



Designing Trials to Reduce Patient and Site Burden

Jenny Higley, Director, Feasibility Center of Excellence
April 2024

Confidential and Proprietary



Designing Trials to Reduce Patient and Site Burden

How to create a patient-centric clinical protocol to obtain the necessary data and validate your primary objective

The importance of developing/applying tools and managing different stakeholders to pressure test our plans to have less complicated protocols

The importance of creating a collaborative relationship with sites during protocol development targeting reducing patient burden



What does it mean to create a patient-centric protocol?

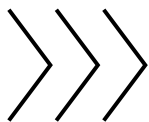
Designing a study that **prioritizes the well-being and convenience of the patients** while ensuring the collection of accurate and relevant data to validate the primary objective

Kyle, living with
Friederich's ataxia

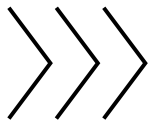
Patient-Centric Approach to Protocol Design

4

Biogen is in the process of implementing new capabilities to enable protocol simplification and reduce patient burden



Developing protocols from with authoring tools that enable measurement of complexity and patient burden from initial draft



Pressure testing draft protocols throughout the study design and planning process



7 of 13 Feasibility groups that are part of the ZS Consortium are now doing protocol analytics in addition to 'traditional' feasibility work



All of the Feasibility groups doing protocol analytics are using their own **in-house designed systems and tools**



