



TACT Newsletter



NCCAM National Center for
Complementary and Alternative Medicine

July 2004



**Our congratulations to Site 234!
Dr. Rajiv Chandra, Terry Murphy
and Susan Hewitt from Tru Med
ED of Melbourne, Florida. They represent the
highest enrolling site, with 33 patients**

Message from the Principal Investigator – Gervasio A. Lamas, MD

We are happy to report that since our last quarterly Newsletter we have met our enrollment goals each month. Thanks to all of very your hard work, we currently have 281 patients enrolled in the trial, with 33 at Dr. Chandra's site alone!

As our enrollment increases, however, other problems become evident. Therefore, this Newsletter will focus on patient retention and compliance with the study regimen. Specifically, the Newsletter will address why patient retention is so important and discuss methods to maximize patient compliance. Having patients complete their infusions, maintain vitamin regimens, and continue for follow-up is essential for this trial.

It is likewise critically important that, when patients decide not to continue in the study, we understand the difference between refusal to continue treatment, and withdrawal of consent. Since we cannot collect any data on a patient that withdraws consent, it costs us dearly in terms of data acquisition and reduces our statistical power. If you can maintain a cordial relationship with the patient who is discontinuing therapy, then withdrawal of consent should be a very rare event, indeed.

We hope you will find this information useful. If you have any concerns about a patient and compliance with this trial please contact the Clinical Manager, Dr. Kayvan Amini. We will help you through the treatment options that will ensure maximum compliance.

Have a wonderful summer!

All things being EQOL...

The TACT Economics and Quality of Life team has identified the following items on the Baseline QOL Questionnaire that frequently trigger queries.

Bedrest and restricted activities:

Questions 8 and 9 of the Baseline QOL Questionnaire ask about the number of days patients stayed in bed and days restricted in their activities over the past 6 weeks: a maximum 42 days total. In calculating the number of days with restricted activities (Question 9), make sure to exclude the days the patient said he/she stayed in bed (Question 8) from the possible total. For example, if the patient stayed in bed for 12 days, there is up to a possible 30 days (42 minus 12) that the patient may have had restricted activities. The sum of days in bed plus days with restricted activities must be ≤ 42 . If the sum entered is greater than 42, you will have a Validation result attached to question 8.

Defining a patient's work status:

Work is defined as a **job for pay** in Question 25 because we are measuring the effects of the study treatments on economic work loss. Persons are considered working if they are paid employees (paid in wages, salary, commission or "in kind"). Volunteer work/activities or activities around the house should not be included as "work".

Get good descriptions of job duties:

Information provided in Questions 31 and 32 contribute to the coding of the patient's job class by the EQOL Coordinating Center. Be sure to obtain a **detailed, descriptive job title as well as job tasks, duties and activities**. A manager who "manages" or supervisor who "supervises" are not specific enough for EQOL to assign a job classification. A manager at a fast-food restaurant has very different responsibilities and activities than a construction site manager or nursing home manager. The type of industry in which the patient works can be helpful information. If you have any questions concerning EQOL issues, please contact Jason at 919-668-8640 or Diane at 919-668-8221.

