MONOCLONAL ANTIBODY THERAPY FOR COVID-19

CONSIDERATIONS FOR EMS AND MEDICAL CONTROL AUTHORITIES

WILLIAM FALES, MD, FACEP, FAEMS

STATE MEDICAL DIRECTOR

MICHIGAN DEPARTMENT OF HEALTH AND HUMAN SERVICES

BUREAU OF EMS, TRAUMA, AND PREPAREDNESS

DIVISION OF EMS AND TRAUMA

1

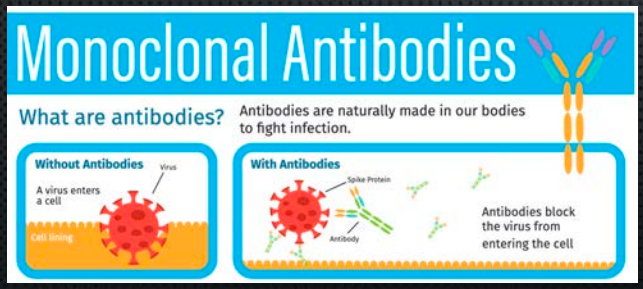
DISCLOSURES AND CONFLICTS

- **DISCLOSURES**
  - WESTERN MICHIGAN UNIVERSITY HOMER STRYKER MD SCHOOL OF MEDICINE
    - PROFESSOR OF EMERGENCY MEDICINE
    - CHIEF, DIVISION OF EMS AND DISASTER MEDICINE
  - KALAMAZOO COUNTY MEDICAL CONTROL AUTHORITY
    - EMS MEDICAL DIRECTOR
- **CONFLICTS**
  - NONE KNOWN

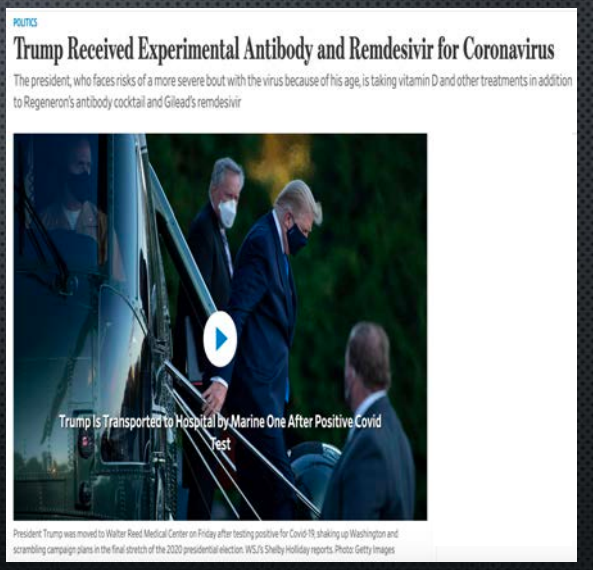
2

MONOCLONAL ANTIBODY THERAPY

- MONOCLONAL ANTIBODIES ARE LABORATORY-MADE PROTEINS THAT MIMIC THE IMMUNE SYSTEM'S ABILITY TO FIGHT OFF HARMFUL ANTIGENS SUCH AS VIRUSES. (FDA NOV 9, 2020)



Source: Lilly Bamlanivimab Playbook



Source: Wall Street Journal, Oct 3

3

MONOCLONAL ANTIBODY THERAPY

- **OCT 3:** PRESIDENT TRUMP TREATED WITH MAB THERAPY
- **NOV 9:** LILLY RECEIVES FDA EMERGENCY USE AUTHORIZATION (EUA)FOR BAMLANIVIMAB
- **NOV 19:** FIRST PATIENTS IN MI TREATED WITH MAB AS IV INFUSION
- **NOV 21:** REGENERON RECEIVES FDA EUA FOR CASIRIVIMAB AND IMDEVIMAB "COCKTAIL"
- **DEC 19:** MICHIGAN TREATS 800 PATIENTS

