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POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Mitapivat Treatment Reduces Levels of Interference in Work/School Activity for Adult Patients with Pyruvate Kinase Deficiency

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Background: Pyruvate kinase (PK) deficiency is a rare hereditary disease resulting in chronic hemolytic anemia. It is associated with a range of acute and long-term complications and negatively impacts health-related quality of life. Patients (pts) with PK deficiency report daily social and physical limitations, which negatively impact various aspects of their lives, including the ability to perform at their full potential at work or school. Mitapivat is a first-in-class, oral, allosteric activator of PK, approved by the United States Food and Drug Administration for the treatment of hemolytic anemia in adults with PK deficiency, and by the European Union European Medicines Agency and the Medicines and Healthcare products Regulatory Agency in Great Britain for the treatment of PK deficiency in adults. Mitapivat has shown sustained and clinically meaningful improvements in the disease impact of PK deficiency measured by two disease-specific patient-reported outcome (PRO) instruments, the PK Deficiency Impact Assessment (PKDIA) and the PK Deficiency Diary (PKDD), in the pivotal ACTIVATE trial (NCT03548220) and its long-term extension (LTE) study (NCT03853798) in adult pts with PK deficiency who were not receiving regular transfusions. In this post hoc analysis, new PRO data are reported from ACTIVATE and its LTE study focusing on the impact of PK deficiency on work or school performance and how treatment with mitapivat impacts this over time in these pts.
Methods: In the global, phase 3, placebo (PBO)-controlled ACTIVATE trial, adult pts with PK deficiency who were not receiving regular transfusions were randomized 1:1 to receive mitapivat (5/20/50 mg twice daily) or PBO for 24 weeks (wks). Pts who completed ACTIVATE were eligible to continue in the open-label LTE study, where all pts received mitapivat (5/20/50 mg twice daily or dose at last visit of ACTIVATE). Pts from ACTIVATE who participated in the LTE study were categorized into either the mitapivat-to-mitapivat arm (M/M) or the PBO-to-mitapivat arm (P/M). In the PKDIA questionnaire, pts who worked or went to school over the 7 days prior to a scheduled visit were asked to rate how often their PK deficiency interfered with their ability to perform to their full potential at work or school, using an 11-point numeric rating scale (work/school interference score; ranging from 0 [none of the time] to 10 [all of the time]). Changes in the work or school interference score from baseline (BL; defined as the last complete assessment before start of study treatment in ACTIVATE) were summarized descriptively by treatment arm over the fixed-dose period of ACTIVATE (24 wks) and up to Wk 60 of the LTE study (84 wks overall).
Results: Among the 80 randomized adult pts with PK deficiency who were not receiving regular transfusions in ACTIVATE, 54 (67.5%) attended work/school at BL (28 pts randomized to mitapivat, 26 pts to PBO), 3 pts found it too difficult to attend, 21 did not attend for reasons unrelated to PK deficiency, and data were unavailable for 2. The mean (SD) work/school interference score for the 54 pts at BL was 4.0 (2.49) and was similar for the mitapivat (4.2 [2.42]) and PBO (3.9 [2.61]) arms. At Wk 24, 37 pts worked or went to school (including 22 in the mitapivat arm and 15 in the PBO arm), 5 pts found it too difficult to attend, 32 pts did not attend for reasons unrelated to PK deficiency, and data were unavailable for 6 pts. Change from BL in work/school interference score was compared for the 33 pts who attended work/school at both BL and Wk 24. Pts treated with mitapivat (n=19) had a reduction in the work/school interference score (mean [SD] change: -1.5 [1.74]) while negligible change (0.1 [2.41]) was observed among PBO pts (n=14). Notably, this reduction in score was sustained among M/M pts up to Wk 60 of the LTE. Furthermore, P/M pts experienced a reduction in the work or school interference score after starting mitapivat treatment in the LTE period, which was consistent with the improvements seen in the M/M arm during the ACTIVATE trial (Figure).
Conclusions: In this post hoc analysis, interference in work or school performance was observed in adult pts with PK deficiency who were not receiving regular transfusions. Treatment with mitapivat showed sustained improvements in work or school performance over time. These data continue to support the potential for mitapivat to provide long-term benefits and reduced interference in work or school performance in these pts.

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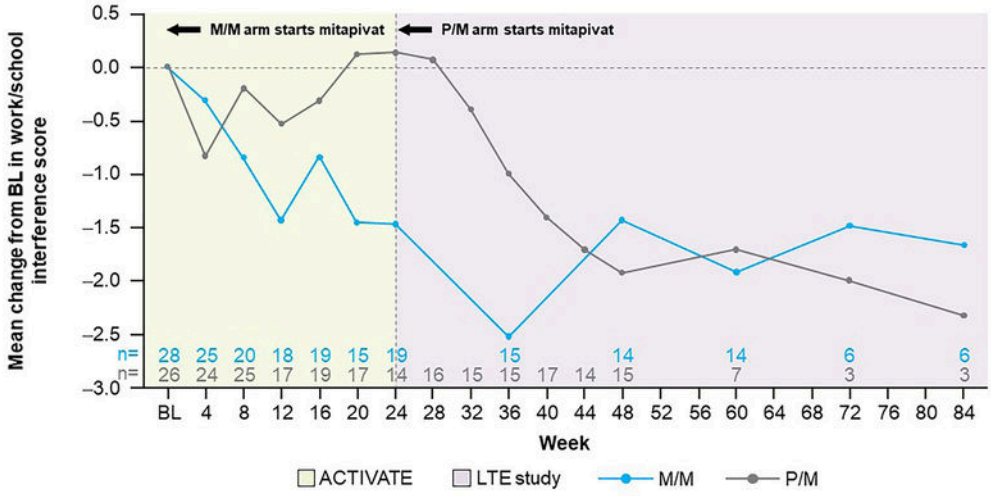
Figure. Change from BL[a] in work/school interference score[b] in adult pts with PK deficiency at scheduled visits in ACTIVATE and the LTE study



[a]BL is defined as the last complete assessment before start of study treatment in ACTIVATE.

[b]Work/school interference score: Pts who worked or went to school over the 7 days prior to a scheduled visit were asked to rate how often their PK deficiency interfered with their ability to perform to their full potential at work or school, using an 11-point numeric rating scale (work/school interference score; ranging from 0 [none of the time] to 10 [all of the time]). This analysis includes only pts who worked or attended school at BL, and who had available data for comparison through Week 84.

BL, baseline; LTE, long-term extension; M/M, mitapivat-to-mitapivat; PK, pyruvate kinase; P/M, placebo-to-mitapivat; pts, patients.

Figure 1

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