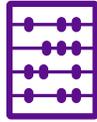


Addressing the Relationship Between Genotype and Phenotype in the Response to Treatment: APV and GPV



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 treatment¹⁻³



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 genotype³



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**