Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

Remdesivir: From research to Emergency Use to FDA approval and Stewardship

Christopher McCoy, Ryan Chapin, Jamie LeVash, Julius Yang, Katy Stephenson, Howard Seth Gold.
Department of Pharmacy, Division of Infectious Diseases, Division of Health Care Quality, Beth Israel Deaconess Medical Center

Introduction/Problem

Remdesivir was an early front runner for therapeutic agents of interest given activity against other coronaviruses, some experience with Ebola and a relatively clean adverse event profile.

Notably the agent was used in the first published experience of a patient in Washington state who received the drug as part of his hospitalization for CoVID-19

Gilead and the NIH had designed early trials to examine its usefulness in hospitalized patients in a placebo controlled fashion but also in trials to examine the duration of therapy (5 vs. 10 days) in patients with varying degrees of illness

Prior to initiation of these trials, the only access to the agent was through compassionate use via the FDA and Gilead.

Once BIDMC was selected as a trial site for two trials, a process of rapid evaluation and enrollment was necessary before patients received unapproved therapies, notably hydroxychloroquine which would become exclusionary.

Remdesivir was then approved for Emergency Use Authorization just four months into the pandemic requiring a level of regulatory compliance not seen at BIDMC.

Four months after EUA approval, the drug was FDA approved in full with limited restrictions to use lending to the need for a stewardship process to ensure safe, equitable and responsible prescribing.

Aim/Goal

To enable access to remdesivir through its life cycle from compassionate use to emergency use to FDA approval while meeting regulatory requirements and conscious stewardship.

The Team

Jamie Levash, MSW	Project Manager	Healthcare Quality
Katy Stephenson, MD	Attending Physician-Viral Vaccine researcher	Infectious Diseases
Ryan Chapin, PharmD	Clinical Specialist- Infectious Disease	Pharmacy
Julius Yang, MD	Director	Health Care Quality
Howard Seth Gold, MD	Medical Director-Antimicrobial Stewardship	Health Care Quality, Infectious Dis
Christopher McCoy, PharmD	Clinical Manager- Infectious Diseases	Pharmacy

The Interventions

- Initiated compassionate use access to remdesivir through an FDA-Gilead-BIDMC pathway for patients with limited treatment options
- Incorporated remdesivir into treatment guidelines for review for research enrollment
- Reviewed CoVID 19 admissions for hydroxychloroquine initiation requests through stewardship and directed primary teams to the remdesivir local study team
- Developed the Emergency Use Pathways for important inclusions and exclusion details and daily treatment tracking with Health Care Quality
- Once study results were published, provided education and review for the treatment collaborative
- Tracked adverse events of concern from the Emergency Use experience
- Worked with Health Care Quality to devise an allocation scheme when early release of product did not meet demand
- With EUA transition to FDA approval, worked collaboratively to develop a treatment guideline and stewardship review
- Continually reviewed study data publication, local results, national guidance and provided BILH network guidance for best practice

Results

Early review of access limited to a restrictive compassionate use process with limitations to degree of illness

US Remdesivir compassionate use (link)

Inclusion	Exclusion
Hospitalized only (severe disease) Open label trial Male or non-pregnant female adult ≥18 years of age Laboratory-confirmed SARS-CoV-2 infection by PCR **< 72 hours** prior Illness of any duration and at least one of the following: Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.) Clinical assessment (evidence of rales/crackles on exam) AND SpO2 ≤ 94% on room air. OR Requiring mechanical ventilation and/or supplemental oxygen	Multi-organ failure Pressor requirement ALT > 5 x ULN Estimated CrCl <30mL/min or iHD or CRRT Other study agents (chloroquine, LPV/r)

