
VIT
VICTORY

Lotte & John Hecht Memorial Foundation

CDMRP

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A phase III multi-center randomized trial:

VItamin C in Thermal injuRY: The VICToRY Trial

Clinical trials.gov ID #NCT04138394

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Critical Care Nutrition

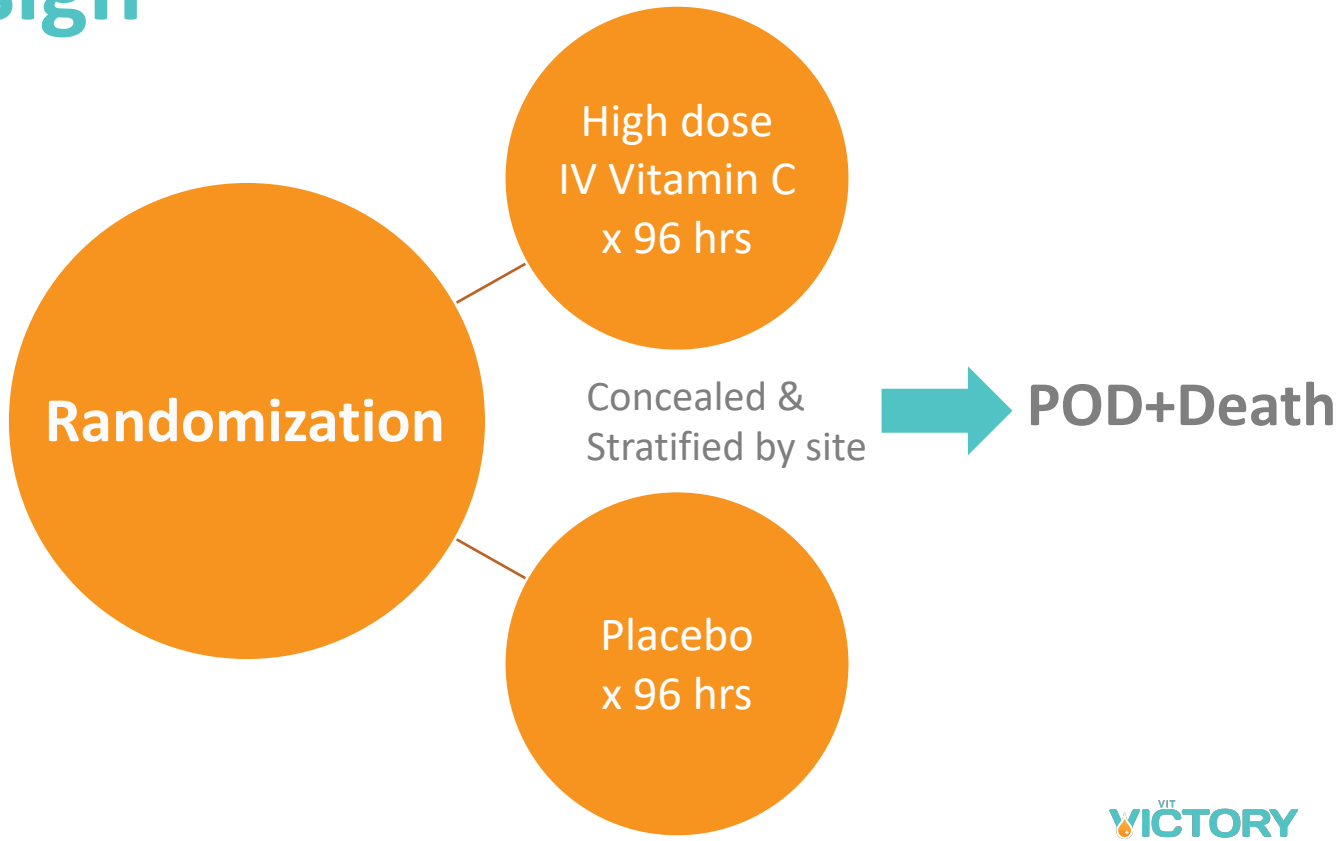
Queen's University

Clinical Evaluation Research Unit

Study Design

Double blind

666 patients
≥18 years of age
Deep 2nd and/or 3rd degree burns requiring skin grafting with TBSA ≥ 20%.