Source: NPR, Nov 25, 2020

4

MAB THERAPY – THE SCIENTIFIC EVIDENCE

	Lilly Bamlanivimab	Regeneron Casirivimab and Imdevimab
Primary Clinical Trial for EUA	Interim analysis of phase 2 randomized dosing trial	Interim analysis of phase 2 randomized dosing trial
Study population	Mild to moderate COVID-19 symptoms w/o hospitalization	Mild to moderate COVID-19 symptoms w/o hospitalization
Number of patients (mAb vs placebo)	465 (**101/107/101** vs 156)	799 (**266/267** vs 266)
Primary outcome: Change in viral load	No difference at 11 days	mAb better than placebo at 7 days
Secondary outcome: Percent admitted (or ER visits) in high risk patients	**3%** (mAb) vs **10%** (placebo) FDA **4%** (mAb) vs **15%** (placebo) NEJM	**3%** (mAb) vs **9%** (placebo) FDA
Peer-reviewed publications	NEJM 10/28/2020	None
Number needed to treat (**NNT**) to prevent 1 admission (or ER visit)	**14.3** (FDA) / **9.1** (NEJM)	**16.7** (FDA)

Source: FDA and NEJM

5

FEDERAL AND STATE PERSPECTIVES

- **Food and Drug Administration**
  - mAb not approved for anything, only authorized
- **HHS Assistant Secretary for Preparedness and Response and OWS**
  - States should work to make this mAb widely available, "game changer"
- **NIH COVID-19 Treatment Recommendations Panel**
  - mAb not standard of care. Cannot support or discourage use
- **Centers for Medicare and Medicaid Services**
  - Medicare will cover and pay for infusions ($310)
- **Michigan Department of Health and Human Services**
  - Clinicians make decision to use. Cannot support or discourage use
  - MDHHS committed to making mAb widely available to patients/clinicians

6

MONOCLONAL ANTIBODY EUA CRITERIA

- COVID-19 **POSITIVE**, AND
- **MILD TO MODERATE** DISEASE IN ADULTS AND PEDIATRIC PATIENTS (AGE ≥12 & ≥40 KG), AND
- **NOT REQUIRING HOSPITALIZATION** OR SUPPLEMENTAL OXYGEN, AND
- **WITHIN 10 DAYS OF SYMPTOM ONSET** (IDEALLY WITHIN 3 DAYS) , AND
- **HIGH RISK** FOR PROGRESSING TO SEVERE DISEASE

7

HIGH RISK ADULTS

- **AGE ≥65 YEARS OR**
- **BODY MASS INDEX (BMI) ≥35,** OR
- AGE ≥55 YEARS, AND
  - CARDIOVASCULAR DISEASE, OR
  - HYPERTENSION, OR
  - COPD/OTHER CHRONIC RESPIRATORY DISEASE
- CHRONIC KIDNEY DISEASE, OR
- DIABETES, OR
- IMMUNOSUPPRESSIVE DISEASE, OR
- RECEIVING IMMUNOSUPPRESSIVE TREATMENT.

Separate high-risk pediatric criteria

8

HIGH RISK PEDIATRICS (ADOLESCENTS)

- BMI ≥85TH PERCENTILE FOR THEIR AGE AND GENDER, OR
- SICKLE CELL DISEASE, OR
- CONGENITAL OR ACQUIRED HEART DISEASE, OR
- NEURODEVELOPMENTAL DISORDERS, (E.G.,CEREBRAL PALSY) OR
- A MEDICAL-RELATED TECHNOLOGICAL DEPENDENCE, FOR EXAMPLE, TRACHEOSTOMY, GASTROSTOMY, OR POSITIVE PRESSURE VENTILATION (NOT RELATED TO COVID-19), OR
- ASTHMA, REACTIVE AIRWAY OR OTHER CHRONIC RESPIRATORY DISEASE THAT REQUIRES DAILY MEDICATION FOR CONTROL.

9

LIMITATIONS OF AUTHORIZED USE

- **MONOCLONAL ANTIBODY THERAPY IS NOT AUTHORIZED FOR**
  - HOSPITALIZED PATIENTS DUE TO COVID-19, OR
  - PATIENTS REQUIRING O2 THERAPY, OR
  - PATIENTS ON HOME O2 REQUIRING AN INCREASE FROM BASELINE OXYGEN
- **BENEFIT OF TREATMENT WITH MAB HAS NOT BEEN OBSERVED IN PATIENTS HOSPITALIZED DUE TO COVID-19.**
  - MAY BE ASSOCIATED WITH WORSE CLINICAL OUTCOMES WHEN ADMINISTERED TO HOSPITALIZED PATIENTS ON HIGH FLOW OXYGEN OR VENTILATORS

