

AWARD NUMBER: W81XWH-17-1-0665

TITLE: Prevention of Post-Traumatic Contractures with Ketotifen II (PERK II)

PRINCIPAL INVESTIGATOR: Kevin A. Hildebrand

CONTRACTING ORGANIZATION: University of Calgary, Calgary, Alberta CANADA

REPORT DATE: October 2023

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
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				5b. GRANT NUMBER OR160026	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Kevin A. Hildebrand E-Mail: hildebrk@ucalgary.ca				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Governors of the University of Calgary 2500 University Drive NW Calgary, Alberta CANADA T2N 1N4				8. PERFORMING ORGANIZATION REPORT NUMBER	
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13. SUPPLEMENTARY NOTES					
14. ABSTRACT 380 participants recruited by September 29, 2023. The 12% withdrawal rate outlined in the protocol has been met, meaning that we may encounter issues reaching our 80% power. Appropriate regulatory submissions have been completed and our REB has approved enrolling past our 384 sample size to offset these withdrawals. Screening and enrollment procedures will continue until December 21 st , 2023. With our current 10 participant enrollments per month average, we may reach close to 400 participants. Health Canada Sponsor inspection has been completed and closed successfully. Royal Columbian Hospital, site 10, has responded to their site level inspection by Health Canada, expecting a response in October 2023.					
15. SUBJECT TERMS Randomized Clinical Trial; Multicenter; Placebo; Ketotifen; Contractures; Post-traumatic; Elbow fractures or dislocations; Surgery; Range of motion; Disability Arm Shoulder Hand; Oxford Elbow Score; Pain Catastrophizing Scale.					
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

This proposal pertains to the FY16 PRORP CTA Focus Area on Surgical Care – Extremity Fractures. This research optimizes patient outcomes through prevention of post-traumatic joint contractures following fractures. We are conducting a multicenter, multidose randomized clinical trial comparing Ketotifen fumarate to a Lactose placebo started within 7 days of elbow fractures or dislocations. The primary outcome measure is elbow extension-flexion arc range of motion 12 weeks after randomization. Secondary outcome measures are range of motion at other selected time points and patient reported outcome measures at these time points and 12 weeks.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Randomized Clinical Trial; Multicenter; Placebo; Ketotifen; Contractures; Post-traumatic; Elbow fractures or dislocations; Surgery; Range of motion; Disability Arm Shoulder Hand; Oxford Elbow Score; Pain Catastrophizing Scale

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

Major Task 1: Complete Clinical Trial Development Award – this was OR140142

Major Task 2: Phase III RCT Implementation

Major Task 3: Study Performance

Major Task 4: Knowledge Translation

What was accomplished under these goals?

Major Task 1: Complete CTDA OR140142

1. Major Activities:

- a. Regulatory Compliance
- b. Core Study Functions
- c. Recruiting Sites

2. Specific Objectives:

- a. Complete contract negotiations with recruiting sites.
- b. Obtain Ethics Internal Review Board and Department of Defense Human Research Protection Office (HRPO) approval for 17 participating sites.

3. Results:
 - a. Nothing to report.

Major Task 2: Phase III RCT Implementation

1. Major Activities:
 - a. Organizational Transitions
 - b. Site Initiations
 - c. Organizing Screening, Enrollment and Randomization Procedures
2. Specific Objectives:
 - a. Start at Calgary Sites
 - b. Site roll out outside of Calgary
3. Results:
 - a. 15 active sites across North America continue screening/enrollment procedures. As a result, 380 participants have been recruited and randomized into the clinical trial by September 29, 2023. Appendix reflects 380 participants randomized by the end of the reporting period. **See appendices page 13 – 36.**

Major Task 3: Study Performance

1. Major Activities:
 - a. Trial Committees
 - b. Support Organizations
2. Specific Objectives:
 - a. Three performance committee meetings
 - b. Regular meetings with Core facilities – EPICORE, CIPAC, BARL
3. Results:
 - a. PERK 2 Monthly Newsletters for July, August, and September 2023. **See pages 37 – 39.**
 - b. PERK 2 Trial Management Group meeting minutes for July and September 2023. **See pages 40 – 46.**
 - c. PERK 2 Trial Steering Committee Group meeting minutes for September 18, 2023. **See pages 47 – 49.**
 - d. Health Canada completed a Sponsor level inspection of the PERK 2 trial and provided an inspection closure letter confirming satisfactory response to all observations. **See page 50.**

Major Task 4: Knowledge Translation

1. Major Activities:
 - a. Publications/Meetings
 - b. Trial Results
 - c. Site Engagement and Updates
2. Specific Objectives
 - a. Trial protocol manuscript, Specialty meetings abstracts and attendance
 - b. Trial results – Primary paper, secondary papers, presentations specialty societies
 - c. Site engagement
3. Results
 - a. The Sponsor team has submitted an abstract to the 2024 Orthopaedic Research Society Annual Meeting. This abstract presents a view of COVID-19 closeouts, its effects on the PERK 2 trial, and our recovery efforts to reach out recent success. **See pages 51 – 52.**

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

Our objective for year 7 is to continue enrollment and randomization procedures with 15 active sites until December 21, 2023, maintaining our current average of 10 new participants per month. We have reached our 12% withdrawal rate and are in need of offsetting the withdrawals with further enrollments. Our REB has approved the proposed plan to continue enrollments past our 384-sample size, and we have submitted appropriate notification to all regulatory agencies. Further, we will continue our monthly TMG and quarterly TSC meetings to inform next steps need for continued success with the trial. A DMC closed meeting is being scheduled for December 2023 (Y7, Q1) to maintain proper oversight of safety and efficacy endpoints. Finally, continuing manuscript and presentation development, with eyes set in further literature development efforts towards Year 7, Quarter 2.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

- 5. CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:

Changes in approach and reasons for change

After review of enrolment status based on the sample size outlined in our approved protocol trial design (n=384), the trial has met the 12% withdrawal rate at 380 participants enrolled. In order to address meeting this withdrawal rate, which affects the collection of data necessary to reach 80% power, and by confirmation from our Trial Steering Committee and Data Monitoring Committee of the safety of this trial, continuation of recruitment beyond the current total sample size is needed. December 21, 2023, has been set as the last day for screening/recruitment to enroll enough participants to address meeting and/or surpassing the withdrawal rate of 12% reported in our protocol.

Actual or anticipated problems or delays and actions or plans to resolve them

We do not expect any anticipated problems or delays during this year. However, as outlined before, we will continue enrollments past our current sample size to reach the 80% power in the protocol. By enrolling more participants we could be able to offset the experienced withdrawals and reach our protocol goals.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS

- **Publications, conference papers, and presentations**

Journal publications.

Sponsor and Trial Steering Committee have discussed a possible publication plan for the upcoming years. The plan includes writing a statistical analysis plan paper, a primary outcome paper, and a secondary outcome paper, pending completion of data collection from sites. We expect to have all data collected by December 2024. In addition, to better direct the publication efforts, a publication committee is being considered for further manuscripts. For notes on these efforts, **see pages 47 – 49.**

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers and presentations.

The Sponsor team has submitted an abstract to the 2024 Orthopaedic Research Society Annual Meeting. This abstract presents a view of COVID-19 closeouts, its effects on the PERK 2 trial, and our recovery efforts to reach out recent success. **See pages 51 – 52.**

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Kevin Hildebrand
Project Role:	Principal Investigator
Research Identifier:	orcid.org/0000-0001-8786-9021
Nearest Person Month worked:	12
Contribution to Project:	Overall management. Writing grants, study design. Recruiting sites. Obtaining data management, medication partners.
Funding Support:	Department of Surgery University of Calgary
Name:	Gerardo Duque
Project Role:	Program Manager
Research Identifier:	None
Nearest Person Month worked:	12
Contribution to Project:	Regulatory application (IND, HRPO, Health Canada). Database Development and quality assurance. Case report forms and consent writing. Screening, recruitment, randomization, and participant follow-ups. Contracts. Regulatory processing. Monitoring and site management.
Funding Support:	Department of Defense.
Name:	Isabella Salazar
Project Role:	Clinical Research Assistant
Research Identifier:	None
Nearest Person Month Worked:	12
Contribution to Project:	Clinical trial implementation and ongoing development. Screening, recruitment, randomization, and participant follow-ups. Case report form development. Institutional Review Board processing.
Funding Support:	Department of Defense
Name:	Joshua Burkart
Project Role:	Summer Student – Research Assistant
Research Identifier:	None
Nearest Person Month Worked:	3
Contribution to Project:	Screening, recruitment, randomization, and participant follow-ups.
Funding Support:	Department of Defense

Name:	Tolulope Sajobi
Project Role:	Trial Statistician
Research Identifier:	orcid.org/0000-0002-5696-5552
Nearest Person Month worked:	1
Contribution to Project:	Statistical support. Recruitment and co-supervise PhD student.
Funding Support:	Department of Community Health Sciences, University of Calgary

Name:	Ayoola Ademola
Project Role:	PhD Graduate Student
Research Identifier:	None
Nearest Person Month worked:	1
Contribution to Project:	Statistical support
Funding Support:	Department of Defense

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

Organization Name:	Bay Area Research Logistics
Location:	Hamilton, ON, CANADA
Contribution:	Sourcing Ketotifen, Lactose Placebo, manufacturing and distribution study medication
Organization Name:	EPICORE Centre
Location:	University of Alberta, Edmonton, AB, CANADA
Contribution:	Development of RedCap Electronic Data Capture, Randomization process (Drug Tracking System), Project management, servers to support study
Organization Name:	Calgary Image Processing and Analysis Centre
Location:	Calgary, AB, CANADA
Contribution:	Archiving and analysis centre for radiographic evaluation of fracture healing
Organization Name:	Alberta Health Services
Location:	Peter Lougheed Centre, Calgary, AB, CANADA
Contribution:	Office space, computer support, clinic space for recruitment and follow up of participants

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments. See **appendices page 14**.

- 9. APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Prevention of Post-Traumatic Contractures with Ketotifen II (PERK II)

0R160026

W81XWH-17-1-0665



PI: Kevin A. Hildebrand

Org: Governors of the University of Calgary

Award Amount: \$2,440,796

Study/Product Aim(s)

- Major Task 1: Complete Clinical Trial Development Award – CTDA (OR140142)
- Major Task 2: Phase III RCT Implementation
- Major Task 3: Study Performance
- Major task 4: Knowledge Translation

Approach

PERK II is a multicenter RCT led from Calgary, CANADA with US centers included. Completing the CTDA will have the infrastructure in place to perform the RCT. This trial will compare 2 different doses of ketotifen fumarate to a lactose placebo in preventing post-traumatic contractures following elbow injuries that require an operation. The medication is randomized, while operation requirement is not.