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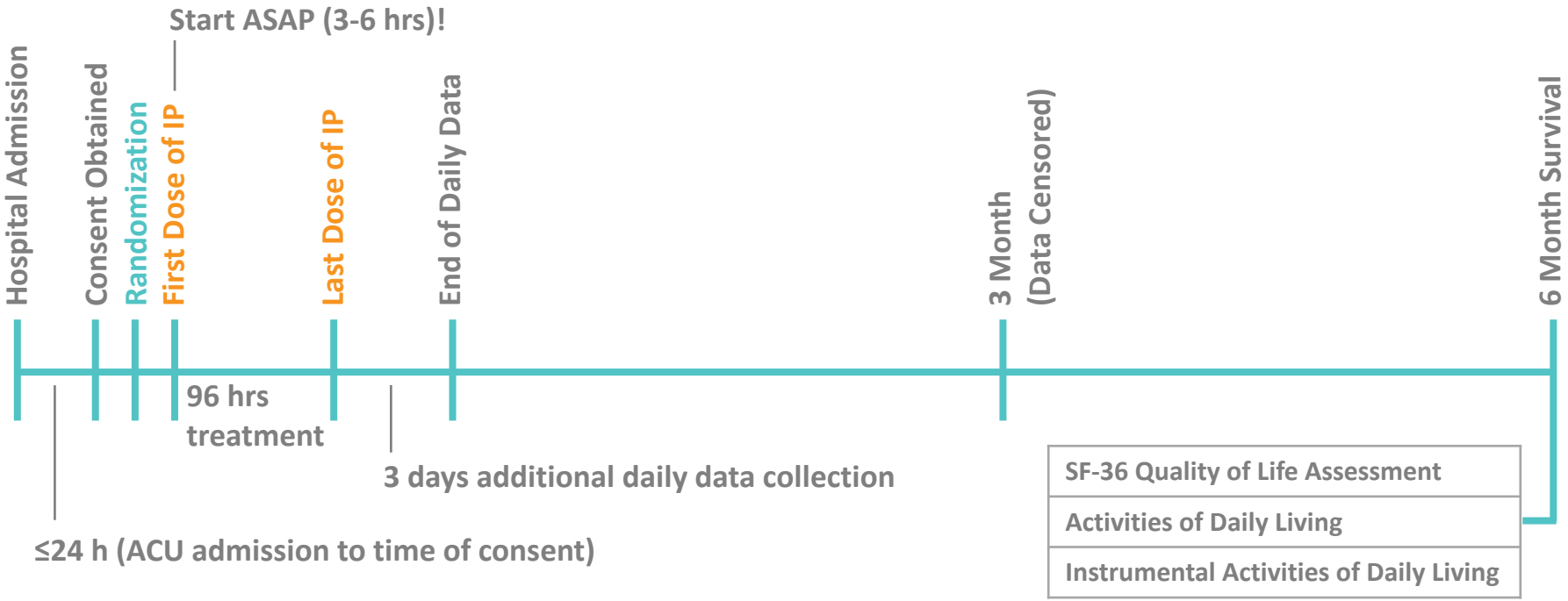
Overall Aim

The overall aim of the VICToRY study is to reduce the burden of illness associated with significant burn injury using a naturally occurring substance, vitamin C!

Study Overview



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IP Administration and Protocol Violations

Investigational Product (IP)

Active
Vitamin C

OR

Control/Placebo
D5W or Saline

IP Dosing and Administration

- Vitamin C at 200mg/kg/day in divided doses, q6h for up to 96 hours (4 days/16 doses) or until hospital discharge.
- Patients who weigh more than 150kg will be dosed based on a weight of 150 kg.
- The total daily dose (mg/day) and single dose (mg/dose) will be calculated by the Central Randomization System (CRS). Additional calculations will be done by pharmacy.
- Vitamin C will be diluted in D5W or 0.9% NaCl to a concentration between 36 mg/mL and 92 mg/mL.
- Infusion rate ≤ 100 mg/min.

Timing of Study Intervention

- IP should start as soon as possible following randomization.
- IP will be given every 6 hours for 96 hours (16 doses).
- If IP starts at 2:00 pm on a Tuesday the doses will be:
  - Tuesday 14:00, 20:00
  - Wednesday 02:00, 08:00, 14:00, and 20:00
  - Thursday 02:00, 08:00, 14:00, and 20:00
  - Friday 02:00, 08:00, 14:00, and 20:00
  - Saturday 02:00, 08:00

Timing of Study Intervention

- To ensure the first dose of IP is administered in a timely manner, vitamin C doses may be prepared in advance and are stable for 14 days protected from light and refrigerated.
- Advanced doses will be prepared using a patient weight of 120 kg.
  - NOTE: Both vitamin C and placebo bags need to be pre-prepared.
- Prepared bags must be stored at 2-8° C and protected from light.
- The bags will be stored in a secure location accessible by the research and Ip administration teams.
- The prepared product expiration must be clearly displayed on each bag.