Beth Israel Deaconess Medical Center | Harvard Medical School Teaching Hospital

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Results and Progress

US Clinical trial development and linkage

Sponsor: US	Design and link:	Primary outcome:
NIAID: **Recruiting**	Adaptive treatment trial Hospitalized only (any severity) Randomized double blind placebo controlled	Day 15 disposition
Gilead **Not yet recruiting**	Phase 3 treatment trial Severe Disease Hospitalized only with pulmonary infiltrates, altered oxygen saturation and fever Randomized duration trial (5 versus 10 days)	Day 14 Clinical recovery (sx)
Gilead **Not yet recruiting**	Phase 3 treatment trial Moderate Disease Hospitalized only with pulmonary infiltrates, altered oxygen saturation and fever Randomized duration trial (5 versus 10 days) vs. Standard of care (supportive)	Day 14 disposition

K Stephenson/BIDMC selected as site for two trials

US trial 5 vs 10 days: Severe disease

Arms

1. Remdesivir 200 mg IV once, then 100 mg IV daily x **5** days total
2. Remdesivir 200 mg IV once, then 100 mg daily x **10** days total

Inclusion	Exclusion
1.>18 years 2.lab-confirmed novel coronavirus (SARS-CoV-2) infection as determined by (PCR), **≤ 96** hours prior to randomization. 3.Hospitalized with fever and SpO2 </= 94% on room air 4.Pulmonary infiltrates on imaging 5.Women of childbearing potential must agree to use at least one primary form of contraception for the duration of the study	1.No other clinical trial or COVID-19 experimental treatment **2.Multiorgan failure** **3.Mechanical ventilation at screening** 4.(ALT/AST) > 5 times the upper limit of normal. **5.(eGFR) < 50)**

US trial 5 vs 10 days: Moderate disease

Arms

1. Remdesivir 200 mg IV once, then 100 mg IV daily x **5** days total
2. Remdesivir 200 mg IV once, then 100 mg daily x **10** days total
3. Standard of care per hospital

Inclusion	Exclusion
1.>18 years 2.lab-confirmed novel coronavirus (SARS-CoV-2) infection as determined by (PCR), **≤ 96** hours prior to randomization. 3.Hospitalized with fever and SpO2 </= 94% on room air 4.Pulmonary infiltrates on imaging	1.No other clinical trial or COVID-19 experimental treatment 2.Mechanical ventilation at screening 3.(ALT/AST) > 5 times the upper limit of normal. 4.(eGFR) < 50)

Initiated compassionate use prior to study launch

Remdesivir (RDV; GS-5734)
for the Treatment of Selected Coronavirus (CoV) Infection

Single Patient Protocol
(Patient X-X)

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

25 February 2020

38 yo M transferred from BI-Milton for ICU admission

Work with trial team and Research Pharm given rapid enrollment

Remdesivir daily evaluation: 9 am

Review that patient has not experienced a serious hypersensitivity reaction.

Review that the following labs have been ordered or resulted for the calendar day.

O Chem7 including importantly (creatinine, BUN)

O Liver function tests (including ALT, AST, bilirubin, and alkaline phosphatase)

O Hematology (complete blood count and prothrombin time)

If they are available, then review as below:

If not available, then remind the team to draw levels.

- Ensure that the Cr has not risen to a point that estimated CrCl falls below 30mL/min.
- Ensure that ALT has not risen to ≥5 x ULN
- Ensure that no other significant laboratory abnormality possibly associated with drug has occurred
- Ensure that the patient has not lost IV access
- Ensure that the patient does not require iHD or CRRT

If any of the above, will need to hold drug and contact Gilead directly.

Otherwise, wait until 1p to give the OK to release for the 2pm dose.

If all are within range, contact the research pharmacy M-F to release drug or Sa/Su, contact the West box, 617 754 3005 for drug release.

Patient excluded from two trials due to need for ventilation enrolled in compassionate use protocol

58 yo M, high risk w/ obesity, hypertension had to be rapidly intubated.

Created a reference document, snippet below for compassionate use consideration to ensure accepted and not study eligible

Remdesivir Compassionate Use Steps — Beth Israel Deaconess Medical Center

1. Review for inclusion/exclusion (note: pregnancy may no longer be excluded, time from last dose of chloroquine/hydroxychloroquine)

   Once ruled in and you've discussed with the ICU team.