380 participants recruited by September 29, 2023. The 12% withdrawal rate outlined in the protocol has been met, meaning that we may encounter issues reaching our 80% power. Appropriate regulatory submissions have been completed and our REB has approved enrolling past our 384-sample size to offset these withdrawals. Screening and enrollment procedures will continue until December 21st, 2023. With our current 10 participant enrollments per month average, we may reach close to 400 participants. Health Canada Sponsor inspection has been completed and closed successfully. Royal Columbian Hospital, site 10, has responded to their site level inspection by Health Canada, expecting a response in October 2023.

Timeline and Cost

Activities	CY	17	18	19	20	21	22	23	24	25
Complete CTDA										
Phase III RCT Implementation										
Study Performance										
Knowledge Translation										
Estimated Budget (\$K)		\$154	\$638	\$704	\$536	\$408	\$0	\$0	\$0	\$0

Updated: (September 29th, 2023)

Goals/Milestones

CY17 Goal – Complete CTDA

☒ IND Approval

✓ Database and Medication Manufacture Development

CY18 Goals – Regulatory/IRB/Contracts

✓ All sites completed all steps

CY19 Goal – Continue recruitment

☐ Complete CTDA

✓ Recruit first participant

✓ Add other sites

CY20 Goal – Continue recruitment, follow up

✓ All sites recruiting

Comments/Challenges/Issues/Concerns

12% withdrawal rate has been met for the 12-week primary endpoint. Additional enrolments will be done to offset withdrawals.

Budget Expenditure to Date

Projected Expenditure: \$2,440,795

Actual Expenditure: \$1,615,174

Data Exports, Reports, and Stats

Number of results returned: 380

Total number of records queried: 9,817

('records' = total available data across all designated events)

Randomized Subjects

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5358-4 (Participant ID 01-001)	Screening/ Randomization			Peter Loughheed Centre	10008	2019-06-29
5362-2 (Participant ID 05-001)	Screening/ Randomization			South Health Campus	10072	2019-07-02
5362-13 (Participant ID 05-002)	Screening/ Randomization			South Health Campus	10049	2019-07-26
5358-5 (Participant ID 01-002)	Screening/ Randomization			Peter Loughheed Centre	10001	2019-07-27
5358-47 (Participant ID 01-003)	Screening/ Randomization			Peter Loughheed Centre	10006	2019-08-29
5362-31 (Participant ID 05-003)	Screening/ Randomization			South Health Campus	10073	2019-09-03
5362-34 (Participant ID 05-004)	Screening/ Randomization			South Health Campus	10066	2019-09-04
5358-56 (Participant ID 01-004)	Screening/ Randomization			Peter Loughheed Centre	10020	2019-09-11
5362-39 (Participant ID 05-005)	Screening/ Randomization			South Health Campus	10050	2019-09-17
5358-70 (Participant ID 01-005)	Screening/ Randomization			Peter Loughheed Centre	10012	2019-10-11
5362-46 (Participant ID 05-006)	Screening/ Randomization			South Health Campus	10068	2019-10-15
5370-1 (Participant ID 13-001)	Screening/ Randomization			Sturgeon Community Hospital	10113	2019-10-16
5370-3 (Participant ID 13-002)	Screening/ Randomization			Sturgeon Community Hospital	10107	2019-10-28
5370-4 (Participant ID 13-003)	Screening/ Randomization			Sturgeon Community Hospital	10101	2019-10-29
5362-56 (Participant ID	Screening/ Randomization			South Health Campus	10053	2019-11-05

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
05-007)						
5358-77 (Participant ID 01-006)	Screening/ Randomization			Peter Lougheed Centre	10009	2019-11-08
5370-6 (Participant ID 13-004)	Screening/ Randomization			Sturgeon Community Hospital	10102	2019-11-20
5358-87 (Participant ID 01-007)	Screening/ Randomization			Peter Lougheed Centre	10011	2019-11-29
5370-8 (Participant ID 13-005)	Screening/ Randomization			Sturgeon Community Hospital	10108	2019-12-04
5360-1 (Participant ID 03-001)	Screening/ Randomization			Foothills Medical Centre	10037	2019-12-06
5360-3 (Participant ID 03-002)	Screening/ Randomization			Foothills Medical Centre	10036	2019-12-09
5362-71 (Participant ID 05-008)	Screening/ Randomization			South Health Campus	10070	2019-12-10
5362-72 (Participant ID 05-009)	Screening/ Randomization			South Health Campus	10079	2019-12-10
5358-93 (Participant ID 01-008)	Screening/ Randomization			Peter Lougheed Centre	10030	2019-12-20
5360-5 (Participant ID 03-003)	Screening/ Randomization			Foothills Medical Centre	10028	2019-12-23
5362-81 (Participant ID 05-010)	Screening/ Randomization			South Health Campus	10056	2019-12-26
5368-1 (Participant ID 11-001)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	10155	2020-01-10
5358-103 (Participant ID 01-009)	Screening/ Randomization			Peter Lougheed Centre	10203	2020-01-23
5358-104 (Participant ID 01-010)	Screening/ Randomization			Peter Lougheed Centre	10197	2020-01-24
5362-92 (Participant ID 05-011)	Screening/ Randomization			South Health Campus	10233	2020-01-27
5362-94 (Participant ID 05-012)	Screening/ Randomization			South Health Campus	10239	2020-02-04
5360-10 (Participant ID 03-004)	Screening/ Randomization			Foothills Medical Centre	10219	2020-02-05

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5359-10 (Participant ID 02-001)	Screening/ Randomization			University of Maryland Medical Center	10131	2020-02-07
5369-1 (Participant ID 12-001)	Screening/ Randomization			The Ottawa Hospital, General Campus	10185	2020-02-11
5360-12 (Participant ID 03-005)	Screening/ Randomization			Foothills Medical Centre	10209	2020-02-12
5370-11 (Participant ID 13-006)	Screening/ Randomization			Sturgeon Community Hospital	10103	2020-02-17
5370-12 (Participant ID 13-007)	Screening/ Randomization			Sturgeon Community Hospital	10114	2020-02-21
5374-1 (Participant ID 17-001)	Screening/ Randomization			University of Vermont Medical Center	10245	2020-02-27
5358-120 (Participant ID 01-011)	Screening/ Randomization			Peter Lougheed Centre	10204	2020-03-02
5362-104 (Participant ID 05-013)	Screening/ Randomization			South Health Campus	10227	2020-03-02
5359-14 (Participant ID 02-002)	Screening/ Randomization			University of Maryland Medical Center	10125	2020-03-03
5358-122 (Participant ID 01-012)	Screening/ Randomization			Peter Lougheed Centre	10198	2020-03-05
5358-125 (Participant ID 01-013)	Screening/ Randomization			Peter Lougheed Centre	10191	2020-03-12
5374-2 (Participant ID 17-002)	Screening/ Randomization			University of Vermont Medical Center	10251	2020-03-16
5358-126 (Participant ID 01-014)	Screening/ Randomization			Peter Lougheed Centre	10192	2020-06-30
5362-108 (Participant ID 05-014)	Screening/ Randomization			South Health Campus	10234	2020-07-17
5374-3 (Participant ID 17-003)	Screening/ Randomization			University of Vermont Medical Center	10257	2020-07-27
5368-16 (Participant ID 11-002)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	10166	2020-08-20

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5369-10 (Participant ID 12-002)	Screening/ Randomization			The Ottawa Hospital, General Campus	10186	2020-09-22
5369-11 (Participant ID 12-003)	Screening/ Randomization			The Ottawa Hospital, General Campus	10173	2020-10-01
5358-141 (Participant ID 01-015)	Screening/ Randomization			Peter Lougheed Centre	10193	2020-10-02
5358-142 (Participant ID 01-016)	Screening/ Randomization			Peter Lougheed Centre	10199	2020-10-14
5358-143 (Participant ID 01-017)	Screening/ Randomization			Peter Lougheed Centre	10205	2020-10-22
5362-118 (Participant ID 05-015)	Screening/ Randomization			South Health Campus	10235	2020-10-24
5358-144 (Participant ID 01-018)	Screening/ Randomization			Peter Lougheed Centre	10206	2020-10-27
5359-16 (Participant ID 02-003)	Screening/ Randomization			University of Maryland Medical Center	10119	2020-10-31
5371-20 (Participant ID 14-001)	Screening/ Randomization			St. Michael's Hospital	10143	2020-11-10
5371-21 (Participant ID 14-002)	Screening/ Randomization			St. Michael's Hospital	10149	2020-11-10
5373-4 (Participant ID 16-001)	Screening/ Randomization			St. Paul's Hospital	20263	2020-11-18
5370-13 (Participant ID 13-008)	Screening/ Randomization			Sturgeon Community Hospital	20326	2020-11-20
5358-154 (Participant ID 01-019)	Screening/ Randomization			Peter Lougheed Centre	10200	2020-11-23
5369-16 (Participant ID 12-004)	Screening/ Randomization			The Ottawa Hospital, General Campus	20317	2020-12-01
5362-131 (Participant ID 05-016)	Screening/ Randomization			South Health Campus	10228	2020-12-15
5358-164 (Participant ID 01-020)	Screening/ Randomization			Peter Lougheed Centre	10194	2020-12-29

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5373-6 (Participant ID 16-002)	Screening/ Randomization			St. Paul's Hospital	20275	2021-01-13
5362-136 (Participant ID 05-017)	Screening/ Randomization			South Health Campus	10240	2021-01-18
5358-167 (Participant ID 01-021)	Screening/ Randomization			Peter Lougheed Centre	10195	2021-01-19
5362-137 (Participant ID 05-018)	Screening/ Randomization			South Health Campus	10229	2021-01-19
5373-7 (Participant ID 16-003)	Screening/ Randomization			St. Paul's Hospital	20269	2021-01-19
5358-168 (Participant ID 01-022)	Screening/ Randomization			Peter Lougheed Centre	10196	2021-01-20
5370-14 (Participant ID 13-009)	Screening/ Randomization			Sturgeon Community Hospital	20327	2021-01-20
5369-26 (Participant ID 12-005)	Screening/ Randomization			The Ottawa Hospital, General Campus	20318	2021-01-22
5360-29 (Participant ID 03-006)	Screening/ Randomization			Foothills Medical Centre	10220	2021-02-08
5360-30 (Participant ID 03-007)	Screening/ Randomization			Foothills Medical Centre	10214	2021-02-08
5364-1 (Participant ID 07-001)	Screening/ Randomization			Queen Elizabeth II Health Sciences Centre	20351	2021-02-09
5372-1 (Participant ID 15-001)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20358	2021-02-11
5369-28 (Participant ID 12-006)	Screening/ Randomization			The Ottawa Hospital, General Campus	20319	2021-02-12
5370-16 (Participant ID 13-010)	Screening/ Randomization			Sturgeon Community Hospital	20328	2021-03-03
5372-2 (Participant ID 15-002)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20359	2021-03-04
5359-36 (Participant ID 02-004)	Screening/ Randomization			University of Maryland	20299	2021-03-05

