Phase 3 PRISM studies: Efficacy and safety of pegvaliase in patients 16-17 years of age with phenylketonuria

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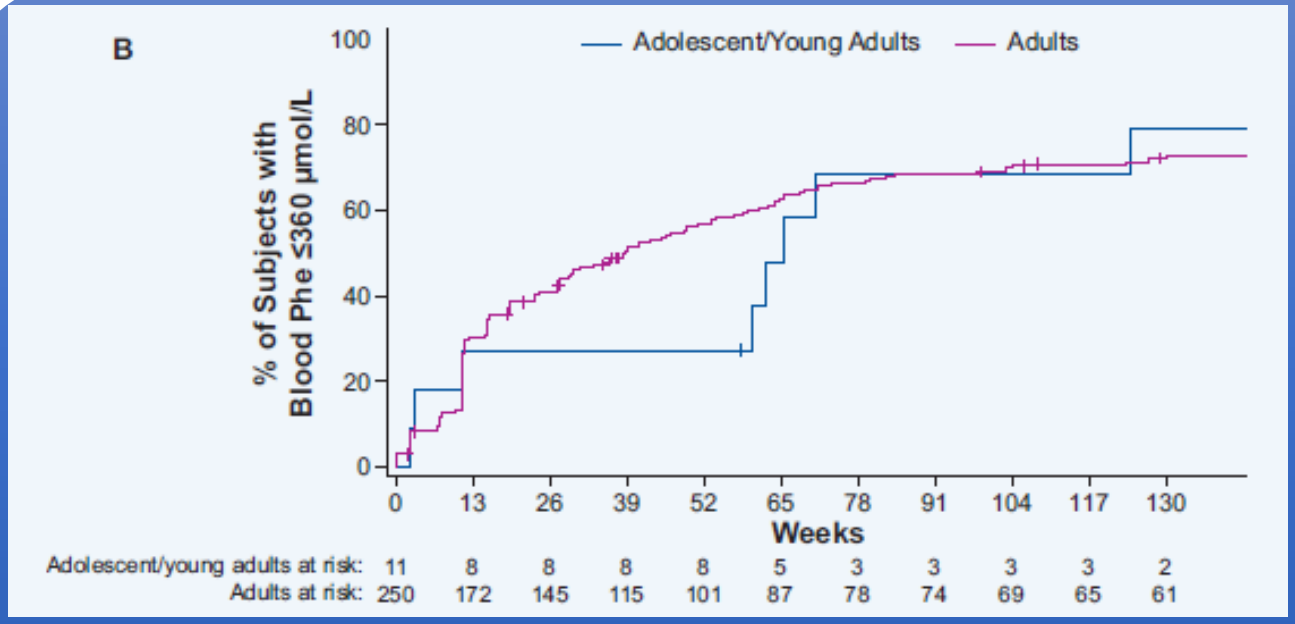
Objective

- **To report on the safety, efficacy, and immunogenicity of pegvaliase for the 11 subjects who were aged 16 - 17 years (adolescents/young adults) at the time of consent compared with adults (aged ≥18 years)**

- Pegvaliase (Palynziq®) is approved for PKU patients with uncontrolled blood Phe concentrations (>600 µmol/L) on existing management for adults at doses of up to 40 mg/day in the US and for patients ≥16 years old at doses of up to 60 mg/day in Europe
- Prior to a protocol amendment in PRISM, 11 subjects aged 16 or 17 yrs at time of consent were enrolled and permitted to continue in the study.



- **Like adults, adolescents/young adults were able to achieve clinically relevant blood Phe thresholds (<600 µmol/L, <360 µmol/L, <120 µmol/L [upper limit of normal]) – based on Kaplan-Meier analyses**
- **The Kaplan-Meier for adults and adolescent/young adults achieving blood Phe levels lower than the upper limit of the ACMG Guideline recommended level (≤360 µmol/L) is shown**

Safety

Table 2. Summary of adverse event rates by age group for subjects enrolled in PRISM-2

	Adolescent/Young Adults (n=11)	Adults (n=204)
Adverse event (AE)	**11 (100.0%)**	**200 (98.0%)**
Any AE assessed by the investigator as drug related	10 (90.9%)	192 (94.1%)
Any AE causing permanent study drug discontinuation	3 (27.3%)	9 (4.4%)
Serious adverse event (SAE)	**2 (18.2%)**	**38 (18.6%)**
SAE assessed by the investigator as drug related	1 (9.1%)	18 (8.8%)
SAE causing permanent study drug discontinuation	0	5 (2.5%)
SAE assessed by the investigator as drug related causing study discontinuation	0	3 (1.5%)
SAE causing study discontinuation	0	3 (1.5%)
Any hypersensitivity AE	**10 (90.9%)**	**175 (85.8%)**
Acute systemic hypersensitivity reaction	1 (9.1%)	7 (3.4%)
Severe acute systemic hypersensitivity reaction	0	0
Generalized skin reaction (≥14 Days)	0	90 (44.1%)
Injection site skin reaction (≥14 Days)	6 (54.5%)	84 (41.2%)
Arthralgia	7 (63.6%)	140 (68.6%)
Injection site reaction	10 (90.9%)	154 (75.5%)
Death	**0**	**0**

Overall summary of incidence of adverse events by age group (adolescent/young adults vs. adults) from subjects who entered PRISM-2 (N=215).

- AEs occurred at a similar rate in both age groups
- SAEs occurred in 2 (18.2%) of adolescents young adults vs 38 (18.6%) of adults
- None of the acute systemic hypersensitivity reactions were associated with drug-specific IgE and all events resolved without sequelae
- Immunogenicity and PK/PD profile were consistent between the two age groups

Conclusions

- Subjects aged 16 or 17 yrs achieved substantial & sustained Phe reductions with pegvaliase dosages <60 mg/day with a manageable safety profile for most subjects with long-term treatment
- Efficacy, safety, and immunogenicity results are consistent with those found in adults, demonstrating a positive benefit:risk profile
- As adherence to dietary management begins to deteriorate during adolescence, pharmacotherapy should be considered to achieve optimum blood Phe control in this patient population