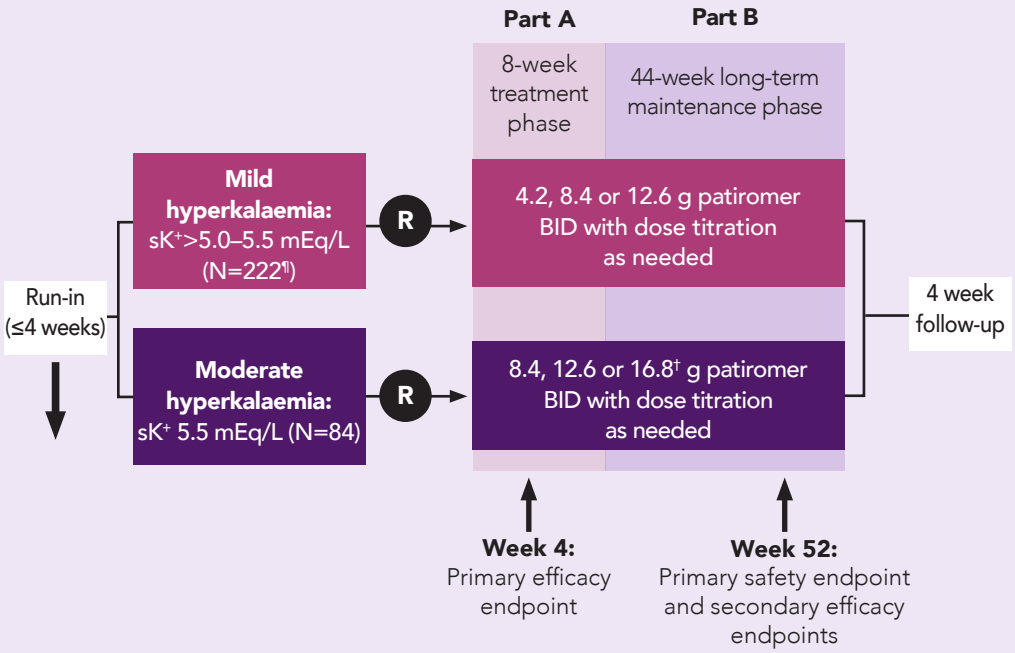
AMETHYST-DN STUDY

AMETHYST-DN: long-term safety and efficacy of patiromer for management of hyperkalaemia in patients with hypertension and diabetic nephropathy

STUDY DESIGN

Phase 2, **52-week**, multicentre, open-label, **dose-ranging study** in 306 outpatients with T2DM

Inclusion criteria: CKD*, T2DM, stable RAASi dose ≥4 weeks AND ACR ≥30 mg/g with sK^+ 4.3–5.0 mEq/L (Cohorts 1 and 2) OR sK^+ >5.0–<6.0 mEq/L (Cohort 3)



Primary efficacy endpoint

Mean change in serum potassium level from baseline to Week 4 or prior to initiation of dose titration

