REGION 1
Regional Disaster Health Response System

RDHRS Region 1 Webinar: Planning Considerations for Monoclonal Antibody Therapies for COVID-19

December 15, 2020

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- The speakers have no affiliation or financial interests/relationships to disclose.

Speakers

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- Gary J. Kleinman
  Regional Administrator, Region 1 (New England), Assistant Secretary for Preparedness and Response, US Department of Health and Human Services
- Russell Webster
  Regional Administrator, FEMA Region 1
  Region 1 Federal Coordinating Officer for COVID-19
- Emily Rubin, MD, JD, MSHP
  Division of Pulmonary and Critical Care, Massachusetts General Hospital
- Inga Lennes, MD, MPH, MBA
  Senior Vice President for Service Excellence and Practice Improvement, Massachusetts General Hospital

Key Background

- Two emergency use authorizations issued for monoclonal antibody therapy for outpatients with mild to moderate Covid-19 at high risk of progressing to severe disease
- Multiple challenges
  - Outpatient infusions for infectious patients
  - Scarce drug and infusion capabilities
  - Need to infuse patients early in course of disease
  - Serious concerns about equitable distribution
  - Shared decision making in setting of weak evidence base

Bamlanivimab

- Neutralizing IgG1 monoclonal antibody that binds to the receptor binding domain of the spike protein of SARS-CoV-2 (Eli Lilly)
- Phase II trial published in *NEJM* suggests reduction in composite endpoint of hospitalizations + ED visits for outpatients with SARS-CoV-2 and mild to moderate symptoms
- Not primary endpoint, small numbers, not statistically significant
  - All participants - 5/309 (1.6%) v. 9/143 (6.3%)
  - Age ≥ 65 or BMI ≥ 35 - 4/95 (4%) v. 7/48 (15%)
- All patients in trials received mAb within 72 hours of test being sent
- Some trials of hospitalized patients have been halted due to lack of benefit and/or harm signal
- Clinical trials are ongoing (largely involving dual Ab cocktail)

Casirivimab + Imdevimab

- Dual Ab cocktail (Regeneron) with two antibodies that bind to different regions of the receptor binding domain of the spike protein of SARS-CoV-2
- No published data
- By report, reduction in hospitalization/ED visits
- Similarly small numbers
  - All participants: 8/434 (2%) in tx group vs 10/231 (4%) in placebo
  - High risk patients: 4/151 (3%) in tx group vs 7/78 (9%) in placebo group

Emergency use authorizations

- Outpatients with mild or moderate symptoms
- No more than 10 days of symptoms
- Age ≥ 65
- Adults with BMI ≥ 35
- CKD, diabetes, immunosuppressed
- Age ≥ 55 with cardiovascular disease, hypertension, COPD or other chronic respiratory conditions
- Age 12-17 with variety of conditions (e.g., sickle cell, obesity)
- Excluded if newly hypoxic or requiring more than baseline supplemental O2

