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Advancing care for critically ill patients with acute traumatic brain injuries

Submission date
14/12/2025

Recruitment status
Recruiting

Registration date
17/12/2025

Overall study status
Ongoing

Last Edited
17/12/2025

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol
Background and study aims
Traumatic brain injury (TBI) is a major cause of death and disability worldwide. Among survivors, moderate and severe TBI can lead to lasting neurological and functional impairments, including problems with mobility, communication, cognition, and independence. Despite improvements in critical care, current treatments rely on limited evidence, and management practices vary significantly between hospitals. The BRAINapt trial aims to identify the most effective interventions to improve survival and recovery after moderate or severe TBI. It is an international, multicentre, adaptive platform trial evaluating multiple interventions simultaneously, including drugs, devices, and other treatment strategies used in the intensive care unit (ICU).

Who can participate?
Adult patients aged 18 years or older admitted to the ICU with an acute moderate or severe acute TBI

What does the study involve?
Participants are randomly assigned to one or more intervention domains for which they are eligible and have consented to participate. Each intervention begins soon after randomization and continues until ICU discharge, death, or a decision to withdraw life-sustaining therapy. The main outcome assessed is the neurological functional status at 6 months. Secondary outcomes include death rates, quality of life, cognition, and depression, organ support-free days and ICU-free days.

What are the possible benefits and risks of participating?
Participants may not directly benefit but their involvement will contribute to improving TBI care for future patients. All participants are closely monitored by ICU physicians throughout the study, and any intervention can be stopped at any time if it is not in the patient's best interest.

Where is the study run from?
The trial is coordinated by the CHU de Québec–Université Laval Clinical Trial Unit (CTU). The chief investigator is Pr. Alexis Turgeon at CHU de Québec–Université Laval (Hôpital de l'Enfant-Jésus).

When is the study starting and how long is it expected to run for?
BRAINapt is a perpetual adaptive platform trial, meaning it is designed to continue as long as funding and new intervention domains are available. New domains, interventions within existing domains, and participating sites will be added over time.

Who is funding the study?
The trial is funded by the Canadian Institutes of Health Research (CIHR/IRSC), with institutional support from Université Laval and CHU de Québec–Université Laval.

Who is the main contact?
Prof. Alexis Turgeon, alexis.Turgeon@crchudequebec.ulaval.ca

Contact information

Type(s)
Public, Principal investigator, Scientific

Contact name
Prof Alexis Turgeon

ORCID ID
https://orcid.org/0000-0001-5675-8791

Contact details
Department of Critical Care Medicine
CHU de Québec-Université-Laval (Hôpital de l'Enfant-Jésus)
1401, 18e rue
Québec
Canada
G1J1Z4
+1 (0)418-525-4444 #64056
alexis.turgeon@crchudequebec.ulaval.ca

Type(s)
Public, Scientific

Contact name
Mrs Larissa Belardin

Contact details
CHU de Québec-Université Laval Clinical Trials Unit
Hôpital de l'Enfant-Jésus
1401, 18e rue
Québec
Canada
G1J1Z4
+1 (0)418-525-4444 #64145
larissa.berloffa-belardin@crchudequebec.ulaval.ca

Additional identifiers

Study information

Scientific Title
BRAINapt – TBI International Adaptative Platform Trial

Acronym
BRAINapt

Study objectives
The objective of BRAINapt is to identify i) drugs, iii) devices, or iii) or other interventions (excluding drugs and devices) that can improve long term outcomes in critically ill adult patients with moderate to severe TBI.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 09/12/2025, CHU de Québec-Université Laval Research Ethics Board (Bureau de l'éthique de la recherche CHU de Québec-Université Laval HSFA - local D7-704 10, rue de L'Espinay, Québec, G1L 3L5, Canada; +1 (0)418-525-4444; gurecherche@chudequebec.ca), ref: MP-20-2026-8206

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Traumatic brain injury

Interventions
BRAINapt is a platform trial evaluating several interventions, which may sometimes be tested within the same participant if eligibility criteria are met. These interventions are organized into “domain families,” categorized as (i) drugs, (ii) devices, and (iii) other interventions (neither drugs

nor devices). Below, the current interventions are listed along with their respective domain family and domain.

Beta-blockers Domain
Domain-specific Exclusion Criteria: Contraindications to beta-blockers as per treating physician.

