**Biogen Extant Study- Data Required (ALL QUESTIONS)**

Note that if any of data described below is sent to Dublin in more than one file per site, site researchers should include an ID code allowing us to link the patients in one file to those in another.

* Core clinical data for as many patients at each site as is available
* age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
  + all ALSFRS assessments available including all subscores
* Endpoint data
  + Vital status, if deceased- date of death
  + NIV usage >/= 23Hrs/day- if so, date reached
  + Invasive ventilation/Tracheotomy status- if invasively ventilated- date of ventilation]
  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.
* Ambulation/mobility, feeding e.g. gastrostomy/date of gastrostomy, and respiratory support data, e.g. NIV status and usage, other respiratory supports including breath stacking, cough assist, etc., on as many patients at each site as possible
* Prescribed drugs/Treatments including Riluzole use data, Edaravone use data, any data available on other symptomatic treatments
* All available data on respiratory function, e.g. FVC, SVC, SNIP, PCF
* All available data on hospitalizations
* All available data on other health resource utilization
* All available data on working status (e.g., currently working, those who have reduced work, etc.), autonomy index & level of assistance from caregivers

**Biogen Extant Study- Data Required by Question**

**Question 1**

*To determine the frequency of ALS patients in European registers with known gene variants (SOD1, C9orf72, FUS, TARDBP)*

* 1. *Characterize the population (overall and genetic subsets) by fast/non-fast progression and determine the known factors that contribute to disease progression.*
  2. *Characterize the population (overall and genetic subsets) by disease severity (as defined by use of ambulation, feeding or respiratory support), clinical staging (based on ALSFRS-R, King’s and MiToS staging), and region of disease onset (e.g., limb vs bulbar)*

Data required;

* Core clinical data for as many patients at each site as is available
  + age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
  + all ALSFRS assessments available including all subscores
* Endpoint data
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  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.
* Ambulation/mobility, feeding e.g. gastrostomy/date of gastrostomy, and respiratory support data, e.g. NIV status and usage, other respiratory supports including breath stacking, cough assist, etc., on as many patients at each site as possible

**Question 2**

*Estimate the mean and median 3-month and annual rates of decline in ALSFRS-R in specified years of follow-up since diagnosis and mean and median rate of decline based on 3-month time frames (length of follow up to be informed by data availability)*

* 1. *Perform additional analyses to clarify the range of rates of decline*
  2. *Perform analyses of the overall population and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets.*
  3. *Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset)*
  4. *Joint analyses of ALSFRS and survival*

Data required;

* Core clinical data for as many patients at each site as is available
  + age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
  + all ALSFRS assessments available including all subscores
* Endpoint data
  + Vital status, if deceased- date of death
  + NIV usage >/= 23Hrs/day- if so, date reached
  + Invasive ventilation/Tracheotomy status- if invasively ventilated- date of ventilation]
  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.

**Question 3**

*Conduct time-to-event (Kaplan-Meier) analyses from symptom onset or diagnosis to (a) use of ambulation support such as cane or wheelchair, (b) non-invasive ventilation, (c) invasive ventilation, (d) use of tube feeding (e) each King’s and MiToS stage, (f) death (specific milestones to be informed by data availability)*

* 1. *Analysis to be performed on the overall population and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets.*
  2. *Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset)*

Data required*;*

* Core clinical data for as many patients at each site as is available
  + age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
  + all ALSFRS assessments available including all subscores
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  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.
* Ambulation/mobility, feeding e.g. gastrostomy/date of gastrostomy, and respiratory support data, e.g. NIV status and usage, other respiratory supports including breath stacking, cough assist, etc., on as many patients at each site as possible

**Question 4**

*Estimate the proportion of patients treated with Riluzole (and edaravone, if data available); ever treated and current treatment. Estimate the proportion of patients treated with various symptomatic therapies. Include stratifications by stage of disease (King’s and MiToS).*

* + *Conduct overall and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets. Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset)*

Data required;

* Core clinical data for as many patients at each site as is available
  + age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
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  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.
* Prescribed drugs/Treatments including Riluzole use data, Edaravone use data, any data available on other symptomatic treatments

**Question 5**

*Potentially estimate: (based on data availability)*

* 1. *The mean and median 3-month and annual rate of decline in a measure of respiratory function* 
     1. *Conduct overall and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets. Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset). Include stratifications by stage of disease (King’s and MiToS).*
  2. *Where data is available, provide rates of hospitalization, overall as well as in the SOD1, C9orf72 and GT-negative sub-populations: mean and median 3-month and annual number of hospitalizations*
     1. *Conduct overall and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets. Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset). Include stratifications by stage of disease (King’s and MiToS).*
  3. *Other health resource utilization*
     1. *Conduct overall and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets. Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset). Include stratifications by stage of disease (King’s and MiToS).*

Data required;

* Core clinical data for as many patients at each site as is available
* age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
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  + If still alive and none of the other endpoints have been reached- last date of follow up
* All genetic testing status data on SOD1, C9orf72, FUS, TARDBP, as available, for each site.
* All available data on hospitalizations
* All available data on other health resource utilization
* All available data on respiratory function, e.g. FVC, SVC, SNIP, PCF

**Question 6**

*Where data is available, provide current working status (e.g., % currently working, % who have reduced work, etc.), autonomy index & level of assistance from caregivers*

* 1. *Conduct overall and by genetic (SOD1, C9orf72, FUS and TARDBP) subsets. Stratify analyses by fast/non-fast progressor (overall and within a given genetic subset). Include stratifications by stage of disease (King’s and MiToS).*

Data required;

* Core clinical data for as many patients at each site as is available
* age/date of birth
  + sex of patient
  + site/region of onset
  + date of/age at onset
  + date of/age at diagnosis
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* All available data on working status (e.g., currently working, those who have reduced work, etc.), autonomy index & level of assistance from caregivers