Timing of Study Intervention (continued)

- Vitamin C and placebo bags will be placed in separate containers and labelled with a code that can be clearly communicated to the study team via phone, such as ‘A’ and ‘B’.
- Only the unblinded pharmacy team member(s)/delegate(s) will know which product is in each of the two containers.
- After the patient is randomized, the pharmacy team member will access the CRS, determine the treatment allocation, and then instruct the study team from which container to retrieve a bag.
  - To ensure continued blinding of the research team, pharmacy/delegate should periodically rotate the study products and allocate new labels. Pharmacy/delegate team must maintain detailed records of what is in each container and the associated labels at all times.

Timing of Study Intervention (continued)

- The pharmacy/delegate will also communicate the following:
  - Total volume of the pre-prepared bag to be infused based on the patient's pre-burn dry weight *(per weight entered in the CRS)*.
  - Minimum infusion time to ensure a rate ≤ 100 mg/minute.
- The pharmacy/delegate and research team member must verify together:
  - Randomization number
  - Date and Time of randomization
  - Patient's pre-burn dry weight *(as entered in the CRS)*.

Timing of Study Intervention (continued)

- The research team will verify with the pharmacy/delegate team member:
  - The expiration date documented on the bag.
  - The container from which the bag was taken
- For patients with a pre-burn dry weight of >120 kg, it is not necessary to infuse more than 1 bag as the initial dose. Record the initial dose as a one-time order. Prepare subsequent doses per the patient's pre-burn dry weight. There is no need to make up for this dose shortage.

Timing of Study Intervention (continued)

- The pharmacy team will document the following on the pharmacy randomization confirmation:
  - The container from which the team was instructed to take the bag.
  - The total volume to be infused that was communicated to the team.
  - The minimum infusion time communicated to the research team.
- The research team will document the following on the patient randomization confirmation:
  - The container from which the bag was taken.
  - The total volume to be infused that was communicated to them.
  - The minimum infusion time that was communicated to them.

IP Administration Procedures

- IP must be administered using infusion pump and can be given through a central or peripheral line.
- Prepare and hang IV bag per local standard procedures.
  - Assess the site, flush according to local SOP, clean the port, hang bag.
- Infuse per pharmacy instructions on the bag (≤100mg/min).
- Do Not co-administer with any other medication.
  - There is no information available concerning compatibility of IP with other drugs. Therefore, IP should not be co-administered with any other medications.

IP Administration Procedures

- Infuse IP through a dedicated port:
  - One port of a triple lumen
  - Piggyback ONLY with NaCl 0.9% (normal saline) or D5W
  - May be given through a port containing Ringer's lactate IF the port is flushed before and after infusion of IP

IP Administration Procedures

- The IP bag and tubing do not need to be protected from light during infusion. According to stability testing, vitamin C concentration between 36 – 92 mg/mL (diluted in NaCl 0.9% or D5W) is physically and chemically stable for up to 75 hours at room temperature not protected from light.
- The IV tubing should be primed with IP solution. Be careful not to waste IP when priming the lines.
- Antibiotic tubing is recommended for IP administration.
- Following completion of infusion, flush line with NaCl 0.9% to ensure patient receives full dose.

IP & ACU Re-admissions < 24 hours

- If a participant is transferred out of the ACU before the 16-dose protocol is completed, the treatment will be continued on the step-down unit or ward until the last (16^{th}) dose of investigational product (IP) is administered or the patient is discharged from the hospital, whichever comes first.
- IP should only be discontinued prior to administration of all 16 doses if the patient is discharged from the hospital.

Infusion Time Examples

kg	mg/day	mg/dose	mL	minutes
Dosing Weight	Daily Dose (based on 200 mg/kg/day)	Single Dose (dosing q6h)	Min volume/dose (based on max conc. 92mg/mL)	Min infusion rate (based on max rate 100mg/min)
50	10,000	2,500	27	25
75	15,000	3,750	41	37.5
100	20,000	5,000	54	50
125	25,000	6,250	68	62.5
150	30,000	7,500	82	75

Interrupted or Missed Dose of IP

- If possible, do not stop IP for procedures or surgery.
- If IP is stopped, restart as soon as possible and complete the infusion.
- Record the start and stop time of the infusion and any interruptions.
- REDCap allows you to record up to 3 interruptions per dose.

