Trial in Progress: TuberOus SClerosis Registry to IncreAse Disease Awareness (TOSCA)

*Carla Fladrowski on behalf of TOSCA Consortium*

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Who is Carla?

- Mother of Leo and Jake
- Wife of Stefano
- Devoted Daughter

From 2010 onwards: As above +

- Responsible for International Relations within the Italian Tuberous Sclerosis Complex Association
- Co President, European Tuberous Sclerosis Complex Association (E-TSC)
- Working Group member, Tuberous Sclerosis Complex International (TSCi)
- Point person for European TSC associations in EU disease registry in collaboration with Novartis
- Member of TOSCA Working Committee and Scientific Advisory Board
Tuberous Sclerosis Complex (TSC)

- Genetic disorder that affects children and adults
- Multiple benign tumors throughout the body
  - Mutations of TSC1 or TSC2, resulting in constitutive mTOR activation, are found in 80%-85% of patients with TSC
- With an estimated prevalence of 1-2 million people worldwide and an estimated incidence of 1:6000 live births, it is a rare disease

TSC: A Multi-organ Disease

Brain
- Cortical tubers
- SEGs
- SEGAs
- Seizures
- TSC-Associated Neuropsychiatric Disorders (TAND)

Eye
- Retinal hamartoma

Kidney
- Angiomyolipoma
- Renal cysts
- Polycystic kidney disease

Heart
- Cardiac rhabdomyomas

Lungs
- LAM

Skin
- Hypomelanotic macules
- Shagreen patches


LAM=lymphangioleiomyomatosis; SEG=subependymal giant cell astrocytoma; SEN=subependymal nodule.
The Gaps in Understanding TSC

- Variability of manifestations
- Rare signs and symptoms
- Concomitant diseases
- Surgery, treatments and their outcomes
- Quality of life
Why the need of a registry?

• Round table discussions organized by Novartis
  – European experts in TSC and patient representatives evaluated the need for a TSC registry in Europe

• Surveys
  – Surveys conducted in Europe in 2010 demonstrated that a national TSC registry did not exist in most of the European countries

• There was a clear consensus to establish an European registry to address some of the gaps in understanding TSC by collecting data from patients across Europe

• Collaborative working with an academic steering committee and a pharmaceutical company was to be a key component of the registry

• Some non-European countries also expressed their desire to join the registry at a later stage
TuberOus SClerosis registry to increAse disease awareness (TOSCA)

- A multicenter, international disease registry
- Designed to collect data from patients with TSC across many countries worldwide
- Aims to address the gaps in understanding the clinical course of TSC and the therapeutic outcomes
TOSCA: Registry Design

In addition, TOSCA Post-Authorization Safety Study (PASS), a drug safety sub-study is designed to provide data for the European Medicines Agency to assess the long-term safety and tolerability profile of everolimus in the treatment of TSC patients residing in the European Union, for the approved indications.
TOSCA: Participation

- It is estimated that ~2000 patients will be enrolled from about 250 sites across more than 30 countries worldwide
  - TOSCA PASS, the safety sub-study, will enroll ~150 patients from about 100 sites in 15 countries
- The initial enrollment period is anticipated to be approximately 24 months with a follow-up observation period of up to 5 years
- More than 750 patients in 17 countries worldwide have already accepted to participate in TOSCA as of September 2013
- The first patient was entered in the registry in August 2012
TOSCA: Registry Organization

- Novartis Oncology Region Europe
- Patient Representatives
- TSC Experts in Participating Countries

Scientific Advisory Board

Working Committee

- Research Group
- Research Group
- Research Group
- Research Group
TOSCA: Countries involved

Europe:
Austria, Belgium, Czech Republic, Denmark, Estonia, France, Germany, Greece, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom

Australasia:
Australia

Asia:
China, Israel, Korea, Taiwan, Thailand, Turkey

Eurasia:
Russia

Africa:
South Africa
E-TSC experience in TOSCA

I believe in total “patient experience” and that interaction with all health care providers and relative agencies is paramount.

Why is a database so necessary?

• E-TSC has always felt that data collection is fundamental and should come before anything else
• To date, quality information collected across the nation is severely lacking and problems encountered and similarities in cases may not be accessed and compared
• By incorporating patients with TSC across the EU, knowledge and surveillance on a rare disease and orphan drugs will be increased, outcomes will be registered, and the effectiveness of treatment will be assessed
• This registry could provide the healthcare professionals with an excellent instrument for research
• Participants of TOSCA remain the owners of their information but this information clearly needs to be processed by the medical community
TOSCA: A petal dedicated to patients

- A separate petal dedicated explicitly to the needs and requests of those affected has been in the registry design right from the beginning and is now under construction.

- This was initially one of the conditions of E-TSC to participate with Novartis in the creation of this registry and at a later point also strongly recommended by both members of the Working Committee and Novartis.

- Various TSC patient communities have contributed to this petal by offering ideas on what they feel is missing regarding certain aspects of the disease to ensure that the petal is true to life.

- To create a TSC socio-economics specific questionnaire for the patients/family

- To evaluate the impact of the disease in the real life of the involved families

- To measure the quality of life of TSC patients using validated questionnaires
A special thanks to:

A very special thanks to all those affected with TSC who have kindly given me their support and input into creating the patient petal and also importantly for giving permission to use their data for the Registry. Without this contribution and their consent the Registry would not have come to life.

Members of TSC Europe for entrusting me with such an important role. Members of TOSCA Working Committee and SAB alike for giving me such genuine support and encouragement and Novartis for making this actually happen.
"A map of the World that does not include Utopia is not even worth glancing at, for it leaves out the one country that Humanity is always landing. And when Humanity lands there, it looks out and sets sail, progress is the realisation of Utopia".
(The Soul of Man under Socialism - Oscar Wilde 1891)