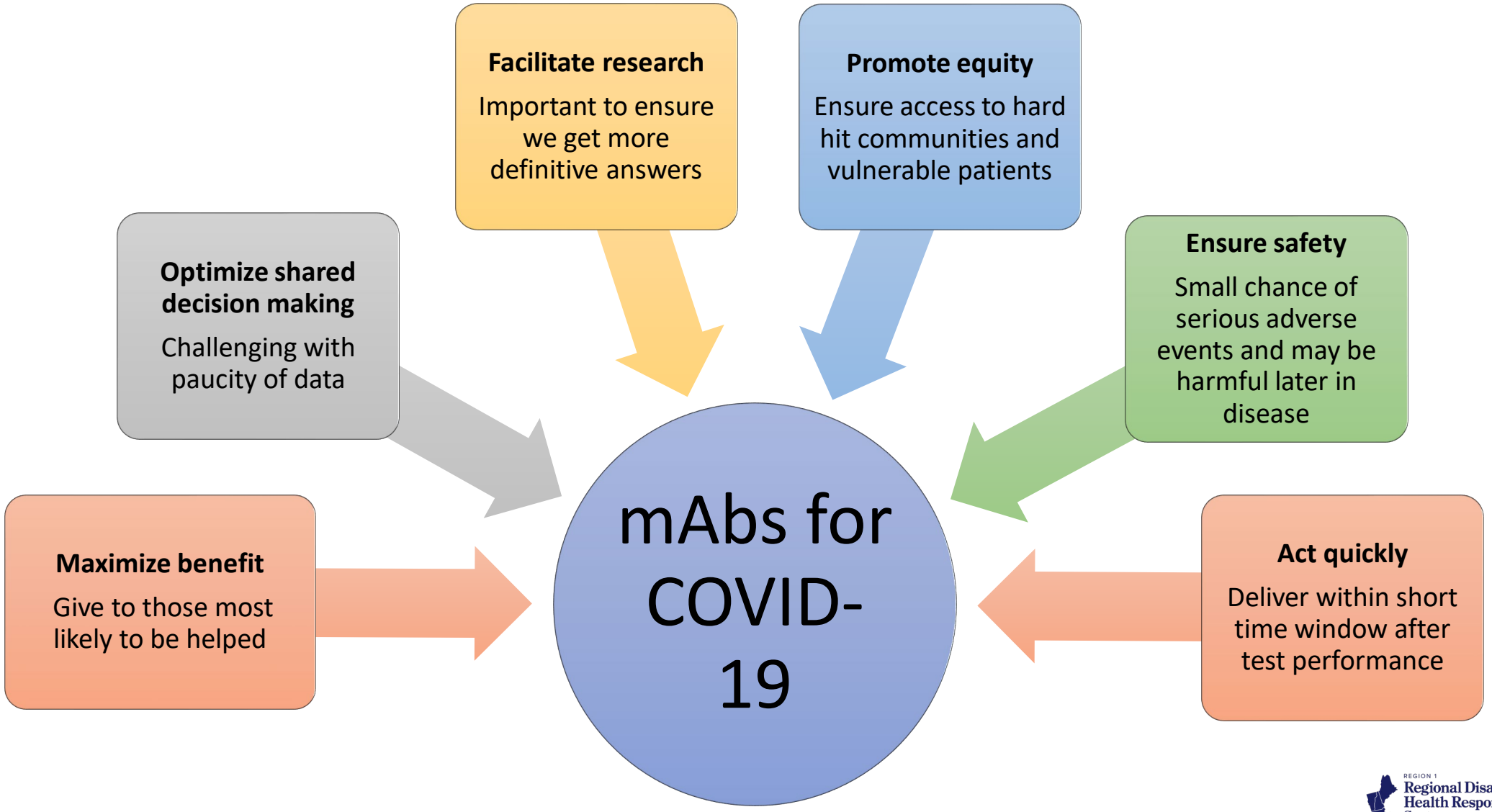
NIH and IDSA on BAM

- NIH
  - Insufficient data to recommend for or against
  - Should not be considered standard of care
- IDSA
  - Recommends against routine use of BAM in ambulatory patients with COVID-19 (Conditional recommendation, very low certainty of evidence)
  - In patients at increased risk, BAM is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events

Core allocation principles

- Maximize benefit
  - Challenging to define given paucity of evidence
- Ensure equity
  - Particularly important here because of disproportionate impact of disease on certain communities
- Be transparent

Complex balance



MA Distribution

- Drug distributed to institutions capable of infusing a certain number of patients and willing to adhere to state guidance
- Allocations based on infusion capabilities
- Priority for patients with age ≥ 65; and/or ≥ 18 with BMI ≥ 35
  - These are the only high risk patients who experienced events in the published data
  - Known to be at risk for morbidity and mortality
  - Identifiable
- Critical to distribute equitably with socially vulnerable groups represented in proportion to impact of disease

MA Distribution

- Random allocation by reserve lottery in event of scarcity
  - 80% of units allocated in a lottery available to all patients
  - 20% of units allocated in a lottery open only to socially vulnerable patients defined by SVI and/or residence in city/town with high incidence
- Participating hospitals/systems must:
  - Accept referrals from outside their system
  - Provide transportation if needed
  - Provide regular reporting demonstrating equitable process