SOURCE: FDA MAB EUAS

10

MONOCLONAL ANTIBODY ALLOCATION

- Medication provided at no cost by federal government
- Weekly allocations to states based on COVID-19 admissions
- MDHHS responsible for allocating to hospitals and others
- Every hospital has received an allocation
- Project SPEED: Allocation directly to LTCs and FQHCs
- Supply >>>>>>>Demand

11

INITIAL ALLOCATION IN MICHIGAN

- ~50% allocated to all hospitals with EDs as baseline (11 vials per hospital)
- ~50% allocated based on COVID-19 admissions
- Capped at 50 vials per hospital
- Supplies to hospitals intended for broad community

Number/Range of Vials to be Distributed	Number of Hospitals Receiving this Quantity*	Percent of Hospitals Receiving this Quantity
11 (Base)	44	27%
12 to 15	43	26%
16 to 20	19	12%
21 to 25	16	10%
26 to 30	10	6%
31 to 40	6	4%
41 to 49	2	1%
50 (Cap)	24	15%
Total	164	100%

12

MONOCLONAL ANTIBODY THERAPY ADMINISTRATION

- **ADMINISTRATION**
  - REQUIRES INTRAVENOUS INFUSION OVER AT LEAST 60 MINUTES, AND
  - 60 MINUTE OBSERVATION
- **PREPARATION**
  - DOES NOT REQUIRE PHARMACIST
  - MAY BE PREPARED AT BEDSIDE, NO PUMP
- **EMERGENCY CAPABILITIES**
  - INITIAL TREATMENT OF ANAPHYLAXIS

13

OPTIONS FOR INFUSION

- EMERGENCY DEPARTMENT
- INFUSION CLINIC
  - HOSPITAL OR INDEPENDENT
- DEDICATED INFUSION AREA OF HOSPITAL
- OUTPATIENT CLINIC
- LONG-TERM CARE
- HOME CARE SETTING (INCLUDING EMS)

