Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

ACHIEVE

Aldosterone blo**C**kade for **H**ealth **I**mprovement **EV**aluation in **E**nd-stage renal disease

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Can-SOLVE CKD Network

Strategy for Patient-Oriented Research
SPOR
Putting Patients First

1. BACKGROUND

- The average life expectancy on dialysis is only 3 years
- 40% of dialysis patients will die from heart disease
- Dialysis causes heart disease due to:
  - Pressure and fluid overload
  - Heart muscle injury and scarring
  - Narrowing of blood vessels to the heart
  - Abnormal heart rhythms leading to sudden cardiac death
- Effective treatments for heart disease in dialysis are lacking
- Aldosterone is a hormone that is implicated in heart disease related to dialysis
- Drugs that block aldosterone are effective in non-dialysis settings
- A large clinical trial is needed to study these medications in dialysis because extrapolating evidence from non-dialysis can be misleading

Research question

Does spironolactone improve survival and prevent heart failure in dialysis patients?

2. PROJECT GOAL

- To determine if spironolactone reduces cardiovascular morbidity and mortality for patients treated with chronic dialysis

3. PROJECT TEAM

- Role of **patient partners**:

Explore barriers to recruitment and potential solutions:

- Focus on simplicity of study: 1 pill per day, minimal study visits and data collection
- Preparing study medication in blister packs to minimize its daily impact
- Emphasize the importance of participant contribution to research
- Engage dialysis nurses, nurse practitioners and pharmacists as stakeholders
- Explore the possibility of including satellite dialysis units
- Re-approach initial screen fails
- If a participant is not open to discussion, approach them at a later date

Patient partners:
Gwen Herrington
Lucy Delgado
Paul Duperron
Roger Hillier

Other:
Steering committee
Data safety monitoring committee
Adjudication committee
Statisticians
Programmers
National Leaders
Qualified Investigators
Research Coordinators

Principal Investigator:
Michael Walsh

Project Team:
Study Chair: PJ Devereaux
Scientific Officer: David Collister
APM: Jessica Tyrwhitt
Research coordinator: Joanne Wilkinson, Kayla Pohl

4. WHAT IS THE STUDY DESIGN?

A) Eligibility Criteria

Inclusion

1. Age
   a) ≥45 years or
   b) ≥18 with a history of diabetes
2. On dialysis ≥ 90 days
3. On either
   a) Hemodialysis at ≥2 tx/week or
   b) Peritoneal dialysis ≥1 exchange/day
4. Provides informed consent

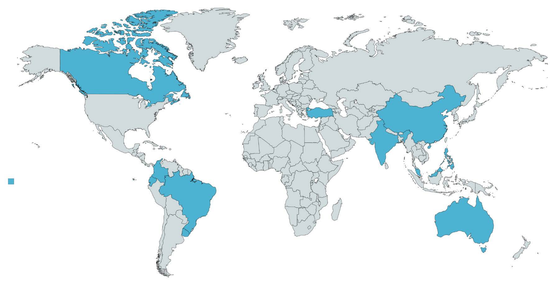
Exclusion

1. Hyperkalemia
   a) Serum potassium >5.8 mmol/L in 6 weeks prior
   b) Serum potassium >6.0 mmol/L during active run-in
2. Currently taking & unable to withdraw MRA
3. Known sensitivity or allergy to spironolactone
4. Current or planned pregnancy or breastfeeding
5. Scheduled living related donor renal transplant
6. Life expectancy < 6 months in the opinion of a treating nephrologist
7. Enrolled in another interventional trial testing a MRA or drug that has a known/likely interaction with spironolactone

Hemodialysis **AND** Peritoneal Dialysis are included in the study

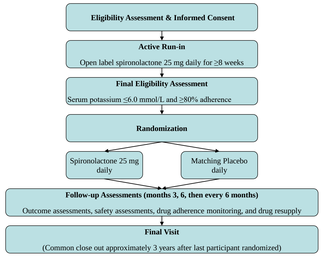
C) Sample size

N=at least 2750
20+ centers across Canada
over 10 countries



B) Study design

open label active run-in period
identification + exclusion
1) high blood levels of potassium
2) non-adherence



double blind post-randomization
spironolactone 25mg orally daily vs placebo
follow-up every 6 months during dialysis

Primary Outcome: composite of cardiac death or hospitalization for heart failure
Secondary Outcomes: safety and efficacy

- Cause specific death (cardiac, other vascular, non-vascular)
- Hospitalization for heart failure
- All-cause death
- All-cause hospitalizations
- Severe hyperkalemia

One of the largest clinical trials in dialysis ever performed

More Canadian participants than any other previous trial in dialysis with a similar design

Applicable to almost all dialysis patients

ClinicalTrials.gov

https://clinicaltrials.gov/ct2/show/NCT03020303

5. ACHIEVEMENTS/LESSONS LEARNED

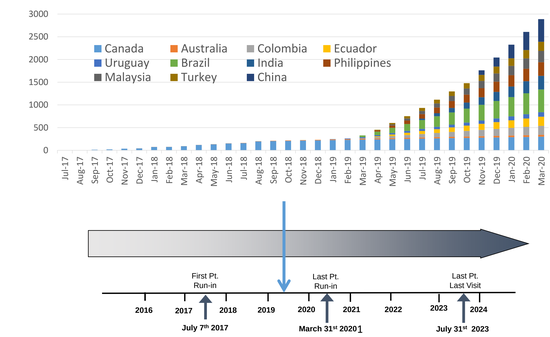
- Publications
- Recruitment in Canada = largest to date, inclusion of new centers
- Countries nearing activation:
  - Spring 2019 = Brazil, the Philippines, others
- Additional funding: MRRF $2,850,898

CHALLENGES

- Regulatory and ethics approval internationally
- Drug supply
- Ongoing recruitment targets

Patient partners can provide valuable information to improve clinical trial recruitment and retention

6. PROJECT TIMELINE



7. COMMENTS

yes, write here!!!

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Ask me about our study within a trial regarding the ACHIEVE run-in period