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
				Medical Center		
5360-34 (Participant ID 03-008)	Screening/ Randomization			Foothills Medical Centre	10215	2021-03-08
5360-35 (Participant ID 03-009)	Screening/ Randomization			Foothills Medical Centre	10210	2021-03-09
5364-5 (Participant ID 07-002)	Screening/ Randomization			Queen Elizabeth II Health Sciences Centre	20352	2021-03-11
5362-138 (Participant ID 05-019)	Screening/ Randomization			South Health Campus	10241	2021-03-12
5358-171 (Participant ID 01-023)	Screening/ Randomization			Peter Lougheed Centre	10201	2021-03-14
5374-11 (Participant ID 17-004)	Screening/ Randomization			University of Vermont Medical Center	10258	2021-03-18
5362-141 (Participant ID 05-020)	Screening/ Randomization			South Health Campus	10242	2021-03-24
5359-52 (Participant ID 02-005)	Screening/ Randomization			University of Maryland Medical Center	20300	2021-03-26
5362-143 (Participant ID 05-021)	Screening/ Randomization			South Health Campus	10236	2021-03-31
5370-18 (Participant ID 13-011)	Screening/ Randomization			Sturgeon Community Hospital	20329	2021-04-03
5358-174 (Participant ID 01-024)	Screening/ Randomization			Peter Lougheed Centre	10202	2021-04-07
5359-53 (Participant ID 02-006)	Screening/ Randomization			University of Maryland Medical Center	20301	2021-04-08
5370-21 (Participant ID 13-012)	Screening/ Randomization			Sturgeon Community Hospital	20330	2021-04-09
5360-36 (Participant ID 03-010)	Screening/ Randomization			Foothills Medical Centre	20374	2021-04-19
5374-13 (Participant ID 17-005)	Screening/ Randomization			University of Vermont Medical Center	20392	2021-04-24

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5358-175 (Participant ID 01-025)	Screening/ Randomization			Peter Loughheed Centre	20365	2021-05-04
5362-144 (Participant ID 05-022)	Screening/ Randomization			South Health Campus	20383	2021-05-06
5370-22 (Participant ID 13-013)	Screening/ Randomization			Sturgeon Community Hospital	20331	2021-05-06
5358-177 (Participant ID 01-026)	Screening/ Randomization			Peter Loughheed Centre	20366	2021-05-07
5372-3 (Participant ID 15-003)	Screening/ Randomization			Peter Loughheed Centre	20360	2021-05-07
5359-54 (Participant ID 02-007)	Screening/ Randomization			University of Maryland Medical Center	20302	2021-05-10
5359-55 (Participant ID 02-008)	Screening/ Randomization			University of Maryland Medical Center	20303	2021-05-11
5360-37 (Participant ID 03-011)	Screening/ Randomization			Foothills Medical Centre	20375	2021-05-17
5359-56 (Participant ID 02-009)	Screening/ Randomization			University of Maryland Medical Center	20304	2021-05-18
5358-179 (Participant ID 01-027)	Screening/ Randomization			Peter Loughheed Centre	20367	2021-05-20
5363-5 (Participant ID 06-001)	Screening/ Randomization			Carolinas Medical Center	20344	2021-05-21
5369-48 (Participant ID 12-007)	Screening/ Randomization			The Ottawa Hospital, General Campus	20320	2021-05-25
5362-147 (Participant ID 05-023)	Screening/ Randomization			South Health Campus	20384	2021-05-28
5373-8 (Participant ID 16-004)	Screening/ Randomization			St. Paul's Hospital	20270	2021-06-02
5360-39 (Participant ID 03-012)	Screening/ Randomization			Sturgeon Community Hospital	20376	2021-06-03
5374-18 (Participant ID 17-006)	Screening/ Randomization			University of Vermont Medical Center	20393	2021-06-05

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5374-19 (Participant ID 17-007)	Screening/ Randomization			University of Vermont Medical Center	20394	2021-06-10
5374-20 (Participant ID 17-008)	Screening/ Randomization			University of Vermont Medical Center	20395	2021-06-11
5362-149 (Participant ID 05-024)	Screening/ Randomization			South Health Campus	20385	2021-06-14
5360-41 (Participant ID 03-013)	Screening/ Randomization			Foothills Medical Centre	20377	2021-06-15
5360-44 (Participant ID 03-014)	Screening/ Randomization			Foothills Medical Centre	20378	2021-06-18
5362-151 (Participant ID 05-025)	Screening/ Randomization			South Health Campus	20386	2021-06-18
5370-23 (Participant ID 13-014)	Screening/ Randomization			Sturgeon Community Hospital	20332	2021-06-18
5362-152 (Participant ID 05-026)	Screening/ Randomization			South Health Campus	20387	2021-06-23
5358-180 (Participant ID 01-028)	Screening/ Randomization			Peter Lougheed Centre	20368	2021-06-24
5360-47 (Participant ID 03-015)	Screening/ Randomization			Foothills Medical Centre	20379	2021-06-24
5374-22 (Participant ID 17-009)	Screening/ Randomization			University of Vermont Medical Center	20396	2021-06-25
5374-23 (Participant ID 17-010)	Screening/ Randomization			University of Vermont Medical Center	20397	2021-06-28
5362-153 (Participant ID 05-027)	Screening/ Randomization			South Health Campus	20388	2021-06-29
5370-24 (Participant ID 13-015)	Screening/ Randomization			Sturgeon Community Hospital	20431	2021-07-02
5362-154 (Participant ID 05-028)	Screening/ Randomization			South Health Campus	20389	2021-07-05
5360-49 (Participant ID 03-016)	Screening/ Randomization			Foothills Medical Centre	20380	2021-07-06

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5371-23 (Participant ID 14-003)	Screening/ Randomization			St. Michael's Hospital	20437	2021-07-12
5367-2 (Participant ID 10-001)	Screening/ Randomization			Royal Columbian Hospital	20416	2021-07-13
5362-158 (Participant ID 05-029)	Screening/ Randomization			South Health Campus	20390	2021-07-15
5362-160 (Participant ID 05-030)	Screening/ Randomization			South Health Campus	20391	2021-07-16
5365-1 (Participant ID 08-001)	Screening/ Randomization			St. Joseph's Hospital	20413	2021-07-16
5367-3 (Participant ID 10-002)	Screening/ Randomization			Royal Columbian Hospital	20417	2021-07-16
5360-56 (Participant ID 03-017)	Screening/ Randomization			Sturgeon Community Hospital	20381	2021-07-20
5359-57 (Participant ID 02-010)	Screening/ Randomization			University of Maryland Medical Center	20398	2021-07-27
5369-63 (Participant ID 12-008)	Screening/ Randomization			The Ottawa Hospital, General Campus	20425	2021-07-27
5364-10 (Participant ID 07-003)	Screening/ Randomization			Queen Elizabeth II Health Sciences Centre	20407	2021-07-28
5362-164 (Participant ID 05-031)	Screening/ Randomization			South Health Campus	20473	2021-08-04
5367-4 (Participant ID 10-003)	Screening/ Randomization			Royal Columbian Hospital	20418	2021-08-06
5367-7 (Participant ID 10-004)	Screening/ Randomization			Royal Columbian Hospital	20419	2021-08-12
5358-184 (Participant ID 01-029)	Screening/ Randomization			Peter Lougheed Centre	20369	2021-08-14
5365-2 (Participant ID 08-002)	Screening/ Randomization			St. Joseph's Hospital	20414	2021-08-17
5367-9 (Participant ID 10-005)	Screening/ Randomization			Royal Columbian Hospital	20420	2021-08-19

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5371-24 (Participant ID 14-004)	Screening/ Randomization			St. Michael's Hospital	20438	2021-08-19
5358-186 (Participant ID 01-030)	Screening/ Randomization			Peter Loughheed Centre	20370	2021-08-25
5374-25 (Participant ID 17-011)	Screening/ Randomization			University of Vermont Medical Center	20485	2021-08-25
5360-60 (Participant ID 03-018)	Screening/ Randomization			Foothills Medical Centre	20382	2021-08-27
5362-168 (Participant ID 05-032)	Screening/ Randomization			South Health Campus	20479	2021-08-30
5359-81 (Participant ID 02-011)	Screening/ Randomization			University of Maryland Medical Center	20399	2021-08-31
5362-169 (Participant ID 05-033)	Screening/ Randomization			South Health Campus	20476	2021-09-02
5360-61 (Participant ID 03-019)	Screening/ Randomization			Foothills Medical Centre	20467	2021-09-03
5360-62 (Participant ID 03-020)	Screening/ Randomization			Foothills Medical Centre	20464	2021-09-03
5362-170 (Participant ID 05-034)	Screening/ Randomization			South Health Campus	20477	2021-09-06
5360-63 (Participant ID 03-021)	Screening/ Randomization			Foothills Medical Centre	20470	2021-09-08
5374-27 (Participant ID 17-012)	Screening/ Randomization			University of Vermont Medical Center	20488	2021-09-09
5360-64 (Participant ID 03-022)	Screening/ Randomization			Foothills Medical Centre	20465	2021-09-15
5374-30 (Participant ID 17-013)	Screening/ Randomization			University of Vermont Medical Center	20486	2021-09-16
5372-5 (Participant ID 15-004)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20443	2021-09-17
5362-172 (Participant ID 05-035)	Screening/ Randomization			South Health Campus	20480	2021-09-18

