

**Participant Information and Consent Form**

1. **Title of Study**

**Celecoxib versus placebo as an adjunct to treatment-as-usual in children and youth with obsessive compulsive disorder: A single-site randomized quadruple-blind phase II study**

**Short title:** Adjunctive CElecoxib in childhood-onset OCD (ACE-OCD) study

**2. Study Personnel**

***Principal Investigator (Sponsor-Investigator):***

**Dr. S. Evelyn Stewart, MD**

Director, Provincial OCD Program, BC Children’s Hospital (BCCH)

Director of Research for Child, Youth and Reproductive Mental Health, BCCH

Professor, Department of Psychiatry, University of British Columbia (UBC)

P4 – Mental Health Building

4500 Oak Street, Vancouver BC, V6H 3N1

Telephone: 604-875-2000 (ext. 4725)

Fax: 604-875-3871

***Co-Investigators:***

**Dr. Clara Westwell-Roper, MD PhD**

Resident Physician, Department of Psychiatry, UBC

Research Track Resident, BCCH Provincial OCD Program

Email: cwestwellroper@bcchr.ubc.ca

Telephone: 778-837-4946

**Dr. John Best, PhD**

Biostatistician / Data Analyst

BCCH Provincial OCD Program

**Dr. Susan Baer, MD, PhD**

Child and Adolescent Psychiatrist, BCCH

Clinical Assistant Professor, Department of Psychiatry, Faculty of Medicine, UBC

**Dr. Dean Elbe, PharmD, BCPP**

Investigator, BCCH

Pharmacy Specialist, Child and Adolescent Psychiatry, BCCH

Clinical Instructor, Faculty of Pharmaceutical Sciences, UBC

**Dr. Bradley Locke, MD**

Child and Adolescent Psychiatrist, BCCH

Clinical Instructor, Department of Psychiatry, Faculty of Medicine, UBC

**Dr. Megan MacFadden, MD**

Child and Adolescent Psychiatrist, BCCH

Clinical Instructor, Department of Psychiatry, Faculty of Medicine, UBC

***Other Study Team Members:***

Zainab Naqqash, BA, Research Coordinator, Provincial OCD Program, BCCH

Boyee Lin, BSc, Research Assistant, Provincial OCD Program, BCCH

Cynthia Lu, BA, Research Assistant, Provincial OCD Program, BCCH

***Funding sources:***

International OCD Foundation Young Investigator Award

Private donor funding to the BCCH Provincial OCD Program

***Emergency telephone number:***

Dr. Evelyn Stewart (Principle Investigator): 604-809-6622

Dr. Clara Westwell-Roper (Psychiatry Resident): 778-837-4946

Please call 911, go to your nearest emergency room (or have a parent take you), or call KIDS HELP LINE (1-800-668-6868) for immediate help at any time.

***Non-emergency contact number:***

Boyee Lin or Cynthia Lu: 604-875-2000 (ext. 3068)

Dr. Evelyn Stewart: 604-875-2000 (ext. 4725)

**3. Invitation**

You are being invited to participate in this research study because you have a diagnosis of obsessive compulsive disorder (OCD) and are between the ages of 7-18. This study will evaluate the effects of the anti-inflammatory medication celecoxib on OCD symptoms during 12 weeks of treatment.

**4. Your participation is voluntary**

Your participation is entirely voluntary, so it is up to you to decide whether or not to take part. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time. If you do not wish to participate, you do not have to provide any reason for your decision nor will you lose the benefit of any medical care, education, or other services to which you are entitled or presently receiving.

Before you decide, it is important for you to understand what is involved. This consent form will tell you about what happens when you participate, what will happen to the collected data and samples, and the possible benefits, risks, and discomforts of participation.

You should be aware that there is a difference for both you and your doctor(s) between being a patient and being a research participant. As a patient, all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant, you and your study doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes treatment and assessment procedures that are being carried out for research purposes.

Please take time to read the following information carefully and to discuss it with your family before deciding. If you wish to participate, you will be invited to sign the consent/assent forms either on paper or electronically. The content of the electronic version of the form is the same as the paper version. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

**5. Who is conducting the study?**

This study is being conducted by Dr. Evelyn Stewart and her team at the Provincial OCD Program (“OCD Program”) at BC Children’s Hospital (BCCH). Dr. Stewart is the Principal Investigator or “Sponsor-Investigator” as designated by Health Canada. Dr. Stewart and her team have no conflicts or potential conflicts of interest with respect to remuneration for conducting or being involved with this study. There is no intention to commercialize the research findings. This research is funded by an International OCD Foundation Young Investigator Award as well as research funds to the OCD Program provided by a private donor. This study is not receiving funds from an external sponsor.

**6. Background**

OCD is a psychiatric disorder affecting 1-3% of the population. It occurs in both children and adults and can be a life-long illness. It can interfere with daily activities, such as socializing, self-care, and school functioning. People with OCD experience both “obsessions” and “compulsions”. Obsessions are unwanted, intrusive thoughts, images, impulses, or fears that cause distress and anxiety. Compulsions are deliberate behaviours (e.g. handwashing, checking, ordering) or mental acts (e.g. counting, repeating words) that are often performed to **reduce the distress** caused by obsessions. The usual treatments include cognitive behavioural therapy and medications called serotonin reuptake inhibitors, but almost half of children continue to experience symptoms despite these treatments.

Both genetic and environmental factors contribute to the development of OCD, but not all of these factors are understood. Research studies have suggested that proteins and cells related to inflammation may be affected in children and adults with OCD. Celecoxib belongs to a medication class called non-steroidal anti-inflammatory drugs (NSAIDS). A common NSAID that many children have taken previously is ibuprofen (Advil/Motrin), but it requires multiple doses per day to effectively reduce inflammation, whereas celecoxib is taken twice daily. NSAIDs such as celecoxib may limit inflammation and improve the function of neurons in parts of the brain involved in OCD symptoms.

Celecoxib has been shown to improve symptoms in adults with OCD who are also taking selective serotonin reuptake inhibitors. NSAIDs are recommended by doctors treating children with some forms of OCD including pediatric acute neuropsychiatric syndrome (PANS) or pediatric autoimmune disorder associated with streptococcal infections (PANDAS), but they have not been tested in a rigorous research study that compares them with a control or placebo treatment. Other children with OCD that has not improved enough with usual treatments are sometimes prescribed NSAIDs as part of their usual clinical care and may feel that they are helpful, but no controlled studies have evaluated how well they work.

This study will assess the effect of celecoxib on OCD symptom severity. Symptoms in participants receiving celecoxib (added to their usual treatment) will be compared to those receiving placebo, an inactive substance that looks identical to the test drug but contains no therapeutic or experimental ingredients. We expect that a total of 80 participants with OCD will be enrolled in this study, which is a single-site trial based at BCCH.

Health Canada, the regulatory body that oversees the use of natural health products/drugs/devices in Canada, has not approved the sale or use of celecoxib for OCD in either children or adults. Health Canada has allowed celecoxib to be used in this study.

**7. What is the purpose of this study?**

The goal of this study is to determine whether 12 weeks of treatment with celecoxib added on to usual treatment results in improvement in OCD symptoms compared to placebo. This study is a randomized placebo-controlled trial, which means that half of participants will receive celecoxib and half will receive placebo, an identical capsule that does not contain the active drug. Participants may be assigned to either treatment. They will also continue their regular treatment (medication and/or psychotherapy) under the care of their regular doctor(s).

This is a Phase II study, which is undertaken after preliminary safety testing on a drug or treatment. Celecoxib has already been tested in previous studies for safety in children. Phase II studies are usually conducted on a small number of individuals. In this case, it will allow researchers to begin to find out what effect celecoxib has on OCD and to further evaluate its safety.

Some assessments and procedures in this study have not been included in previous trials of medications to treat OCD in children in BC. Results from this study – including parent and child perspectives on participation – will be used to determine the feasibility of future, larger studies, although there is no guarantee that they will be conducted. Participation in this study does not mean that you will be eligible to participate in a future larger study. Knowledge gained from pilot or feasibility studies may be used to develop future studies that may benefit others.