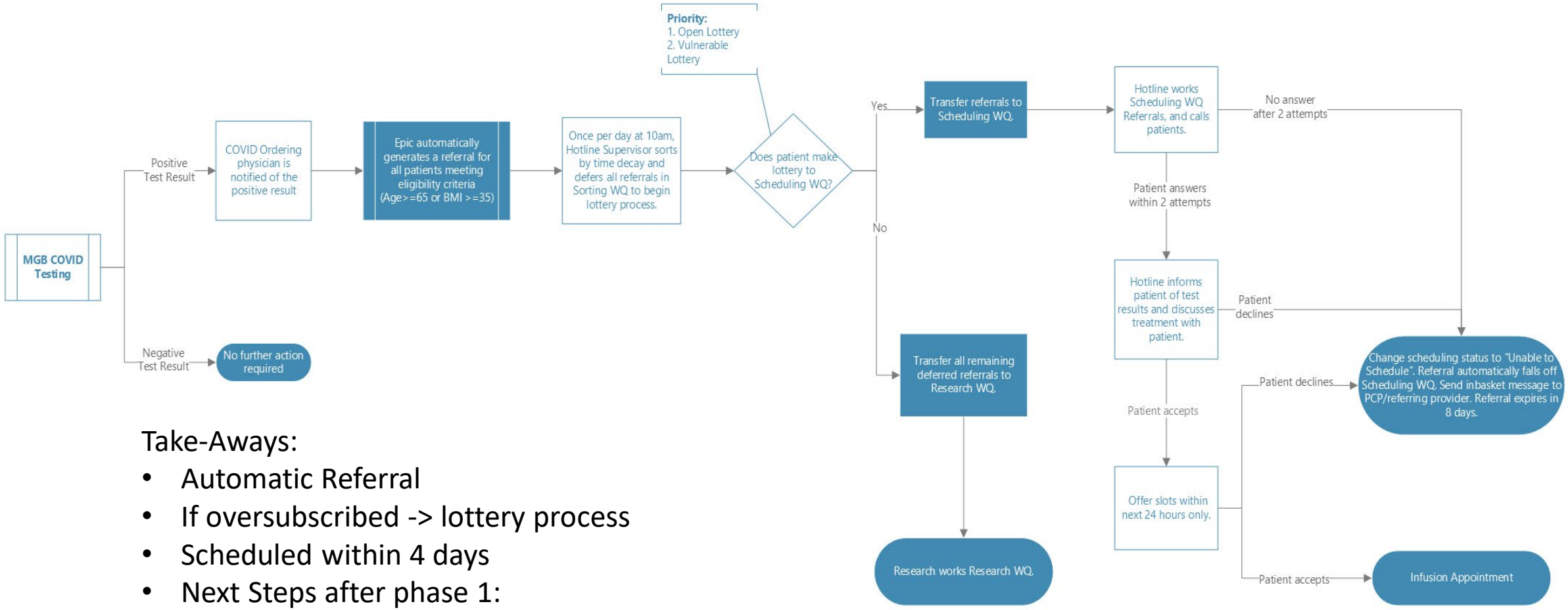
Key Challenges

- How are patients identified for entry into a lottery to minimize referral bias in favor of those with access and privilege?
  - Equity favors entering patients automatically if eligible
  - But may get low yield and have unused capacity
- How is shared decision making done and by whom?
  - Challenging messaging given unclear benefits
- How is research preserved?
  - Prior EUA's have interfered with ability to enroll in trials
- What does it mean to equitably distribute a therapy that might not work?

MGB Phase 1: Bamlanivimab (BAM) Administration

- **Eligibility:** Patients age >=65 or with BMI >=35 are considered eligible for this treatment in phase 1.
- **Automated (internal) referral pathway** to ensure timely process
- **Option to Opt Out:** If a provider does not wish for their patient to be considered for this treatment, they may opt out when submitting the COVID test order
- **Lottery to Ensure Equity:** All patients tested within the MGB system meeting this eligibility criteria are automatically referred to a lottery and may be contacted by our COVID hotline to offer the option of receiving this treatment
- **Shared Decision Making:** Assent process prior to scheduling with provider
- **At Home** treatment pathway option
- **External Referral Pathway:** Development of a referral pathway for patients tested outside the MGB system in progress