Screening ID screen_id	Event Name redcap_ event_ name	Repeat Instrument redcap_ repeat_ instrument	Repeat Instance redcap_ repeat_ instance	Data Access Group redcap_ data_ access_ group	BOTTLE ID rand_ group	Date of randomization rand_dt
5360-67 (Participant ID 03-023)	Screening/ Randomization			Foothills Medical Centre	20471	2021-09-22
5360-68 (Participant ID 03-024)	Screening/ Randomization			Foothills Medical Centre	20468	2021-09-24
5362-175 (Participant ID 05-036)	Screening/ Randomization			South Health Campus	20474	2021-10-04
5367-13 (Participant ID 10-006)	Screening/ Randomization			Royal Columbian Hospital	20421	2021-10-04
5370-26 (Participant ID 13-016)	Screening/ Randomization			Sturgeon Community Hospital	20432	2021-10-05
5363-35 (Participant ID 06-002)	Screening/ Randomization			Carolinas Medical Center	20404	2021-10-06
5374-32 (Participant ID 17-014)	Screening/ Randomization			University of Vermont Medical Center	20489	2021-10-11
5369-73 (Participant ID 12-009)	Screening/ Randomization			The Ottawa Hospital, General Campus	20426	2021-10-14
5367-16 (Participant ID 10-007)	Screening/ Randomization			Royal Columbian Hospital	20505	2021-10-18
5360-69 (Participant ID 03-025)	Screening/ Randomization			Foothills Medical Centre	20466	2021-10-20
5362-178 (Participant ID 05-037)	Screening/ Randomization			South Health Campus	20478	2021-11-04
5371-25 (Participant ID 14-005)	Screening/ Randomization			St. Michael's Hospital	20562	2021-11-04
5358-193 (Participant ID 01-031)	Screening/ Randomization			Sturgeon Community Hospital	20461	2021-11-05
5362-179 (Participant ID 05-038)	Screening/ Randomization			South Health Campus	20475	2021-11-10
5362-180 (Participant ID 05-039)	Screening/ Randomization			South Health Campus	20481	2021-11-10
5360-73 (Participant ID 03-026)	Screening/ Randomization			Foothills Medical Centre	20472	2021-11-16
5365-3 (Participant ID 08-003)	Screening/ Randomization			St. Joseph's Hospital	20496	2021-11-19

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5360-74 (Participant ID 03-027)	Screening/ Randomization			Foothills Medical Centre	20469	2021-11-26
5358-195 (Participant ID 01-032)	Screening/ Randomization			Peter Lougheed Centre	20458	2021-12-01
5360-76 (Participant ID 03-028)	Screening/ Randomization			Foothills Medical Centre	20518	2021-12-06
5362-186 (Participant ID 05-040)	Screening/ Randomization			South Health Campus	20530	2021-12-07
5374-37 (Participant ID 17-015)	Screening/ Randomization			University of Vermont Medical Center	20574	2021-12-13
5363-56 (Participant ID 06-003)	Screening/ Randomization			Carolinas Medical Center	20532	2021-12-16
5369-83 (Participant ID 12-010)	Screening/ Randomization			The Ottawa Hospital, General Campus	20547	2021-12-16
5372-6 (Participant ID 15-005)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20568	2021-12-16
5358-197 (Participant ID 01-033)	Screening/ Randomization			Peter Lougheed Centre	20455	2021-12-28
5367-29 (Participant ID 10-008)	Screening/ Randomization			Royal Columbian Hospital	20500	2021-12-29
5358-198 (Participant ID 01-034)	Screening/ Randomization			Peter Lougheed Centre	20462	2021-12-31
5358-199 (Participant ID 01-035)	Screening/ Randomization			Peter Lougheed Centre	20456	2022-01-11
5360-85 (Participant ID 03-029)	Screening/ Randomization			Foothills Medical Centre	20521	2022-01-11
5374-40 (Participant ID 17-016)	Screening/ Randomization			University of Vermont Medical Center	20580	2022-01-13
5373-20 (Participant ID 16-005)	Screening/ Randomization			St. Paul's Hospital	20571	2022-01-14
5358-200 (Participant ID 01-036)	Screening/ Randomization			Peter Lougheed Centre	20459	2022-01-17

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5367-33 (Participant ID 10-009)	Screening/ Randomization			Royal Columbian Hospital	20503	2022-01-19
5358-202 (Participant ID 01-037)	Screening/ Randomization			Peter Lougheed Centre	20457	2022-01-21
5358-204 (Participant ID 01-038)	Screening/ Randomization			Peter Lougheed Centre	20463	2022-01-25
5362-190 (Participant ID 05-041)	Screening/ Randomization			South Health Campus	20524	2022-01-25
5358-206 (Participant ID 01-039)	Screening/ Randomization			Peter Lougheed Centre	20460	2022-01-26
5373-21 (Participant ID 16-006)	Screening/ Randomization			St. Paul's Hospital	20572	2022-02-02
5362-195 (Participant ID 05-042)	Screening/ Randomization			South Health Campus	20527	2022-02-11
5358-210 (Participant ID 01-040)	Screening/ Randomization			Peter Lougheed Centre	20593	2022-02-16
5364-18 (Participant ID 07-004)	Screening/ Randomization			Queen Elizabeth II Health Sciences Centre	20535	2022-02-17
5367-38 (Participant ID 10-010)	Screening/ Randomization			Royal Columbian Hospital	20501	2022-02-22
5359-86 (Participant ID 02-012)	Screening/ Randomization			University of Maryland Medical Center	20510	2022-02-28
5372-7 (Participant ID 15-006)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20565	2022-02-28
5360-86 (Participant ID 03-030)	Screening/ Randomization			Foothills Medical Centre	20522	2022-03-01
5369-100 (Participant ID 12-011)	Screening/ Randomization			The Ottawa Hospital, General Campus	20545	2022-03-01
5362-197 (Participant ID 05-043)	Screening/ Randomization			South Health Campus	20531	2022-03-07
5374-43 (Participant ID 17-017)	Screening/ Randomization			University of Vermont Medical Center	20577	2022-03-07

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5369-101 (Participant ID 12-012)	Screening/ Randomization			The Ottawa Hospital, General Campus	20548	2022-03-08
5360-87 (Participant ID 03-031)	Screening/ Randomization			Foothills Medical Centre	20519	2022-03-11
5358-211 (Participant ID 01-041)	Screening/ Randomization			Peter Lougheed Centre	20590	2022-03-16
5369-103 (Participant ID 12-013)	Screening/ Randomization			The Ottawa Hospital, General Campus	20546	2022-03-16
5358-212 (Participant ID 01-042)	Screening/ Randomization			Peter Lougheed Centre	20594	2022-03-17
5368-86 (Participant ID 11-003)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20541	2022-03-22
5370-36 (Participant ID 13-017)	Screening/ Randomization			Sturgeon Community Hospital	20554	2022-03-23
5368-88 (Participant ID 11-004)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20542	2022-03-24
5371-55 (Participant ID 14-006)	Screening/ Randomization			St. Michael's Hospital	20563	2022-03-28
5358-214 (Participant ID 01-043)	Screening/ Randomization			Peter Lougheed Centre	20591	2022-03-29
5363-78 (Participant ID 06-004)	Screening/ Randomization			Carolinas Medical Center	20533	2022-03-30
5360-95 (Participant ID 03-032)	Screening/ Randomization			Foothills Medical Centre	20515	2022-04-02
5359-92 (Participant ID 02-013)	Screening/ Randomization			University of Maryland Medical Center	20512	2022-04-04
5374-44 (Participant ID 17-018)	Screening/ Randomization			University of Vermont Medical Center	20578	2022-04-04
5373-22 (Participant ID 16-007)	Screening/ Randomization			St. Paul's Hospital	20573	2022-04-05
5359-93 (Participant ID 02-014)	Screening/ Randomization			University of Maryland Medical Center	20513	2022-04-12

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5374-45 (Participant ID 17-019)	Screening/ Randomization			University of Vermont Medical Center	20581	2022-04-18
5358-215 (Participant ID 01-044)	Screening/ Randomization			Peter Loughheed Centre	20596	2022-04-19
5367-42 (Participant ID 10-011)	Screening/ Randomization			Royal Columbian Hospital	20506	2022-04-21
5373-23 (Participant ID 16-008)	Screening/ Randomization			St. Paul's Hospital	20603	2022-04-28
5371-61 (Participant ID 14-007)	Screening/ Randomization			St. Michael's Hospital	20559	2022-05-12
5365-4 (Participant ID 08-004)	Screening/ Randomization			St. Joseph's Hospital	20491	2022-05-13
5371-62 (Participant ID 14-008)	Screening/ Randomization			St. Michael's Hospital	20560	2022-05-19
5367-46 (Participant ID 10-012)	Screening/ Randomization			Royal Columbian Hospital	20507	2022-06-02
5370-40 (Participant ID 13-018)	Screening/ Randomization			Sturgeon Community Hospital	20556	2022-06-03
5372-61 (Participant ID 15-007)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20570	2022-06-08
5359-99 (Participant ID 02-015)	Screening/ Randomization			University of Maryland Medical Center	20509	2022-06-13
5362-206 (Participant ID 05-044)	Screening/ Randomization			South Health Campus	20528	2022-06-14
5365-5 (Participant ID 08-005)	Screening/ Randomization			St. Joseph's Hospital	20494	2022-06-15
5367-52 (Participant ID 10-013)	Screening/ Randomization			Royal Columbian Hospital	20504	2022-06-17
5368-96 (Participant ID 11-005)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20543	2022-06-17
5371-63 (Participant ID 14-009)	Screening/ Randomization			St. Michael's Hospital	20561	2022-06-20
5374-56 (Participant ID	Screening/ Randomization			University of Vermont	20575	2022-06-20

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
17-020)				Medical Center		
5369-120 (Participant ID 12-014)	Screening/ Randomization			The Ottawa Hospital, General Campus	20549	2022-06-21
5358-220 (Participant ID 01-045)	Screening/ Randomization			Peter Loughheed Centre	20595	2022-06-24
5365-6 (Participant ID 08-006)	Screening/ Randomization			Sturgeon Community Hospital	20497	2022-06-27
5362-211 (Participant ID 05-045)	Screening/ Randomization			South Health Campus	20583	2022-06-28
5360-99 (Participant ID 03-033)	Screening/ Randomization			Foothills Medical Centre	20516	2022-07-06
5360-100 (Participant ID 03-034)	Screening/ Randomization			Foothills Medical Centre	20520	2022-07-06
5367-54 (Participant ID 10-014)	Screening/ Randomization			Royal Columbian Hospital	20502	2022-07-06
5360-101 (Participant ID 03-035)	Screening/ Randomization			Foothills Medical Centre	20517	2022-07-08
5365-7 (Participant ID 08-007)	Screening/ Randomization			St. Joseph's Hospital	20495	2022-07-08
5360-104 (Participant ID 03-036)	Screening/ Randomization			Foothills Medical Centre	20523	2022-07-15
5358-221 (Participant ID 01-046)	Screening/ Randomization			Peter Loughheed Centre	20592	2022-07-18
5367-58 (Participant ID 10-015)	Screening/ Randomization			Royal Columbian Hospital	20508	2022-07-18
5363-100 (Participant ID 06-005)	Screening/ Randomization			Carolinas Medical Center	20534	2022-07-20
5368-110 (Participant ID 11-006)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20611	2022-08-03
5359-105 (Participant ID 02-016)	Screening/ Randomization			University of Maryland Medical Center	20514	2022-08-10
5365-8 (Participant ID 08-008)	Screening/ Randomization			St. Joseph's Hospital	20498	2022-08-10