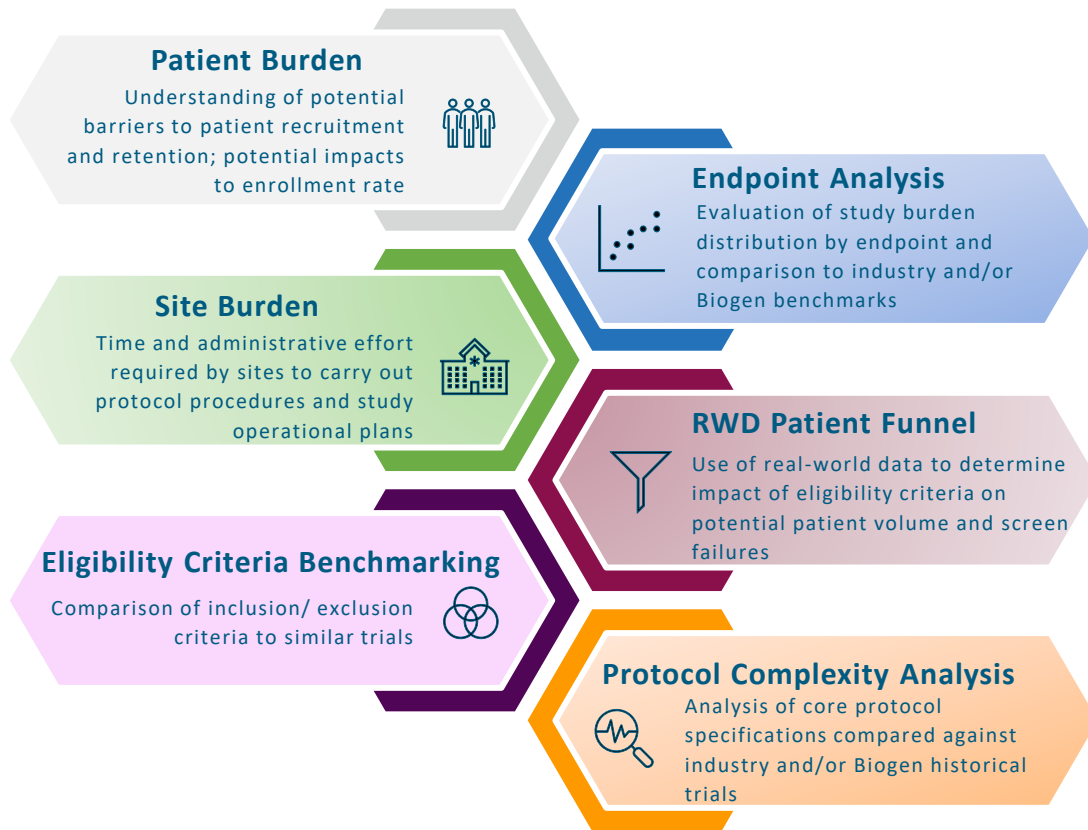
Clinical Feasibility Consortium



Pressure Testing Protocols to Reduce Complexity

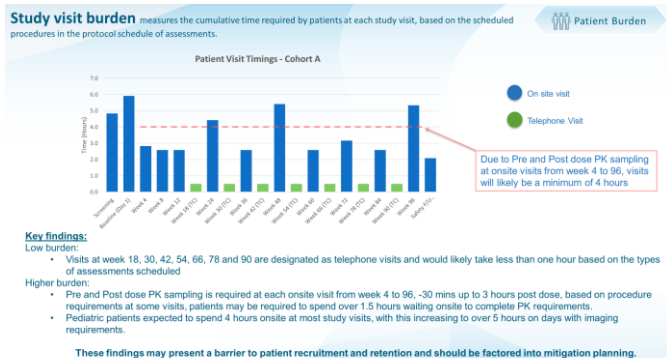
Protocol Feasibility Analysis

Each protocol is evaluated using a combination of a Biogen-developed “Protocol Assessment Tool,” benchmarking of similar studies, patient insights published industry protocol complexity metrics.



Protocol Feasibility Assessment Output

A comprehensive report details the 8 core PFA components



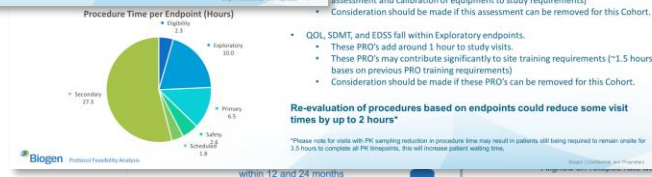
Biogen Protocol Feasibility Analysis

Item	Impact (Considered, not Prioritized)	Score
IMP Dosing Regime		
Discontinue current treatment	High	3
Percent of visits with blood draw	High	3
Invasive procedure: LP, biopsy, colonoscopy, endoscopy	High	3
Caregiver requirements	High	3
Imaging requirements: MRI, X-ray, PET, etc.	Medium	3
Overall Score		3.3

Key findings:

- The total treatment length for this study is 24 months, with 20 visits spanning that timeframe.
- Previous pediatric MS focus group highlighted patient and caregiver concerns with studies over 2 years in length and 15 onsite visits due to school and work commitments.
- Most visits are in-clinic and require over 4 hours to complete, with an imaging procedure and blood draw being required. These visit lengths and procedure requirements may add additional levels of burden and complexity for this pediatric population.
- A caregiver will be required for all patients participating, long study visits may prove to be a barrier to this working population.

These findings may present a high potential barrier to patient recruitment and retention. Study team should develop recruitment strategies to address this risk and should factor this into enrollment rate projections.



Aligned with industry on minimum age of 10 years for a paediatric MS trial

Majority of medicine exclusion align across industry i.e. Fingolimod, Immunomodulators, Natalizumab, Corticosteroids etc.