**8. Who can participate in this study?**

Children and young adults between 7-18 who live in BC may be eligible to participate in this study if:

* They have previously been diagnosed with OCD.
* Results of a diagnostic screening phone interview are consistent with OCD.
* They have moderate to severe symptoms based on a standardized rating scale, as determined by a study doctor at their first study visit.
* They are able to take medication twice daily in capsule form, or to sprinkle the capsule on food.
* Results of a negative pregnancy test from baseline blood-work (either serum or urine) in female participants after menarche (i.e. after their first period)
* They use highly effective and/or double barrier contraception, or abstinence, in participants with child-bearing potential who could become pregnant.

**9. Who should not participate in this study?**

Children and young adults are not eligible to participate in this study if any of the following apply:

* They have been previously diagnosed with or develop conditions that would increase their risk of harm with NSAID use, including kidney or liver disease, gastrointestinal bleeding or peptic ulcer disease, inflammatory bowel disease, bleeding disorders, severe asthma, or NSAID allergy.
* They have a current major depressive episode, psychosis, suicidality, or active substance use.
* They have an active infection or are taking antibiotics.
* They have used any NSAID at any dose more than 3 times per week in the 2 months prior to participation.
* They currently take steroids (IV, oral, or inhaled) or drugs that may interact with celecoxib (detailed list included in Appendix A).
* There is an abnormality identified on baseline blood work including liver enzymes, kidney function, and blood cell counts, or they have a form of an enzyme that metabolizes celecoxib that will significantly increase their levels.
* Changes have been made to CBT or other psychotherapy in the 4 weeks prior to participation
* They have started a new medication started in the 10 weeks prior to participation.
* There are planned changes to their usual treatment during the study period.
* They or their parents are unable to provide informed consent or assent, or to participate in study procedures or assessments in English.
* They do not have a doctor (family physician or specialist) or other primary care provider (e.g. nurse practitioner) providing regular medical care.
* Because there are risks associated with NSAID use in pregnancy, you should avoid becoming pregnant during this study. She should be aware of the risks to an unborn baby/fetus, and will be advised by study staff to work with her study doctor to find the best solution to make sure she does not get pregnant, if she wishes to be in the study.
* They are unable to have blood pressure measured within 2 months prior to enrollment (either on-site at BCCH or by a primary care provider).
* They have an intention of pregnancy.

A complete list of inclusion/exclusion criteria is included in Appendix A.

**10. What does the study involve?**

**Overall design**

Your usual treatment (medications and/or psychotherapy that are standard therapy) should not change during the study and should be monitored by your regular treating doctor(s). The study procedures and treatment described below are in addition to this standard therapy.

*Screening:*

Following a phone screening interview, there will be three study visits with a study doctor and Research Assistant for participants who remain eligible. After the first visit, you will complete blood work and have your blood pressure, height, and weight measured to help ensure that an NSAID can be safely taken. Blood work and measurements will take place either at LifeLabs in the community, at BCCH, or (for height, weight, and blood pressure only) by your regular doctor or primary care provider. The first study visit and this blood work are considered part of the screening process. If conditions are identified that affect your eligibility then you will not proceed to randomization or treatment but will be referred for further assessment and treatment by their regular doctor or primary care provider.

*Randomization:*

This study has two “arms”: participants will be randomized to receive either celecoxib or placebo capsules for a total of 12 weeks. Randomization is like the flip of a coin so that there is an equal chance of being in any of the groups. The study will also be quadruple blinded – participants (as well as doctors/care providers, study investigators, and team members assessing outcomes) will not know which group they are in. However, this information is available in case of an emergency.

*Study visits:*

After beginning treatment, there will be two additional study visits after 6 and 12 weeks. Treatment and study participation will end at the 12-week visit. This study is designed to allow for study visits at BCCH in person only if it is safe to do so (according to current health authority and BCCH COVID-19 guidelines) and if this is preferred by you and your parent. Alternatively, study visits will take place remotely using the videoconferencing platform Zoom.

*Duration of the study:*

The screening process may take up to 4 weeks to allow scheduling of the telephone screening interview, first study visit, blood work, and height/weight/blood pressure measurements at your convenience, and to allow study doctors to review the results. Following randomization to celecoxib or placebo, you will receive treatment for 12 weeks. The maximum study duration is therefore 16 weeks or approximately 4 months. The estimated time required for each study component is included in Table 1.

*Questionnaires and interviews:*

This study involves multiple questionnaires and interviews, listed in Table 1. In addition to the screening interview and study visits at which you will answer questions, participants and parents will complete online questionnaires prior to and following each visit. Participants do not need to answer questions that they are not comfortable answering, and may take breaks from questionnaires or interviews at any time.

**If you decide to join this study: Specific procedures**

If you decide that you will take part in this study, the procedures and visits you can expect will include the following.

**A. Screening (before you begin the study):**

An initial screening assessment will take place by telephone between the parent and Research Assistant. This will include review of inclusion/exclusion criteria followed by a diagnostic interview to assess for psychiatric diagnoses. It will take approximately 1 hour. The results of the screening interview will be reviewed by the study doctors and you will be informed of the results. If there is concern that you require further assessment or care, this will be communicated to you/your parent and your regular doctor(s) or an appropriate community psychiatric referral will be made.

If you remain eligible to participate, you and your parent will complete online medical, demographic, and perspective questionnaires prior to the first study visit. These surveys will include questions about your current and past OCD severity and specific symptoms, current and past mental and physical health, and expectations and experiences related to this study. You will also be asked demographic questions about your age, ethnicity, and gender, along with medical questions including your OCD and medication history. At this visit, a study doctor will assess your OCD severity and ask about symptoms of PANS/PANDAS and tics. If your OCD symptoms are moderate-to-severe, you will remain eligible to receive treatment and will subsequently complete the following:

* Required blood work (at BCCH, or in the community), if you have not had the same blood work done with normal results in the past 2 months or you do not consent to sharing of those results with study doctors. Required blood work includes assessment of liver enzymes (AST, ALT), blood (CBC), electrolytes (sodium, potassium, and chloride) and kidney function (creatinine) to ensure that NSAID treatment is as safe as possible. A pregnancy test (either urine or serum) will also be performed at this visit with participants of child-bearing potential to further determine eligibility. hsCRP (high-sensitivity C-reactive protein, a measure of inflammation) may also be measured; if all labs except hsCRP have been completed in the past 2 months and are normal, then you may opt out of collection. Total collected blood volume will be approximately 15 ml or 1 tablespoon. Blood work may be completed prior to the first visit if it is clear that you likely have moderate-to-severe OCD symptoms based on the questionnaires that you complete.
* Optional blood work (an extra 3-5 ml or 1 teaspoon will be collected to store in the BCCH BioBank for future studies; this requires a separate consent process as described below).
* Height, weight, and blood pressure measurement (at BCCH, or by your primary care provider). These measurements will be used to ensure you do not have high blood pressure and to determine the appropriate dose for treatment. If you will see a primary care provider or regular physician/specialist as part of regular care during the screening period and would like them to provide these measurements rather than repeating the same procedures for the study, you will be provided with a form informing your care provider of your participation on which they can provide these measurements. They will be reimbursed for form completion by the study team. You may also measure your height and weight at home with help from a parent. A research assistant would walk you through how to do this.

At the first study visit, you will also be able to discuss the study treatment, procedures, and potential risks and benefits further with a study doctor. Any questions you have about the treatment, potential side effects, and alternatives will again be addressed.

**B. Randomization and treatment:**

Once the results of the blood work and height/weight/blood pressure measurements have been reviewed by a study doctor, participants eligible to receive treatment will be randomized to either celecoxib or placebo. These capsules will be dispensed by the BCCH Research Pharmacy and will be either picked up by you or delivered to your home, depending on your location and preference. Participants 25 kg and under will receive capsules containing celecoxib 50 mg twice daily; those over 25 kg will receive 100 mg twice daily. Participants between 10 to 25 kg will receive capsules containing celecoxib 50mg twice daily. Placebo capsules will appear identical and contain only non-medicinal ingredients. The capsule should be taken with food (ideally breakfast and dinner) and may be swallowed whole or sprinkled on moist food such as applesauce. The entire contents of the capsule should be consumed.