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5365-9 (Participant ID 08-009)	Screening/ Randomization			St. Joseph's Hospital	20492	2022-08-10
5360-109 (Participant ID 03-037)	Screening/ Randomization			Foothills Medical Centre	20629	2022-08-11
5374-60 (Participant ID 17-021)	Screening/ Randomization			University of Vermont Medical Center	20576	2022-08-15
5360-112 (Participant ID 03-038)	Screening/ Randomization			Foothills Medical Centre	20630	2022-08-16
5362-217 (Participant ID 05-046)	Screening/ Randomization			South Health Campus	20529	2022-08-16
5367-63 (Participant ID 10-016)	Screening/ Randomization			Royal Columbian Hospital	20638	2022-08-22
5372-62 (Participant ID 15-008)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20566	2022-08-23
5370-48 (Participant ID 13-019)	Screening/ Randomization			Sturgeon Community Hospital	20550	2022-08-26
5365-10 (Participant ID 08-010)	Screening/ Randomization			St. Joseph's Hospital	20493	2022-08-30
5363-109 (Participant ID 06-006)	Screening/ Randomization			Carolinas Medical Center	20605	2022-08-31
5372-63 (Participant ID 15-009)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20569	2022-09-01
5358-228 (Participant ID 01-047)	Screening/ Randomization			Peter Lougheed Centre	20597	2022-09-02
5364-32 (Participant ID 07-005)	Screening/ Randomization			Queen Elizabeth II Health Sciences Centre	20539	2022-09-09
5360-123 (Participant ID 03-039)	Screening/ Randomization			Foothills Medical Centre	20631	2022-09-13
5368-122 (Participant ID 11-007)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20612	2022-09-14
5365-11 (Participant ID 08-011)	Screening/ Randomization			St. Joseph's Hospital	20499	2022-09-15

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5368-128 (Participant ID 11-008)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20613	2022-09-22
5359-115 (Participant ID 02-017)	Screening/ Randomization			University of Maryland Medical Center	20511	2022-09-23
5359-116 (Participant ID 02-018)	Screening/ Randomization			University of Maryland Medical Center	20632	2022-09-26
5367-69 (Participant ID 10-017)	Screening/ Randomization			Royal Columbian Hospital	20639	2022-09-27
5358-232 (Participant ID 01-048)	Screening/ Randomization			Peter Lougheed Centre	20598	2022-09-28
5370-51 (Participant ID 13-020)	Screening/ Randomization			Sturgeon Community Hospital	20557	2022-10-03
5359-118 (Participant ID 02-019)	Screening/ Randomization			University of Maryland Medical Center	20633	2022-10-05
5370-54 (Participant ID 13-021)	Screening/ Randomization			Sturgeon Community Hospital	20558	2022-10-05
5374-68 (Participant ID 17-022)	Screening/ Randomization			University of Vermont Medical Center	20582	2022-10-07
5367-73 (Participant ID 10-018)	Screening/ Randomization			Royal Columbian Hospital	20640	2022-10-11
5367-74 (Participant ID 10-019)	Screening/ Randomization			Royal Columbian Hospital	20641	2022-10-12
5367-78 (Participant ID 10-020)	Screening/ Randomization			Royal Columbian Hospital	20642	2022-10-19
5358-235 (Participant ID 01-049)	Screening/ Randomization			Peter Lougheed Centre	20668	2022-10-21
5358-236 (Participant ID 01-050)	Screening/ Randomization			Peter Lougheed Centre	20665	2022-10-24
5362-227 (Participant ID 05-047)	Screening/ Randomization			South Health Campus	20635	2022-10-29
5360-136 (Participant ID 03-040)	Screening/ Randomization			Foothills Medical Centre	20674	2022-11-01

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5373-26 (Participant ID 16-009)	Screening/ Randomization			St. Paul's Hospital	20698	2022-11-02
5358-237 (Participant ID 01-051)	Screening/ Randomization			Peter Lougheed Centre	20662	2022-11-07
5360-137 (Participant ID 03-041)	Screening/ Randomization			Foothills Medical Centre	20675	2022-11-08
5363-127 (Participant ID 06-007)	Screening/ Randomization			Carolinas Medical Center	20606	2022-11-16
5367-84 (Participant ID 10-021)	Screening/ Randomization			Royal Columbian Hospital	20643	2022-11-17
5372-64 (Participant ID 15-010)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20653	2022-11-24
5368-146 (Participant ID 11-009)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20614	2022-11-25
5358-241 (Participant ID 01-052)	Screening/ Randomization			Peter Lougheed Centre	20669	2022-12-05
5358-242 (Participant ID 01-053)	Screening/ Randomization			Peter Lougheed Centre	20666	2022-12-05
5360-142 (Participant ID 03-042)	Screening/ Randomization			Foothills Medical Centre	20676	2022-12-10
5367-90 (Participant ID 10-022)	Screening/ Randomization			Royal Columbian Hospital	20644	2022-12-12
5362-232 (Participant ID 05-048)	Screening/ Randomization			South Health Campus	20636	2022-12-22
5367-92 (Participant ID 10-023)	Screening/ Randomization			Royal Columbian Hospital	20645	2022-12-22
5362-233 (Participant ID 05-049)	Screening/ Randomization			South Health Campus	20637	2022-12-28
5370-57 (Participant ID 13-022)	Screening/ Randomization			Sturgeon Community Hospital	20690	2023-01-04
5369-159 (Participant ID 12-015)	Screening/ Randomization			The Ottawa Hospital, General Campus	20617	2023-01-06
5359-123 (Participant ID 02-020)	Screening/ Randomization			University of Maryland	20634	2023-01-09

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
				Medical Center		
5371-76 (Participant ID 14-010)	Screening/ Randomization			St. Michael's Hospital	20647	2023-01-10
5359-124 (Participant ID 02-021)	Screening/ Randomization			University of Maryland Medical Center	20701	2023-01-11
5368-155 (Participant ID 11-010)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20615	2023-01-12
5368-156 (Participant ID 11-011)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20616	2023-01-13
5362-238 (Participant ID 05-050)	Screening/ Randomization			South Health Campus	20677	2023-01-25
5373-27 (Participant ID 16-010)	Screening/ Randomization			St. Paul's Hospital	20699	2023-01-26
5362-240 (Participant ID 05-051)	Screening/ Randomization			South Health Campus	20679	2023-02-06
5359-127 (Participant ID 02-022)	Screening/ Randomization			University of Maryland Medical Center	20702	2023-02-07
5372-65 (Participant ID 15-011)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20654	2023-02-08
5374-74 (Participant ID 17-023)	Screening/ Randomization			University of Vermont Medical Center	20656	2023-02-10
5358-251 (Participant ID 01-054)	Screening/ Randomization			Peter Lougheed Centre	20663	2023-02-13
5373-28 (Participant ID 16-011)	Screening/ Randomization			St. Paul's Hospital	20700	2023-02-14
5374-75 (Participant ID 17-024)	Screening/ Randomization			University of Vermont Medical Center	20657	2023-02-15
5358-252 (Participant ID 01-055)	Screening/ Randomization			Peter Lougheed Centre	20670	2023-02-16
5358-253 (Participant ID 01-056)	Screening/ Randomization			Peter Lougheed Centre	20667	2023-02-16
5362-242 (Participant ID	Screening/ Randomization			South Health Campus	20680	2023-02-23

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
(Participant ID 17-025)	Screening/ Randomization			Medical Center	20658	2023-03-06
5374-79 (Participant ID 17-026)	Screening/ Randomization			University of Vermont Medical Center	20659	2023-03-06
5367-98 (Participant ID 10-024)	Screening/ Randomization			Royal Columbian Hospital	20646	2023-03-08
5371-123 (Participant ID 14-011)	Screening/ Randomization			St. Michael's Hospital	20648	2023-03-16
5362-246 (Participant ID 05-053)	Screening/ Randomization			South Health Campus	20681	2023-03-17
5374-80 (Participant ID 17-027)	Screening/ Randomization			University of Vermont Medical Center	20660	2023-03-23
5358-256 (Participant ID 01-057)	Screening/ Randomization			Peter Lougheed Centre	20664	2023-03-28
5358-257 (Participant ID 01-058)	Screening/ Randomization			Peter Lougheed Centre	20683	2023-03-29
5359-132 (Participant ID 02-023)	Screening/ Randomization			University of Maryland Medical Center	20703	2023-03-30
5371-124 (Participant ID 14-012)	Screening/ Randomization			St. Michael's Hospital	20649	2023-03-31
5374-81 (Participant ID 17-028)	Screening/ Randomization			University of Vermont Medical Center	20661	2023-04-06
5358-260 (Participant ID 01-059)	Screening/ Randomization			Peter Lougheed Centre	20685	2023-04-10
5358-262 (Participant ID 01-060)	Screening/ Randomization			Peter Lougheed Centre	20684	2023-04-13
5362-247 (Participant ID 05-054)	Screening/ Randomization			South Health Campus	20678	2023-05-03
5367-110 (Participant ID 10-025)	Screening/ Randomization			Royal Columbian Hospital	20704	2023-05-05
5370-59 (Participant ID 13-023)	Screening/ Randomization			Sturgeon Community Hospital	20691	2023-05-08
5367-111 (Participant ID 10-026)	Screening/ Randomization			Royal Columbian	20705	2023-05-12

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
10-026)				Hospital		
5367-114 (Participant ID 10-027)	Screening/ Randomization			Royal Columbian Hospital	20706	2023-05-18
5358-267 (Participant ID 01-061)	Screening/ Randomization			Peter Lougheed Centre	20620	2023-05-26
5358-268 (Participant ID 01-062)	Screening/ Randomization			Peter Lougheed Centre	20618	2023-05-29
5368-189 (Participant ID 11-012)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20710	2023-05-30
5358-270 (Participant ID 01-063)	Screening/ Randomization			Peter Lougheed Centre	20622	2023-05-31
5358-274 (Participant ID 01-064)	Screening/ Randomization			Peter Lougheed Centre	20623	2023-06-06
5372-66 (Participant ID 15-012)	Screening/ Randomization			Sunnybrook Health Sciences Centre	20655	2023-06-06
5362-250 (Participant ID 05-055)	Screening/ Randomization			South Health Campus	20682	2023-06-08
5360-170 (Participant ID 03-043)	Screening/ Randomization			Foothills Medical Centre	20626	2023-06-10
5370-65 (Participant ID 13-024)	Screening/ Randomization			Sturgeon Community Hospital	20693	2023-06-13
5360-179 (Participant ID 03-044)	Screening/ Randomization			Foothills Medical Centre	20741	2023-06-28
5367-124 (Participant ID 10-028)	Screening/ Randomization			Royal Columbian Hospital	20707	2023-06-30
5358-276 (Participant ID 01-065)	Screening/ Randomization			Peter Lougheed Centre	20725	2023-07-04
5358-280 (Participant ID 01-066)	Screening/ Randomization			Peter Lougheed Centre	20726	2023-07-07
5360-183 (Participant ID 03-045)	Screening/ Randomization			Foothills Medical Centre	20744	2023-07-07
5370-67 (Participant ID 13-025)	Screening/ Randomization			Sturgeon Community Hospital	20778	2023-07-07
5370-68 (Participant ID	Screening/ Randomization			Sturgeon Community	20773	2023-07-11

