Fighting for YOU: On the Frontlines of PSP Research

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• "I understand that one person in 100,000 suffers from the disease and I am also aware that there are 100,000 members of my union, the Screen Actors Guild, who are working every day."

• "I think, therefore, it is in some way considerate of me that I have taken on the disease for myself, thus protecting the remaining 99,999 members from this fate."

Dudley Moore, upon announcing his illness in 1999. He died from complications of PSP in 2002.
Hope through Research

- Earlier, more accurate diagnosis
- Understanding the cause of PSP
- Treatments for symptoms
- Efforts at slowing the disease
What are Clinical Trials?

• Research using human volunteers to answer specific disease questions or to test treatments. Can include both observational and interventional types.
  – *Observational* studies generally observe the natural course of the disease, to guide design of treatment trials.
  – *Interventional* trials investigate whether potential treatments are safe and effective.
PSP Observational Studies

- 4 Repeat Tau Imaging Initiative
- CURE PSP Brain Bank
- Genetic and Environmental Risk Factors for PSP
  - Patients were compared to their spouses as well as unaffected healthy people
Risk Factor Study Findings

• No definite links found with a specific chemical or occupational exposure
• Risk of PSP was associated with number of years spent drinking well water
Recent Genetic Discoveries from PSP Brain Donation

- Very rarely, patients have familial PSP (1q13.1, MAPT-17)
- Two copies of the “H1” tau gene are (nearly) necessary (90%) but far from sufficient for PSP (60% controls) to develop
- H1c sub-type confers further PSP risk (increased tau and bad “4 repeat” tau)
- Two copies of a European tau “H2” gene variant is protective

Recent Genetic Discoveries from PSP Brain Donation

- Recent studies suggested slight increases in risk from a few other genes.
  
  - Syntaxin-6, EIF2AK3, and MOBP
  
  - MOBP (myelin associated oligodendrocyte protein) linked to CBD and PSP
  
  - N-acetyltransferase 2 rapid acetylator phenotype is associated with PSP, suggesting it may be responsible for activation of a xenobiotic whose metabolite is neurotoxic


What goes wrong in PSP?

Tau aggregates in neurons and glia:
- a=NFT;
- b=tufted astrocyte;
- c=threads;
- d=coiled body
What is tau and how is it involved in PSP?

Stamelou et al Brain 2010
How PSP treatment may work

Stamelou et al. Brain 2010
Phases of Clinical Trials

• Pre-Clinical – testing in the lab, such as testing in mice or flies
• Phase I – small trials that test for safety usually in unaffected, healthy humans
• Phase II – small trials testing for safety and dosage-finding in those with the disease
Phases of Clinical Trials

• Phase III – trials testing for effectiveness in those with the disease, are often longer trials with larger numbers of volunteers

• Phase IV – AKA “post marketing studies” after drug has received approval. Provides additional information on risks, benefits, and optimal use.
Unsuccessful treatments

- Mitochondrial Enhancers
  - Coenzyme Q10
- Microtubule stabilizer
  - Davunetide
- Anti-aggregation therapies
  - Lithium
  - Valproic acid
  - Tideglusib
New Treatments in Studies

• “Anti-aging”
  – Young plasma infusions

• Anti-Aggregation
  – Salsalate (block tau-acetylation)

• Anti-Tau Therapies
  – ABBV-8E12
  – BMS-986168
Anti-Tau Therapies

• Tau is a protein normally found in brain cells
• Tau is thought to play a role in causing PSP, especially when it leaks outside of cells (a.k.a. extracellular tau, or e-tau)
• BMS-986168 is an antibody that binds to, and reduces, eTau.
Anti-Tau Therapies

• In a Phase 1 single ascending (increasing) dose study in normal healthy volunteers, BMS-986168 was well tolerated, with no safety issues identified.

• This study demonstrated that BMS-986168 reduces eTau in cerebrospinal fluid. These data support further study of BMS-986168 in patients with PSP. ¹

Anti-Tau Therapies

• An ongoing study (CN002-003) is evaluating the safety, tolerability, pharmacokinetics (the study of the movement of the drug in your body), and pharmacodynamics (the study of drug effects on your body) of multiple ascending doses with intravenous infusions (a solution administered into a vein) of BMS-986168 in patients with PSP. This study is taking place in the US, but is now closed for enrollment.
Anti-Tau Therapies

• However, a study that will take place in various countries will soon be recruiting.
• Bristol-Myers Squibb is planning a global, randomized (participants are assigned at random, by chance alone), double-blind (neither the participants nor the study team know who is getting the study drug versus inactive placebo), placebo-controlled (a method of research in which an inactive substance, a placebo, is given to one group of participants, while the investigational drug being tested is given to another group) study in PSP, CN002-012 that is projected to start in 2017.
Anti-Tau Therapies

– The duration of the double-blind period of the study, when your doctor nor you will know whether you are taking the active, investigational drug or inactive placebo (2:1 chance of receiving the active BMS- 986168), is 52 weeks.

– An open-label period, when active study drug is given to all participants, will continue in a long-term follow-on phase.

– Similar to CN002-003 and other PSP studies, the study will plan to enroll patients with PSP who are still able to walk.
Anti-Tau Therapies

– Home visits and travel support may be available for patients in this study.
– Bristol-Myers Squibb is currently investigating possible study site options in the US, and further country selection will be finalized over the next few months. You can subscribe to receive study updates by visiting BMSStudyConnect.com.
Why Participate in Clinical Trials?

• To meet regularly with PSP experts.

• To help others by contributing to medical research and treatment advances, though there may be no direct benefit to you.

• To provide hope to yourself and others.
How to be an Educated Consumer

• What are the credentials of the author (Is the journalist trained in the field, interviewing someone who is?)
• What are the financial ties, other sources of bias, of researcher
• What does your doctor or support group medical adviser think of the results?
How to get involved

• Search www.clinicaltrials.gov

• Go to the website listing active trials at local academic centers
  – www.bannershri.com
  – www.barrowneuro.org
  – http://www.mayoclinic.org/
  – https://neurosciences.ucsd.edu
    • Closest PSP observational research program

• Brain Donation: www.cure PSP.org
Summary

• PSP is not easy to diagnose
• The cause is still poorly understood
• We need better treatments for symptoms and to slow down this illness
• Treatments being developed today are more likely to succeed because of the contributions of patients and their families