2. Contact Katy Stephenson and Jess (RA): Katy, Jessto let them know. Decide on who to enter info to Gilead website for enrollment and FDA paperwork. Don't initiate Gilead entry before chatting with Katy and Jess:

24 yo F pregnant excluded from trials enrolled in compassionate use acces

Developed an early review by Stewardship team for potential enrollment in remdesivir trials

1	Completed 5 days hydroxychloroquine
2	Completed 5 days hydroxychloroquine
3	None
4	Hydroxychloroquine
5	None
6	Hydroxychloroquine
7	HCQ 3/17-18, stopped
8	Lopinavir/ritonavir
9	Hydroxychloroquine
10	Hydroxychloroquine
11	Hydroxychloroquine
12	Hydroxychloroquine
13	Hydroxychloroquine
14	Remdesivir compassionate use
15	Completed 5 days hydroxychloroquine
16	Completed 5 days hydroxychloroquine
17	None
18	Hydroxychloroquine
19	None
20	Hydroxychloroquine
22	Lopinavir/ritonavir
23	Hydroxychloroquine
24	Hydroxychloroquine
25	Hydroxychloroquine
26	Hydroxychloroquine
27	Hydroxychloroquine

Developed a primer for primary teams to enable study drug release given high volume

Remdesivir studies 5773 and 5774
Primary Team Responsibilities for Daily Labs

On the same calendar day please obtain labs to be resulted

six hours prior to daily drug infusion

in order to meet study requirements for safety monitoring and to avoid preparatory delays

- CBC with differential
- Chem7 (Scr, Na, K, Cl, Bicarb, BUN, glucose)
- Liver panel: specifically total bilirubin, ALT, AST

Response to primary team demand

To: BIDMC Clinicians and Managers

From: COVID-19 Treatment Guideline Task Force

Subject: **Remdesivir Outside of Clinical Trials**

We are writing in regard to the use of use of remdesivir in the clinical care setting. Please read the important updates below.

What You Need to Know:

1. Remdesivir is currently being studied in a number of clinical trials. Two trials are active at BIDMC in an open label fashion examining the effect of the drug on clinical outcomes in patients that meet specific criteria. Another clinical trial sponsored by the NIAID is a placebo controlled trial being conducted at other sites around the U.S.
2. The only other way to obtain remdesivir is through a compassionate use process for individual patients, which is currently limited to pregnant patients.
3. Results of the compassionate use uncontrolled observational trial were released a few weeks ago in The New England Journal of Medicine that demonstrated a high rate of treatment response, limited by its observational uncontrolled design.
4. On April 29, the National Institute of Allergy and Infectious Diseases (NIAID) released a news brief announcing that the interim results of the placebo controlled trial indicated a more rapid time to recovery with remdesivir (11 days vs. 15 days). No other details were made available.
5. This prompted news and media outlets to expound on the benefits and the possibility for the FDA to release the drug broadly.

Neither Gilead nor the Food and Drug Administration (FDA) have provided further information on any timeline for the FDA to release the drug in a broader fashion.

What We Ask of You:
Please do not request drug release outside of our clinical trials and await more formal communication from our group, which is in direct contact with Gilead and the FDA, regarding expanded drug release.

Thank you for your cooperation and understanding.

May 2020 Emergency Use Authorization granted but allocation process in question

The U.S. Food and Drug Administration's emergency use authorization of remdesivir on May 1 will expand its use in hospitals across the country.[i] While remdesivir remains an investigational drug, the FDA made this decision based on preliminary clinical trial data suggesting that the benefits or potential benefits of treatment with remdesivir in patients with severe COVID-19 outweigh the risks.

Following the EUA approval, Gilead Sciences announced that they would donate 1.5 million individual doses of remdesivir -- with a 10-day treatment course this will be enough drug to treat 140,000 patients.[ii] This inventory is likely to fall short of demand given that tens of thousands of patients per month are projected to require hospitalization nationwide due to COVID-19 throughout the summer months,[iii] and that the majority of hospitalized patients have acute severe disease and will meet the FDA criteria for treatment.