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
13-026)				Hospital		
5374-84 (Participant ID 17-029)	Screening/ Randomization			University of Vermont Medical Center	20779	2023-07-13
5367-129 (Participant ID 10-029)	Screening/ Randomization			Royal Columbian Hospital	20708	2023-07-17
5359-137 (Participant ID 02-024)	Screening/ Randomization			University of Maryland Medical Center	20734	2023-07-18
5367-130 (Participant ID 10-030)	Screening/ Randomization			Royal Columbian Hospital	20709	2023-07-19
5374-85 (Participant ID 17-030)	Screening/ Randomization			University of Vermont Medical Center	20782	2023-07-21
5359-139 (Participant ID 02-025)	Screening/ Randomization			University of Maryland Medical Center	20735	2023-07-26
5367-133 (Participant ID 10-031)	Screening/ Randomization			Royal Columbian Hospital	20763	2023-08-02
5358-287 (Participant ID 01-067)	Screening/ Randomization			Peter Lougheed Centre	20720	2023-08-09
5359-142 (Participant ID 02-026)	Screening/ Randomization			University of Maryland Medical Center	20728	2023-08-09
5358-288 (Participant ID 01-068)	Screening/ Randomization			Peter Lougheed Centre	20716	2023-08-11
5374-88 (Participant ID 17-031)	Screening/ Randomization			University of Vermont Medical Center	20784	2023-08-11
5367-137 (Participant ID 10-032)	Screening/ Randomization			Royal Columbian Hospital	20764	2023-08-15
5362-259 (Participant ID 05-056)	Screening/ Randomization			South Health Campus	20756	2023-08-18
5368-213 (Participant ID 11-013)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20711	2023-08-18
5368-215 (Participant ID 11-014)	Screening/ Randomization			The Ottawa Hospital, Civic Campus	20712	2023-08-24
5374-90 (Participant ID	Screening/ Randomization			University of Vermont	20785	2023-08-28

Screening ID screen_id	Event Name redcap_event_name	Repeat Instrument redcap_repeat_instrument	Repeat Instance redcap_repeat_instance	Data Access Group redcap_data_access_group	BOTTLE ID rand_group	Date of randomization rand_dt
5362-262 (Participant ID 01-069)	Screening/Randomization			Lougheed Centre	20721	2023-09-05
5367-142 (Participant ID 10-033)	Screening/Randomization			Royal Columbian Hospital	20761	2023-09-06
5369-207 (Participant ID 12-016)	Screening/Randomization			The Ottawa Hospital, General Campus	20770	2023-09-08
5369-208 (Participant ID 12-017)	Screening/Randomization			The Ottawa Hospital, General Campus	20771	2023-09-11
5358-293 (Participant ID 01-070)	Screening/Randomization			Peter Lougheed Centre	20717	2023-09-18
5362-262 (Participant ID 05-057)	Screening/Randomization			South Health Campus	20749	2023-09-26

PERK 2 TRIAL NEWSLETTER

Dr. Kevin A. Hildebrand

July 2023 Edition



GOALS

By July 31st:

- Reach 362 total recruitments for the trial
- Complete query resolution at sites
- Complete updated AE/SAE Logs

MILESTONES

Current Overall Enrollment Status:

Peter Lougheed Centre (n=64)
South Health Campus (n=55)
Foothills Medical Centre (n=44)
University of Vermont Medical Center (n=28)
Royal Columbian Hospital (n=28)
Sturgeon Community Hospital (n=24)
University of Maryland Medical Center (n=23)
The Ottawa Hospital, General Campus (n=15)
St. Michael's Hospital (n=12)
The Ottawa Hospital, Civic Campus (n=12)
Sunnybrook HSC (n=12)
St. Joseph's Hospital (n=11)
St. Paul's Hospital (n=11)
Carolinas Medical Center (n=8)
Queen Elizabeth II HSC (n=5)



June 2023 Enrollment Hall of Fame:

1. Foothills Medical Centre (n=2)
2. Peter Lougheed Centre (n=1)
3. South Health Campus (n=1)
4. Royal Columbian Hospital (n=1)
5. Sunnybrook HSC (n=1)
6. Sturgeon Community Hospital (n=1)

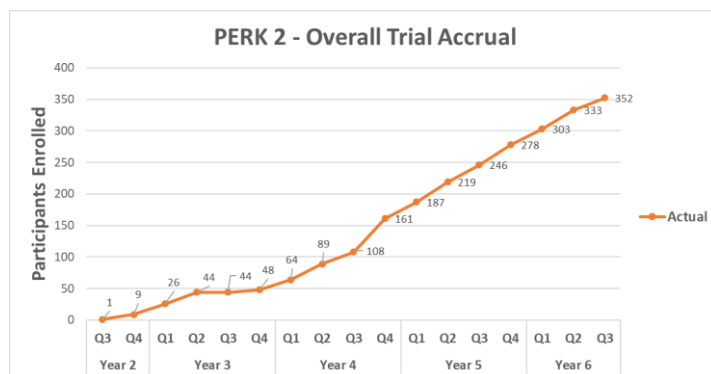
TRIAL UPDATES

- With 7 participants enrolled in June, we have reached 352 participants!
- The next Trial Management Group meeting with active sites proposed for **Monday, September 11th, 2023 at 1:00pm MDT (12:00pm PDT, 3:00pm EDT).**
- **REMINDER:** AE/SAE Logs are being phased out. Please send us your last log signed and dated by your PI with all adverse events reported up until June 30th, 2023.

PERK 2 TEAM

Trial PI/Sponsor: Kevin Hildebrand 403-220-7282

Research Coordinator: Isabella Salazar 403-943-5556



PERK 2 TRIAL NEWSLETTER

Dr. Kevin A. Hildebrand

August 2023 Edition



GOALS

By August 31st:

- Reach 374 total recruitments for the trial
- Complete query resolution at sites
- Complete updated AE/SAE Logs

MILESTONES

Current Overall Enrollment Status:

Peter Lougheed Centre (n=66)
South Health Campus (n=55)
Foothills Medical Centre (n=45)
University of Vermont Medical Center (n=30)
Royal Columbian Hospital (n=30)
Sturgeon Community Hospital (n=26)
University of Maryland Medical Center (n=25)
The Ottawa Hospital, General Campus (n=15)
St. Michael's Hospital (n=12)
The Ottawa Hospital, Civic Campus (n=12)
Sunnybrook HSC (n=12)
St. Joseph's Hospital (n=11)
St. Paul's Hospital (n=11)
Carolinas Medical Center (n=8)
Queen Elizabeth II HSC (n=5)



July 2023 Enrollment Hall of Fame:

1. Peter Lougheed Centre (n=2)
2. Sturgeon Community Hospital (n=2)
3. University of Vermont Medical Center (n=2)
4. University of Maryland Medical Center (n=2)
5. Royal Columbian Hospital (n=2)
6. Foothills Medical Centre (n=1)

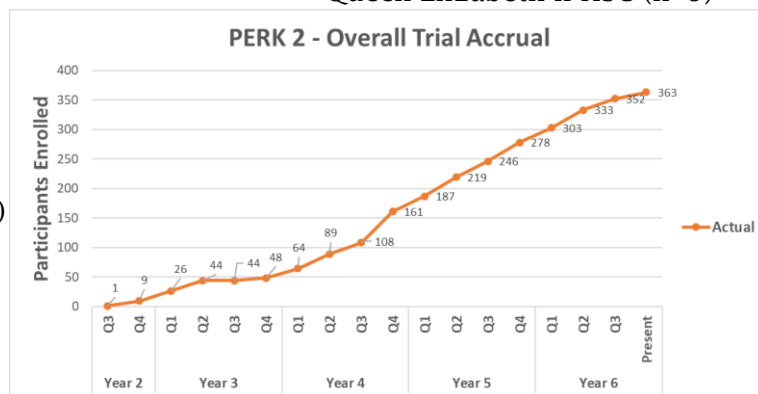
TRIAL UPDATES

- With 11 participants enrolled in July, we have reached 363 participants!
- The next Trial Management Group meeting with active sites proposed for **Monday, September 11th, 2023 at 1:00pm MDT (12:00pm PDT, 3:00pm EDT).**
- **REMINDER:** Please send us your last AE/SAE log signed and dated by your PI with all adverse events reported up until June 30th, 2023.