You will be asked to inform the study team of the date/time of your first dose, and to enter this as well as your preferred medication form (capsule or sprinkles) in an electronic participant diary. You will continue to use this diary to record concerns about side effects or any missed doses for the duration of the study. No changes will be made to your usual treatment or regular medical care.

**C. Follow-up visits:**

Study Visits 2 and 3 will take place after 6 and 12 weeks of treatment, respectively. You and your parent will complete online questionnaires prior to these visits; these will take approximately 40 minutes each and include reporting of missed doses, potential side effects, symptom severity, and perspectives on study participation. At the study visit, you will meet with a Research Assistant and a study doctor. You and your parent will again be asked about your symptoms. The doctor will complete several standardized measures of symptom severity, which are listed in Table 1. You will also perform required blood work at Visit 12 identical to the baseline blood work, with the exception of the pregnancy test (if applicable), and can be done at BCCH or in the community.

**Table 1.** Schedule of study visits and procedures

|  |  |  |  |
| --- | --- | --- | --- |
| **TIMEPOINT (weeks of treatment)** | -4 to -1  | 6  | 12  |
| **Study Visit****or Procedure** | Screening | 1 | 2 | 3 |
| **ENROLLMENT(phone interview; approx. 60 min total):** |
| Pre-screening consent | x |  |  |  |
| Review of inclusion/exclusion criteria | x |  |  |  |
| Informed consent form review  | x |  x | As needed |
| Diagnostic interview | x |  |  |  |
| **ADDITIONAL SCREENING ASSESSMENTS (60 min total):** |
| Medical and demographics questionnaires (Online, 20 min, prior to visit) |  | x |  |  |
| Height, weight, blood pressure, heart rate (10 min, at or following visit) |  | x |  |  |
| Blood work: CBC, AST, ALT, Cr, electrolytes, pregnancy test (visit 1)(30 min, following visit) |  | x |  | x |
| Blood collection for BioBank (optional, with other blood work following visit) |  | x |  |  |
| **INTERVENTIONS:** |
| Pharmacy: Randomization and dispensing (following Visit 1 and all screening assessments)  |  | x  |   |   |
| Celecoxib (weeks 0-12)  |  |   |   |   |
| Placebo (weeks 0-12)  |  |  |  |  |
| **PARTICIPANT-/PARENT-REPORTED MEASURES (120 min total):** |
| Participant perspective questionnaire (Online, 30 min, prior to visit) |  | x | x | x |
| Adverse event monitoring questionnaire (Online, 20 min, prior to visit) |  |   |  x | x  |
| Adherence assessment (Online, 5 min, prior to visit) |  |  | x | x |
| Participant electronic diary (Adverse events, missed doses) |  | As needed |
| **CLINICIAN-REPORTED MEASURES (completed at study visit, each 30-60 min = 90-180 min total):** |
| OCD symptom severity (CY-BOCS; Clinician Global Impression of Improvement and Severity) |  | x | x | x |
| PANS/PANDAS and tic symptom assessments |  | x | x | x |
| Treatment expectancy |  | x | x | x |
| **TOTAL TIME PER VISIT (min):** | ~60  | 120-150 | 85-115 | 85-115 |
| **TOTAL PARTICIPANT/PARENT TIME:** | 330-420 min (5-7 hours) + additional time to take drug twice daily and complete electronic diaryas needed |

**D. Where will my information be stored and analyzed?**

You will be assigned a unique study number as a participant. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity (i.e., name, personal health number, birth date) or any other information that could identify you as a participant in this study will be kept confidential. Information that contains your identity will remain only with Dr. Stewart and/or designate in a locked filing cabinet in a locked office. The list that matches your name to the unique identifier that is used on your research-related information will not be removed or released without your consent unless required by law.

Your study information will be stored at the BCCH Research Institute Building (BCCHR), Vancouver. De-identified data entered from the questionnaires you have completed will be entered into an online platform called REDCap, which will also be used to collect information from you in electronic form. This will only be accessed by limited, authorized members of the research team with appropriate electronic signatures. Your electronic consent form will also be stored (separately from your other study information) in the BCCHR’s secured network in Vancouver, BC; only authorized personnel will be able to access it.

The BCCHR Clinical Research Support Unit (CRSU) stores the data in a secure, firewall-protected server; the web-server uses secure technology for the transfer of data between the participating computer and the server. The actual data center is a physically secured and protected area, with very limited access. BCCHR information technology and security personnel control and record authorization and access linked to identification cards in this area. The data center is patrolled by onsite security personnel, monitored by surveillance cameras, and protected by a fire-suppression system.

Data will be stored for 25 years after study termination per Health Canada requirements. After this time period has passed the destruction of the data will be initiated.

Storage of blood samples:

No samples will be stored as part of this study once baseline lab work has been completed, reported, and reviewed; remaining sample will be destroyed by the laboratory. No genetic information will be obtained. Samples will not be sold and will only be used for the laboratory analysis described in this consent document.

Use of email and text messaging:

We are asking to collect your email address and/or cell phone number so that we can send study-related reminders to you and/or your parent via email or email-to-text message (SMS). Emails sent to some webmail services (e.g. Gmail, Hotmail, etc.), may be stored/routed outside of Canada (for example, in the United States) and governed by foreign laws. Due to the fact that future emails may contain personal information about you, including your name and information about your health, the Freedom of Information and Protection of Privacy Act requires that we obtain your consent. All of the information you provide to us will be kept completely confidential. Providing your email address means that you voluntarily agree and give your consent for the study team to use email to communicate with you. Providing a phone number for text messages means you agree to receive study-related reminders by SMS message on your cell phone (these will be sent by email to your phone; you may reply by email or by sending a text-to-email if this is an option with your cell phone provider).

☐ No, I do not wish to be contacted by email or text. Please contact me/my parents by phone only.

Preferred phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Back-up phone 1: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Back-up phone 2: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

☐ I agree to receiving study-related communications by email. Please use the email(s) below:

Email 1: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Email 2: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Email 3: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

☐ I agree to receiving study-related communications by text. Please use the number(s) below:

Phone 1: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Service provider (e.g. Rogers, Telus):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Phone 2: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Service provider (e.g. Rogers, Telus):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Phone 3: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Service provider (e.g. Rogers, Telus):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Participant initials**:\_\_\_\_\_\_\_\_**

**Use of teleconferencing tools**

In this study, Zoom will be used to complete Study Visits 1-3 if in-person visits are not permitted on site according to COVID-19 guidelines, or if you prefer this to an in-person visit. While virtual care has some privacy and security risks, several security measures have been implemented to safeguard your privacy and to ensure that data is collected in a secure manner. These include using Zoom that has been licensed by UBC or PHSA (Zoom for Healthcare); the virtual visit links are private (i.e. not shared on public outlets); once the virtual visit with you has started, the meeting will be locked so no other people can join; and the visits will not be recorded. Two participant identifiers will be verified at the beginning of the Zoom appointment. Your location will also be noted, in case an emergency arises; the location of the study clinician will also be stated. This information about location is confidential and will only be made known to those other than the study staff in an emergency or in an instance that you may be in danger to themselves or others. Prior the starting the Zoom appointment, the study staff will review the limits of confidentiality.

Access to the Zoom meeting will also require a password. This will be sent to the contact information provided in the consent form before the virtual visit. You will be placed in a waiting room on Zoom before meeting the research staff.

To better protect the identity of participants, you should use only a nickname or a substitute name (i.e. not their real names) when joining the Zoom session. While you can also turn off the camera and mute the microphone if you would like to, there are certain components of the study which would require your involvement, such as answering questionnaires and verifying the recording of height, weight, and blood pressure measurements. In these instances, the research staff may ask you to turn on the camera and microphone to verify the data being collected.

**E. Use of data from other sources:**

If you have had normal blood work done in the past 2 months, you may choose to allow study doctors to access that data via the Provincial eHealth Viewer, which means that additional blood work may not be required for you to participate in this study. No other information in your medical record will be accessed in this study.

