



The NEXT Generation of Neurologic Treatments
NIH-Network for Excellence in Neuroscience Clinical Trials

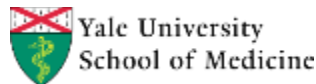


**Recruitment Strategies Implemented in the
“B Cell Targeted Treatment in Myasthenia Gravis (BeatMG)” Trial:
Understanding the Approach to Successful Recruitment for a Rare
Disease Population Utilizing a Clinical Trial Network**

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Montreal

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NeuroNEXT

- The NeuroNEXT: Network funded by NINDS
- Network consists of:
 - The Clinical Coordinating Center (CCC) at Massachusetts General Hospital
 - The Data Coordinating Center (DCC) at the University of Iowa
 - 25 Clinical Study Sites (CSS) across the US
 - Approximately 60 institutions part of the Network
 - BeatMG Study: Yale University (PPI Institution)

Myasthenia Gravis Overview

- Myasthenia Gravis (MG): rare, chronic autoimmune neuromuscular disease
 - Annual incidence: about 1-2 per 100,000
 - Prevalence: as high as 20-50 per 100,000
 - Affects approximately 75,000 individuals in the US
 - Causes muscle weakness
 - MG can occur at any age, gender, ethnicity

Myasthenia Gravis Overview (cont.)

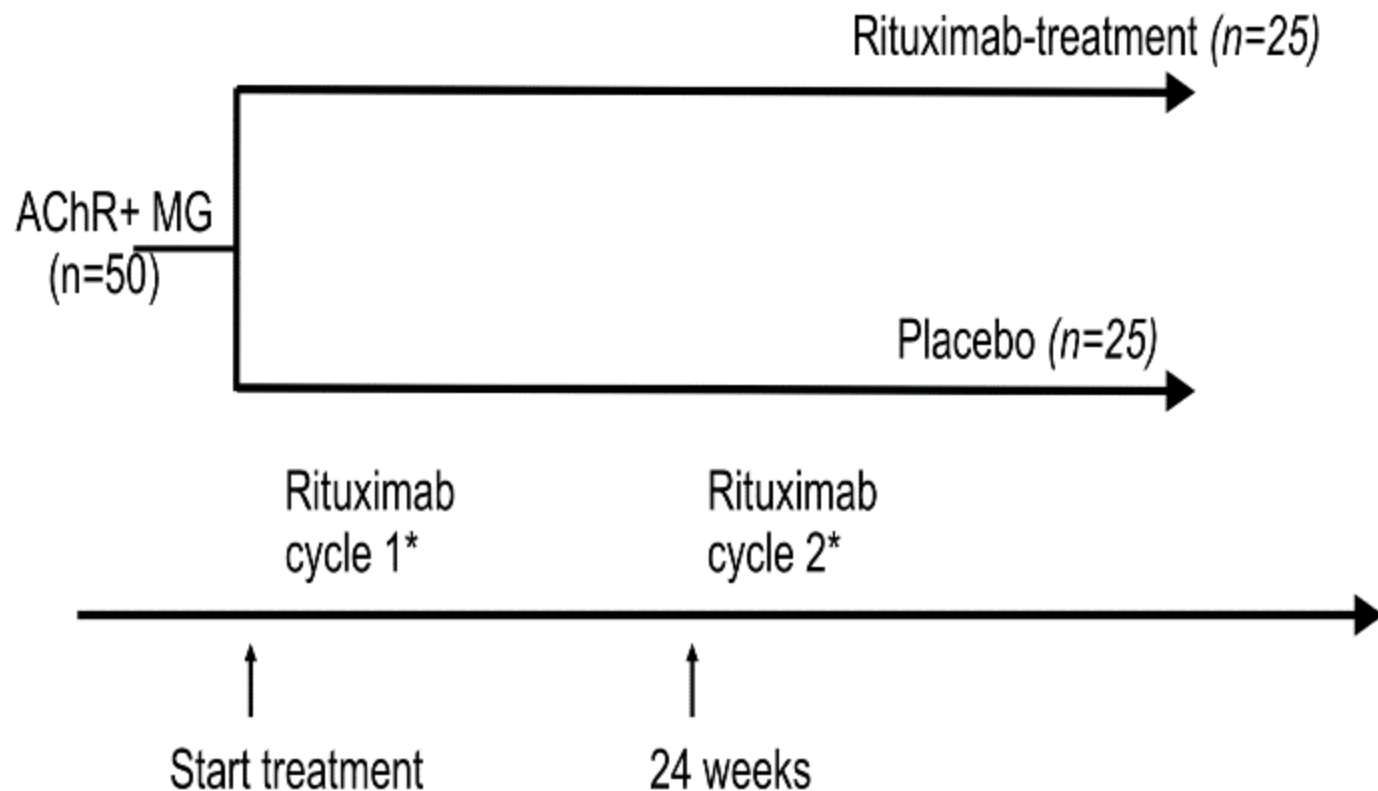
- There is no known cure for MG
- Steroids (i.e. prednisone) continue to be the gold standard treatment
 - People with MG often require treatment with steroids for many years
 - Prednisone has many unwanted side effects