PERK 2 TEAM

Trial PI/Sponsor: Kevin Hildebrand 403-220-7282

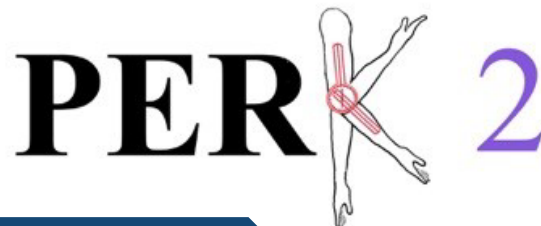
Research Coordinator: Isabella Salazar 403-943-5556



PERK 2 TRIAL NEWSLETTER

Dr. Kevin A. Hildebrand

September 2023 Edition



GOALS

By September 30th:

- Reach 381 total recruitments for the trial
- Complete query resolution at sites
- Complete updated AE/SAE Logs

MILESTONES

Current Overall Enrollment Status:

Peter Lougheed Centre (n=68)
South Health Campus (n=56)
Foothills Medical Centre (n=45)
University of Vermont Medical Center (n=32)
Royal Columbian Hospital (n=32)
Sturgeon Community Hospital (n=26)
University of Maryland Medical Center (n=26)
The Ottawa Hospital, General Campus (n=15)
The Ottawa Hospital, Civic Campus (n=15)
St. Michael's Hospital (n=12)
Sunnybrook HSC (n=12)
St. Joseph's Hospital (n=11)
St. Paul's Hospital (n=11)
Carolinas Medical Center (n=8)
Queen Elizabeth II HSC (n=5)



August 2023 Enrollment Hall of Fame:

1. Peter Lougheed Centre (n=2)
2. Royal Columbian Hospital (n=2)
3. University of Vermont Medical Center (n=2)
4. The Ottawa Hospital, Civic Campus (n=2)
5. University of Maryland Medical Center (n=1)
6. South Health Campus (n=1)

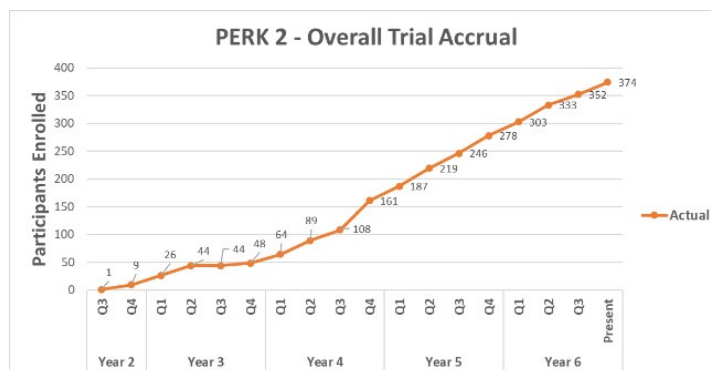
TRIAL UPDATES

- With 10 participants enrolled in August, we have reached 374 participants!
- The next Trial Management Group meeting with active sites proposed for **Monday, September 18th, 2023 at 1:00pm MDT (12:00pm PDT, 3:00pm EDT).**
- **REMINDER:** Please send us your last AE/SAE log signed and dated by your PI with all adverse events reported up until June 30th, 2023.

PERK 2 TEAM

Trial PI/Sponsor: Kevin Hildebrand 403-220-7282

Research Coordinator: Isabella Salazar 403-943-5556



PERK 2 Trial Management Group Meeting #42

June 26th, 2023, 1:00pm - 2:00pm MDT

Attendees: Isabella Salazar, Tosin Ogunleye, Christine Churchill, Kyrsten Payne, Katie McIlquham, Muskan Sethi, Ashmanie Brijmohan, Christine Schemitsch, Zafeiria Glaris, and Gerardo Duque

Regrets: Dr. Kevin Hildebrand, Ayoola Ademola, Casey Loudermilk, Adina Tarcea, Katrina Munro, Melanie Dodd-Moher, Saranjan Moganathas, Katrine Milner, and Melissa Cuke

Meeting start: 1:00 pm MDT

1. TMG #42 Report Review

- a. Screening/recruitment from sites since last meeting.
 - i. 28 new screens
 - ii. 6 screened were eligible; 5 recruited and 1 not recruited.
- b. AEs reported continue to be within expected patterns.
 - i. 6 new adverse events reported:
 1. 5 mild (3 dry mouth, 1 constipation, and 1 Neurological (Radial Pain)
 - a. Dry Mouth is an expected adverse event of Ketotifen as outlined in the protocol and product monograph
 - b. Constipation has been observed early on post-surgery
Expected adverse event from use of pain medication
 - c. Radial nerve pain is an expected complication after surgery
 2. 1 Moderate (Nausea/Vomiting)
 - a. Expected complication post-surgery. Especially after coming off from anesthesia and starting use of narcotic pain medication
- c. 2 new SAEs were reported during this time.
 - i. Symptomatic Hardware Removal – Elective surgery done between 6 – 12 months. Not related to use of IP/Placebo. Expected elective surgery post elbow open reduction external fixation (ORIF)
 - ii. Post-surgical ankle superficial infection – Not related to use of IP/Placebo. Expected complication post ankle surgery. Infection found after treatment period ended.

2. CIPAC Imaging and uploads for PERK 2

- a. Calgary Image Processing and Analysis Centre (CIPAC)**
 - i.** Team in charge of receiving, holding, and analyzing images obtained for the PERK 2 trial
 - ii.** They provide an upload platform to all sites. Images are to be uploaded through the platform in DICOM format
 - iii.** Some sites have not uploaded any images. We have emailed all sites directly, CC'ing the manager at CIPAC to provide support to the sites
 - 1.** The Ottawa Hospital sites, Calgary sites (PLC, SHC, and FMC), Sturgeon Community Hospital, Carolinas Medical Centre, St. Paul's Hospital, and the University of Vermont have uploaded all images without any issues
 - 2.** University of Maryland, St. Joseph Hospital, and Sunnybrook Health Sciences Center has not been able to upload images. CIPAC team has emailed the coordinators and PI's. Please respond and work with them to address this task

3. Updated Itemized Data Breakdowns and Invoices

- i.** Updated itemized data breakdowns have been sent to sites. These are used to review outstanding data, and current data availability for payment
- ii.** Sites are to review and build invoices from this document
- iii.** Please send updated invoices by June 30, 2023. Otherwise, we will address payments by September 2023

4. Changes from Health Canada Inspection

- a. Case Report Form updated to Version 4.0**
 - i. Addition of:**
 - 1.** Notice for surgeon sign/date added to the screening form, injury classification form, operative imaging, and adverse event forms
 - 2.** Bisphosphonates listed in the medication form
 - 3.** Adverse event form includes expectedness, attribution, and updated grading system to Mild, Moderate, and Severe only
 - 4.** Return to work date added to the in person follow up forms
 - ii.** Sponsor will be submitting these changes for approval and then provide to sites for local submissions

b. End of AE/SAE logs – We will be transitioning to sites sending us completed, signed and dated source/CRFs for reported AE's and SAE's. However, a final log needs to be completed to cover all reported up to now, with needed information included.

1. Updated log should include all AE's and SAE's reported up until June 30th, 2023
2. The log should be reviewed and signed off by the local PI
3. A Signed/dated copy is to be sent to the coordinating center
4. Once done, the coordinating center will be requesting individual AE forms completed, signed/dated for filing

c. Protocol deviation and violation logs

- i. Health Canada inspectors found reconciliation issues with these logs and REDcap entry
- ii. Sites needs to review their logs to make sure that deviations and violations are reported in the appropriate logs, and all violations need to be reported in REDcap
- iii. Coordinating center will be following up with sites to complete this request

d. Updated Trial Manual to version 4.0 (Dated May 19th, 2023)

- i. Trial Manual now includes all recent changes done during Protocol amendment v7.0
- ii. Manual includes steps and procedures related to all activities involved in the trial (i.e. reporting adverse events, pregnancy test expectations, data entry troubleshooting, etc.)

5. Upcoming changes to PERK 2 Coordinating team

- a. Gerry will be going on leave for the months of July and August. Next TMG meeting is scheduled for September 11th, 2023
- b. Centralized monitoring visits will continue while Gerry is away
- c. Isabella Salazar will become the PERK2 sponsor point of contact during this time. Please reach out to her with all questions/for support
- d. Safety related concerns/questions or reports need to go directly to Dr. Hildebrand and CC'ing Isabella Salazar. As a reminder, all Serious Adverse Events have to be reported to Dr. Hildebrand within 48 hours of learning of the event



Meeting adjourned 1:35pm MDT.

Next TMG Meeting: September 11th at 1:00 pm MDT (12:00pm PDT and 3:00pm EDT)

PERK 2 Trial Management Group Meeting #43

September 18th, 2023, 1:00pm - 2:00pm MDT

Attendees: , Dr. Kevin Hildebrand, Gerardo Duque, Isabella Salazar, Tosin Ogunleye, Adina Tarcea, Christine Churchill, Kyrsten Payne, Melissa Cuke, Casey Loudermilk, Melanie Dodd-Moher, Katie McIlquham, and Ashmanie Brijmohan

Regrets: Muskan Sethi, Ayoola Ademola, Katrina Munro, Saranjan Moganathas, and Katrine Milner

Meeting start: 1:00 pm MDT

1. TMG #43 Report Review

- a. Screening/recruitment from sites since last meeting
 - i. 156 new screens
 - ii. 42 screened were eligible; 28 recruited and 14 not recruited
 - iii. 5 new withdrawals reported
- b. AEs reported continue to be within expected patterns
 - i. 21 new adverse events reported:
 1. Mild AEs included: 5 Neurologic (5 Radial/Median, 2 Feet/Arm pain), 5 Dry Mouth, 3 Sedation, 2 GI Issues (2 constipation), 1 Nausea/Vomiting, 1 Compensatory Hyperhidrosis, 1 Soft Tissue/Wound Healing (Blisters), 1 Headache, and 1 Dizziness
 - i. Dr. Hildebrand says compensatory hyperhidrosis is not a very common post-op issue in orthopedics. Sweating is not expected. However, this participant experienced this side effect mildly
 2. Moderate AEs include: 1 GI Issue (Diarrhea)
- c. 3 new SAEs were reported during this time
 - i. Participant with baseline Lupus diagnosis experienced lupus flare-up related to a kidney infection. Participant still in recovery
 - ii. Deep Infection occurred 8 months after surgery, outside of treatment period. Infection developed in surgical area. Participant is doing well, infection addressed
 - iii. Contralateral wrist surgery planned at baseline. Participant recovered well

2. CIPAC Imaging and uploads for PERK 2

- a. Calgary Image Processing and Analysis Centre (CIPAC)
 - i. Some sites have not uploaded any images. Images need to be uploaded as soon as possible!
 - ii. We hope to start uploading processes now so by the time close-out procedures are beginning, images from sites are mostly uploaded

3. Updated Itemized Data Breakdowns and Invoices

- a. Every invoice received prior to Gerry's leave has been paid out
- b. Please send invoices by September 30th if you want an updated payment for your site

4. 12-Week ROM Data Collection and Withdrawals

- a. Non-injured ROM bilateral comparison done at 12-week timepoint. Very important for our primary analysis outcome; this is considered the most important follow-up visit for the study
- b. Sample size of 381 was calculated with a 12% withdrawal rate at 80% statistical power for this primary end point
- c. We are at a 90% collection rate, with 10% withdrawal rate as we stand. At very least, we would like to ask sites to get 24-week bilateral ROM if 12-week timepoint was not collected
- d. We want to stay clear of the 12% withdrawal rate/loss of data collection in order to maintain statistical power

5. Upcoming Recruitment

- a. Current recruitment stoppage date is December 21, 2023. If there are any changes to this date, we will advise your site immediately via email
- b. Please continue screening and enrolling as you have been until directed otherwise; we are close but have not yet reached our goal

6. Health Canada Sponsor and Site Inspection

- a. Compliant rating for both sponsor level and site level inspections!
- b. Queries longer than 30 days were brought up by Health Canada. Sponsor was advised to not allow sites to remain with open queries longer than 30 days. Health Canada expectation is that queries are to be addressed as immediately as possible. Some sites currently have queries open for longer than a year. Please address queries on REDCap ASAP. We are sending out emails to sites with open query lists and time open for prompt resolution

7. Expectations before next TMG

- a. We will begin an administrative push to get documents sent and data uploaded by sites for the end of October, prior to the next TMG meeting. Our goal is to resolve outstanding tasks before the end of recruitment if possible, and certainly before the end of this year
- b. In response to Health Canada findings, we have updated our Case Report Forms to Version 4.0, which includes a change to AE Logs. Please note that CRFs do not need to be approved by your local REB because they are not patient facing documents
- c. We have asked sites to send us UTD AE/SAE Logs up to June 30th, 2023.
- d. As of July 1st, 2023, the new AE documentation process is for sites to send the sponsor an email with attached AE source document, signed by local PI
- e. In the coming weeks, we will be sending out a list of missing AE CRFs that have not yet been received by the sponsor for review

Meeting adjourned 1:30pm MDT.