The plan for distributing remdesivir should be transparent and should be based on state and regional COVID-19 case data and hospitalization rates. Supplies of remdesivir should be distributed on a regional basis with equitable distribution within the region to states and within states to hospitals. This will be imperative to ensure appropriate patient access, reduce the significant health disparities and adverse outcomes already experienced by Black Americans, Latinx communities and other populations, and to prevent a surge in patients at institutions known or thought to have access to the drug or a crush of requests to transfer patients to these hospitals from those who may not have remdesivir access.

Data on the distribution of remdesivir under the EUA should be publicly available. In addition, data from the Adaptive COVID-19 Treatment Trial (ACTT) should be publicly released so that hospitals with a limited supply have the best possible data to inform how to distribute it among patients.

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Results and Progress

Remdesivir EUA guideline developed locally

Includes an algorithm to allow for continued enrollment in the clinical trials to avoid dipping into the EUA limited supply

PHARMACY & THERAPEUTICS
ANTIMICROBIAL SUBCOMMITTEE

Remdesivir Emergency Use Authorization Guidelines

(Note: Remdesivir is only available for use in a clinical trial or under FDA Emergency Use Authorization)

This guideline has been designed to assist the clinician in the utilization of Remdesivir in the medical center under the recent FDA EUA. It is not intended to replace clinical judgment where individual patient characteristics may require modification.

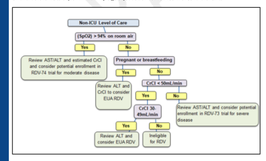
Remdesivir is a RNA-dependent RNA polymerase inhibitor which is currently under investigation as a potential treatment for SARS-COV2, or COVID-19. Clinical trials are currently ongoing. In May 2020, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) to permit use of remdesivir outside of clinical trials for hospitalized patients with severe disease.

BIDMC is currently (5/20) a registered site for two open label trials of the drug for moderate and severe disease, the criteria of which are defined via link (moderate-RDV76/severe-RDV73). If possible, enrolling patients in these trials over the EUA supply is advisable.

General criteria for use for EUA are broad

- Patients hospitalized with confirmed COVID-19
- Patients with severe disease defined as
  - Oxygen saturation (SpO2) ≤94% on room air
  - Requiring supplemental oxygen
  - Requiring mechanical ventilation
  - Requiring extracorporeal membrane oxygenation (ECMO)

Given the broad inclusion, for an initial rapid guide, use below for non-ICU and ICU level of care.



Stewardship team daily tracking and dose release approval to avoid waste

NEW PATIENTS

Patient name/MRN: xxxx
xxxx
CC7 C 796
Approval by EUA exec: Yes
Education Documentation in OMR: Yes
Dose scheduled: **needs loading dose, RN to time ASAP**
Lab clearance for today's dose: yes: watch LFT trend: 106/139 currently
Received yesterday's dose: no, today is day 1
Course planned: 5 days – 5/23
Mechanical Ventilation or ECMO: NO
Planning discharge: No

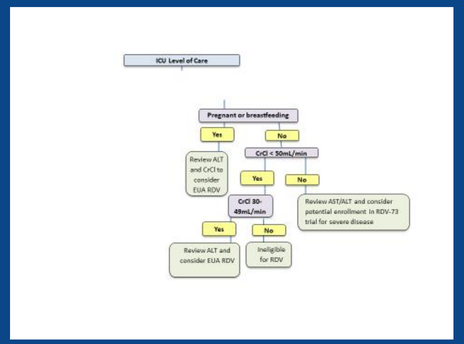
Patient lacking safety lab LFT panel 5/19/20

Patient name/MRN: xxx
xxx
Approval by EUA exec: Yes
Education Documentation in OMR: Yes
Dose GIVEN: 1420
Lab clearance for today's dose: NO: missing liver panel
Received yesterday's dose: 1627
Course planned: 5 days – 5/20
Mechanical Ventilation or ECMO: NO
Planning discharge: No

Afternoon/Evening doses given or timed

Patient name/MRN: xxxx
xxx
Approval by EUA exec: Yes
Education Documentation in OMR: Yes
Dose scheduled: **timed for 2pm**
Lab clearance for today's dose: yes: LFT trend similar today
Received yesterday's dose: yes, loaded at 20:15
Course planned: 5 days – 5/22
Mechanical Ventilation or ECMO: NO
Planning discharge: No

Algorithm for trial versus EUA



Development of unique guidance for an Emergency Use Authorization to meet regulatory compliance and receive further allocation

Unique Requirements for the EUA by Discipline:

Prescribers

Fact Sheet for Health Care Providers

Page the Remdesivir Allocation Pager (#94844) for approval prior to Pharmacy release and consent from patient.