Intervention Arms: Participants will be randomly assigned in a 2:2:3 ratio to one of three arms:
1. Propranolol
Generic drug name: propranolol.
Dosage and administration: As per ICU protocol at sites; PO (recommended) or IV. Recommended initial daily dose 40 mg (10 mg q 6h). Recommended target daily dose 80 mg (20 mg q 6h). Recommended maximal daily dose 160 mg (40 mg q 6h). IV:PO ratio is 1:10
Frequency: As clinically indicated. Recommended frequency in divided doses every 6, 8 or 12 hours
Duration: From randomization until ICU discharge, death, or withdrawal of life-sustaining therapies.
2. Metoprolol
Generic drug name: metoprolol.
Dosage and administration: As per ICU protocol at sites; PO (recommended) or IV. Recommended initial daily dose 50 mg (25 mg q 12h). Recommended target daily dose 100 mg (50 mg q 12h). Recommended maximal daily dose 200 mg (100 mg q 12h). IV:PO ratio is 1:2.5
Frequency: As clinically indicated. Recommended frequency in divided doses every 12 hours
Duration: From randomization until ICU discharge, death, or withdrawal of life-sustaining therapies.
3. Control (No beta-blocker)
Participants receive standard ICU care without beta-blockers.
Follow-up and Duration: Participants are followed for six months post-randomization.
Domain-specific secondary outcome: Day 28: myocardial ischemic events.

Anticonvulsants Domain
Domain-specific Exclusion Criteria: Contraindications to anticonvulsants per treating physician; Pre-existing anticonvulsant therapy for seizure disorder; Early seizure requiring anticonvulsants; More than 72 hours elapsed since ICU admission.
Intervention Arms: Participants will be randomly assigned in a 2:2:3 ratio to one of three arms:
4. Phenytoin
Generic drug name: phenytoin.
Dosage and administration: As per local ICU clinical protocols at sites; PO or IV. Recommended loading dose 15 mg/kg (max 2000 mg). Recommended maintenance daily dose 5 mg/kg or 300 mg (100 mg q 8h). May be titrated according to serum level, as per local practice.
Frequency: As per local ICU clinical protocols. Recommended frequency in divided doses every 8 or 12 hours.
Duration: From randomization until ICU discharge, death, or withdrawal of life-sustaining therapies.
5. Levetiracetam
Generic drug name: levetiracetam.
Dosage and administration: As per local ICU clinical protocols at sites; PO or IV. Recommended loading dose 20 mg/kg. recommended maintenance daily dose 2000 mg (1000mg q 12h). The dose should be titrated down to 500 mg q12h in patients aged ≥ 75 years or with a creatinine clearance ≤ 50 mL/min.
Frequency: As per local ICU clinical protocols.
Duration: From randomization until ICU discharge, death, or withdrawal of life-sustaining therapies.

6. Control (No anticonvulsant)
Participants receive standard ICU care without prophylactic anticonvulsants.
Follow-up and Duration: Participants are followed for six months post-randomization.
Domain-specific secondary outcome: Day 7: occurrence of seizures.

Intervention Type
Mixed

Primary outcome(s)
1. Neurologic functional outcome measured using Glasgow Outcome Scale extended questionnaire at 6 months

Key secondary outcome(s))
1. Mortality measured using medical records, public registries or questionnaire at Hospital and 6 months

2. Quality of life measured using EuroQoL Visual Analogue Scale (VAS) and 5-Dimension 5-Level (EQ-5D-5L) at 6 months

3. Cognition measured using Telephone-Montréal Cognitive Assessment test (T-MoCA) at 6 months

4. Depression measured using Patient Health Questionnaire-9 (PHQ-9) at 6 months

5. Organ-support free days (mechanical ventilation, vasopressors, renal replacement therapy) measured using medical records at 28 days

6. ICU-free days measured using medical records at 28 days

Completion date
31/12/2035

Eligibility

Key inclusion criteria
1. Adults aged ≥18 years
2. Admitted to the intensive care unit following acute TBI
3. Moderate or severe acute TBI (GCS ≤12 [on a scale of 3 to 15])

Each domain may have additional inclusion criteria

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit

100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Platform trial exclusion criteria:
1. A decision to withdraw life-sustaining therapies was made

Domain exclusion criteria:

Beta-blocker domain:
1. Contraindications to use beta-blockers based on clinical risk (as per treating physician)

Anticonvulsant domain:
1. Contraindications to use anticonvulsants based on clinical risk (as per treating physician)
2. Patient on anticonvulsants for seizure disorder prior to hospital admission
3. Early seizure requiring anticonvulsants
4. More than 72 hours have elapsed since ICU admission

Date of first enrolment
19/01/2026

Date of final enrolment
31/12/2032

Locations

Countries of recruitment
Australia

Belgium

Brazil

Canada

Colombia

France

Ireland

Italy

Netherlands

New Zealand

Switzerland

Study participating centre
CHU de Québec-Université Laval (Hôpital de l'Enfant-Jésus)
1401, 18e rue
Québec
Canada
G1J1Z4

Sponsor information

Organisation
Université Laval

ROR
https://ror.org/04sjchr03

Organisation
Centre de recherche du CHU de Québec-Université Laval

ROR
https://ror.org/04rgqcd02

Funder(s)

Funder type

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date