Next TMG Meeting: October 30th at 1:00 pm MDT (12:00pm PDT and 3:00pm EDT)



PERK 2 Trial Steering Committee

Meeting #15 – Minutes

September 18, 2022, 3:30 – 4:30pm MDT

Attendees:

Dr. Nicholas Mohtadi – Chair/Clinical Trialist

Dr. Kevin Hildebrand – Chief Investigator

Dr. Michael Bosse – Sponsor’s Medical Expert

Dr. Neil White – Site Principal Investigator, South Health Campus

Katie McIlquham – Clinical Research and Quality Program Coordinator, The Ottawa Hospital, General Campus

Gerardo “Gerry” Duque, MA – Clinical Trials Unit, Facilitator

Regrets:

Dr. Tolulope Sajobi – Biostatistician

Meeting called to order: 5:30 pm MDT

1. Trial Steering Committee (TSC) – Meeting #15 Call to Order

- a. Minutes of TSC Meeting #14 reviewed. No comments from the committee members. Minutes approved at this time
- b. No additional agenda items proposed by the team

2. Trial Steering Committee Report #15

- a. PERK 2 – Recruitment through Q4 Year 6 (Jul/Aug/Sep 2023)
 - i. Current recruitment is 379. We are 5 participants away from 384 total listed in the protocol’s trial design
- b. AE/SAE change from last report
 - i. Discussion of Research Monitor’s opinion on latest SAEs reported, including possible review of infection rates if they surpass the 1% mark. We are looking at an .8% infection rate for the trial at this moment. Committee members agree, and continue to not expect this to be a concerning event for the remainder of the trial
- c. Primary outcome measure completion (12 week ROM = ~311 out of 346 collected / 90% collection)
 - i. 12 week Bilateral ROM is close to our 12% withdrawal rate
 - ii. We could lose 46 participants to reach our 12% withdrawal rate, leaving the total at 335 patients with available data



PERK 2

- iii. We have enough investigational product to reach a sample size of 423 participants, helping us offset the current withdrawals
- iv. Data Monitoring Committee thought during our last meeting that we should not over recruit significantly. However, they recommended following up with regulatory entities to confirm ethics related
- v. Trial Steering Committee members present agree with the following:
 - 1. Continuing enrollment would be ethical if it leads to having a well powered study that answers our primary endpoint question
 - 2. Additionally, contact the appropriate regulatory entities to submit a possible amendment/notification to the protocol that includes the additional participants needed
 - 3. An email has been sent to Health Canada inquiring what is expected from us in explaining our plans and moving forward with more enrollments
 - 4. The majority of the TSC agrees that due to the current withdrawal rate of the trial, we would like to maximize the data we can gather based on available resources and time. Therefore, based on the safety of the trial and the above, we would continue enrollments beyond our current goal of 384. The team will engage the Data Monitoring Committee for opinion while also getting input from regulatory agencies (eg. REB, Health Canada, and DoD)

3. Health Canada Sponsor Inspection – Possible Amendment

- a. Outlining collection of Weight and Height – In-Person or Self Report
 - i. Sites will be informed to include weight that is gathered in-person through a scale. However, if there is a need to do so through self-report, it is allowed

4. Dr. Hildebrand's to present on his meeting with Dr. Sajobi and Ayoola Ademola

- a. Building a statistics plan, a publication committee, and setting a data sharing policy
 - i. This is a need so we have a set guideline on how and who will have access to the data, and at what time will it be available. A publication committee would help in setting these expectations. In addition, a statics plan is in



PERK 2

the works to set up future PERK 2 papers up for success in publication. Dr. Sajobi and Ayoola Ademola are working with Dr. Hildebrand to get this paper together

- ii. The TSC agrees that an inclusionary standpoint is best while setting up authorship in publication. If a governing committee for authorship or sharing is put together, it should be comprised of people already involved in the trial. This could include qualified investigators and/or other stakeholders
- iii. Dr. Mohtadi recommended contacting Dr. Mohit Bhandari for direction. Dr. Bosse recommended contacting Dr. Renan Castillo at Hopkins for direction on publications and committees
- iv. Regarding publication committees, Dr. Hildebrand expects authorship to be as a group of involved investigators. However, he would like more involvement from investigators, so he proposes a possible investigators meeting soon to discuss
- v. Dr. Bosse will share the data sharing policy SOP from METRC with Dr. Hildebrand

Meeting adjourned 4:40 pm MDT

Next TSC meeting: Monday, December 11th, 2023 at 3:30pm – 4:45pm MDT

Regulatory Operations and Enforcement Branch
Clinical Trial Compliance Program
101 Roland-Therrien
Longueuil, Quebec J4H 4B9

Sent by electronic mail

September 29, 2023

Dr. Kevin A. Hildebrand
University of Calgary
3280 Hospital Drive NW
Calgary, Canada, T2N 4Z6
hildebrk@ucalgary.ca

**Subject: Clinical Trial Final Inspection Exit Notice – Clinical Trial Application (CTA) # 218219,
Protocol # PERK2_KAH**

This letter is to acknowledge the receipt of your responses dated June 19, July 28 and September 8, 2023 to the final Inspection Exit Notice issued in respect of the University of Calgary clinical trial inspection. This inspection was conducted on-site by Marie Laganier and Jennifer Evans on April 24 to April 28, 2023.

The corrective and preventive actions submitted were assessed in accordance with Part C, Division 5 of the *Food and Drug Regulations* “*Drugs for Clinical Trials Involving Human Subjects*”.

We would like to let you know that as a good clinical practice, when a document is reviewed/modified, it is best to use a different (i.e. next in sequence) document version number when the original document was final and signed-off. The Trial Manual, Monitoring Plan and Data Management Plan provided in your response on September 8, 2023, were bearing the same version numbers as the signed-off versions provided in your response dated June 19, 2023. Please keep the original versions of all and write a note-to-file to identify why two same version numbers of these documents but bearing different version dates were created.

- Trial Manual: V4 dated 19MAY2023 and V4 dated 17AUG2023
- Monitoring Plan: V5 dated 19MAY2023 and V5 dated 17AUG2023
- Data Management Plan: V4 dated 19MAY2023 and V4 dated 17AUG2023

Lastly, take note that the Appendix A of the Monitoring Plan indicates for the Risk Scores to see Appendix 1. This Appendix 1 is not detailed in this document.

Health Canada deems the corrective and preventive actions as presented satisfactory.

No further response in respect of this clinical trial inspection is required. This inspection is now considered closed.

Regards,

Marie Laganier
Compliance Specialist, Clinical Trial Compliance Program
Regulatory Operations and Enforcement Branch
Tel.: 514-910-8276
Email: marie.laganier@hc-sc.gc.ca

From: [Kevin A. Hildebrand](#)
To: [Josh Burkart](#); [Gerardo Duque](#); [Isabella Salazar](#); [Ayoola Ademola](#)
Subject: Re: ORS Abstract Confirmation
Date: Monday, August 28, 2023 12:24:49 PM

Thanks Josh for getting this in and to everyone for your contributions.

Kevin

Kevin A. Hildebrand, MD, FRCSC, FACS, CCPE (he/his/him)

Academic Head and Professor, Department of Surgery
Cumming School of Medicine, University of Calgary
Zone Clinical Department Head, Department of Surgery
Alberta Health Services, Calgary Zone
Room 1033 North Tower
1403 – 29th Street NW
Calgary, AB
T2N 2T9
Phone: +1-403-944-1697

I acknowledge the traditional territories of the people of Treaty 7 region in Southern Alberta. The City of Calgary is also home to Métis Nation of Alberta, Region 3.

From: Josh Burkart <josh.burkart@ucalgary.ca>
Date: Monday, August 28, 2023 at 11:26 AM
To: Kevin A. Hildebrand <hildebrk@ucalgary.ca>, Gerardo Duque <gerardo.duque@ucalgary.ca>, Isabella Salazar <isabella.salazar@ucalgary.ca>, Ayoola Ademola <ayoola.ademola@ucalgary.ca>
Subject: ORS Abstract Confirmation

Hi All,

Please see below a confirmation of the submitted abstract for the ORS annual meeting. Also see attached a copy of the final version of the abstract.

Thanks for everyone's help on this!

Best,

Josh Burkart

University of Calgary

4th Year Undergraduate | Faculty of Kinesiology
BSc, KIN: Exercise and Health Physiology

From: cOASIS Abstract System <ors@support.ctimeetingtech.com>

Date: Monday, August 28, 2023 at 11:12 AM

To: Josh Burkart <josh.burkart@ucalgary.ca>

Subject: ORS 2024 Annual Meeting Abstract Submitted

[△EXTERNAL]

Congratulations on submitting your abstract(s) to the ORS 2024 Annual Meeting, February 2-6, 2024, in Long Beach, CA. We look forward to seeing you in Long Beach, CA!!!

Your Submission, Control Number 2024-A-1749-ORS, is complete. If you need to make an edit to your abstract you will be able to access your submission until August 28, 2023, at midnight (pacific time). You will need your login and password to access the submission site. No edits can be made after this date/time.

If you have questions, please contact the ORS by e-mail at orsabstracts@ors.org or by phone at 847-823-5770.

Join the ORS Nation!

ORS provides awards and grants based on high-quality abstracts. To be considered for an award or grant, presenting authors must be an ORS member in good standing no later than the abstract submission deadline Monday, August 28, 2023 and have paid 2023 membership dues. Membership application can be completed online at: <https://ors.memberclicks.net/join-the-ors>.

If you have questions regarding membership and/or award eligibility, please contact the ORS office, 847-823-5770 or email ors@ors.org.

Additional information for the ORS 2024 Annual Meeting Information can be found at www.ors.org/2024annualmeeting. Registration will open in October 2023!