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Interrupted or Missed Dose of IP

- In the event of a missed dose, please work to make up the missed dose as soon as possible, using the following guidelines:
  - Do not administer make-up doses with scheduled doses.
  - Leave at least one hour between the end of one administration and the start of the next.
  - The patient must be off study product infusion for a minimum of 60 minutes before you begin infusing the next dose.
  - Delay the start of the next scheduled dose to accommodate the make-up dose.
- It is vital that all doses of IP are administered.

Unused IP

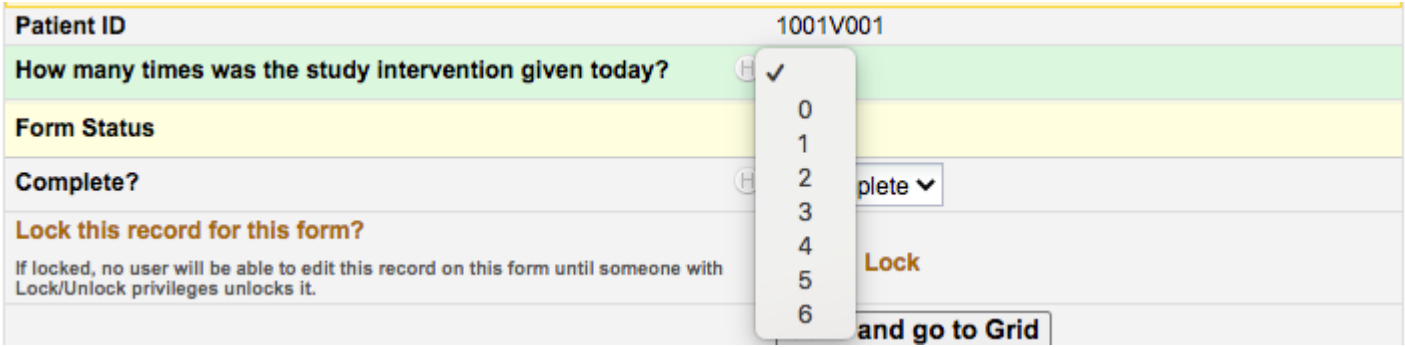
- Please follow local procedures for destruction of unused IP.
- Please follow local procedures for disposal of empty IP bags after the IP has been administered.

IP Non-Compliance

- Work closely with your bedside clinical staff to ensure the IP is delivered appropriately and consistently.
- The majority of issues related to IP administration in other studies have been attributable to bedside clinical staff non-compliance.
- Instruct bedside clinical staff to record and inform the study team of any interruptions in IP administration.
- Bedside clinical staff should continue administering the study investigational product until they are advised by the study team that the patient is no longer on the study.

