

The REDOXS[®] Circular

As of August 31st, 2009

Total Patients Enrolled: 583 **Patients enrolled in August: 21**
(includes 80 patients from pilot)

Congratulations to the sites who enrolled patients in August

| | | | |
|-------------------------|---|---------------------------------|---|
| St. Joseph's Healthcare | 1 | CHUV | 1 |
| Ottawa General | 2 | Royal Jubilee Hospital | 1 |
| Hopital du Sacre-Coeur | 7 | University of Colorado | 2 |
| Grey Nun's Hospital | 1 | Miami Valley, Ohio | 1 |
| Halifax Capital Health | 1 | Fletcher Allen, Vermont | 1 |
| Montreal General | 2 | Asklepios Klinik Altona-Hamburg | 1 |

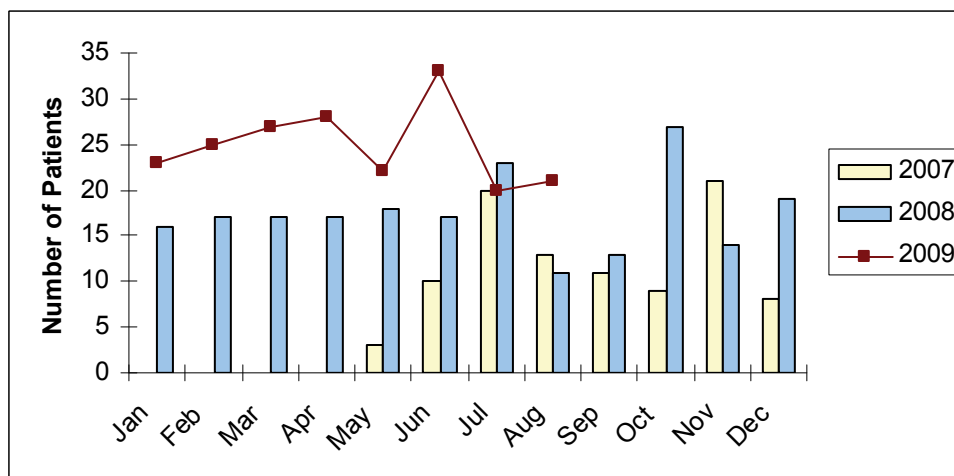
Enrolment News

- ◆ Große Arbeit team Altona-Hamburg for enrolling your 1st patient this month!
- ◆ The team at Hôpital Sacré-Coeur has tied the current monthly enrolment record with 7 patients enrolled in August. Incredible work!
- ◆ Keep you eyes on the group at Ottawa General they now have a total of 99 patients enrolled. We look forward to seeing them reach the milestone of 100 patients enrolled at their site. ☺
- ◆ We are 17 patients away from reaching the half-way mark of the study, let's work towards reaching this REDOXS[®] study landmark in September!!!

Enrolment Trends

We have made great strides with the REDOXS Study over the past 3 years!

We began enrolling patients at one site in May of 2007, by the end of that year we had 8 sites enrolling patients and recruited a total of 175 patients. Staggered start-up continued through 2008 adding 14 additional sites to the team. By the end of 2008 there were 384 patients enrolled overall. As we progress towards the final quarter of 2009 we have a total of 31 sites recruiting patients. Our goal is for each site to enroll 2 patients/month resulting in a total projected monthly enrolment of 62 patients.



Some reasons for lower than expected enrolment have included: staffing shortages, tight timelines for inclusion of patients (i.e. within 24 hours of admission to ICU), contraindications to enteral nutrition and competing ICU studies. Together we have worked towards limiting these obstacles as much as possible.

The table to the left illustrates the actual monthly enrolment achieved since the commencement of the study. The addition of new sites has resulted in a significant increase in enrolment.

We would like to see the bold line continue to climb to our projected enrolment of 62 patients/month!

STUDY CHAIR

Daren Heyland
dkh2@queensu.ca

PROJECT LEADERS

Rupinder Dhaliwal
dhaliwar@kgh.kari.net
Janet Overvelde
overvelj@kgh.kari.net

DATA MANAGEMENT

Jennifer Korol
korolj@kgh.kari.net
Shawna Froese
froeses@kgh.kari.net

PROJECT ASSISTANTS

Suzanne Biro
biros@kgh.kari.net
Susan Campbell
campbes3@kgh.kari.net

When to Report a Protocol Violation

We have recently received many questions regarding when a Protocol Violation (PV) should be reported. A PV is defined as a patient receiving the following volumes of Study Supplements in a study day:

Enteral = 0-383 mL Parenteral = 0-215 mL

All PVs should be reported to the Project Leader for the duration of the study with the exception of the following:

- ◆ **Day of randomization**
If there are < 12 hours left in the study day on the day of randomization, then it will not be possible for the patient to receive the full prescription of the study supplements.
- ◆ **Day of discharge from ICU & Day of Death**
Because patients depart the ICU at various times, for various reasons, it is reasonable that the patient may not receive the full daily prescription of study supplements on the day of ICU discharge or death. Also, it is common for life-sustaining therapies to be withheld preceding death.
- ◆ **Days Following Extubation**
We require a PV on the day of extubation, however we do NOT require any PVs to be reported following the day of extubation.

If a patient is discharged from the ICU before they have received a total of 5 days of study supplements, continue to report any PVs until the patient has received 5 days of study supplements.

Calories from Propofol



Are you including calories from propofol in your daily nutrition calculations?

Remember that if a patient receives at least 6 consecutive hours of propofol during a study day, the calories from propofol should be included in your daily calorie calculations.

Propofol = 1.1 kcal/mL

Contact the Project Leader if you have any questions regarding calculating daily nutrition.

Good Clinical Practices



Did you know that for each patient enrolled in the study you must document that the patient (or substitute-decision maker) granted consent prior to any study related procedures being conducted?

Reference ICH GCP 4.8.8.

Practically speaking this means the date & time of consent and the circumstances surrounding consent must be documented for each patient. This is most easily accomplished through an entry in the patient's medical chart including the following details:

- ◆ Date & time of consent discussions
- ◆ Patient/Substitute-Decision Makers (SDM) comprehension of the material reviewed
- ◆ Patient/SDM being given ample opportunity to review the ICF and decide whether or not to participate in the research
- ◆ Adequate time being given to answer all questions satisfactorily
- ◆ Date & time consent obtained

The Project Leaders will be looking for this documentation at site source verification visits to ensure your site is in compliance with the regulations!!!

Inclusion Criteria—Organ Failure: Hyperperfusion

Can I use dobutamine to meet the hyperperfusion inclusion criteria (2.ii)?

No, dobutamine can NOT be used to qualify a patient for the hyperperfusion criteria. However the following can be used to qualify a patient for the hyperperfusion criteria:

- ◆ Any dose of norepinephrine, epinephrine or vasopressin
- ◆ ≥ 5 mcg/kg/min of dopamine
- ◆ ≥ 50 mcg/min phenylephrine

Remember vasopressor agents must be administered for ≥ 2 hours.