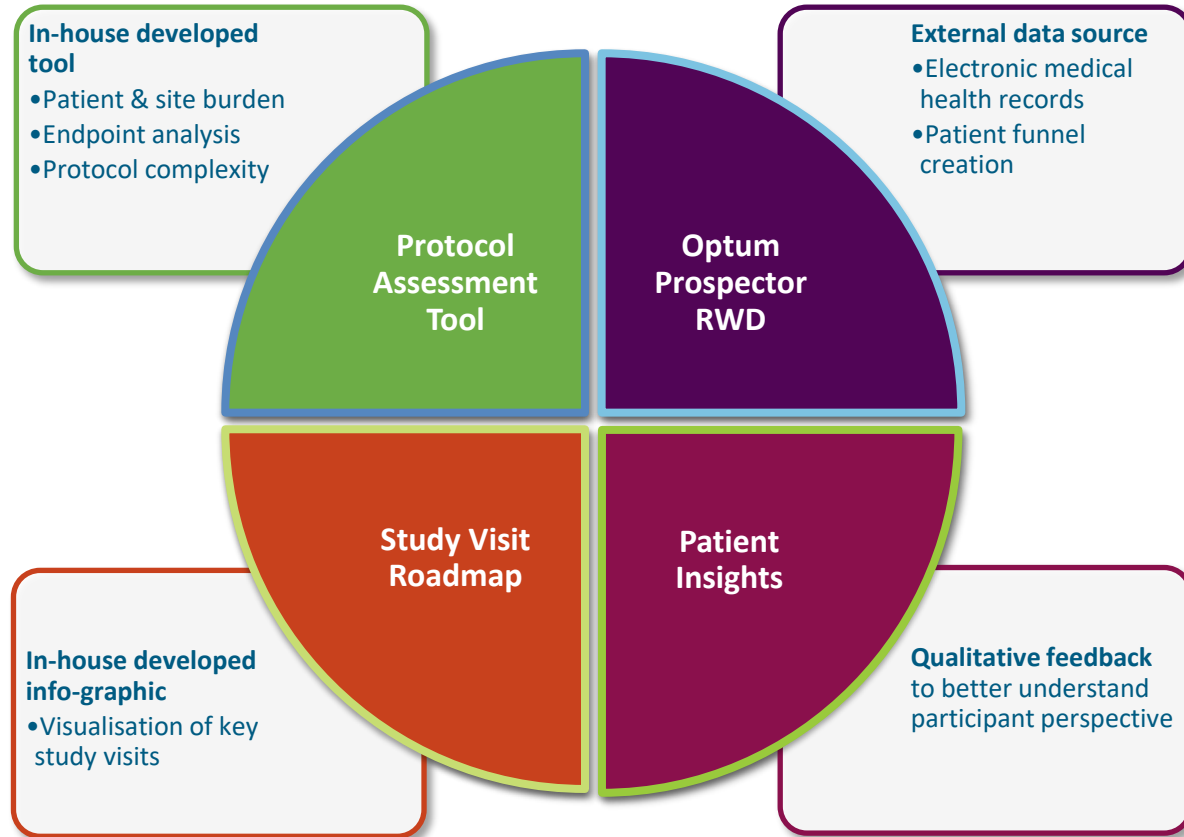
Industry studies measure cognitive function as secondary endpoints

MRI is a primary endpoint for one industry study but aligned as secondary with others

Growth and development endpoints not included in other industry trials

Aligned on most study design factors. Those highlighted in Green show variance from our current study design to that of industry studies.

Tools, technology, and data sources



Patient burden analysis

Evaluates 3 key areas:

- Study visit burden
- Study design burden
- Insights from patients

Study design burden – Cohort A evaluates 12 major categories of protocol design and estimates the potential impact on patients within a given indication. Once areas of higher burden are identified, study teams can develop mitigation plans around any potential risks the burden may present to patient recruitment and retention.

Study Design Factor		Burden Ranking	Burden Score
Number of visits	13*	Medium	3
Visits per month	0.54	Medium	3
Visit type	Solely Outpatient and/or Homebased	Low	1
Number of forms (PROs)	5	Medium-Low	2
Chance of patient receiving placebo	0%	Low	1
Route of study drug administration		Low	1
IMP Dosing Regime		Medium	3
Discontinue current treatment		High	5
Percent of visits with blood draw		High	5
Invasive procedure; LP, biopsy, colonoscopy, endoscopy		None	0
Caregiver requirements		High	5
Imaging requirements: MRI, X-Ray, PET, etc.	Imaging multiple times per study/ year - above SOC requirements	Medium	3
Overall Score			32

*excluding telephone visits

Key findings:

- The total treatment length for this study is 24 months, with 20 visits spanning that timeframe.
 - Previous pediatric MS focus group highlighted patient and caregiver concerns with studies over 2 years in length and 15 onsite visits due to school and work commitments.
 - Most visits are in-clinic and require over 4 hours to complete, with an imaging procedure and blood draw being required. These visit lengths and procedure requirements may add additional levels of burden and complexity for this pediatric population.
- A caregiver will be required for all patients participating, long study visits may prove to be a barrier to this working population.