High Level BAM Workflow



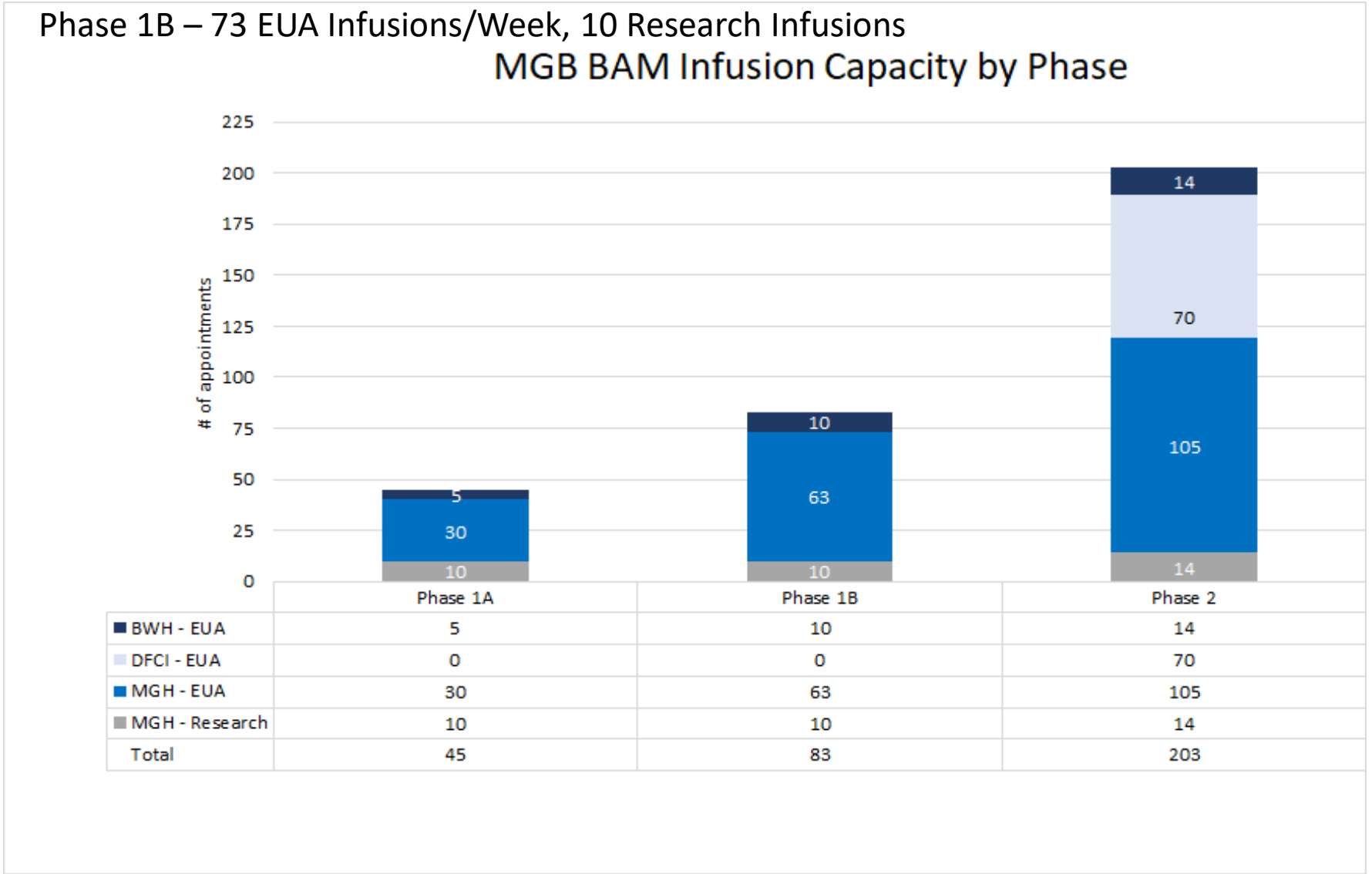
Take-Aways:

- Automatic Referral
- If oversubscribed -> lottery process
- Scheduled within 4 days
- Next Steps after phase 1:
  - Research pathway
  - External referrals

MGB BAM Infusion Capacity (pending drug availability)

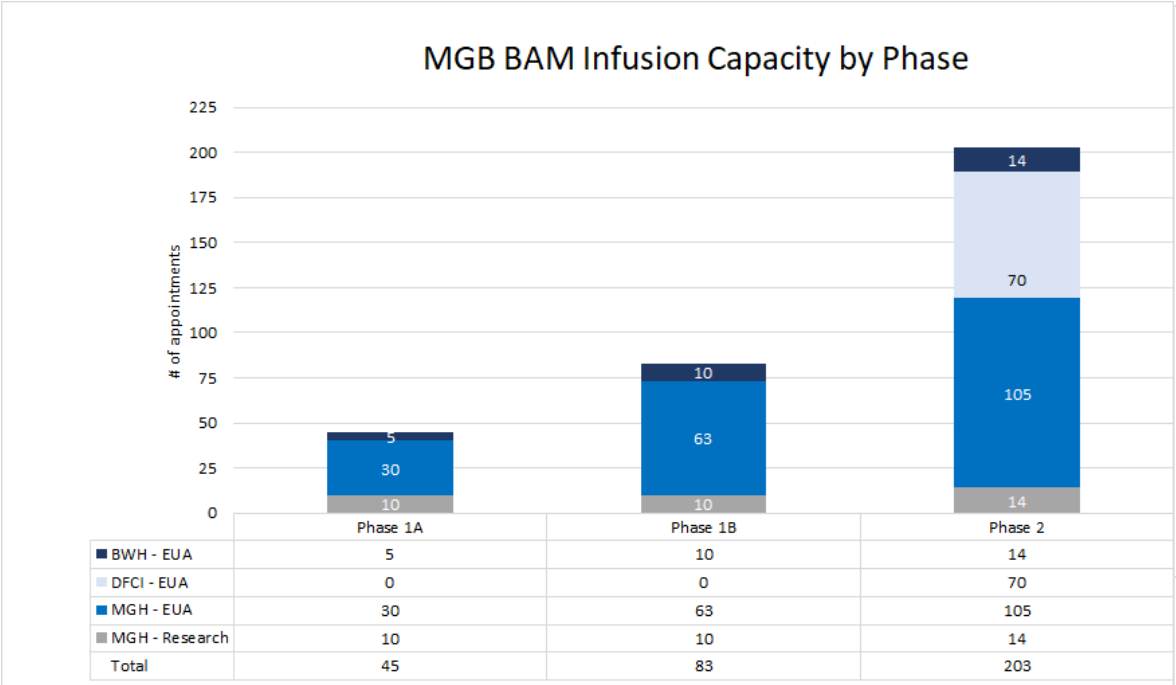
Phase 1A – 35 EUA Infusions/Week, 10 Research Infusions

