Enrollment In ALS Research Studies: A Modifiable Barrier In Our Road Toward a Cure
Why No Cure For ALS Yet?

• We don’t know what causes most cases
• We don’t understand disease progression
• It takes a long time to make a diagnosis
• Our measurement tools are noisy and slow to change
• It is a rare disease with limited resources available for study

• Enrollment in ALS research studies is surprisingly low
Enrollment In ALS Studies Is Low

– Best available data suggest that less than 10% of PALS are enrolling in research studies

– Historically, studies are enrolling at a rate of about 2 patients per site per month (most sites see 50 or more patients in a month)
Why Is This Surprising?

• ALS is one of the most devastating diseases
• There is no markedly effective treatment for it
• Research offers the only path toward more effective future treatments
• Participation in research can provide positive feelings of hope, altruism
• Patients who participate in research studies may “do better” than patients who do not
Does It Matter?

• Huge problem! Poor enrollment means:
  – PALS are being deprived of the benefits of being in trials
  – Trials take longer, are more expensive, may be terminated without a definitive conclusion, may not be generalizable
  – Unless this can be solved, it will take longer than it should to find a cure for ALS
Can We Improve Enrollment?

There is tremendous variability in trial enrollment rate across previously published ALS studies (0.1-7.5 pts/site/mo); this suggests *modifiable factors that might influence enrollment*
Clues: Modeling

- Enrollment in ALS studies is **not** significantly influenced by “trial factors”
  - Primary outcome safety vs. efficacy
  - Intervention available outside trial (y/n)
  - Placebo (y/n)
  - Active to placebo ratio (1 or >1)
  - Invasive (y/n)
  - Geography (USA/outside)
  - Number of sites (single/multiple)
  - Sponsor (pharma/other)
  - FVC restriction (yes/no)
  - Strength restriction (yes/no)
  - Duration restriction (yes/no)
  - Medication restriction (yes/no)
  - Large phase 3 study (yes/no)
  - Publication year
Clues: Other Fields

• ALS is not the only field to experience this problem

• Best studied in cancer
  • Harris Poll of 5,980 cancer patients, 425 physicians
  • ASCO Survey of 3,550 oncologists
  • NCI sponsored focus groups of primary care doctors

• Less than 5% of North American cancer patients enroll in a study

• “Patient factors” and “doctor factors” may play important roles in cancer study enrollment
Patient Factors: Cancer Study Enrollment

- Lack of awareness (80%)
- Burden of travel
- Fear of unexpected costs
- Fear of “being a guinea pig”
- Perceived loss of control over decision making
- Possibility of not receiving “best possible care” especially with placebo designs
- Confusion about research process, specifics
- Choosing an alternative therapy
Doctor Factors: Cancer Study Enrollment

- Lack of awareness
- Concern for doctor-patient relationship
- Perceived loss of control
- Perceived increase in time and paperwork
- Doubts about protocols
Clues: ALS Surveys

• 2007 Veterans Registry, 2008 survey ALSRG, 2009 surveys of online PALS

• Less than 50% of PALS attend specialized multi-disciplinary ALS Clinics, where ALS studies are offered

• There is no good standardization across clinics in terms of how studies are presented
Clues: ALS Surveys

• Only half the PALS in online surveys said they had ever been asked to be in a research study. Most PALS said they would participate *if asked*; most who had participated said they were *never asked to participate again*.

• There is *confusion* among PALS about the research process
  – Concerned about hidden costs, and about things being done to them without their knowledge
  – Unclear as to need for design features such as placebo and need for new samples for each study

• Biggest reasons PALS decline trials
  – *Physical burden*
  – *Seeking an alternative therapy*
How Can You Help?

I WANT YOU
Lead By Example

- Come to multi-disciplinary ALS Clinics
- Enroll in open studies if you can
- Enroll in National ALS Registry and agree to be contacted about future research opportunities
Be Sure You Understand and Are Comfortable With Your Study Options

• Ask your *physician* about your research options
• Ask about things that confuse or trouble you before declining or signing consent
• If you still don’t feel comfortable ask if there are ancillary materials such as a video you can watch (ex. NEALS Ceftriaxone Study)
Be Sure You Understand Alternative and Off Label Treatment Options Before Pursuing Them

• Ask ALSUntangled: Uses social networking to systematically investigate alternative and off-label ALS treatment options (www.alsuntangled.org)
  • Input: twitter, email, clinics, new website
  • Discussion among experts: email
  • Results: Free access publications in the ALS Journal
Help Improve Awareness

- “Use What You Got” to attract attention to your cause
- Once you have their attention, tell your story
- Advertise importance of research and enrollment
- Speak at support groups, fundraisers
- Publish in patient-centric literature (Neurology Now) and write in patient-centric websites
- Attend National ALS Advocacy Days
Help Reduce Travel Burdens

• Identify underserved areas where ALS clinics are needed
  • Contact ALSA, MDA

• Encourage your nearest clinic to get involved with research studies
  • Join a trial consortium (ex. NEALS at 103 sites)

• Suggest ways researchers can make ALS trials more patient friendly, such as home based outcome measures
  • Use NEALS, ALSA, MDA websites
Become Patient Research Advocates

• PD, ALS Clinical Research Learning Institutes
• Modeled after successful programs in cancer
  – “Crash course” in research including ethics, informed consent, trial designs, statistics
  – “Crash course” in advocacy including tips on public speaking, writing letters to the editor, writing letters to congress, internet tools, meeting with the press and congress

To apply for next year’s program call (877) 458-0631 or email alstrials@partners.org
Conclusions

• Surprisingly small numbers of patients enroll in neurology research studies
• There are clues as to why this is happening
• You can help us improve enrollment

• The faster we enroll, the faster we finish our studies, the faster we get to a cure for this dreaded disease