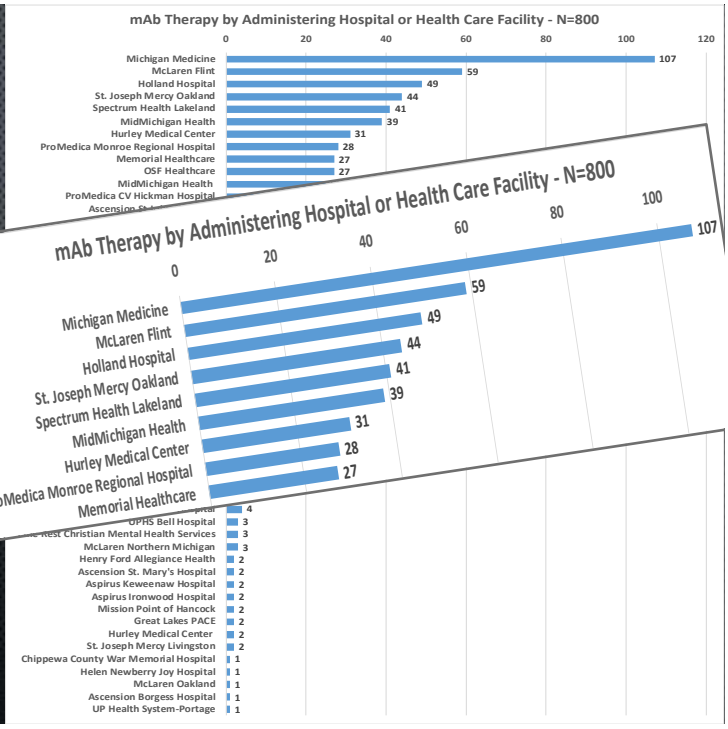
14

MICHIGAN'S FIRST 800 PATIENTS

15

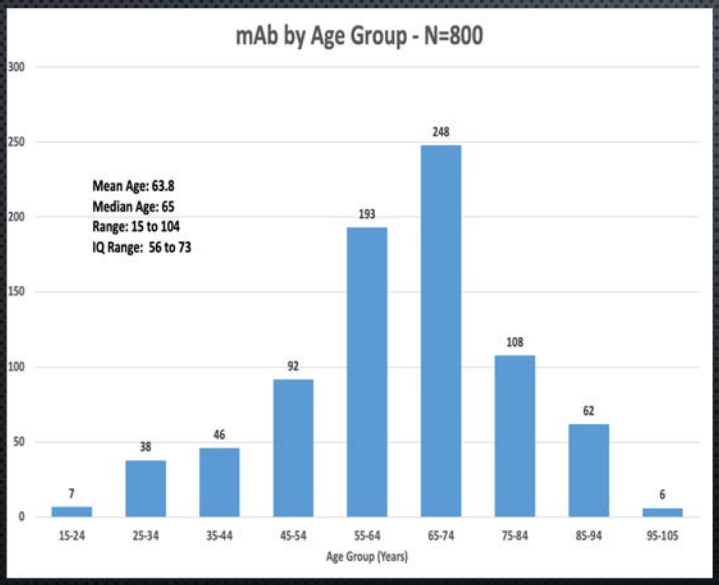
MONOCLONAL ANTIBODY THERAPY BY HOSPITALS

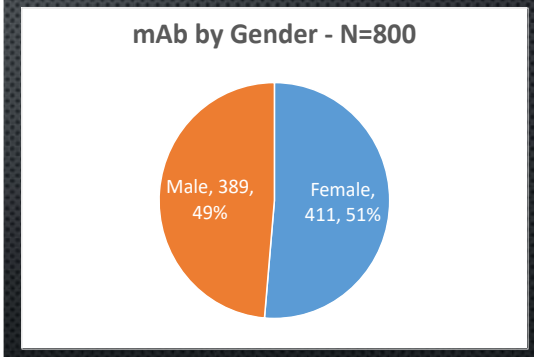
- >25% of hospitals in the UP
- More patients treated in UP (88) than in Detroit (38)
- More Level 3 & 4 trauma centers than Level 1 & 2 trauma centers
- SE MI ~50% of population only 25% of hospitals used mAb
- Most treated at one site in one day were 21 at a SNF



