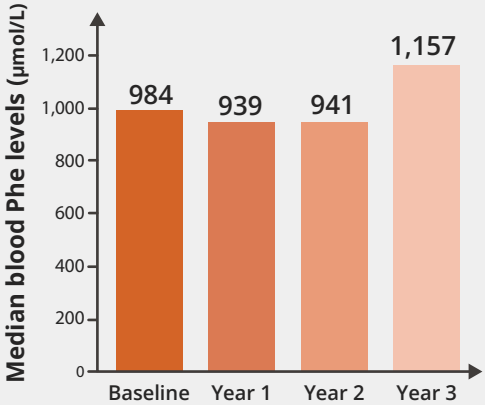
Median intact protein intake was higher in the pegvaliase group than in the sapropterin + MNT and MNT groups

Median blood Phe levels

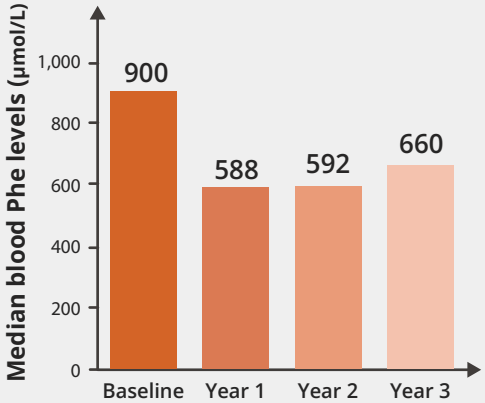
Pegvaliase group



MNT group



Sapropterin + MNT group



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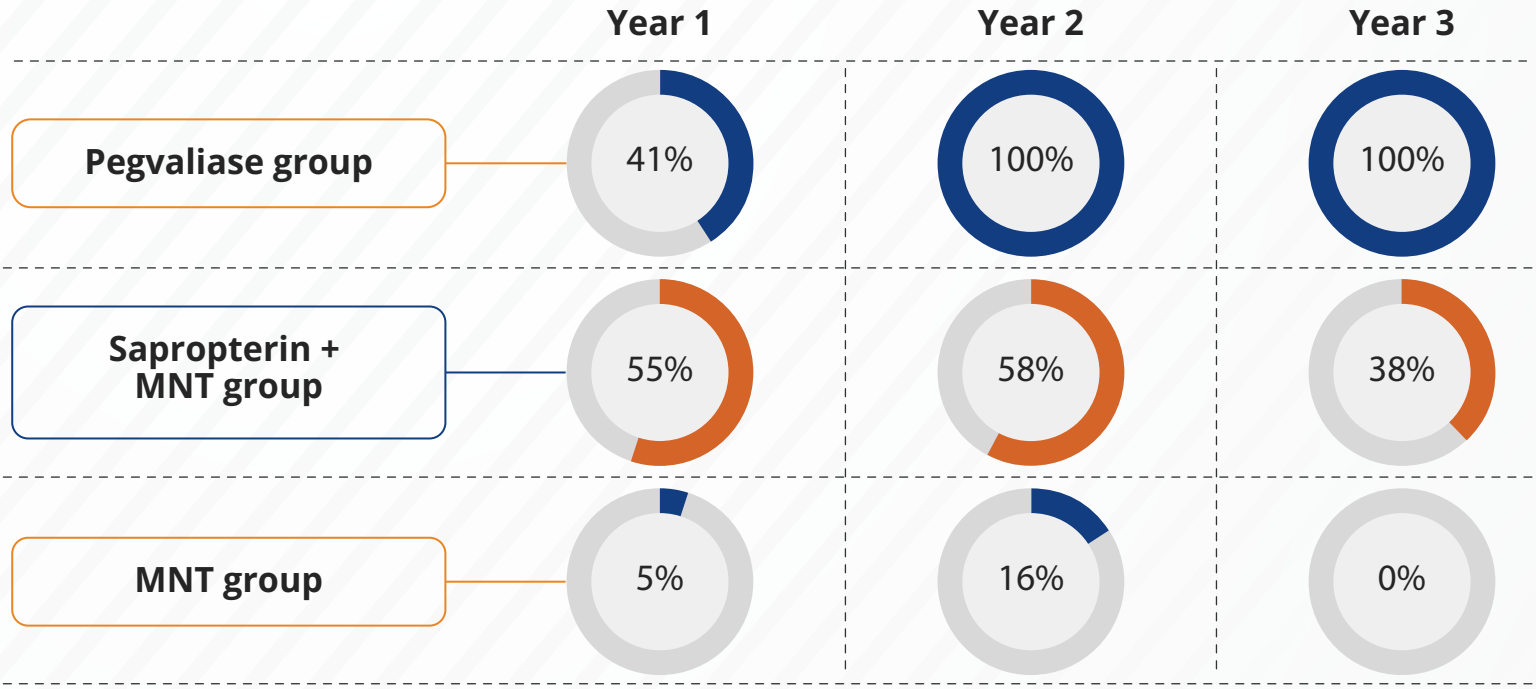
Proportions of participants achieving blood Phe concentrations ≤600 µmol/L



Decrease in blood Phe levels in the pegvaliase group was:

- More substantial compared to standard therapy
- Progressive, increasing with time
- More sustained compared to standard therapy

Study limitations

- Confounding due to differences in baseline characteristics of patients
- A limited number of participants were included in the analysis
- Large standard deviation in mean blood Phe level at year 1 and 2 of follow-up

Key messages

Pegvaliase is a beneficial addition to PKU treatment strategies, as it offers a significant, sustained, and progressively increasing reduction in blood Phe levels over time

Pegvaliase may improve outcomes and quality of life of patients with PKU

Sponsor

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Long-term comparative effectiveness of pegvaliase versus medical nutrition therapy with and without sapropterin in adults with phenylketonuria
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