BeatMG Study: Overview

- The specific primary objective of this study is to determine whether rituximab is a safe and beneficial therapeutic for MG that warrants further study in a phase 3 efficacy trial.
- n=50, generalized AChR antibody positive (AChR+) myasthenia gravis (MG)
- Subjects on prednisone or prednisone + another immunosuppressive therapy (IST)
- Primary outcomes: steroid sparing effect and safety

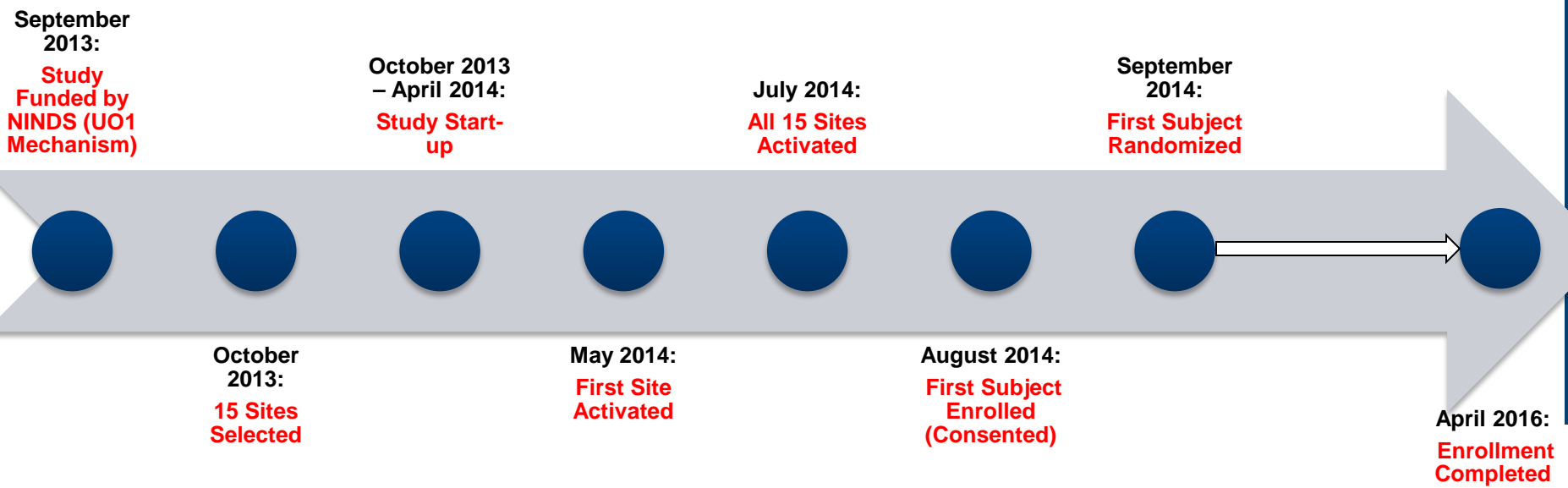
BeatMG Study Design

Prospective, randomized, double-blind, placebo-controlled clinical trial



* Cycle = 4 doses over 4 weeks

BeatMG Study Timeline



Other trials in MG

- MG trials (published and ongoing):
 - azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, IVIg, eculizumab, thymectomy
- Slow recruitment
- Restrictive eligibility criteria

Benatar, M., et al. Muscle & Nerve (June, 2012)

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Other trials in MG (cont.)