16

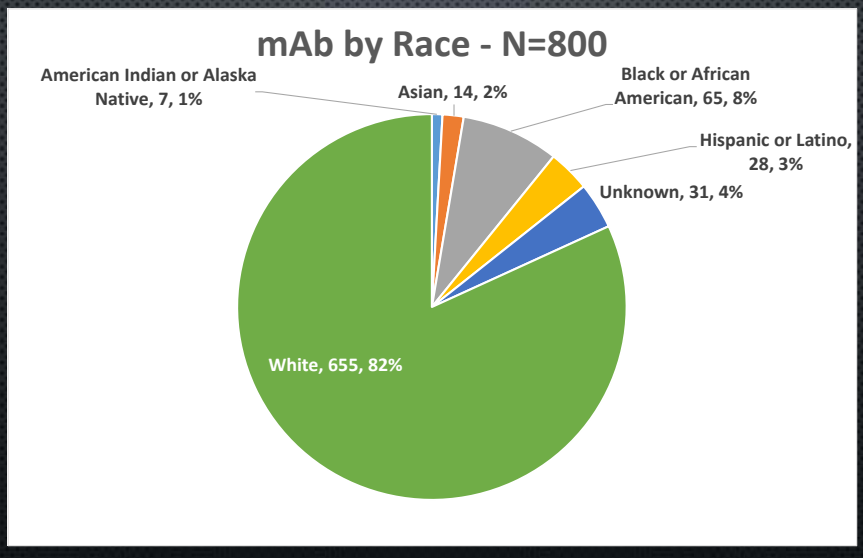
MAB THERAPY BY AGE AND GENDER





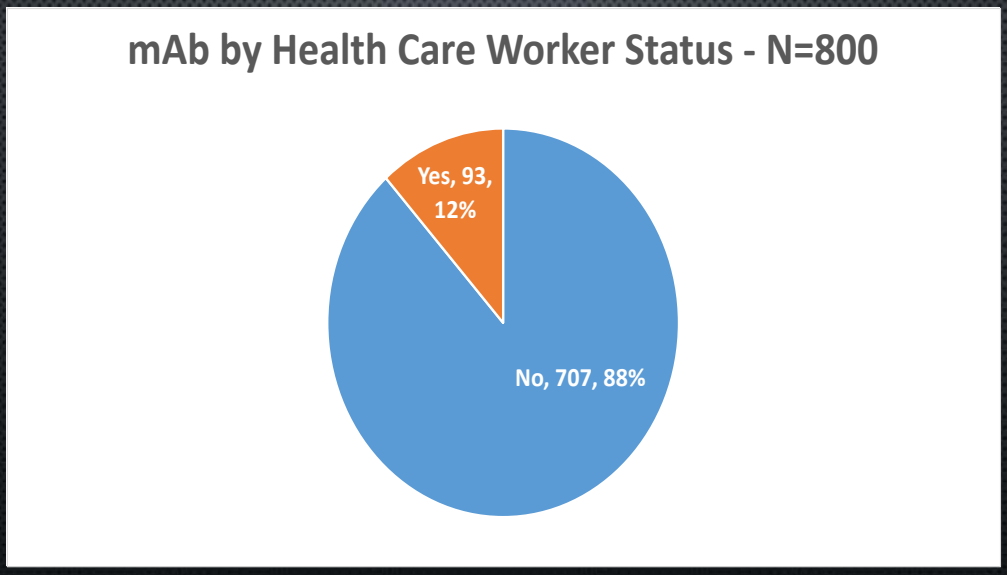
17

MAB THERAPY BY RACE



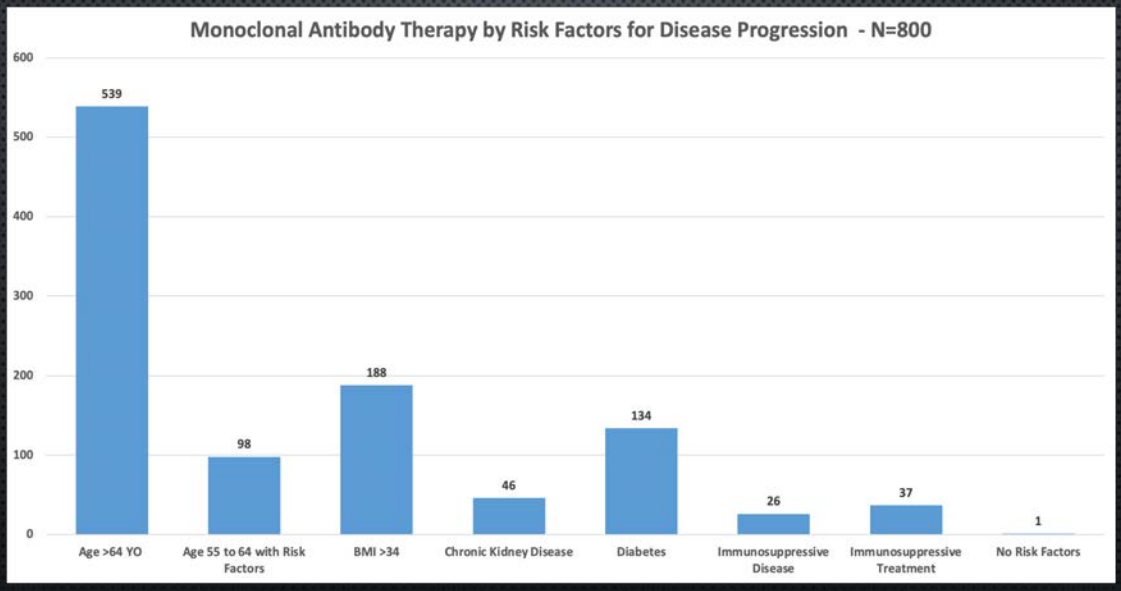
18

HEALTHCARE WORKERS



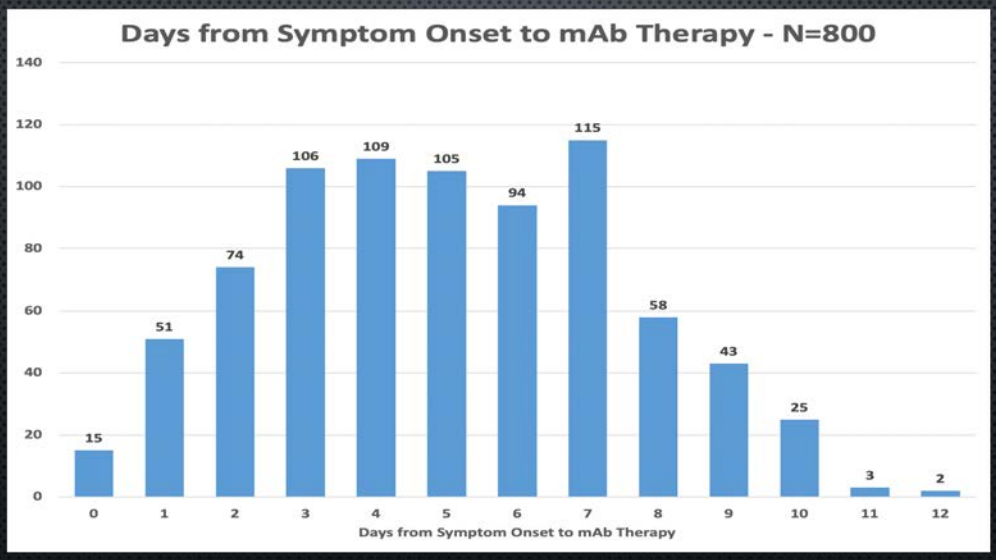
19

RISK FACTORS



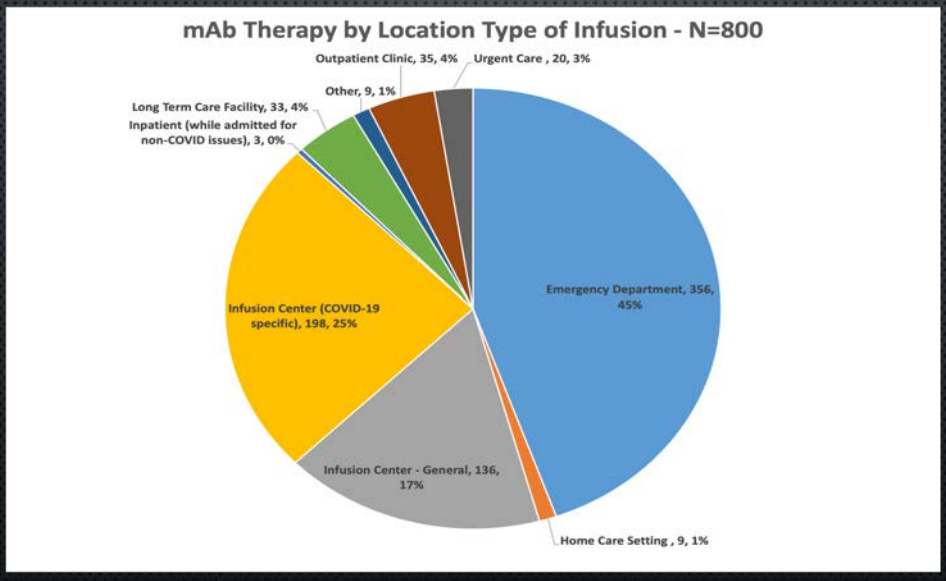
20

DAYS FROM SYMPTOM ONSET TO MAB



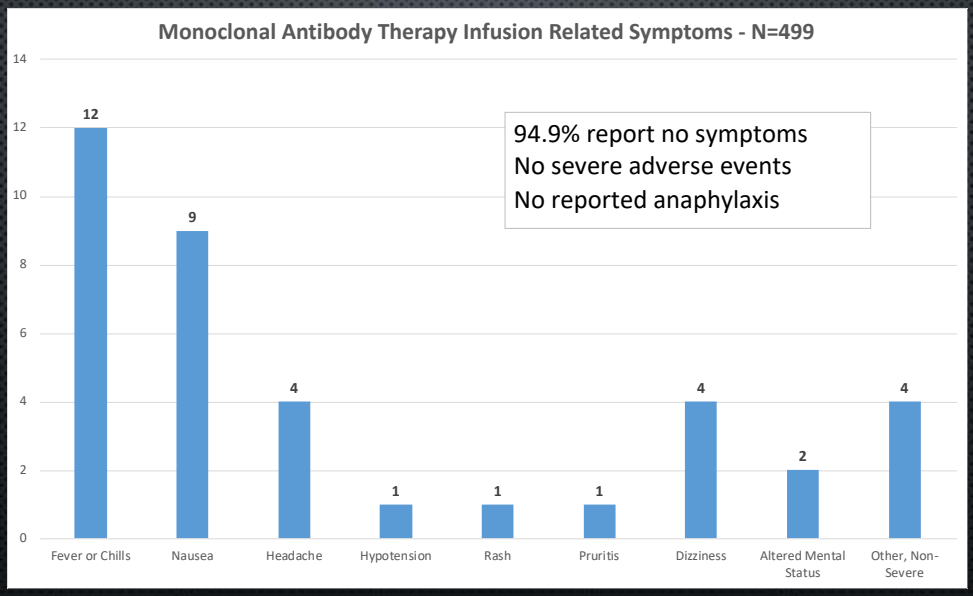
21

INFUSION LOCATION



22

INFUSION RELATED SIDE EFFECTS



23

WILL MONOCLONAL ANTIBODIES MITIGATE COVID-19 ADMISSIONS? SAVE LIVES

- POST-INFUSION ADMISSION RATE 4.4%
  - NO DIFFERENCE IN AGE </> 65 YO,
  - NO DIFFERENCE IN BMI </> 35,
- 2 DEATHS REPORTED TO DATE
- 63 LTC PATIENTS WITH 1 DEATH, 1 ADMISSION BOTH TREATED AFTER 7 DAYS OF SYMPTOMS, 1 GRAVELY ILL AT SNF. REMAINDER CLINICALLY IMPROVED

24

CONSIDERATIONS FOR EMS IN MAB

