Non-Interventional, Exploratory, Phase IV, Single-Blind, Cross-Sectional, Randomised, Cross-over Study Evaluating Patient Palatability and Preference of 3 Potassium Binders, Sodium Polystyrene Sulphonate (SPS) or Calcium Polystyrene Sulphonate (CPS), Sodium Zirconium Cyclosilicate (Lokelma®), and Calcium Patiromer Sorbitex (Veltassa®) in Patients with Chronic Kidney Disease and Hyperkalaemia (APPETIZE)

First published: 08/07/2020

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## Administrative details

**EU PAS number** 

**EUPAS36248** 

#### Study ID

49737

DARWIN EU® study		
No		
Study countries		
Canada		
France		

## **Study description**

**United States** 

Italy

Spain

Sodium zirconium cyclosilicate (hereafter referred to as Lokelma) has been approved in adults for effective and safe treatment of hyperkalaemia (HK), a metabolic condition characterised by elevated serum potassium (K+) levels above the normal range of 3.5-5.0 mmol/L. Patients with chronic kidney disease (CKD), diabetes, and those prescribed renin angiotensin aldosterone system inhibitor (RAASi) therapy are at an increased risk of HK due to abnormal K+ homeostasis, mainly due to impaired renal excretion. Sodium polystyrene sulphonate (SPS) or calcium polystyrene sulphonate (CPS) (hereafter referred to as S/CPS) are traditional K+ binders which are commonly prescribed but are poorly tolerated by patients due to lack of palatability and gastrointestinal (GI) constipation, leading to low adherence. Additionally, S/CPS use has been associated with serious GI adverse events (AEs, bleeding, ischemic colitis, colonic necrosis, colon perforation). Recently approved novel K+ binders, such as sodium zirconium cyclosilicate (Lokelma) and calcium patiromer sorbitex (hereafter referred to as Veltassa), are anecdotally reported to be more palatable and better tolerated in comparison to S/CPS, and provide additional

treatment options to fulfil the unmet need for treatment of HK. There is a need to generate evidence for patients and physicians (nephrologists and cardiologists) on patient palatability and patient preference for currently available K+ binders and how preference could impact the likelihood of adherence and enable long-term HK pharmacological treatment.

#### **Study status**

**Finalised** 

## Research institutions and networks

## Institutions

Multiple centres: 32 centres are involved in the study

## Contact details

## **Study institution contact**

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Study contact

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## **Primary lead investigator**

Wittbrodt Eric

**Primary lead investigator** 

## Study timelines

### Date when funding contract was signed

Planned: 29/05/2020 Actual: 25/03/2020

### Study start date

Planned: 31/08/2020 Actual: 23/10/2020

#### Data analysis start date

Planned: 03/03/2022 Actual: 03/03/2022

### **Date of final study report**

Planned: 16/09/2022 Actual: 21/10/2022

# Sources of funding

• Pharmaceutical company and other private sector

# More details on funding

AstraZeneca AB

## Study protocol

D9480c00016\_Study Protocol\_V2.0\_FINAL\_02 June 2020 with signature.pdf (2.02 MB)

## Regulatory

Was the study required by a regulatory body?			
Is the study required by a Risk Management Plan (RMP)?  Not applicable			
Methodological aspects			
Study type			
Study type list			
Study topic: Human medicinal product Disease /health condition			
Study type: Non-interventional study			
Scope of the study:			
Drug utilisation Other			
If 'other', further details on the scope of the study			
Patient taste preference			
Data collection methods:			
Primary data collection			

#### Main study objective:

To compare patient-reported overall taste between Lokelma and Veltassa, and between Lokelma and S/CPS

# Study Design

### Non-interventional study design

Other

### Non-interventional study design, other

Phase IV, exploratory, cross-over, active comparator controlled study

# Study drug and medical condition

#### Name of medicine

**LOKELMA** 

**VELTASSA** 

## **Anatomical Therapeutic Chemical (ATC) code**

(V03AE01) polystyrene sulfonate

polystyrene sulfonate

#### Medical condition to be studied

Chronic kidney disease

Hyperkalaemia

## Population studied

#### Short description of the study population

The study subjects were patients with dialysis and non-dialysis chronic kidney disease (CKD) and hyperkalaemia (HK) aged 18 years or older treated with sodium zirconium cyclosilicate (Lokelma®), calcium patiromer sorbitex (Veltassa®), sodium polystyrene sulphonate and calcium polystyrene sulphonate (CPS).

