

IMPORTANT CHANGES ABOUT GLUCOSE MONITORING

On September 20, 2019, the LOVIT research protocol version 5 was sent to sites with changes on monitoring of blood glucose immediately effective. These changes were deemed necessary because of a patient who experienced hypoglycemia following falsely elevated glucose results treated with insulin. Fortunately, the patient did not suffer any harm.

To ensure patient safety moving forward, we **mandate that glucose** be measured with one of the 3 following methods:

- 1) **core lab**
- 2) **point-of-care arterial blood gas machine** that has been validated in the setting of high plasma concentrations of vitamin C (manufacturer's documentation to be checked)
- 3) **Nova Biomedical Statstrip glucometer** which has already been validated to be accurate in the presence of high concentrations of ascorbic acid.

Glucose measurements need to be monitored **up to 7 days after the last dose** of the investigational product for all participants receiving insulin or oral hypoglycemic agents.

We are offering to **supply each site with Nova Biomedical Statstrip glucometers and the required strips for free**.

If not already done, please send the following information to the Coordinating Centre:

- 1) Glucometer brand/model used at your site
- 2) Arterial Blood Gas Analyzer (if used for glycemia measurements) at your site
- 3) If you would like to receive Statstrip Glucometer and strips: Yes/No.

RESULTS OF THE CITRIS-ALI TRIAL AND IMPACT ON THE LOVIT TRIAL

On October 1st, 2019, the results of the CITRIS-ALI Trial were published in JAMA. LOVIT uses the same dose regimen for vitamin C than CITRIS-ALI (50 mg/kg of weight for 16 doses during 96 hours). The article can be found at:

<https://jamanetwork.com/journals/jama/fullarticle/2752063>

The CITRIS-ALI was a randomized controlled trial including 170 patients (167 contributing to the final analysis) with sepsis and acute respiratory distress syndrome. The trial was negative on the primary outcomes, but showed a reduction in 28-day mortality (one of 46 secondary outcomes): 30% [25/84] in the vitamin C group vs. 46% [38/82] in the placebo group, $p=0.03$, relative risk [RR] 0.642, 95% CI 0.415-0.984 (RR not provided in paper). The result has a fragility index of 1, meaning that if 1 patient in the vitamin C group were "converted" from alive at day 28 to dead at day 28, the study would lose statistical significance. In addition, other secondary outcomes (e.g. evolution of ventilator parameters, vasopressor use) did not favour vitamin C.

We discussed these results with the LOVIT Steering Committee and Data Safety Monitoring Committee (DSMC). Both groups agree that ongoing enrollment in LOVIT is justified and should be encouraged, given that CITRIS-ALI does not definitively settle the question of whether intravenous vitamin C is beneficial in sepsis. A letter from the DSMC has already been sent to sites.

**THE NEXT ROUND OF PAYMENTS IS PLANNED
ON DECEMBER 1st, 2019**

Interim Analysis

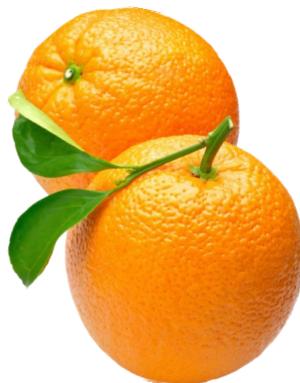
An interim analysis will be held when 250 participants will have completed the study. We are now at 198 patients enrolled. We ask you to already plan the data entry of your participants in iDataFax in order to not delay the analysis.

Manuscript Article Accepted

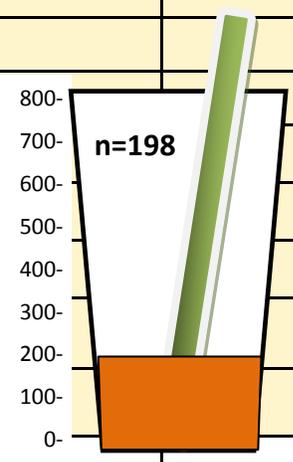
The manuscript article of the LOVIT Trial has been accepted for publication in Trials. We will keep you informed as soon as the article is published.

We thank you for your constant efforts in enrolling patients.

**We are only 2 patients away from reaching
25% of our sample size.**



Sites	Ethics Process started	Ethics Submitted	Final Ethics Approval	Agreement Executed	SIV	Activated	# Patients Enrolled
CIUSSS de l'Estrie - CHUS			👍	👍	26-SEP-2019	👍	89
Kingston HSC			👍	👍	07-FEB-2019	27-FEB-2019	19
IUCPQ			👍	👍	28-FEB-2019	01-MAR-2019	5
CISSS Chaudière-Appalaches			👍	👍	02-APR-2019	05-APR-2019	15
CHUM			👍	👍	03-APR-2019	05-APR-2019	8
Juravinski Hospital			👍	👍	09-APR-2019	17-APR-2019	20
Maisonneuve-Rosemont			👍	👍	09-APR-2019	17-APR-2019	2
Hamilton General Hospital			👍	👍	10-APR-2019	26-APR-2019	2
McGill (RVH)			👍	👍	18-APR-2019	09-JUL-2019	
McGill (MGH)			👍	👍	18-APR-2019	09-JUL-2019	
Trois-Rivières (CIUSSS MCQ)			👍	👍	23-MAY-2019	15-JUL-2019	3
Ottawa General Hospital			👍	👍	03-JUIL-2019	17-JUL-2019	19
Ottawa Civic Hospital			👍	👍	03-JUIL-2019	17-JUL-2019	8
University of Alberta			👍	👍	28-MAY-2019	17-JUL-2019	3
Hôpital Sacré-Cœur			👍	👍	08-JUIL-2019	26-JUL-2019	2
St. Joseph's Healthcare			👍	👍	18-JUN-2019	23-AUG-2019	3
Sunnybrook HSC			👍	👍	21-JUN-2019	12-SEP-2019	
Victoria (VIHA)			👍	👍	13-SEP-2019		
Mount Sinai Hospital			👍				
Regina General Hospital		👍		👍			
St. Michael's Hospital		👍					
CHU de Quebec - Univ. Laval		👍					
Royal Alexandra Hospital		👍					
Apollo Hospital, Chennai, India		👍					
Raymond Poincaré University Hospital, France		👍					
Auckland City Hospital, New Zealand		👍					
London HSC	👍						
Niagara Health Hospital	👍						



DO NOT HESITATE TO CONTACT US FOR ANY INFORMATION OR HELP

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