- Phase II Eculizumab trial (Alexion)
 - 14 subjects across 25 sites (US and Canada) in approximately 2.5 years
- EPITOME trial (University of Miami)
 - Initial target: 88 subjects across 10 sites (US and Canada)
 - Actual enrollment: 11 subjects in 22 months
 - Recruitment rate: 0.5 subjects/month
 - Study suspended due to poor enrollment

BeatMG: Recruitment Issues

- Initial enrollment lag
 - 3-4 months with no enrollment
- Our response:
 - Recruitment and retention plan
 - DSMB and Protocol Steering Committee
 - Loosening of eligibility criteria
 - Protocol amendment – implemented September 2014
 - Addition of sites
 - 11 sites added between August 2014 – August 2015

Impact of Changes

■ Eligibility Criteria

- Protocol amendment allowed subjects to be on prednisone + IST
- 19 subjects were able to enroll due to this eligibility criteria change

■ Addition of sites

- Weighing the balance between time, money and resources required for activating additional sites versus potential increase in enrollment
- Addition of sites during study maintenance
- Only 3 of the 11 reserve sites enrolled

Recruitment Efforts

Ancillary Study Meetings

- Muscle Study Group - September 2014 and 2015
- AANEM - October 2014
- AAN - April 2015 and 2016

Raising Awareness

- MGFA Annual Meeting – April 2014
- MGFA Scientific Session – November 2014
- Local MDA/MGFA presentations
- Brochure, Colleague Letter, Website postings

Recruitment Efforts (cont.)

Raising Awareness – Media

■ Videos

- Myasthenia Gravis Disease Overview video:
<http://player.vimeo.com/video/112884706>
- NN103: Rituximab in Myasthenia Gravis Study video:
<http://player.vimeo.com/video/112942312>

■ Online/Print Articles (MDA, MGFA, YCCI)

■ Clinicaltrials.gov ([NCT02110706](#))

■ Research Match

■ Announcements/Press Releases

■ Patient Information Webinar: April 2015

Recruitment Efforts (cont.)

Social Media

- NINDS Twitter and Facebook
- YCCI Twitter and Facebook
- MDA Facebook



Impact of Recruitment Efforts

- Study information readily available and widely publicized
 - Constant outreach
 - Site engagement
 - Successful completion of enrollment within expected timeline
-
- ❖ Participation survey

Retention Efforts

- Engaged Coordinators and Investigators
- Tools – e.g. birthday cards
- Travel reimbursement

- Retention: 2/50 subjects dropped out

Advantages of Utilizing a Network

- **Team Approach and Effort**
 - CCC (MGH), DCC (Iowa), PPI Institution (Yale)
- **Clinical Study Site Engagement**
 - Monthly site PI Calls
 - Monthly site Coordinator Calls
 - Bi-Weekly calls with PPI Coordinator
- **Internal Communication & Tracking**
 - Study team meetings
 - Core team meetings

Advantages of Utilizing a Network (cont.)

■ Network Resources:

- Recruitment, Retention & Diversity Committee
- Patient advocacy
 - At protocol designing stages and continuing today through PSC
- Recruitment tools
 - All CIRB approved and ready for use at sites
- Invested Clinical Study Staff
 - Network PIs and Coordinators
 - Network milestones and NN grant stipulations

26 Participating Sites

- ❖ Yale University (PI: Richard Nowak)
- ❖ Montefiore/Einstein University (PI: Volkan Granit)
- ❖ Weill Cornell (PI: Jonathan Goldstein)
- ❖ Ohio State (PI: John Kissel)
- ❖ Univ. Alabama Birmingham (PI: Mohammad Alsharabati)
- ❖ Univ. California Davis (PI: David Richman)
- ❖ Univ. California Los Angeles (PI: Perry Shieh)
- ❖ Univ. Cincinnati (PI: Laura Ann Sams)
- ❖ Univ. Colorado Denver (PI: Dianna Quan)
- ❖ Univ. Kansas (PI: Mazen Dimachkie)
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- ❖ Univ. Pittsburgh (PI: Arya Puwanant)
- ❖ Univ. Rochester (PI: Emma Ciafaloni)
- ❖ Univ. Texas Southwestern (PI: Sharon Nations)
- ❖ Univ. Virginia (PI: Ted Michael Burns)
- ❖ University of Utah (PI: A. Gordon Smith)
- ❖ Columbia University (PI: Thomas Brannagan)
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- ❖ Northwestern University (PI: Senda Ajuod-Driss)
- ❖ Oregon Health and Sciences University (PI: Tessa Marburger)
- ❖ Swedish Medical Center (PI: Erik Gierke)
- ❖ Washington University (PI: Muhammad Al-Lozi)
- ❖ SUNY Stony Brook Medical Center (PI: Nurcan Gursoy)
- ❖ Emory University (PI: Vita Kesner)
- ❖ SUNY Downstate Medical Center (PI: Yaacov Anziska)
- ❖ SUNY Buffalo Medical Center (PI: Gil Wolfe)