#### Inclusion criteria:

- Participants must be adults aged ≥18 years, at the time of signing the informed consent.
- Participants should have CKD defined by having an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2 (calculated using CKD-EPI equation) measured twice at least 90 days apart
- Prevalent HK with serum K+ >5 mmol/L
- Male and/or female
- Capable of giving signed informed consent as described in Appendix A which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. Informed consent must be obtained prior to any study-specific procedures performed.

#### Exclusion criteria:

- Screening serum K+ value which, in the opinion of the investigator, requires immediate medical intervention (ie, cannot wait until after tasting procedures)
- As judged by the investigator, any evidence of any condition which in the investigator's opinion makes it undesirable for the participant to participate in the study
- Known history of drug or alcohol abuse within 6 months of screening
- History of QT prolongation associated with other medications that required discontinuation of that medication, including congenital long QT syndrome
- Symptomatic or uncontrolled atrial fibrillation despite treatment, or

asymptomatic sustained ventricular tachycardia. Participants with atrial fibrillation controlled by medication are permitted

- Have a life expectancy of <6 months
- 12-lead ECG with reported QTcF >550 msec at screening
- Are current smoker
- Have mouth ulcers/mouth infection, respiratory infection, nasal congestion, or other condition, medication, or procedure which may interfere with sense of smell or taste, in opinion of the investigator

#### Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

### Special population of interest

Renal impaired

#### **Estimated number of subjects**

148

## Study design details

#### Outcomes

To compare patient-reported overall palatability (composite of taste, texture, smell, and mouthfeel) between Lokelma and Veltassa, and between Lokelma and S/CPS in the United States (US), To compare: patient-reported overall palatability, between Lokelma & Veltassa, and between Lokelma & S/CPS,

patient-reported emotional response to overall palatability, between Lokelma & Veltassa, & between Lokelma and S/CPS. To describe and compare scoring & emotional response for how willing patients would be to take each K+ binder, describe patient-reported preference by ranking the NIMPs.

### Data analysis plan

The primary endpoint is the overall Scoring (0-10) of taste. The primary analysis is to compare the scoring between Lokelma and Veltassa, and between Lokelma and S/CPS. The null hypotheses (H0) are that the oveThe primary endpoint is the overall palatability Scoring (0-40), a composite score of taste, texture, smell, and mouthfeel. The primary analysis is to compare the scoring between Lokelma and Veltassa, and between Lokelma and S/CPS in the US. AstraZeneca hypothesizes that palatability, in terms of taste, texture, smell, and mouthfeel, will score higher (better) for Lokelma, when compared with Veltassa and S/CPS. Additionally, emotional response scores (towards appeal, engagement and empowerment) will score higher (better) for Lokelma, when compared with Veltassa and S/CPS. Each objective will be analysed per country/region. In addition, the difference in results per regions and overall may be explored as outlined in the Study Objectives.

## **Documents**

### **Study results**

APPETIZE Abstract 04Nov2022.pdf (1.88 MB)

## Data management

## **ENCePP Seal**

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### **Data sources (types)**

Other

### Data sources (types), other

Prospective patient-based data collection

## Use of a Common Data Model (CDM)

### **CDM** mapping

No

# Data quality specifications

#### **Check conformance**

Unknown

### **Check completeness**

Unknown

### **Check stability**

Unknown

## **Check logical consistency**

Unknown

# Data characterisation

## **Data characterisation conducted**

No