Phase 1B – 73 EUA Infusions/Week, 10 Research Infusions

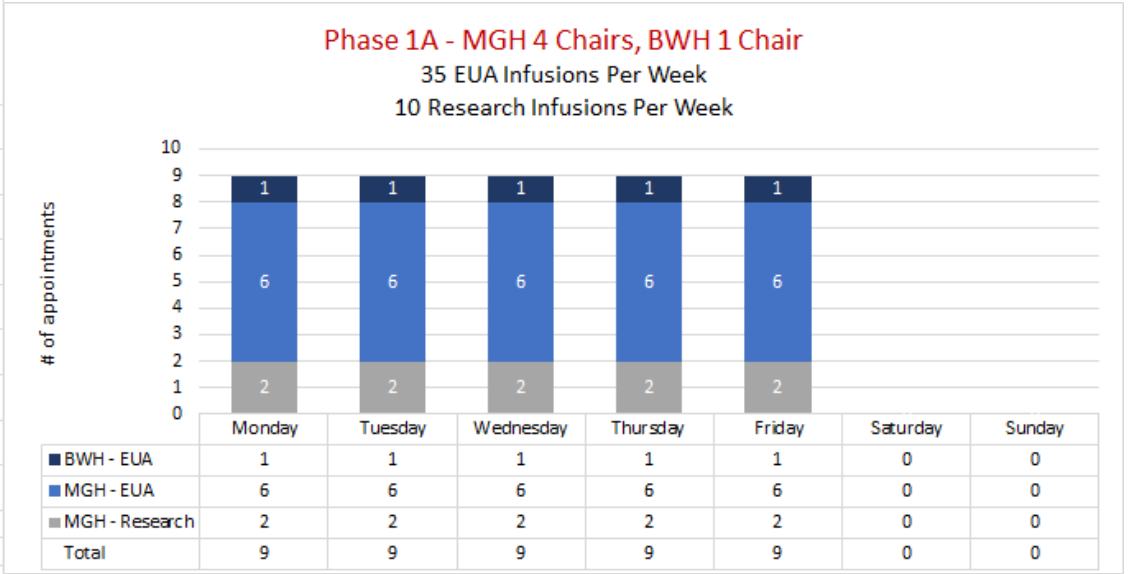


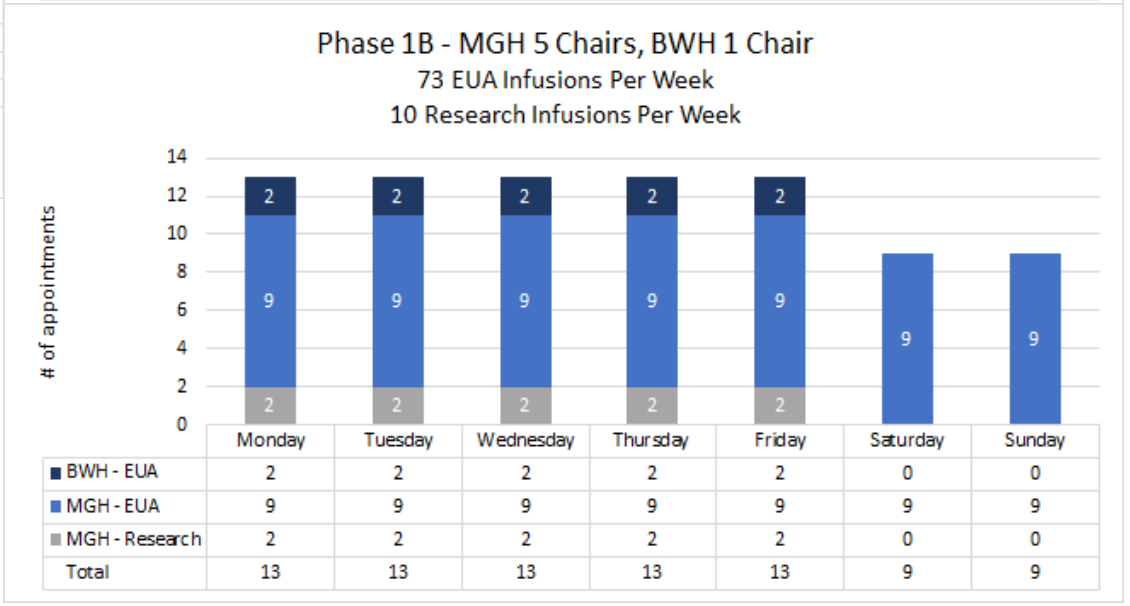
	Phase 1A	Phase 1B	Phase 2
BWH - EUA	5	10	14
DFCI - EUA	0	0	70
MGH - EUA	30	63	105
MGH - Research	10	10	14
Total	45	83	203