[Enrollment

As of May 2, 2016:

- Across 26 Sites

- 4030 chart reviews conducted
- 1823 subjects pre-screened

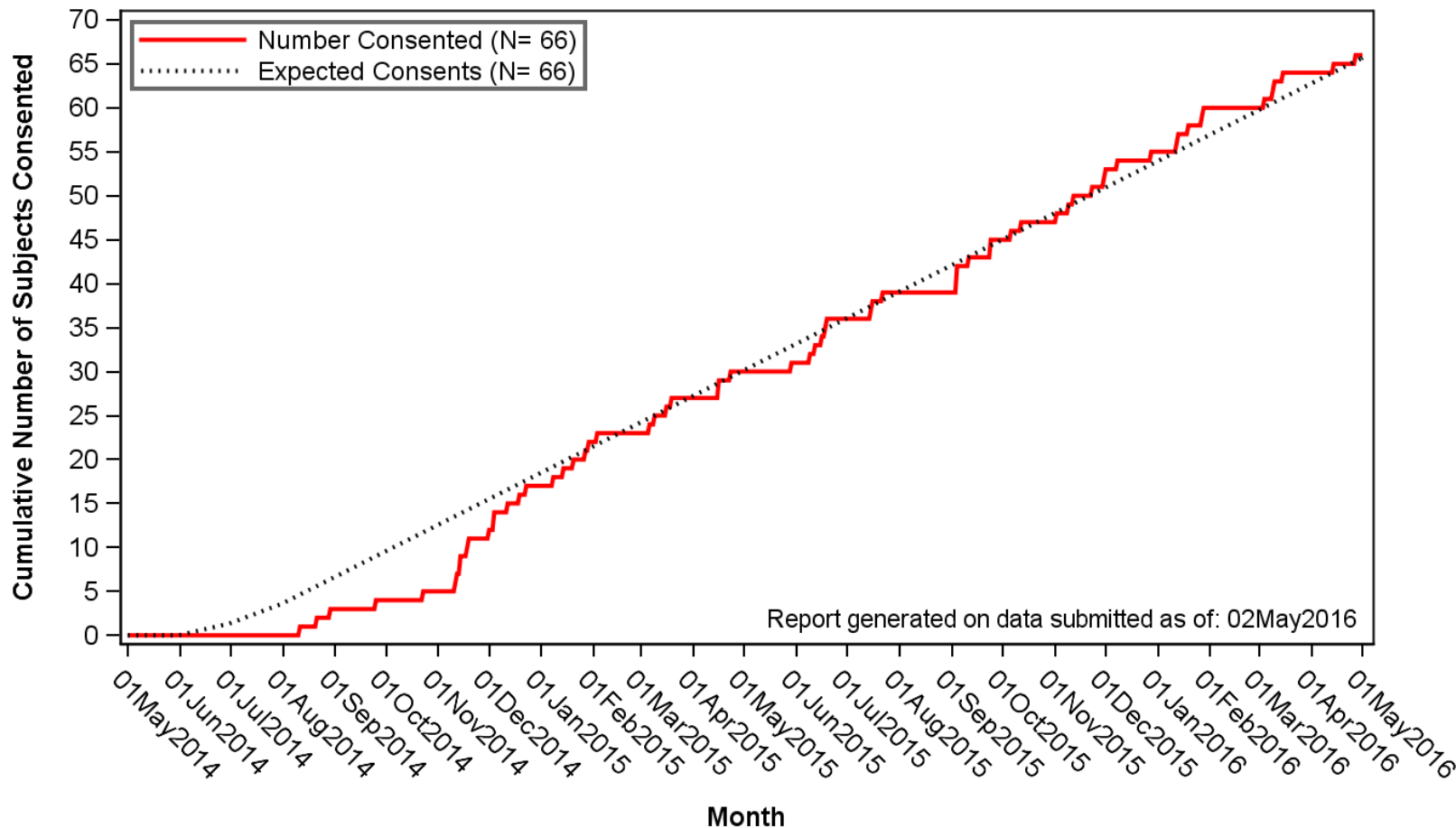
- Across 16 Sites:

- 66 subjects enrolled (signed consent)
- 50 have been randomized and received study drug/placebo