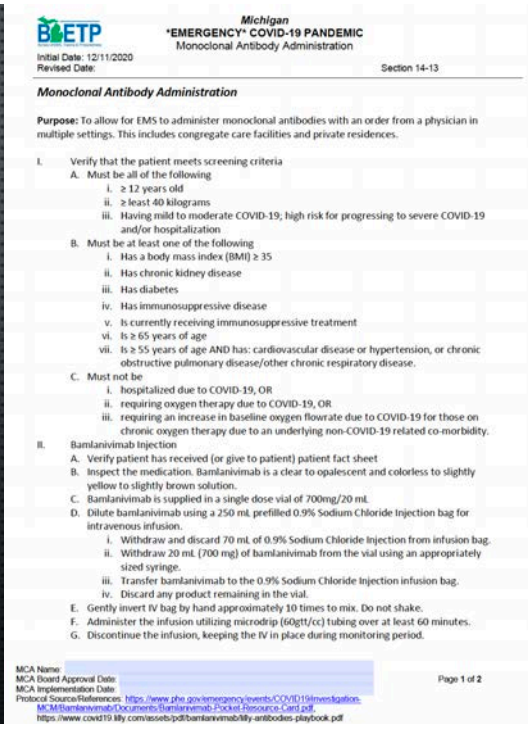
- PROVIDE PARATRANSIT OR AMBULANCE TRANSPORT TO INFUSION CLINIC
- START IVS FOR SNFS AND THEY RUN INFUSIONS
- START IVS AND RUN INFUSIONS*
- PART OF MAB TASK FORCE WORKING WITH HOME HEALTH OR STATE LTC MOBILE CRISIS TEAMS*

*REQUIRES EMERGENCY PROTOCOL

25

MCA EMERGENCY PROTOCOL

- MUST BE ADOPTED BY THE MCA
- VERSION 2.0 COMING



BETP

Michigan
"EMERGENCY" COVID-19 PANDEMIC
Monoclonal Antibody Administration

Initial Date: 12/11/2020
Revised Date:
Section 14-13

Monoclonal Antibody Administration

Purpose: To allow for EMS to administer monoclonal antibodies with an order from a physician in multiple settings. This includes congregate care facilities and private residences.

I. Verify that the patient meets screening criteria
  A. Must be all of the following
    i. ≥ 12 years old
    ii. ≥ least 40 kilograms
    iii. Having mild to moderate COVID-19; high risk for progressing to severe COVID-19 and/or hospitalization
  B. Must be at least one of the following
    i. Has a body mass index (BMI) ≥ 35
    ii. Has chronic kidney disease
    iii. Has diabetes
    iv. Has immunosuppressive disease
    v. Is currently receiving immunosuppressive treatment
    vi. Is ≥ 65 years of age
    vii. Is ≥ 55 years of age AND has: cardiovascular disease or hypertension, or chronic obstructive pulmonary disease/other chronic respiratory disease.
  C. Must not be
    i. hospitalized due to COVID-19, OR
    ii. requiring oxygen therapy due to COVID-19, OR
    iii. requiring an increase in baseline oxygen flowrate due to COVID-19 for those on chronic oxygen therapy due to an underlying non-COVID-19 related co-morbidity.