If you have had height, weight, and blood pressure measured by a primary care provider (e.g. doctor or nurse practitioner) or specialist within the past 2 months, you may choose to allow study doctors to communicate with that care provider to obtain these values rather than repeat these measurements. If you are seeing another doctor or primary care provider anyway, you may also choose to have him or her complete a form that includes these measurements, and then provide this form to the Research Assistant. Care providers will be reimbursed by the study team for form completion.

Optional BioBank participation:

If you choose to participate in this study, you have the option of also participating in the BCCH BioBank for storage of blood components (plasma and white blood cells) that could be used in future research. You will be provided with a separate consent form that describes the details of BioBank participation, and you will be required to sign this form if you wish to participate. You can take part in the main study and not take part in the BCCH BioBank. If you decide not to take part the BCCH BioBank, your usual care and participation in this study will not be affected.

Optional sharing of data for future studies:

We are asking your permission to use your health information collected for this particular study. This includes data from questionnaires that you complete as well as assessments completed by study doctors. However, we would also like you to consider sharing this information for other future research studies. Any shared information would be coded and de-identified, which means it would not include your name, date of birth, personal health number, or any other identifiers that would allow researchers to link the data with you. If you wish to participate in data sharing, please indicate your answers in the relevant section at the end of this consent form.

**11. What are the possible harms and discomforts?**

Risks associated with celecoxib or placebo

The risks and side effects of any usual treatment that you are receiving will be explained to you as part of your standard care by your regular doctor(s). If you are unclear about what is standard of care and what is specifically part of this study, please discuss this with your study doctor.

Participants/parents should immediately contact the study team if they are experiencing possible side effects. They should discuss the known side effects of celecoxib with a study doctor prior to their decision to participate. These are listed in Appendix B.

In the US, celecoxib is approved for use in children over 2 years of age for treatment of juvenile idiopathic arthritis; in Canada, it is used off-label in children. Studies of celecoxib in children that have included a placebo group have shown no increase in risk with the drug compared to the placebo. The risks have been documented in several larger studies in children with other health conditions and are detailed in Appendix B. Effects in combination with other treatments are not fully known in children with OCD. It is possible that OCD symptoms could get worse while you are taking either celecoxib or placebo.

NSAIDs are well-tolerated in children at doses and durations exceeding those delivered in this trial, with the most common treatment-related adverse events including mild gastrointestinal symptoms that are mitigated by taking the medication with food. These include abdominal pain, nausea, diarrhea, and stomach upset. Participants unable to tolerate 100 mg twice daily may be switched to 50 mg twice daily at the discretion of a study doctor; if symptoms are ongoing despite this dosing change then the study drug will be discontinued.

Serious adverse events are very rare in children (<0.01%); these include gastrointestinal bleeding, ulcer, or perforation; kidney disease; and allergic reactions. If symptoms are not recognized and treated, these events could be severe or cause death. In particular, celecoxib may increase the risk of severe gastrointestinal bleeding when used concomitantly with serotonin reuptake inhibitors (SRIs). Participants will be asked to seek urgent care if they experience any signs or symptoms of gastrointestinal bleeding as detailed in Appendix B, including persistent abdominal pain, light-headedness, or black/tarry stool.

Treatment-related effects on the cardiovascular and blood clotting systems reported in adults have not been documented in children. Celecoxib can affect kidney function particularly in individuals with low body water content (commonly called dehydration). The drug will therefore be held during any illness involving vomiting or diarrhea, or during any other known period of volume depletion. NSAIDs can also (rarely) cause other kidney problems (electrolyte and acid-base disorders; acute interstitial nephritis, which may be accompanied by nephrotic syndrome; and papillary necrosis). Participants will be monitored for signs and symptoms of these rare complications, and asked to contact study staff and seek medical care for significant changes in weight or volume status including swelling around the eyes/ankles/feet; change in urine appearance; back/flank pain or pain with urination; and feeling generally unwell. Treatment-related risks will be minimized by baseline measurement of kidney function and liver enzymes and monitoring of symptoms throughout the course of the study.

Administration of celecoxib during the latter part of pregnancy may cause harm to the fetus and mother. There are no controlled data in human pregnancy. Participants should not become pregnant while on this study. An effective method to avoid pregnancy should be used if needed during study treatment. You may ask the study doctor or regular doctor about for more information about preventing pregnancy, and should notify a study doctor if you become pregnant during this study.

Detailed safety information related to celecoxib and its potential side effects is described in Appendix B. Some medications should not be taken while on the study are also listed here.

Side effects as per the Product Monograph (listed in Appendix B) are as follows:

1. Common side effects:
* [headache](https://www.rxlist.com/headache/article.htm),
* [abdominal pain](https://www.rxlist.com/abdominal_pain_causes_remedies_treatment/article.htm),
* [indigestion](https://www.rxlist.com/dyspepsia/article.htm),
* [diarrhea](https://www.rxlist.com/diarrhea/article.htm),
* [nausea](https://www.rxlist.com/nausea/symptoms.htm),
* upset stomach,
* bloating,
* gas,
* [dizziness](https://www.rxlist.com/dizziness_dizzy/article.htm),
* nervousness,
* headache,
* runny or [stuffy nose](https://www.medicinenet.com/stuffy_nose/definition.htm),
* [sore throat](https://www.rxlist.com/sore_throat_pharyngitis/article.htm),
* skin [rash](https://www.rxlist.com/rash/article.htm), and
* [insomnia](https://www.rxlist.com/insomnia/article.htm).
1. Reasons to stop taking the drug and get emergency medical attention immediately:
* Chills, fever, muscle aches or pains, or other flu-like symptoms (especially if they occur together with a skin rash, these may be the first signs of a serious allergic reaction to this medication)
* Bloody or black tarry stools
* Shortness of breath, wheezing, any trouble breathing or chest tightness
* Skin rash, hives, swelling, or itching
* Blurred vision or other visual disturbance
* Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech, or weakness or numbness in the face, arm, or leg
* Change in urine (amount or colour; dark or red brown)
1. Reasons to stop taking the drug and talk to the study team or your regular health care provider:
* Serious skin reactions: skin rash, blisters or breakdown of your skin, fever, swollen glands
* Pain or difficulty urinating
* Feet or lower leg swelling; weight gain
* Vomiting or persistent indigestion, nausea, stomach pain, or diarrhea
* Yellow discolouration of the skin or eyes with or without itchy skin
* Malaise, fatigue, or loss of appetite
* Headaches, stiff neck
* Mental confusion or depression
* Dizziness or light-headedness
* Hearing problems
* Pneumonitis (symptoms include trouble breathing, dry cough, tiredness)
* Drowsiness or fatigue

If at any point you wish to discontinue participation or treatment, you may do so. You may withdraw your consent from this study at any time and you do not have to provide a reason. If you receive care through the OCD Program or BCCH, your medical care will not be affected.

Risks related to blood draws

There are mild risks associated with blood draws that may include bruising or swelling at the site of the blood draw. There is minimal chance of infection. Any discomfort you experience will likely go away quickly and may be reduced by the application of a topical anesthetic prior to the blood draw.

Other study risks

There are potential non-physical risks associated with this type of research, such as the possibility of discrimination towards you or your family members by others if it is discovered that you and/or your family are participating in research involving a psychiatric illness. The risk of this information being released is very small. No genetic information will be collected in this study.

Some questions regarding mental or physical health may make participants feel uncomfortable; you will be informed that you have the option to discontinue questionnaires or interviews at any time, and you do not have to answer any questions that you do not wish to answer. In addition, if there is any risk of harm to you uncovered during the study as part of the mental health assessment or at other times, study staff will notify Dr. Stewart immediately. You will also be informed. Dr. Stewart (or, in her absence, another study doctor) will assess the level of risk and establish a management plan. In the case of children who are deemed to be in imminent danger of harm or of harming others, an appropriate psychiatric referral will be made (e.g. to the BCCH Emergency Department if there is concern for ongoing risk, or to your local Child and Youth Mental Health Team if outpatient follow-up is appropriate). It may be necessary to disclose personal information to relevant authorities in this scenario, and in the case where an incident that involves abuse and/or neglect of a child or vulnerable adult or in response to any other lawful requirements to do so. More information regarding the confidentiality of your information can be found in section 18 of this consent form.