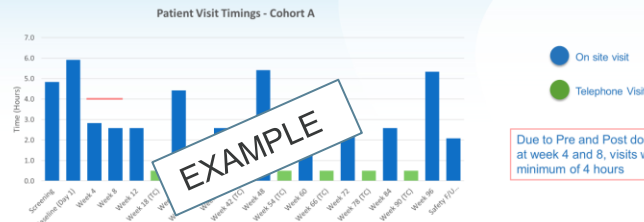
These findings may present a high potential barrier to patient recruitment and retention. Study team should develop recruitment strategies to address this risk and should factor this into enrollment rate projections.

Biogen Protocol Feasibility Analysis

Patient Burden

Study visit burden – Cohort A measures the cumulative time required by patients at each study visit, based on the scheduled procedures in the protocol schedule of assessments.

Patient Burden



Key findings:

Low burden:

- Visits at week 18, 30, 42, 54, 66, 78 and 90 are designated as telephone visits and would likely take less than one hour based on the types of assessments scheduled

Higher burden:

- Pre and Post dose PK sampling is required at Baseline, week 4 and 8, ~30 mins up to 3 hours post dose, based on procedure requirements at some visits, patients may be required to spend ~1.5 hours waiting onsite to complete PK requirements.
- Pediatric patients expected to spend 4 hours onsite at most study visits, with this increasing to over 5 hours on days with imaging requirements.

These findings may present a barrier to patient recruitment and retention and should be factored into mitigation planning.

Biogen Protocol Feasibility Analysis

Biogen | Confidential and Proprietary



“Is it possible to decrease burden on patients and sites?”



“Is there an opportunity to reduce visit frequency?”



“Can we reduce lengthy/ burdensome procedures?”

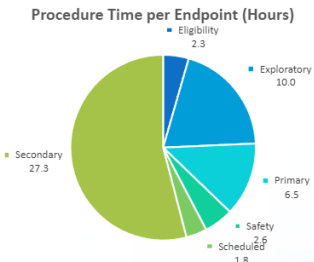
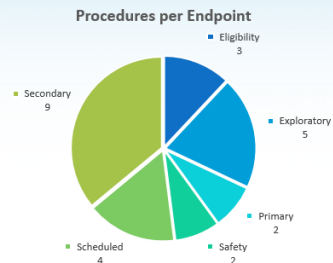


“Can we mitigate burden through recruitment and retention strategies?”

Endpoint analysis

[illegible]

- Distribution of procedures per endpoint type
- Proportion of study time by endpoint type



73.8% of the total study time (37.3 Hours) is dedicated to Secondary and Exploratory endpoints

- Large proportion of endpoints fall within the Secondary category
 - PK sampling, adds 3.5 hours to visit time
 - X-ray adds 30 mins to visit time for patients and 1 hour for sites
 - Consideration if required at all planned visit or reduced frequency can still achieve secondary endpoint.
 - i.e., does last PK dose need to be 3 hours post dose or can this be reduced
 - MRI requirement falls within Exploratory category.
 - MRI adds 45 mins to patient visit time and 1 hour 15 mins for sites
 - MRI requirements add up to 7 hours to training requirements (including assessments of equipment to study requirements)
 - Consideration should be made if this assessment can be removed for this Cohort.
- EXAMPLE**
- PRO's that fall within Exploratory endpoints.
 - PRO's add around 1 hour to study visits.
 - These PRO's may contribute significantly to site training requirements (~1.5 hours bases on previous PRO training requirements)
 - Consideration should be made if these PRO's can be removed for this Cohort.

Re-evaluation of procedures based on endpoints could reduce some visit times by up to 2 hours*

*Please note for visits with PK sampling reduction in procedure time may result in patients still being required to remain onsite for 3.5 hours to complete all PK timepoints. this will increase patient waiting time.

EXAMPLE

?

Is there a relatively high number of exploratory endpoints?

?

Is a large amount of time spent on exploratory endpoints?

?

Can activities and procedures be re-evaluated to focus more on primary endpoints?