MGB BAM Infusion Capacity (pending drug availability)

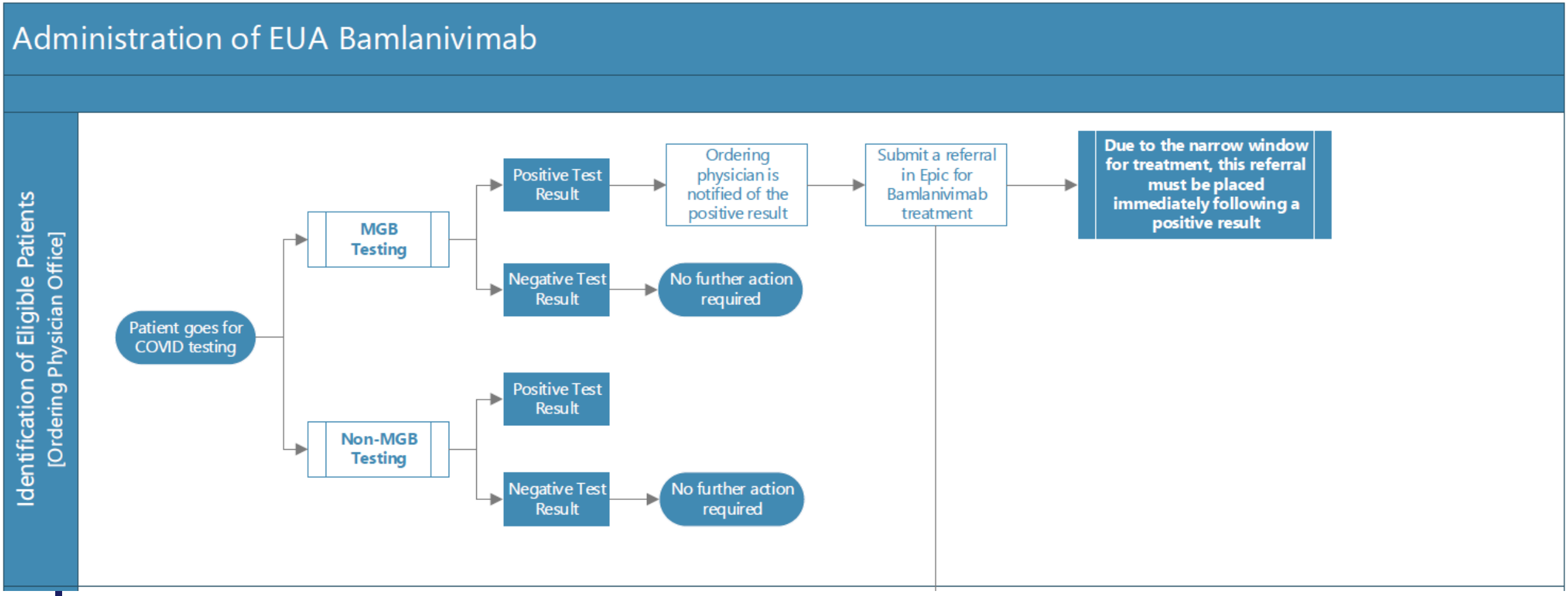


Hours of Operations	
MGH Weekday (Mon-Fri) Short Stay	7:00 – 7:30 (12.5 hrs)
BWH Weekday (Mon-Fri)	9:00 - 1:00pm (4 hours)
MGH Weekend (Sat-Sun) Termeer	8:00-6:30 (10.5 hrs)– Sat 9:00-5:00 (8hrs) - Sun