- Recruitment Rate: 2.7 subjects/month

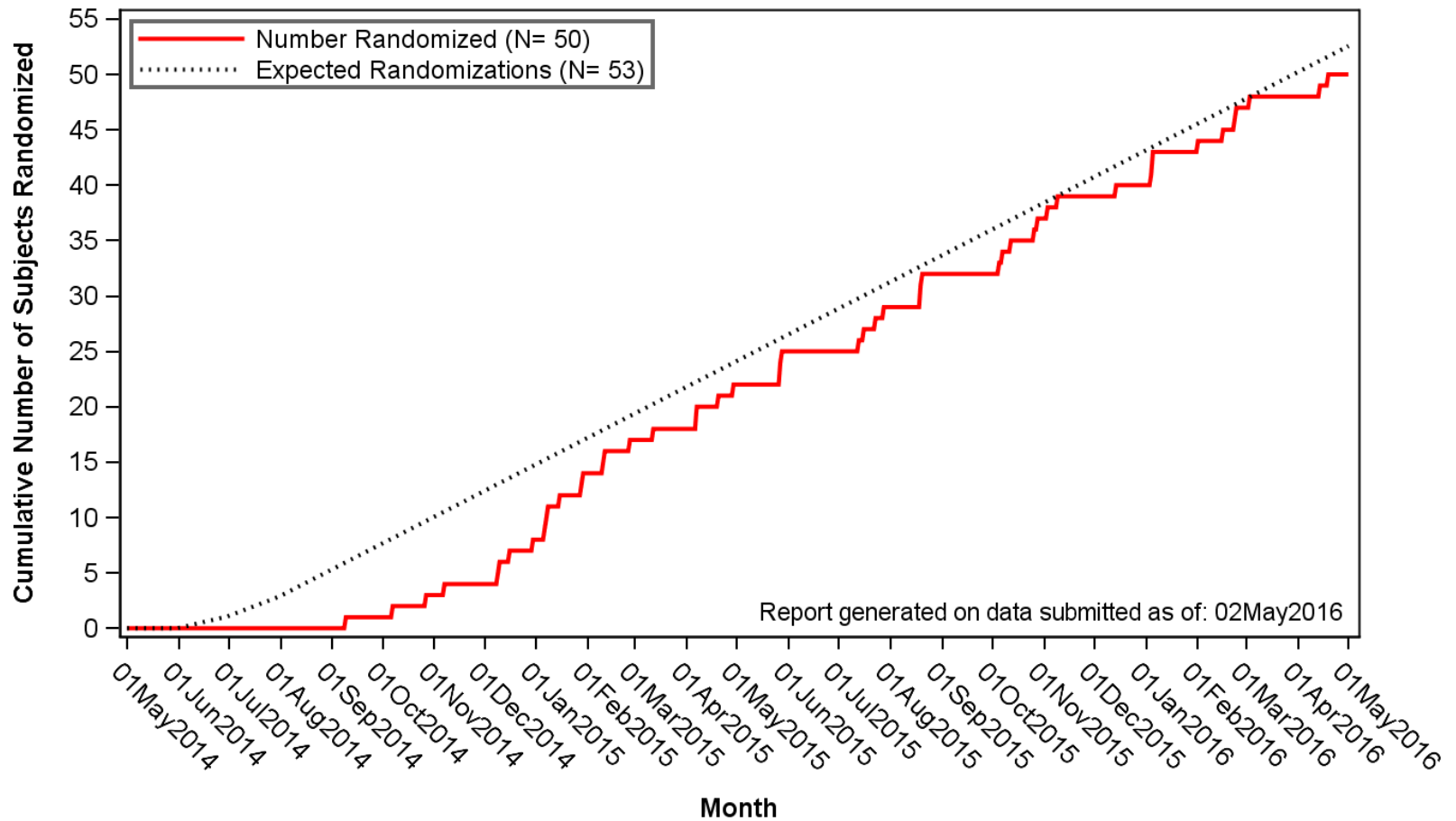
Enrollment: Overall Consents

Figure 6. Overall Consents



Enrollment: Overall Randomizations

Figure 7. Overall Randomizations



Conclusions – Strategies to Improve Enrollment

- Be thoughtful when establishing eligibility criteria, selecting sites and developing a recruitment plan
 - Continuously and proactively monitor and assess the progress of enrollment
 - Adapt as needed
 - Be strategic in how you utilize resources and funding to increase study enrollment
- Utilizing a Network is ideal
 - Engaged teams that are invested in the study both at the site and at the management level
 - Collaboration and effective communication
 - Raise awareness through multiple channels
 - Ability to utilize all available resources

Acknowledgements

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Questions



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