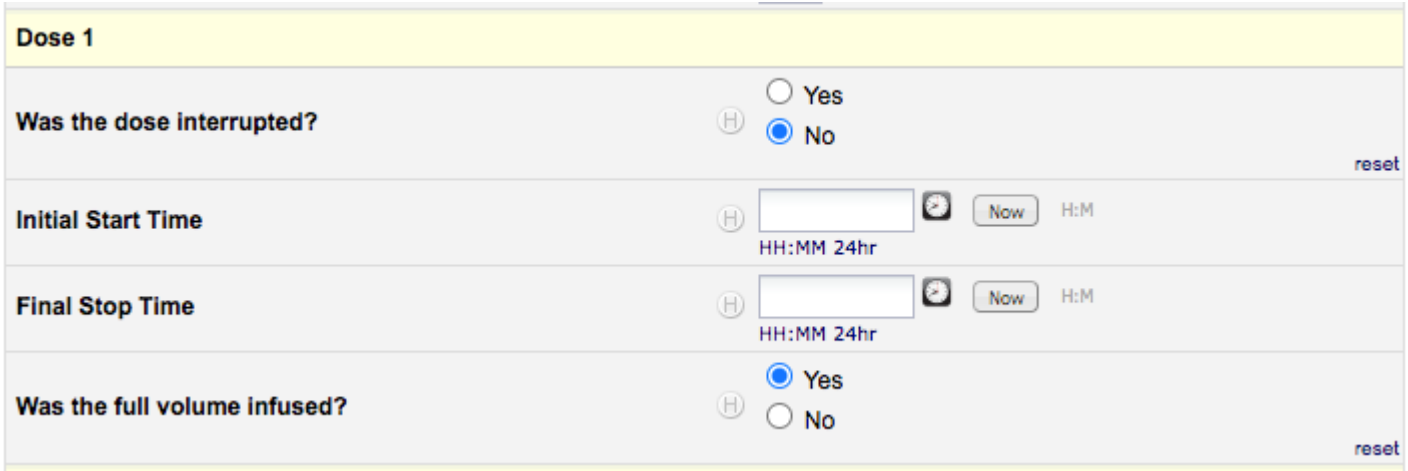
Recording Vitamin C Dosing in REDCAP

+ Record each dose of investigational product given.
+ REDCap allows for up to 6 doses to be given each day should you need to make up doses.



Recording Vitamin C Dosing in REDCAP

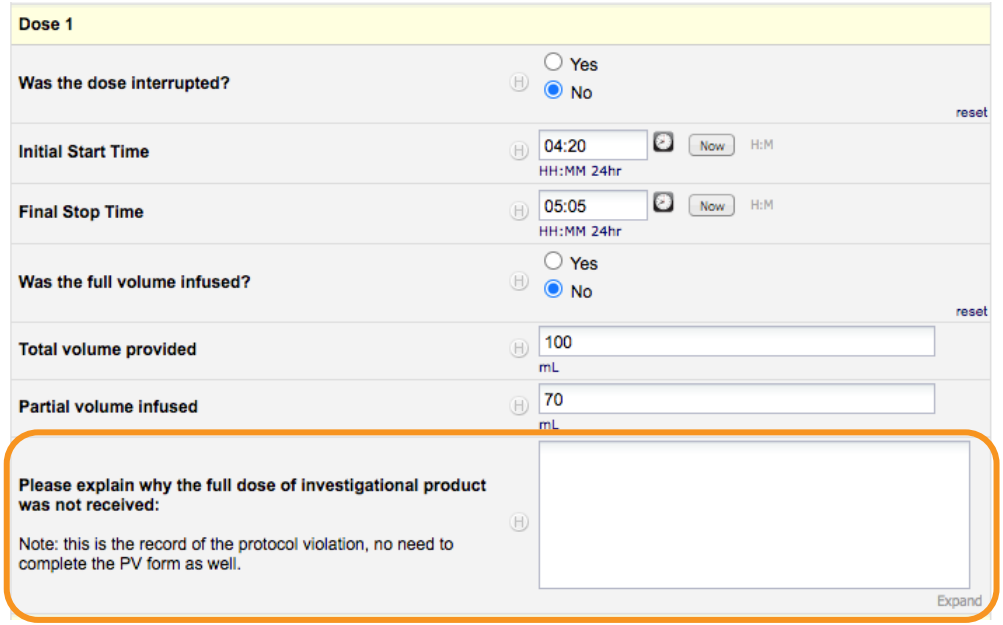
+ For each dose indicate if the dose was interrupted.
+ Record the start and stop time of each dose.
+ Indicate if the full volume was infused.



Incomplete Infusion Record

In the event the full volume was not infused:

+ Record the total volume of the bag as indicated on the label.
+ Record the volume infused.
+ Protocol violations related to incomplete doses will be recorded on the Vitamin C Dosing form.



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Glucose Measurements

+ Due to the similar molecular structure of vitamin C and glucose it is possible that capillary blood sugar point-of-care devices will report artificially high glucose measurements. To that end, we are mandating that glucose may only be measured with one of the following 3 systems:
  1. Core Lab
  2. POC arterial blood gas machine validated in the presence of high plasma concentrations of vitamin C
  3. Nova Biomedical StatStrip glucometer (validated accurate in the presence of high plasma concentrations of vitamin C)

Glucometers and Test Strips

- Nova Biomedical StatStrip glucometers
  - Are being provided to you for use in the study
  - Meters and strips will be shipped to you prior to activation

Glucose Testing Post Treatment

- High plasma concentration of vitamin C may be observed up to 7 days after the last dose of vitamin C is received.
- For patient's receiving oral hypoglycemics or insulin, one of the 3 validated methods must be used to measure glucose for 7 days after the last dose, or a minimum of 36 hours if the hospital device is validated with the approved method. If validated, the hospital device may be used from that point on as needed.
- Hospital method is ok in those patients that do NOT require oral hypoglycemics or intravenous insulin.

Questions

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