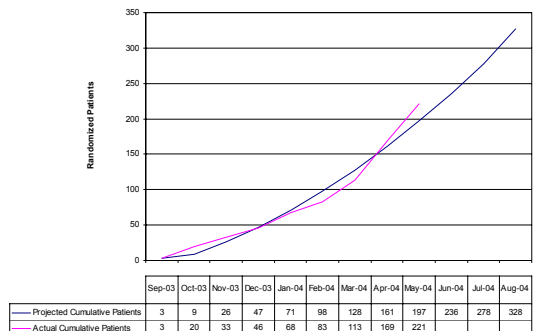
TACT Enrollment

234 Rajiv Chandra/ Terry Murphy 33

- 227 Sangeeta Shah/ Tracey Wilks 21
- 220 Steven Burkholz/ Dolly Corbin 19
- 312 Tammy Born/ Judy Schneider 14
- 239 Randy Hartman/Lynn King/Amy Heineman 14
- 406 Patrick Golden/ Kathy Sasser 13
- 113 Russell Silverman/ Sherri Loucks 12
- 115 Robert Weiss/ Diane Cass 10
- 232 John Griffin/ Terry Mellinger 7
- 112 Reed Snider/ Jean Provencher 7
- 326 Kenneth Ganapini/ Venus Barney 7
- 302 Greg Flaker/ Jamie Easley 7
- 212 Joseph O'Bryan/ Mary Barr 7
- 131 Terry Chappell/Marcia Arnold 7
- 407 Nampalli Vijay/ Melinda Washam 6
- 223 Roy Heilbron/ Celia Heilbron 6
- 249 Connie Ross/Michelle Simpson 6
- 228 James Carter/ Jodie Ledbetter 6
- 238 Lawrence Miller/ Deanna Overbeck 6
- 217 James Carter/ David Maddox 5
- 216 Ricky Schneider/ Amy Abreu 4
- 107 Allan Magaziner/ Betty Ann Persico 4
- 414 Terry Grossman/Kathryn Hurt 4
- 247 Pieter de Wet/Cynthia de Wet 3
- 242 Miguel Trevino/ Tracy Osborn 3
- 120 Majid Ail/ Boobullah Baig 3
- 110 Pamela Ouyang/ Melanie Herr 3
- 215 Shalendra Varma/ Sharon Collins 3
- 221 Robert Cicia-McLean/Pablo Guala 3
- 132 Ralph Miranda/Barbara Cassella 3
- 416 William Voss/ Lorna Gordon 3
- 415 George Wong/Brian Kilpatrick 2
- 122 Harmony Reynolds/ Karen Hager 2
- 327 Robert Randall/Teresa Kohle 2
- 226 Donald Tice/Celeste Altman 2
- 307 Robert Waters/ Karen Fernholz 2
- 140 James Garofalo/Kathleen O'Neill 2
- 208 Yamil Wady Aude/Paige Harrison 2
- 248 Gerald Wootan/Susan Shaw 2
- 128 Stuart Freedenfeld/ Nella Hamtil 2
- 251 Robert Wright/Alma Steffen 1
- 102 Narendra Bhalodkar/Amada Valeria 1
- 408 Herman Casdorff/ Kathy Hutsinger 1
- 237 Smart Idemudia/Eva Hubdy 1
- 108 Raymond Magorien/ JoAnn Homan 1
- 224 Angelique Hart/ Angelique Hart 1
- 206 Steven Borzak/Elizabeth Dagher 1
- 311 Varsha Rathod/Julie Mester 1
- 322 Eric Born / Julie Gonzalez 1

Total 281

TACT Enrollment, Actual and Projected, as of 1 June 2004 (First Year Only)



INFUSION TIMES

The minimum acceptable time for a TACT infusion is three hours. This rate (166 cc per hour) is designed to lower the risks of EDTA therapy. Patients should receive all of the infusion solution. Specific laboratory tests are incorporated into the study as well to ensure patient safety. In particular, renal and liver functions are being monitored, as well as hematological parameters. To maintain your patient's safety, follow the rate dictated by the protocol. A 'window' of plus/minus 15 minutes is considered during monitoring. Should you have any questions about the infusion rate, please contact your regional representative.





Intention to Treat

By **Kerry Lee, PhD, DCRI** Principal Investigator

As indicated in the study protocol, the primary treatment comparisons in TACT will be performed according to the principle of “intention to treat.” This is a well-established guiding principle in the conduct of modern clinical trials. The basic concept is that treatments are compared and endpoints attributed according to the treatment group to which patients are randomized, regardless of crossover, discontinuation of therapy, or subsequent events. That is, patient groups are compared as they were formed by randomization, regardless of what subsequently happens to the patients. This means that patients are not necessarily analyzed according to how they were actually treated, but how it was intended that they be treated. Thus, this approach is referred to as analysis by “intention to treat.”

The primary reason that the “intention to treat” approach has evolved is to minimize bias—the kind of bias that can enter into the treatment and management of patients, especially in an unblinded trial. In well-conducted clinical trials, it should be relatively rare that a patient receives a different treatment than the therapy to which they are randomized. Thus the “intention to treat” analysis is normally consistent with an “as-treated” analysis. However, there may be instances when investigators choose not to treat certain patients with the intervention assigned by randomization or patients may refuse the intervention after being randomized. Analyzing the patients in any way other than as randomized does not preserve the protection provided by randomization, and bias can be introduced. TACT will adhere to this important guiding principle in performing and reporting the primary assessments of the treatments being studied in this trial.

As an additional note related to this issue, it is important to remember that once patients sign informed consent and are randomized, they are included in the trial from that moment forward. Every effort should be made, therefore, to ensure that all patients receive the full course of infusions and vitamins outlined in the study protocol. If patients prematurely discontinue study therapies, it will diminish the ability of the study to determine the true effects of the therapies (i.e., any treatment benefits will be diminished and perhaps no longer be discernible). The study will be criticized by the clinical and scientific community if there is a high discontinuation rate or lack of complete follow-up of patients. Discontinuation of study therapy must be kept to an absolute minimum. If there are patients who insist on prematurely discontinuing the study infusions, they should continue to take the vitamins (high dose or placebo), and quarterly telephone follow-up and annual clinic visits should be maintained. If any patient prematurely discontinues both the chelation infusions and the high dose or placebo vitamin supplementation, they should also continue to be followed via telephone and clinic visits. Once patients are randomized, they remain in the trial and should be followed until either death or the end of the study.

Have a great summer!!