Educate patients/health care proxy of the risk and benefits of the drug based on the FDA's Patient Fact Sheet (English version): Spanish version These are the only language versions as of 5/14/20. An interpreter is recommended to assist in other cases.

- Document in the OMR that the patient/health care proxy understands and accepts the risks of the investigational treatment
- Provide FDA's Patient Fact Sheet to patient/health care proxy

Ordering labs and daily monitoring is required.

- Order entry in cPOE after approval

Built cPOE screens to encourage laboratory screening before entry as well as special considerations for other study meds

REMDESIVIR cPOE

PAGE 1 screener

<FONT COLOR=RED SIZE=5> This order is intended for the use of remdesivir via the Emergency Use Authorization process

<font color=blue size=4><FONT SIZE=4> Evaluate estimated CrCl and ALT before proceeding

Patients who previously or currently are receiving remdesivir, those on active hydroxychloroquine or Sarilumab trials are excluded.

RENAL DOSING

If estimated CrCl <30 mL/min, a warning comes up saying remdesivir is contraindicated for CrCL<30mL/min

Indications and dosing defaults.

Loading Dose: treatment of COVID19 mechanical ventilation and/or ECMO	200mg IV once
Continuation: treatment of COVID19 mechanical ventilation and/or ECMO	100mg IV daily for 9 days
Loading Dose: treatment of COVID19 nonICU	200mg IV once
Continuation: treatment of COVID19 non ICU	100mg IV daily for 4 days

Pharmacists

Fact Sheet for Health Care Providers

cPOE order verification is required.

- Authorization of release of remdesivir MUST include signoff by Remdesivir EUA Collaborative Team (Howard Gold, Molly Hayes, Julius Yang) with considerations detailed previously
- Verification of the above prescriber documentation in OMR that the patient/health care proxy understands and accepts the risks of the investigational treatment must be fulfilled
- A review of the CrCl and ALT should precede verification as above
- After the loading dose, reschedule any subsequent doses to 2pm the following day to allow for safety reviews. If 2pm is within 16h of the last dose, attempt to adjust the dosing time per the standard administration time guidelines.

Dispensing & inventory information

- Given the unique qualities of this EUA and the ongoing clinical trials, inventory will be maintained on count in the narcotic vault. For each new patient, the supply of drug for the course will be sequestered and sent to the Sterile Products area for refrigerated storage.
- The EUA drug supply is a different formulation from the study supply, each requiring different storage and mixing instructions
- The lot number and an appropriate quantity of drug must be logged for each patient with daily sign-out if lot numbers vary

Daily monitoring is required.

- Remind prescriber of their duty to order appropriate daily labs prior to dispensation. This must include Chem-7 including Scr, liver function tests (AST/ALT/bili/alk phos), CBC.
- These labs must be reviewed prior to dispensation each day.
- If CrCl falls below 30 mL/min, or if the ALT rises above 5XULN, the pharmacist should contact the prescriber to discuss discontinuation

Developed and sent out Communications given limited supply and restrictive criteria

Practice Alert
Remdesivir (RDV)– Emergency Use Authorization

Beth Israel Deaconess Medical Center

The Situation:

- The Food and Drug Administration (FDA) approved an Emergency Use Authorization (EUA) for RDV for the treatment of COVID-19 on Friday, May 1, based on preliminary data and in the absence of any currently approved treatment.
- BIDMC has received a small supply of RDV to be used under the EUA, but this quantity is not sufficient to offer treatment to all of our current COVID+ patients.
- The BIDMC Drug Shortage Task Force convened to oversee allocation of RDV under the EUA, with the objective of overseeing and prioritizing administration of this drug to those patients most likely to receive the most benefit.