There may be a possibility of disclosure of personal information in the instance that the participant may be in danger to themselves or others, as determined by the study physician. In this instance, the study physician could contact 911 (if there is concern for imminent harm, such as suicidal or violent ideation) and advise the participant’s guardian, contact a child welfare worker (if there is concern regarding the child’s safety in the home or the need for protection), or refer the child and family to the nearest emergency department if urgent care is deemed to be required. For less urgent follow-up, participants will be provided with a list of community mental health resources and the participant’s primary care provider listed on this consent form will be advised. If required by provincial mandatory reporting, any child protection concerns will be reported to a child welfare worker (1-800-663-9122).

If the diagnostic interview or mental health screening questionnaire suggest that you may have symptoms that would benefit from further assessment, you will be provided with a list of appropriate community resources and this information will be conveyed to your regular doctor(s).

**12. What are the potential benefits of participating?**

There may not be any direct benefits to you from participating in the ACE-OCD Study. Although some doctors have reported benefit for some children with OCD, it is unknown whether celecoxib could be helpful to you. Participation in scheduled visits and assessments with the study team can sometimes be helpful regardless of the assigned treatment. You will be provided with the laboratory results from your blood work as well as results of the screening interview. You will have the opportunity to discuss your symptoms and their severity with a study doctor.

In the longer term, the study may indirectly improve the lives of families with OCD by providing evidence for or against the use of a medication that is increasingly prescribed in patients who do not respond to usual treatments. The information collected may contribute to future clinical trials to better inform the treatment of children with OCD.

**13. What are the alternatives to the study treatment?**

If you choose not to participate in this study or to withdraw at a later date, you may continue usual care as recommended by your regular doctor. This care may include medications or psychotherapy. You can discuss treatment options with your regular treating doctor and a study doctor before deciding whether or not to participate in this research project.

**14. After the study is finished**

You may not be able to receive the study treatment after your participation in the study is completed. You will continue to see your regular treating doctor or care provider and will not have additional follow-up with the study team. Your care provider may have the option of prescribing NSAIDs off-label, if this is part of your regular care. There are several reasons why celecoxib may not be available as a treatment in the long-term:

* The treatment may not turn out to be effective or safe.
* The treatment may not be approved for use in Canada.
* Your caregivers may not feel it is the best option for you.
* The treatment, even if approved in Canada or prescribed off-label by a physician, may not be available free of charge.
* You may decide it is too expensive and insurance coverage may not be available.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

**15. What if new information becomes available that may affect my decision to participate?**

It is unlikely that new treatments will become available over the short 12-week course of this study. However, if you choose to enter this study and at a later date a more effective treatment becomes available, it will be discussed with you. You will be advised by a study doctor of any new information that becomes available that may affect your willingness to remain in this study. If you choose to enter this study and during treatment decide to make changes to your usual medications or psychotherapy, you may do so and withdraw at any time. You may be invited to sign an amended consent to indicate your continued consent to participate in the study.

**16. What happens if I decide to withdraw my consent to participate?**

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, all information about you collected up to the point of your withdrawal (including information obtained from your blood samples) will be retained for analysis in order to protect the integrity of the research, which may benefit future research participants and patients. However, no further information will be collected. If you decide to withdraw, you may still be asked to come in for a final safety visit to ensure your safety. You have the option to find out what treatment you were receiving once all participants have completed the study, which may be more than one year following your participation.

If samples have been collected before you withdraw, they will be destroyed if they have not been already (for example, if laboratory analysis is in progress). There may be exceptions where the samples will not be able to be withdrawn, for example where the sample is no longer identifiable (meaning it cannot be linked in any way back to your identity).

If your participation in this study includes participation in the BCCH BioBank, you will be asked whether you wish to withdraw from this as well. Please refer to the separate BioBank consent form.

You may make the request to withdraw at anytime in writing or verbally by contacting our Research Coordinator at aceocd@bcchr.ca or 604-875-2000 ext. 3068.

**17. Can I be asked to leave the study?**

You may be asked to leave the study if the study team judges it is not in your best interest to continue (for example, if a safety issue arises during the course of a study visit or during treatment), if you are unable to fulfill the requirements for the study, or for any other reason such as a change in eligibility during the course of your participation. If you are asked to leave the study, the reasons for this will be explained to you and you will have the opportunity to ask questions about this decision. You would continue your usual care outside of the study. The study may also be stopped at any time by the Research Ethics Board or Health Canada if new information rises about the safety of the study treatment. The reasons for study stoppage will be explained to you by the study doctor. If you are withdrawn from the study, you will continue to follow-up with your regular care provider. If a study doctor feels that additional care is needed, an appropriate referral will be made.

**18. How will my taking part in this study be kept confidential?**

If you choose to participate in this study, information that discloses your identity will only be used as described in this consent form, unless required by law. We will follow strict guidelines designed to maximize the privacy and security of your information, which is described in more detail in the “Where will my information be stored?” section of this form. In addition to this, the collection, use and disclosure of your information will be held in strict accordance with the Freedom of Information and Protection of Privacy Act and/or the Personal Information Protection Act.

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of Dr. Stewart or her designate by representatives of the Children’s and Women’s Hospital Research Ethics Board or Health Canada for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

Your will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with Dr. Stewart and/or a designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law. Research data or results will not be placed in your health/medical records.

You will not be identified by name or initials in any medical journal publications resulting from this research. This research information may also be used for educational purposes (public awareness events, medical conferences, teaching of healthcare professionals) but your identity will be kept confidential. Collected data will not be stored with identifying information, and identifying information will not be released or published. Your data will be given a unique study number and only this will be on your blood sample questionnaires. Study-related data will not be sent outside of Canada except in coded form (that is, it will not contain your name or personal identifying information) if you consent to its future use / sharing with other researchers.

Personal information may be necessary to be disclosed to relevant authorities if at any point during the study the following is revealed: a clear and substantial risk of serious and imminent harm to yourself or towards someone else; an incident that involves abuse and/or neglect of a child or vulnerable adult; or in response to any other lawful requirements to do so. You are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available upon request to Dr. Stewart.

Disclosure of risk of harm

Please be aware that personal information may be necessary to be disclosed to relevant authorities if at any point during the study the following is revealed: a clear and substantial risk of serious and imminent harm to yourself or towards someone else; an incident that involves abuse and/or neglect of a child or vulnerable adult; or in response to any other lawful requirements to do so.

Disclosure of race/ethnicity

Studies involving humans now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. You should be aware that providing this information is not mandatory.

Primary care physician(s)/specialist notification

Your signed consent form will be part of study-related documentation but not included in your medical record. Please indicate, by checking the applicable box, your consent to notify your primary care physician(s) or specialist(s) of your participation in this study. This may include communication regarding the need for additional follow-up of medical or psychiatric concerns that arise over the course of the study. You will be informed when information will be shared.

⬜ I agree that the study investigator will advise my primary care physician(s) or specialist(s) of my participation in this study and consent to the sharing of medical information with this provider. My primary care physician(s) and/or specialist(s) name(s) is/are:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

The name of the medical clinic I attend is:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

The contact phone number for this clinic is:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Participant Initials: \_\_\_\_\_\_\_\_\_\_\_\_\_

⬜ The study investigator is my primary care physician/specialist.

Name of physician:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Participant Initials: \_\_\_\_\_\_\_\_\_\_\_\_\_

**19. What happens if something goes wrong?**

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan.

In case of a serious medical event, please report to an emergency room and inform them that you are participating in a clinical study and that the following person can then be contacted for further information: Dr. Stewartat telephone number:604-809-6622 (or alternatively Dr. Westwell-Roper: 778-837-4946 or the BCCH Pharmacy: 604-875-2059). You will be given a wallet card to carry with you in the event of an emergency with this emergency contact information. This emergency contact is available 24/7.

**20. What will the study cost me?**

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

You will not be paid for participating. Participants will receive a $25 gift card following visits 1 and 2 and a $50 gift card following visit 3 in lieu of expenses, including transportation required for study-related activities including blood work and drug pick-up. Reimbursement for parking expenses for in-person visits will also be provided. If you choose to attend an in-person appointment at BCCH, please contact Boyee or Cynthia at aceocd@bcchr.ca before your appointment to receive a parking voucher. Other travel expenses will not be reimbursed as all study visits can take place virtually.