Workflow for Patient Allocation



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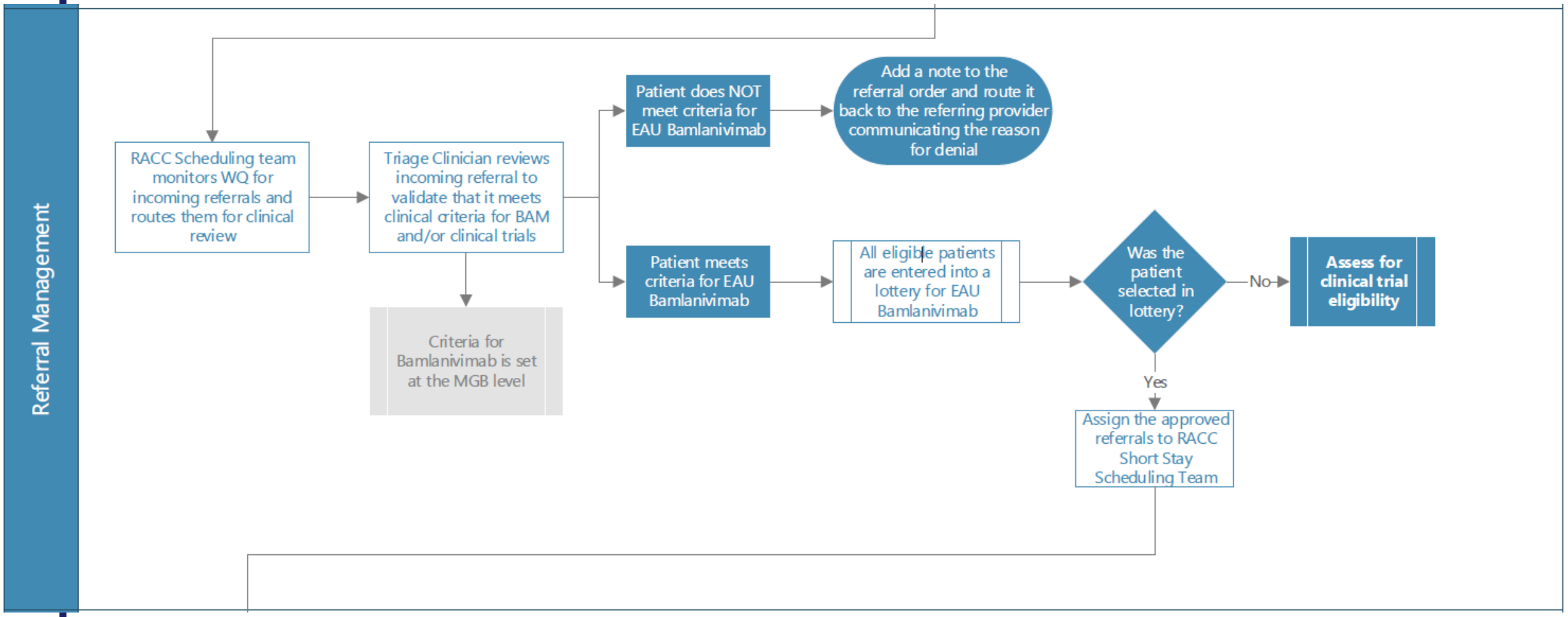

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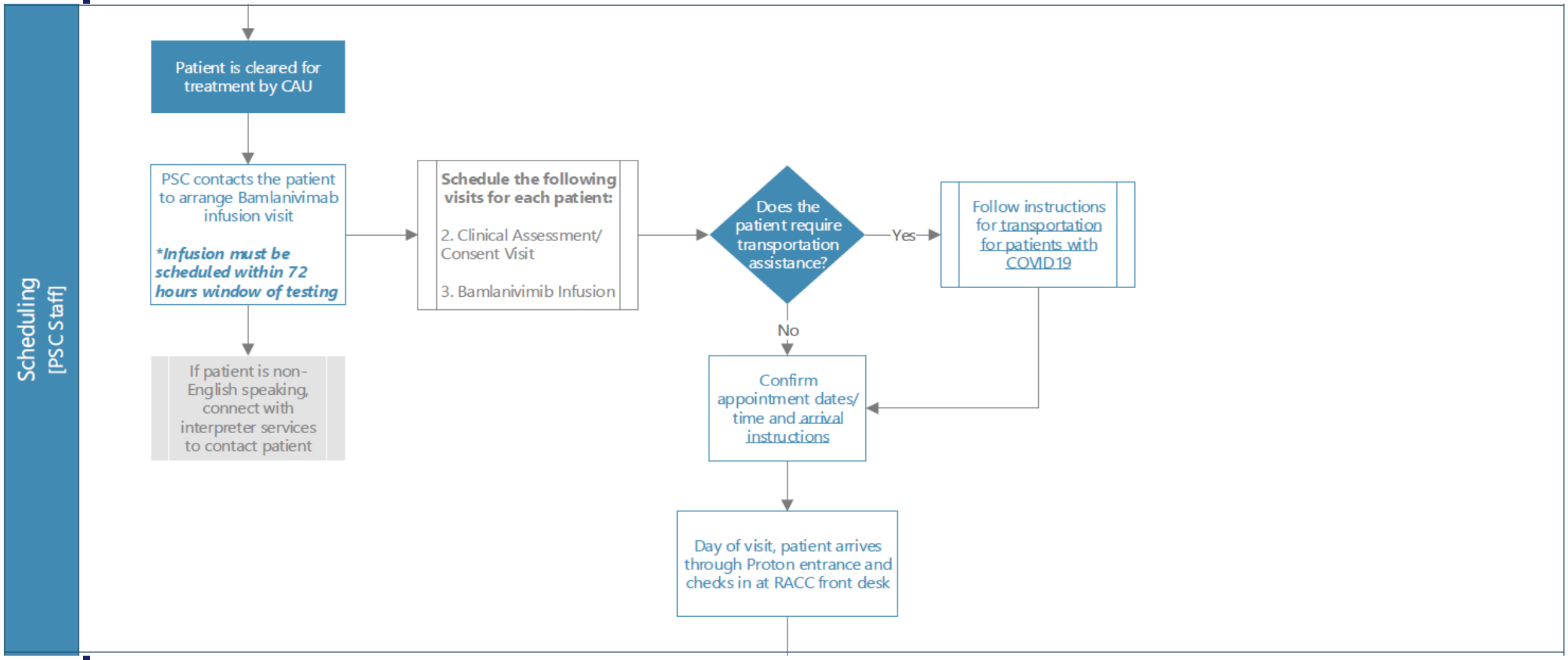

