Addressing the Relationship Between Genotype and Phenotype in the Response to Treatment: APV and GPV

aphenity

Phenotypic variation in PKU is likely driven by **> 750 unique *PAH* variants** and **> 3,500 genotypes**. Given that ~55% of variants occur only in single individuals, *PAH* genotype may not be completely predictive of clinical phenotype or determine response to treatment[1–3]

Allelic phenotypic value (APV) was calculated using data from the BIOPKU database (n = 9336) and was based on the **frequencies of the severity of PKU** for functionally hemizygous phenotypes[1,3]

Like most inborn errors of metabolism, disease severity in PKU is determined by the least severe of the two alleles. Therefore, it is the **highest APV** which determines the **genotypic phenotype value (GPV)** of any given genotype[3]

Phenotype	APV[3]	GPV[3]
Classical PKU	0	0–2.7
Non-classical PKU	5	2.8–6.6
Mild hyperphenylalaninemia	10	6.7–10

Although the majority of APHENITY participants had a non-classical PKU phenotype (121/157), **77.2% (115/149) had GPV consistent with classical PKU (0–2.7)**[4]

APV, allelic phenotypic value; GPV, genotypic phenotype value; PAH, phenylalanine hydroxylase; PKU, phenylketonuria.

1. BioPKU.org. Accessed February 2025. http://www.biopku.org/home/pah.asp. 2. Hillert A, et al. Am J Human Genet. 2020;107:234–250.
3. Garbade SF, et al. Genet Med. 2019;21:580–590. 4. PTC Therapeutics, data on file.

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