Your will also receive a letter of recognition for the voluntary time you have contributed to the research study. The letter will not contain any information regarding diagnosis.

**21. If I have questions about the study during my participation, who should I speak to?**

If you have any questions or concerns or would like more information about this study before or during your participation, or if you experience any adverse effects, you may contact Dr. Stewart at 604-875-2000 (ext. 4725) or the Research Assistant team at 604-875-2000 (ext. 3068).

**22. Who do I contact if I have any questions or concerns about my rights as a participant?**

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598.) Please reference the study number (H19-03886) when calling so the Complaint Line staff can better assist you.

**Celecoxib versus placebo as an adjunct to treatment-as-usual**

**in children and youth with obsessive compulsive disorder:**

**A randomized quadruple-blind phase II pilot study**

**Consent to Participate:**

*My signature on this consent form means:*

* I have read and understood the information in this consent form.
* I have had enough time to think about the information provided.
* I have been able to ask for advice if needed.
* I have been able to ask questions and have had satisfactory responses to my questions.
* I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
* I understand that my participation in this study is voluntary.
* I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
* I understand that I am not waiving any of my legal rights as a result of signing this consent form.
* I understand that there is no guarantee that this study will provide any benefits to me.
* I authorize access to my health records (specifically blood work/serology results from the past 2 months, if applicable), as described in this consent form.
* I agree to sharing of information required for safe medical or mental health follow-up with my primary or usual care provider.

I will receive a signed and dated copy of this consent form for my own records.

**I consent to participate in the ACE-OCD study by signing below. I am signing for my own participation.**

Printed Name of Participant:

*Participant’s Signature Date*

*Signature of Research Team Member Obtaining Consent* *Date*

*Printed name* *Role*

**Celecoxib versus placebo as an adjunct to treatment-as-usual**

**in children and youth with obsessive compulsive disorder:**

**A randomized quadruple-blind phase II pilot study**

**Future Contact**

**Option to be contacted for future related studies:**

❑ I give permission to be contacted for future related studies.

❑ I do NOT give permission to be contacted for future related studies.

Printed Name of Participant: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |  |  |
| --- | --- | --- |
| \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Participant’s Signature | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Printed name of Participant | \_\_\_\_\_\_\_\_\_\_\_\_\_\_Date |

Email address: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Contact telephone number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Mailing address (optional):

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Celecoxib versus placebo as an adjunct to treatment-as-usual**

**in children and youth with obsessive compulsive disorder:**

**A randomized quadruple-blind phase II pilot study**

**Future Use of Data**

Your individual de-identified research data (questionnaire, blood work, and clinician assessment results) may be deposited into a publicly accessible location at the time of publication, or provided to other researchers upon request. This can enhance the transparency of the research data and allows for external validation and fraud control, but it also allows others to access the data for re-analysis of this study or to do other kinds of analyses in the future beyond those you are consenting to in this study. Also, this future use of your data may not be subject to oversight by a research ethics board, and thus the data may be publicly shared and used in currently unknown ways. Once the data are made publicly available, you will not be able to withdraw your data nor will you have the chance to individual consent to this use at the age of majority. Even though the identifying information will be removed from the data, it is possible that others may be able to find out who you are. The chance of this is currently thought to be very low.

❑ I consent to the use of my individual de-identified data (including linkage with BioBank samples) in future studies at the BCCH OCD Program.

❑ I consent to the release of my individual de-identified data for future use by other researchers.

❑ I do NOT consent to any release of my de-identified data for future use. It may be used for the sole purpose of the current study.

Printed Name of Participant: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |  |  |
| --- | --- | --- |
| \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Participant’s Signature | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Printed name of Participant | \_\_\_\_\_\_\_\_\_\_\_\_\_\_Date |

**Celecoxib versus placebo as an adjunct to treatment-as-usual**

**in children and youth with obsessive compulsive disorder:**

**A randomized quadruple-blind phase II pilot study**

**Videoconferencing Consent**

Due to the recent COVID-19 outbreak we are proposing to conduct Study Visits 1-3 remotely, according to the BCCH and Provincial Health Service Authority guidelines for virtual clinical visits.

We will be using a videoconferencing tool called Zoom to complete Study Visits 1-3 if in-person visits are not permitted on site according to COVID-19 guidelines, or if you prefer this to an in-person visit.

The videoconferencing company Zoom is located in the United States. Zoom uses privacy practices and technical security measures including encryption to ensure that data are protected. There is no monitoring, viewing, or tracking of the video or audio content of video meetings or webinars, and this content is not shared with third parties. Nevertheless, any study-related videos sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries, dealing with protection of information, may not be as strict as in Canada. Data transmitted using Zoom are encrypted

By signing this consent form, you are consenting to the use of Zoom to complete study visits 1-3.

I will receive a signed and dated copy of this consent form for my own records.

Participant’s Signature Printed name Date

 Signature of Person Printed name Study Role Date

 Obtaining Consent

**Appendix A.**

**Full inclusion and exclusion criteria.**

|  |  |  |
| --- | --- | --- |
| **Criterion** | **Yes/****Correct** | **No/****Incorrect** |
| **Inclusion criteria** |
| 1. You are between the ages of 7-18.
 |  | ✖ |
| 1. You live in British Columbia.
 |  | ✖ |
| 1. You have been diagnosed with OCD by a doctor *and* the screening interview for this study (MINI-Kid) is consistent with a diagnosis of OCD per consensus of the study team.
 |  | ✖ |
| 1. You currently have OCD symptoms that are moderate or severe (CY-BOCS ≥16).
 |  | ✖ |
| 1. You have a doctor in charge of his/her regular medical or OCD treatment (e.g. family doctor, pediatrician, specialist).
 |  | ✖ |
| 1. You would be able to take a medication twice daily in capsule form (whole or sprinkled).
 |  | ✖ |
| 1. You are able to participate in all study assessments and procedures in English, including informed consent/assent, self-care, adverse event reporting, and follow-up assessments.
 |  | ✖ |
| 1. You, if you are of child-bearing potential, have a negative pregnancy test (either serum or urine)
 |  | ✖ |
| 1. Your, if you are of child-bearing potential, use highly effective and/or double barrier contraception, or abstinence
 |  | ✖ |
| **Exclusion criteria** |
| 1. You do not have any of the following **previously diagnosed** conditions:

Autism spectrum disorder, bipolar disorder, psychotic disorder, intellectual disability, substance use disorder, significant head injury causing loss of consciousness, kidney disease, liver disease, gastrointestinal bleeding, peptic ulcer disease, inflammatory bowel disease, bleeding disorder, severe asthma or uncontrolled asthma, heart disease, heart failure, or hypertension |  | ✖ |
| 1. You do not have a known allergy to celecoxib, ibuprofen or other NSAIDs, or sulfonamide compounds, including aspirin.
 |  | ✖ |
| 1. You do not take regular corticosteroids (IV, oral, or inhaled).
 |  | ✖ |
| 1. You do not take a medication that may interact with celecoxib to represent a potential safety risk. These include but are not limited to CYP2C9 inhibitors (e.g. fluconazole, amiodarone, oxandrolone, methotrexate) and inducers (e.g. rifampin, phenobarbital).
 |  | ✖ |
| 1. You have not had genetic testing that demonstrates they are a poor CY2C9 metabolizer (CYP2C9\*3/\*3 genotype)
 |  | ✖ |
| 1. You have not previously received a regular immune-modulating therapy for treating OCD at an effective anti-inflammatory dose (including NSAIDs, corticosteroids, or biologics).
 |  | \* |
| 1. You do not take any medications that could interact with celecoxib.
 |  | \* |
| 1. You do not have **current** severe depression symptoms, suicidal thoughts, psychosis, substance use, or fluid/drinking restriction.
 |  |  |
| 1. You are not currently pregnant or breastfeeding.
 |  |  |
| 1. No abnormalities have been identified on baseline serology including leukocytosis, leukopenia, thrombocytopenia, anemia, abnormal renal function (Cr > 1.5 x upper limit of normal), or abnormal liver function (ALT, ALP, or AST > 1.5x upper limit of normal)
 |  |  |
| 1. You have not had any new medications started in the past 10 weeks, and there are no planned changes (including to the dose) of medications for OCD treatment during the study period. No dose changes have been made in the 4 weeks prior to randomization.
 |  |  |
| 1. There are no planned changes in CBT or other psychotherapy during the study period, and none have been made in the 4 weeks prior to randomization.
 |  |  |
| 1. There are no other planned or likely treatment changes during the study period.
 |  |  |
| 1. You have not used an NSAID such as ibuprofen, celecoxib, or naproxen 3 or more times per week in the past 2 months.
 |  |  |
| 1. You do not currently have an infection and is not on antibiotics.
 |  |  |
| 1. You, if you are of child-bearing potential, do not have an intention of pregnancy.
 |  |  |
| 1. You do not have an inability to have blood measured within 2 months prior to enrolment (either on-site at BCCH or by a primary care provider)
 |  |  |
| ✖If selected, you are ineligible to participate in this study. |
| If selected, you are *currently* ineligible but may become eligible when criterion no longer applies.  |
| \*If selected, you may or may not be eligible; requires review by study doctor. |