Collaboration with Sites in Study Design

Site burden analysis

Evaluates 3 key areas:

- Site training requirements
- Study visit burden
- Study design burden



“Are there ways we can decrease burden on sites?”



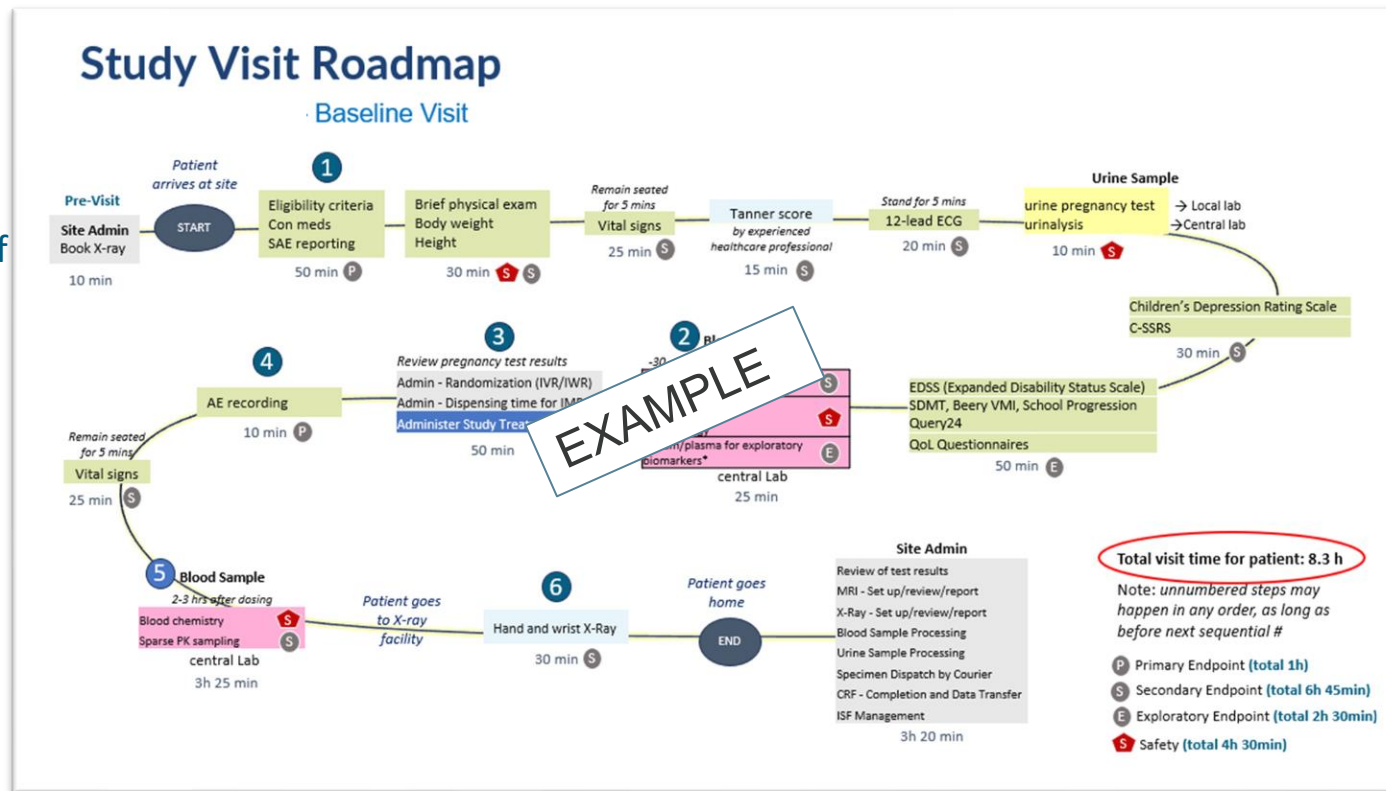
“Can we reduce training requirements for sites?”



“Does the protocol design require a large number of vendors?”

Study visit roadmap

- Step-by-step visualization of burden per visit:
 - Patient
 - Site
 - Study design
- Developed for key study visits





**For additional information or questions contact:
jenny.higley@biogen.com**