What Can I Expect?

Criteria For Use & Allocation:

- Several interdisciplinary workgroups have been formed to develop clinical use guidelines, allocation criteria, and oversight of the EUA process. This will be an iterative process as supply/demand may fluctuate in the coming weeks.

Order Approval & Requirements:

- Any order for RDV requires formal approval by the aforementioned oversight group prior to dispensation by the pharmacy. Additionally, patients must give consent to use this medication under this EUA designation. Both EUA approval & consent should be documented in OMR by physician.

Scheduling in eMAR:

- After the initial one-time load dose, ongoing daily doses should be timed for early afternoon (2pm). This allows for sufficient time to perform the daily monitoring required for continuation of therapy.

Pharmacy Dispensing & Tracking:

- Pharmacy will perform a clinical assessment each day prior to dispensing the afternoon dose.
- To ensure appropriate tracking, nurses will be required to sign for each dose (similar to other investigational agents)

IV Administration and Guideline:

- Infuse dose over 60 minutes. IV guideline is under development and should be posted soon.
- Sigma pumps have been updated to include Remdesivir

Tracking sheet developed to communicate between Health Care Quality and Stewardship team

Admission Date	Last COVID Test	MV at Enrollment	Priority	Date Approved	Consent Completed	Planned RegimEn (day)
05/11/2020	05/11/2020	No	3	05/12/2020	Y	5
05/09/2020	05/08/2020	Day 1	1	05/12/2020	Y	10
05/03/2020	05/03/2020	DAY 9	2	05/12/2020	Y	10
05/11/2020	04/26/2020	DAY 2	1	05/12/2020	Y	10
05/11/2020	05/02/2020	Not at enrollment, now intubated	3, now 1	05/12/2020	Y	10
05/12/2020	05/10/2020	DAY 2	1	05/14/2020	Y	10
05/10/2020	05/12/2020	dAY 1	1	05/14/2020	Y	10
05/11/2020	05/11/2020	DAY 3	1	05/14/2020	Y	10
5/15/2020	5/15/2020	No	3	5/16/20	Y	5
5/15/2020	5/15/2020	No, O2 sat<94%	4	5/16/20	Y	5
5/14/20	5/15/20	Day 3	1	5/18/20	Y	5
5/16/20	5/16/20	No, O2 sat <94% RA, 3L	4	5/17/20	Y	5
5/15/20	5/16/20	No, O2 sat <94% RA, oximizer 10L	3	5/17/20	Y	5
5/17/20	5/17/20			5/18/20	Y	5

Engaged Drug Shortage Task Force for prioritization scheme

Beth Israel Lahey Health

Remdesivir via Emergency Use Authorization (EUA) guideline v 5.0 **LAST UPDATED: 14 May 2020**

The purpose of this guideline is to provide the framework for criteria for use of a limited supply of remdesivir and fulfill the regulatory requirements of this unique EUA. This guideline will not cover all potential clinical scenarios. Given that no treatment has been proven to be safe and effective for COVID-19 and there is a limited supply, this is directed to prioritize patients and use in the context of benefit based on a collective review of available published evidence, accrued COVID management experience, and clinical judgement. Please be aware that this is a LIVING document with frequent updates as supply may change and observations are gathered. The Date is highlighted above.

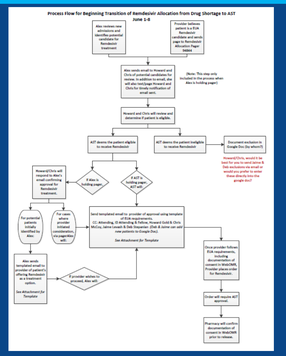
The Interdisciplinary Advisory Workgroup set forth to establish specific clinical criteria for COVID patients with varying degrees of anticipated benefit of RDV administration, as follows:

- Tier 1 allocation (highest priority objective): **Survival benefit**
- Tier 2 allocation: Prevention of **severe morbidity**, including risk of prolonged/permanent vital organ impairment or functional disability
- Tier 3 allocation (valid, but lowest priority objective): Reduction in **illness burden**, including shortening duration of hospitalization

The basic prioritization scheme follows and will be directed by an approval body.