**Appendix B. Celecoxib patient safety information**

**(based on Celebrex product monograph)**

**1. Boxed warnings**

**Celecoxib, particularly at doses higher than 200 mg per day, is associated with an increased risk of serious cardiovascular related adverse events (such as myocardial infarction, stroke or thrombotic events, which can be fatal). Doses of celecoxib >200 mg/day should NOT be used in patients with ischemic heart disease, cerebrovascular disease, patients with congestive heart failure or patients with risk factors for cardiovascular disease. For patients with an increased risk of developing cardiovascular adverse events, other management strategies that do NOT include the use of NSAIDs, particularly celecoxib, diclofenac, or ibuprofen, should be considered first.

For patients with an increased risk of developing gastrointestinal adverse events, other management strategies that do NOT include the use of NSAIDs, including celecoxib, should be considered first.

Use of celecoxib should be limited to the lowest effective dose for the shortest possible duration of treatment in order to minimize the potential risk for cardiovascular or gastrointestinal adverse events.**

**2. Use in pediatric populations**

In Canada, celecoxib is not recommended for use in patients under 18 years of age and the product monograph states that the safety and effectiveness have not been established in these patients. In the US, celecoxib is approved for relief of the signs and symptoms of Juvenile Rheumatoid Arthritis in patients 2 years and older. Safety and efficacy have not been studied beyond six months in children. The long-term cardiovascular toxicity in children exposed to celecoxib has not been evaluated and it is unknown if long-term risks may be similar to that seen in adults exposed to celecoxib or other COX-2 selective and non-selective NSAIDs.

The use of celecoxib in patients 2 years to 17 years of age with juvenile rheumatoid arthritis was studied in a 12-week, double-blind, active controlled, pharmacokinetic, safety and efficacy study. Adverse events from this trial are listed in Section X. Celecoxib has not been studied in patients under the age of 2 years, in patients with body weight less than 10 kg (22 lbs), and in patients with active systemic features.

**3. When it should not be used**

Do not take celecoxib if you have any of the following medical conditions:

* Heart bypass surgery (planning to have or recently had)
* Severe, uncontrolled heart failure
* Allergy to celecoxib or any of the other ingredients in CELEBREX
* Allergy to sulfonamide drugs
* Allergy to ASA or other NSAIDs
* Pregnancy of more than 28 weeks (third trimester)
* Currently breastfeeding or planning to breastfeed
* Ulcer (active)
* Bleeding from the stomach or gut (active)
* Bleeding in the brain or other bleeding disorders
* Inflammatory bowel disease (Crohn’s Disease or Ulcerative Colitis)
* Liver disease (active or severe)
* Kidney disease (severe or worsening)
* High potassium in the blood

**4. Medicinal ingredient**

Celecoxib

**5. Nonmedicinal ingredients in CELEBREX**

Croscarmellose sodium, Ferric oxide edible ink (E172) (200 mg capsules), Gelatin, Indigotine edible ink (E132) (100 mg capsules), Lactose monohydrate, Magnesium stearate, Povidone, Sodium lauryl sulphate, Titanium dioxide (E171)

**6. Medication interactions**

As part of this study you will list all medications you are taking. These should not include the following, which can interact with celecoxib:

* Acetylsalicylic acid (ASA) or other NSAIDs (e.g. diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen)
* Antacids or proton pump inhibitors (omeprazole)
* Antidepressants [Selective serotonine receptor uptake inhibitor (SSRIs) (e.g. citalopram, paroxetine, fluoxetine, sertraline)]
* Blood pressure medications, such as ACE (angiotensin converting enzyme) inhibitors (e.g. enalapril, lisinopril, perindopril, ramipril), ARBs (angiotensin II receptor blockers) (e.g. candesartan, irbesartan, losartan, valsartan), beta blockers (e.g. metoprolol)
* Blood thinners (to prevent blood clots), such as warfarin, apixaban, rivaroxaban, dabigatran, ASA, clopidogrel
* Corticosteroids (including glucocorticoids) e.g. prednisone
* Cyclosporin
* Digoxin
* Diuretics such as furosemide, hydrochlorothiazide
* Fluconazole
* Lithium
* Dextromethorphan (found in some cough medications)
* Tacrolimus

**7. What to know while taking this medication**

* Tell any doctor, dentist, pharmacist, or other health care professional that you see that you are in an OCD treatment trial and may be taking this medication
* Do not drink alcohol beverages while taking this medication because you would be more likely to develop stomach problems
* Take the capsule with food
* Stop taking the medication if you have nausea, vomiting, or dehydration. Inform the study team and do not resume the medication until these symptoms have resolved.
* If you miss a dose, take it as soon as you remember, then take the next dose at the scheduled time. If it is < 4 h until your next dose, skip the dose and record this in your electronic diary.
* If you take more than the prescribed dose, contact the study team or your health care provider immediately. For suspected overdose, go to the emergency department or contact your regional Poison Control Centre, and contact the study team.
* Store the capsules at room temperature between 15-30°C
* Contact the study team if you experience side effects

**8. Side effects and what to do about them**

Stop taking the drug and get emergency medical attention immediately if you experience any of the following:

* Chills, fever, muscle aches or pains, or other flu-like symptoms (especially if they occur together with a skin rash, these may be the first signs of a serious allergic reaction to this medication)
* Bloody or black tarry stools
* Shortness of breath, wheezing, any trouble breathing or chest tightness
* Skin rash, hives, swelling, or itching
* Blurred vision or other visual disturbance
* Sudden severe headache or worsening of headache, vomiting, dizziness, fainting, disturbance of vision or speech, or weakness or numbness in the face, arm, or leg
* Change in urine (amount or colour; dark or red brown)

Stop taking the drug and talk to the study team or your regular health care provider:

* Serious skin reactions: skin rash, blisters or breakdown of your skin, fever, swollen glands
* Pain or difficulty urinating
* Feet or lower leg swelling; weight gain
* Vomiting or persistent indigestion, nausea, stomach pain, or diarrhea
* Yellow discolouration of the skin or eyes with or without itchy skin
* Malaise, fatigue, or loss of appetite
* Headaches, stiff neck
* Mental confusion or depression
* Dizziness or light-headedness
* Hearing problems
* Pneumonitis (symptoms include trouble breathing, dry cough, tiredness)

This is not a complete list. If you develop any other symptoms while on the study treatment, contact the study team.