II. Bamlanivimab Injection
  A. Verify patient has received (or give to patient) patient fact sheet
  B. Inspect the medication. Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
  C. Bamlanivimab is supplied in a single dose vial of 700mg/20 mL
  D. Dilute bamlanivimab using a 250 mL prefilled 0.9% Sodium Chloride Injection bag for intravenous infusion.
    i. Withdraw and discard 70 mL of 0.9% Sodium Chloride Injection from infusion bag.
    ii. Withdraw 20 mL (700 mg) of bamlanivimab from the vial using an appropriately sized syringe.
    iii. Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.
    iv. Discard any product remaining in the vial.
  E. Gently invert IV bag by hand approximately 10 times to mix. Do not shake.
  F. Administer the infusion utilizing microdrip (60gtt/cc) tubing over at least 60 minutes.
  G. Discontinue the infusion, keeping the IV in place during monitoring period.

MCA Name:
MCA Board Approval Date:
MCA Implementation Date:
Protocol Source/References: https://www.phe.gov/emergency/events/COVID19investigation-MCM/Bamlanivimab/Documents/Bamlanivimab-Pocket-Resource-Card.pdf
https://www.covid19.lilly.com/assets/pdf/bamlanivimab/lilly-antibodies-playbook.pdf

Page 1 of 2

26

OPERATION HOLIDAY DELIVERY

- Rapid Response (<24 hours) to SNFs with large Outbreaks
- Resources: MDHHS Mobile Crisis Teams + Local EMS/Paramedics
- Three Operations (19, 21, and 8 patients)
- Request State support through Local Public Health or Regional Health Care Coalitions
- MDHHS can provide technical support

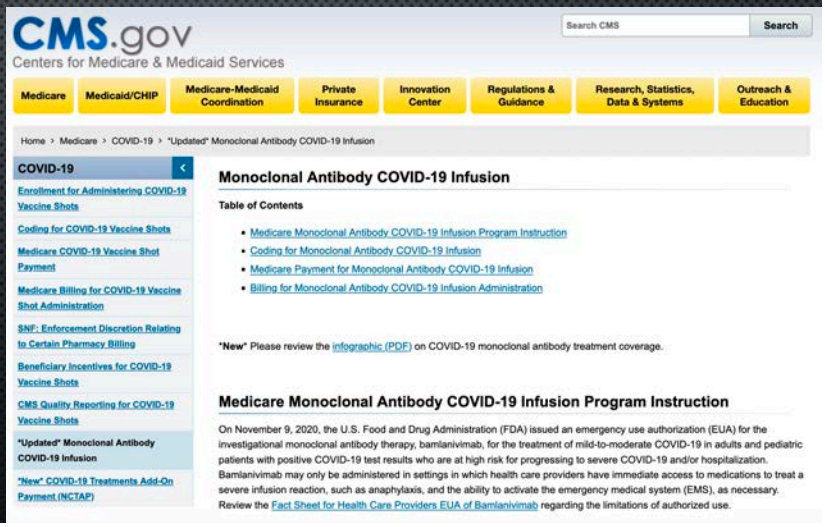
27

OPERATION HOLIDAY DELIVERY

28

FINANCIAL CONSIDERATIONS

- ABILITY FOR EMS TO DIRECTLY BILL MEDICARE, INSURANCE
- BILL FACILITY FOR SERVICES



29

HELPFUL LINKS

- HTTPS://WWW.FDA.GOV/MEDIA/143604/DOWNLOAD
- HTTPS://WWW.FDA.GOV/MEDIA/143603/DOWNLOAD
- HTTPS://WWW.CMS.GOV/MEDICARE/COVID-19/MONOCLONAL-ANTIBODY-COVID-19-INFUSION
- HTTPS://WWW.NEJM.ORG/DOI/FULL/10.1056/NEJMOA2029849

30


MDHHS
Michigan Department of Health & Human Services
BETP
Bureau of EMS, Trauma & Preparedness
THANKS – QUESTIONS?
FALESW@MICHIGAN.GOV

31