The importance of timely diagnosis and effective treatment

Inadequate seizure control can lead to worsening prognosis

- There are 6 FDA-approved AEDs for the treatment of LGS, but 80% to 90% of patients continue to have seizures throughout their lives.\(^1,3\)
- The frequency and severity of seizures can impact the level of cognitive impairment patients experience.\(^1,4,5\)

Careful selection of treatment is needed for better cognitive outcomes and overall improved prognosis.\(^1,4,5\)

The classic description of LGS focuses on typical clinical features\(^1,3\)

- Multiple seizure types: LGS involves a variety of seizure types including tonic and atypical absence; drop seizures occur in at least 50% of patients.\(^1,2,4,5\)

Cognitive impairment

- Many patients with LGS have significant cognitive impairment.\(^1,10\)

Slow spike-wave EEG

- A distinct EEG pattern is the third characteristic feature of LGS for most patients.\(^1,3\)

LGS presentation, however, is variable and not all patients display all components of the classic triad at onset.\(^1,3\)

- Patients with LGS may present with a wide range of characteristics that mimic other epilepsies such as Dravet syndrome, Doose syndrome, and focal cryptogenic epilepsy.\(^1,3\)

LGS signs and symptoms change over time.\(^1,2\)

Understanding the variability in LGS presentation, between individuals and over time, helps ensure accurate diagnosis and effective management.\(^1,2\)

This information is brought to you by Greenwich Biosciences. For more information about Greenwich Biosciences, visit GreenwichBiosciences.com.

©2017, Greenwich Biosciences, Inc.

For more information, visit www.greenwichbiosciences.com.
LGS background and challenges

LGS leads to cognitive and physical impairments that have a significant impact on patients and caregivers. While the heterogeneous clinical presentation of LGS makes it a challenge to recognize, early diagnosis is vital, as appropriate treatment may affect disease course and improve quality of life. It is also important to evaluate adult patients with LGS-like symptoms who may not have been accurately diagnosed earlier.

Onset
Peak onset of LGS is between 3 and 5 years of age, with symptoms typically emerging between 2 and 8 years of age. LGS symptoms persist into adulthood, with 80% to 90% of patients continuing to have seizures.

Prevalence
Up to 4% of children with epilepsy are diagnosed with LGS.

Etiology
70% to 80% of LGS patients have an identifiable cause for their syndrome.

Brain abnormalities play a major role in precipitating LGS.

LGS may be preceded by infantile epilepsy conditions, such as West syndrome.

Research is currently being done to identify genes associated with LGS.

Currently no biomarker
LGS has no consistent genetic variant or biomarker that confirms a diagnosis.

Changes over time and continued evaluation of patients and their symptoms are important to optimize diagnosis.

Signs and symptoms of LGS change as patients age

**Young children/Onset**
- Most commonly generalized tonic, atonic, and atypical absence
- Tonic seizures during sleep
- Seizures occur several times per week with most patients experiencing daily seizures
- Behavioral problems are also often present
- EEG pattern of slow spike-wave complexes

**Adolescents/Adults**
- Generalized tonic-clonic, atonic, and atypical absence seizures continue
- Tonic seizures may or may not be seen during wakefulness
- Tonic seizures are present during sleep and may become the most distinctive seizure type
- Change in seizure frequency and fewer daytime seizures in some patients
- Increase in drop attacks leading to injuries in some patients

**Cognitive impairment**
- Cognitive impairments may become more noticeable at later ages
- Significantly impaired IQ relative to peers: 75% to 95% have cognitive impairments 5 years from onset
- Behavioral problems such as hyperactivity, aggression, and autistic traits are seen in 50% of patients with LGS
- Some patients begin exhibiting symptoms of psychosis

**Seizures**
- Most patients exhibit cognitive impairment in early childhood, but up to 1/3 of children with LGS may show normal functioning prior to or at the time of seizure onset
- Behavioral problems are also often present
- EEG pattern of slow spike-wave complexes

**EEG**
- Cognitive functioning over time correlates with the severity and frequency of seizures
- The changing presentation of LGS in adulthood may reflect a combination of factors, including:
  - Long-term effects of antiepileptic drugs (AEDs)
  - Long-term effects of recurrent seizures on brain function
  - Neurologic maturation
  - Impact of puberty and physical maturation
- Decrease in or disappearance of slow spike-wave complexes

Over time, neurologic deficits such as spastic paraparesis and quadriplegia, hemiparesis, generalized hypotonia, and extrapyramidal features may become more apparent, as do gait deterioration and dysphagia.
- Lifelong functional impairment is seen in patients with LGS; the majority rely on caregivers
- Social and language features falling within the autism spectrum are commonly seen
- As patients move into adulthood, management may involve support from other disciplines including physiotherapists, occupational therapists, and psychiatrists

Timely management of seizures is critical to a patient’s neurologic development and long-term risk for disability and mortality.