**9. Adverse events in previous treatment trials**

Small studies in children have found no increase in adverse events in participants receiving celecoxib compared to placebo for up to 12 weeks. Adverse events are symptoms that occur during treatment and may or may not be related to the drug. In studies reporting serious adverse events in children, none have been attributed to NSAID use. The following tables list adverse events in adult and pediatric treatment trials.

|  |
| --- |
|  Very common (10% or greater) or common (1-10%) adverse events in 12 controlled studies in patients with osteoarthritis and rheumatoid arthritis, per product monograph |
|  | **CELEBREX****100-200mg BID****and 200mg QD** | **Placebo** | **Naproxen****500mg BID** | **Ibuprofen****800mg TID** | **Diclofenac****75mg BID** |
| **Gastrointestinal** |   |   |   |   |   |
| Abdominal pain | 4.1% | 2.8% | 7.7% | 9.0% | 9.0% |
| Diarrhea | 5.6% | 3.8% | 5.3% | 9.3% | 5.8% |
| Dyspepsia | 8.8% | 6.2% | 12.2% | 10.9% | 12.8% |
| Flatulence | 2.2% | 1.0% | 3.6% | 4.1% | 3.5% |
| Nausea | 3.5% | 4.2% | 6.0% | 3.4% | 6.7% |
| **Body as a Whole** |   |   |   |   |   |
| Back pain | 2.8% | 3.6% | 2.2% | 2.6% | 0.9% |
| Peripheral edema | 2.1% | 1.1% | 2.1% | 1.0% | 3.5% |
| Injury-accidental | 2.9% | 2.3% | 3.0% | 2.6% | 3.2% |
| **Central and Peripheral Nervous System** |   |   |   |
| Dizziness | 2.0% | 1.7% | 2.6% | 1.3% | 2.3% |
| Headache | 15.8% | 20.2% | 14.5% | 15.5% | 15.4% |
| **Psychiatric** |   |   |   |   |   |
| Insomnia | 2.3% | 2.3% | 2.9% | 1.3% | 1.4% |
| **Respiratory** |   |   |   |   |   |
| Pharyngitis | 2.3% | 1.1% | 1.7% | 1.6% | 2.6% |
| Rhinitis | 2.0% | 1.3% | 2.4% | 2.3% | 0.6% |
| Sinusitis | 5.0% | 4.3% | 4.0% | 5.4% | 5.8% |
| Upper respiratory tract infection | 8.1% | 6.7% | 9.9% | 9.8% | 9.9% |
| **Skin** |   |   |   |   |   |
| Rash | 2.2% | 2.1% | 2.1% | 1.3% | 1.2% |

|  |
| --- |
| Uncommon adverse events (0.1-1.9%) in adult treatment trials, per product monograph |
| **Gastrointestinal:** | Constipation, diverticulitis, dry mouth, dysphagia, eructation, esophagitis, gastritis, gastroenteritis, gastroesophageal reflux, hemorrhoids, hiatal hernia, melena, stomatitis, tenesmus, tooth disorder, vomiting |
| **Cardiovascular:** | Aggravated hypertension, angina pectoris, coronary artery disorder, myocardial infarction |
| **General:** | Allergy aggravated, allergic reaction, asthenia, chest pain, cyst NOS, edema generalized, face edema, fatigue, fever, hot flushes, influenza-like symptoms, pain, peripheral pain |
| **Resistance Mechanism****Disorders:** | Herpes simplex, herpes zoster, infection bacterial, infection fungal, infection soft tissue, infection viral, moniliasis, moniliasis genital, otitis media |
| **Central, Peripheral** **Nervous System:** | Leg cramps, hypertonia, hypoesthesia, migraine, neuralgia, neuropathy, paresthesia, vertigo |
| **Female Reproductive:** | Breast fibroadenosis, breast neoplasm, breast pain, dysmenorrhea, menstrual disorder, vaginal hemorrhage, vaginitis |
| **Male Reproductive:** | Prostatic disorder |
| **Hearing and** **Vestibular:** | Deafness, ear abnormality, earache, tinnitus |
| **Heart Rate and Rhythm:** | Palpitation, tachycardia |
| **Liver and Biliary System:** | ALT increased, AST increased, hepatic function abnormal |
| **Metabolic and Nutritional:** | Urea increased, CPK increased, diabetes mellitus, hypercholesterolemia, hyperglycemia, hypokalemia, NPN increase, creatinine increased, alkaline phosphatase increased, weight increase |
| **Musculoskeletal:** | Arthralgia, arthrosis, bone disorder, fracture accidental, myalgia, neck stiffness, synovitis, tendinitis |
| **Platelets****(bleeding** **or clotting):** | Ecchymosis, epistaxis, thrombocythemia |
| **Psychiatric:** | Anorexia, anxiety, appetite increased, depression, nervousness, somnolence |
| **Hemic:** | Anemia |
| **Respiratory:** | Bronchitis**,** bronchospasm, bronchospasm aggravated, coughing, dyspnea, laryngitis, pneumonia |
| **Skin and Appendages:** | Alopecia, dermatitis, nail disorder, photosensitivity reaction, pruritus, rash erythematous, rash maculopapular, skin disorder, skin dry, sweating increased, urticaria |
| **Application Site Disorders:** | Cellulitis, dermatitis contact, injection site reaction, skin nodule |
| **Special Senses:** | Taste perversion |
| **Urinary System:** | Albuminuria, cystitis, dysuria, hematuria, micturition frequency, renal calculus, urinary incontinence, urinary tract infection |
| **Vision:** | Blurred vision, cataract, conjunctivitis, eye pain, glaucoma |

|  |
| --- |
| Rare (0.01-0.1%) and very rare (<0.01%) adverse events in adult treatment trials, per product monograph |
| **Cardiovascular:** | Syncope, congestive heart failure, ventricular fibrillation, pulmonary embolism, cerebrovascular accident, peripheral gangrene, thrombophlebitis |
| **Gastrointestinal:** | Intestinal obstruction, intestinal perforation, gastrointestinal bleeding,  colitis with bleeding, esophageal perforation, pancreatitis, cholelithiasis, ileus |
| **Hemic and****Lymphatic:** | Thrombocytopenia |
| **Liver and Biliary System:** | Cholelithiasis, hepatitis, jaundice, liver failure |
| **Metabolic:** | Hypoglycemia |
| **Nervous System:** | Ataxia |
| **Renal:** | Acute renal failure |
| **General:** | Sepsis, sudden death |

|  |
| --- |
| Very common (10% or greater) or common (1-10%) adverse events in children with arthritis treated for 12 weeks (from *Foeldvari et al. Journal of Rheumatology* 36(1):174-182). |
|  | **Celecoxib****3 mg/kg bid** | **Celecoxib****6 mg/kg bid** | **Naproxen****7.5 mg/kg bid** |
| **Any event**  | 63.6 | 69.5 | 72.3 |
| **Eye disorders** | 5.2 | 4.9 | 4.8 |
| **Gastrointestinal disorders** Abdominal pain  Upper abdominal pain Vomiting Diarrhea Nausea | 26.03.97.82.65.26.5 | 24.47.36.16.13.73.7 | 36.17.29.610.88.410.8 |
| **General disorders and administration site conditions** Pyrexia | 13.07.8 | 11.08.5 | 18.110.8 |
| **Infections and infestations** Nasopharyngitis | 24.75.2 | 19.56.1 | 26.54.8 |
| **Injury and poisoning** | 3.9 | 6.1 | 7.2 |
| **Investigations** | 2.6 | 11.0 | 7.2 |
| **Musculoskeletal, connective tissue, and bone disorders** Arthralgia | 7.82.6 | 9.87.3 | 16.93.6 |
| **Nervous system disorders** Headache Dizziness | 16.913.01.3 | 11.09.81.2 | 20.515.77.2 |
| **Respiratory, thoracic, and mediastinal disorders** Cough | 7.86.5 | 14.67.3 | 14.58.4 |
| **Skin and subcutaneous tissue disorders** | 10.4 | 7.3 | 18.1 |

|  |
| --- |
| Adverse events reported in pediatric studies (frequency not defined per Lexicomp drug information) |
| **Cardiovascular**: **Dermatologic**: **Gastrointestinal**: **Hepatic**: **Hypersensitivity**: **Immunologic**: **Renal**: **Respiratory**: **Miscellaneous**:  | Peripheral edemaAcute generalized exanthematous pustulosis, exfoliative dermatitisAbdominal pain, diarrhea, dyspepsia, flatulence, gastroesophageal reflux disease, gastrointestinal perforation, gastrointestinaI ulcer, GI inflammation, intestinal perforation, vomitingIncreased liver enzymes (<3x ULN)AnaphylaxisDRESS syndromeNephrolithiasisDyspnea, local alveolar osteitis (post oral surgery patients), pharyngitis, rhinitis, sinusitis, Upper respiratory tract infectionAccidental injury |