Key secondary efficacy endpoint

Mean change in serum potassium level through 52 weeks

Primary safety endpoint

Adverse events through 52 weeks

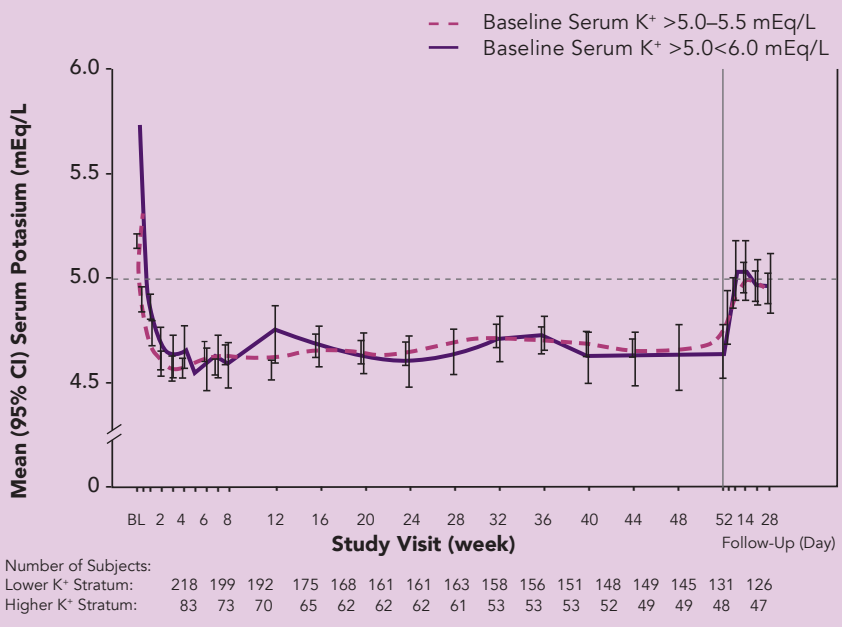
Cohort 1: Discontinue RAASi, start losartan 100 mg/day, add spironolactone after Week 2 if required; **Cohort 2**: Maintain RAASi, start spironolactone 25 mg/day; **Cohort 3**: Skip run-in and maintain current RAASi*

*eGFR 15–60 mL/min/m^2; † Dose studied but not registered. ¶ Two patients with mild hyperkalaemia did not receive patiromer and therefore were not included in the efficacy or safety analyses.

RESULTS

In patients with mild and moderate hyperkalaemia, **significant reductions in sK^+** were observed after 4 weeks of treatment with patiromer, and maintained through 52 weeks in:

- **83.1% to 92.7% of patients with mild hyperkalaemia**
- **77.4% to 95.1% of patients with moderate hyperkalaemia**



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RESULTS

Among treatment related adverse events, the most frequently reported were:

hypomagnesaemia	constipation	diarrhoea
7.2%*	**4.6%**	**2.7%**

Hypokalaemia (sK^+<3.5 mEq/L) occurred in 17 patients (5.6%), with no patients developing a sK^+ level <3.0 mEq/L.

Reductions in systolic and **diastolic blood pressure** were observed in all starting-dose groups in both strata over 52 weeks

Mean SBP/DBP	**Mild hyperkalaemia**	**Moderate hyperkalaemia**
Baseline	153.5/83.6 mmHg	153.8/81.9 mmHg
Reduction from baseline to Week 52	-15.7/-8.0 mmHg	-17.1/9.2 mmHg

*No patients developed severe hypomagnesaemia (<1.0 mg/dL)

CONCLUSIONS

AMETHYST-DN showed that in patients with hyperkalaemia and diabetic nephropathy

patiromer starting doses of **4.2** to **16.8 g** BID → resulted in statistically significant **decreases in sK^+ level** → after 4 weeks of treatment lasting through **52 weeks**

The study data demonstrate the long-term efficacy and safety of patiromer in patients with hypertension and diabetic nephropathy

The recommended starting dose is 8.4 g patiromer once daily[2]

Abbreviations: ACR, albumin creatinine ratio; BID, twice daily; BL, baseline; CKD, chronic kidney disease; DN, diabetic nephropathy; eGFR, estimated glomerular filtration rate; K^+, potassium; R, randomisation; RAASi, renin-angiotensin-aldosterone system inhibitor; sK^+, serum postassium; T2DM, type 2 diabetes mellitus.

*Patients who developed hyperkalaemia at any time during the 4-week run-in were eligible to be randomised into the treatment phase

1. Bakris GL, *et al.* Effect of patiromer on serum potassium level in patients with hyperkalemia and diabetic kidney disease: The AMETHYST-DN Randomized Clinical Trial *JAMA.* 2015;314(2):151–61.

2. European Medicines Agency. Veltassa. Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/veltassa-epar-product-information_en.pdf. Accessed September 2019.

VIFOR PHARMA

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