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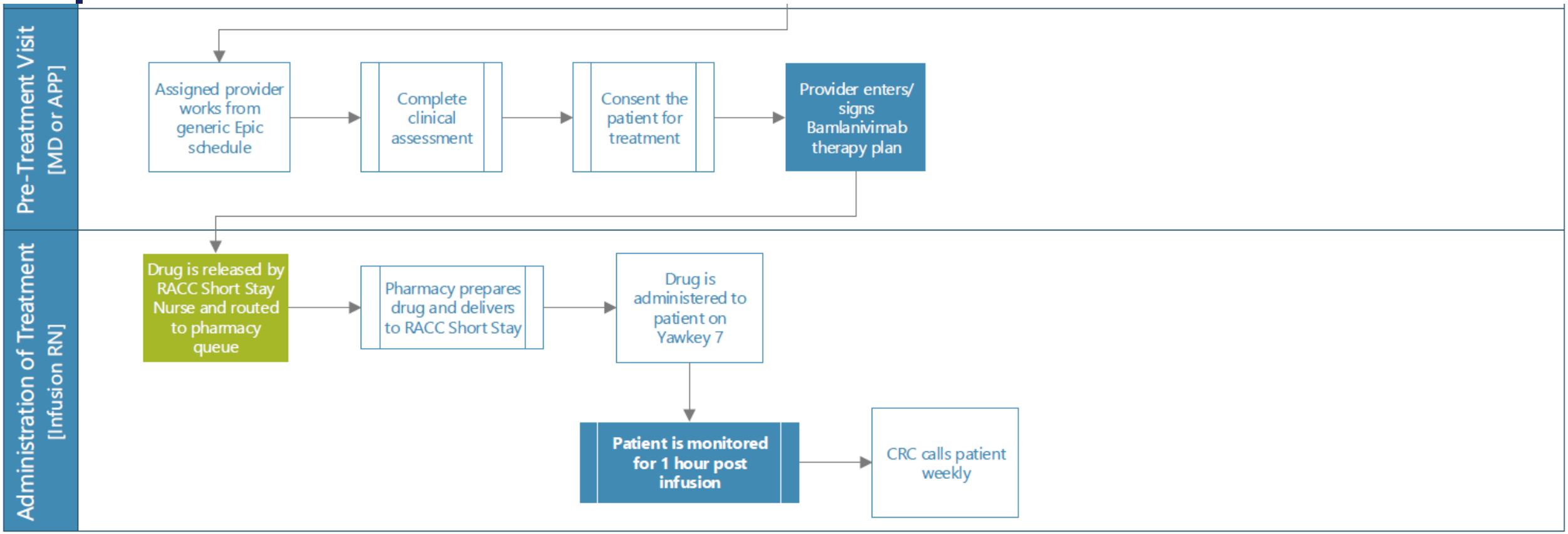

Future Directions

- Home infusion
- Shared decision making with primary providers
- Expanded infusion locations
- External referral pathway

Thank you. Special thanks to Lara Henshaw Archer and the Ambulatory Management team and MGB COVID mAb Task Force.

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Questions?

Additional Webinars on This Topic

https://netec.org/education-and-training/

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THANK YOU!

To contact the Region 1 RDHRS:

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