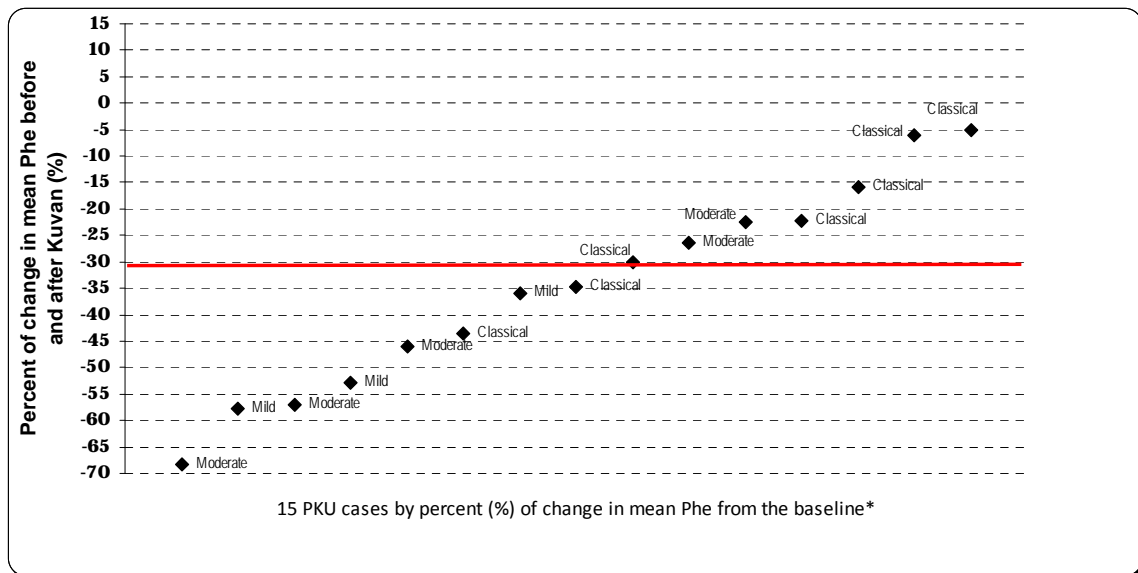


**The evaluation of the response to Kuvan treatment (preliminary results of retrospective analysis of BDCS PKU data).**

There was a cohort of 21 PKU patients who had Kuvan treatment for at least 6 months during the years 2009 - 2012. Six patients were excluded from the analysis, among them: 2 patients who participated in PKU-016 study, and for whom data were not available at the moment, and four patients did not continue Kuvan treatment for at least 6 months, therefore the exposure period was not sufficient. After the exclusion, we analyzed data from 15 eligible patients. The preliminary results are shown below.

**Figure 1: Distribution of the response to Kuvan, by PKU type, based on BCCH PKU data: percentage (%) of the difference between mean Phe levels at the baseline\* and 6 months of Kuvan treatment\*\*. Cut-off point for a “good response” to Kuvan\*\*\* is defined as a 30% decrease in mean Phe levels before and after treatment (red line at -30%).**



\*Baseline or “Before Kuvan” period was defined as 6 months prior starting Kuvan.

\*\* “After Kuvan” was defined a period of the 6 months after starting Kuvan. We decided to exclude the first month Kuvan exposure to get more consistent Phenylalanine values.

\*\*\* “Good response” was defined as 30% decrease from the baseline mean Phe level. We choose a “cut off” of 30% decrease as a good response to Kuvan however the robust standard definition of a “good response” to Kuvan has not yet defined.

When we compared “before” and “after” Kuvan treatment periods, out of 15 PKU patients - 9 (60%) had at least 30% decrease in mean Phe levels, which we considered as a “good response”. Among the “good responders”, 6 (67%) cases were classified as “mild or moderate” PKU type, and 3 (33%) cases were classified as “classical” PKU type. Among 6 “non-responders” (or those with less than 30% change in Phe levels): 2 cases (33%) were “moderate” PKU and four (67%) were “classical” PKU.