Priority	Site of Care	Respiratory failure
1 (highest)	ICU	Mechanical Ventilation ≤5 days
2	ICU	Mechanical Ventilation 6 -10 days
3	Ward/ICU	Requires ≥ 4L O2 NC
4 (lowest)	Ward/ICU	O2 sat < 94% RA

June 2020: Remdesivir supply opens up lending to a transition to Stewardship only approval



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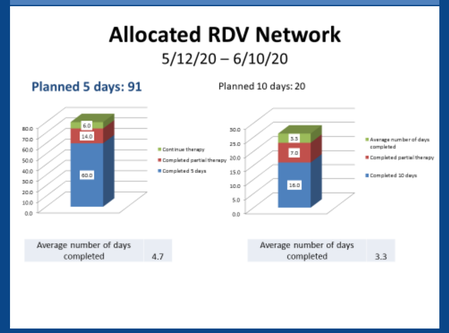
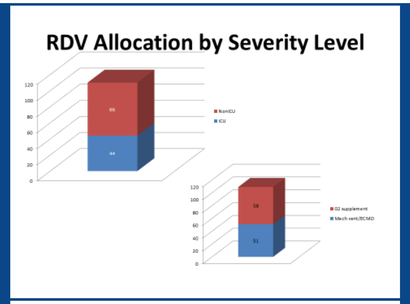
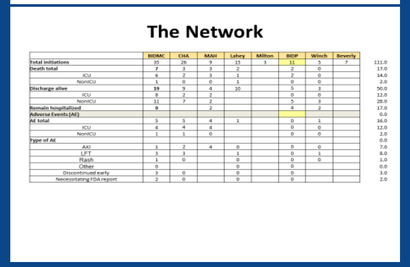
Results and Progress

June 2020

BILH Network Remdesivir EUA review done

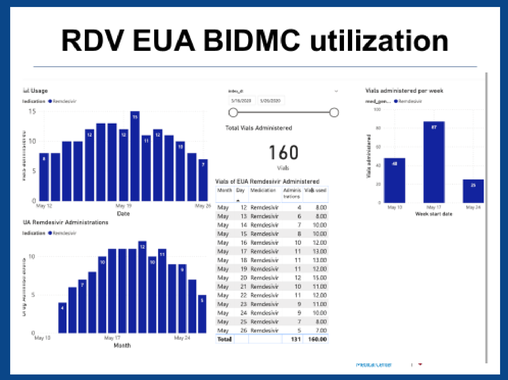




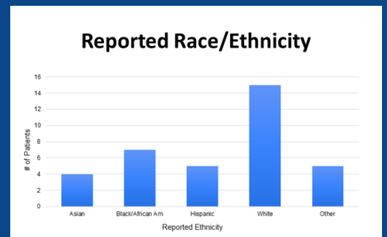


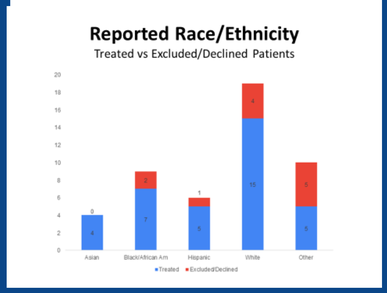
	BIDMC	CHA	MAH	Lahey	Milton	BIDP	Winch	Beverly	
Total initiations	35	26	9	13	3	11	5	7	111.0
Death total	7	3	2	2		2	0		17.0
ICU	6	2	1	1		2	0		14.0
NonICU	1	0	0	1		0	0		2.0
Discharge alive	19	9	4	10		5	3		50.0
ICU	8	2	2			0	0		12.0
NonICU	11	7	2			5	3		28.0
Remain hospitalized	9		2			4	2		17.0
Adverse Events (AE)									6.0
AE total	5	5	4	1		0	1		16.0
ICU	4	4	4			0	0		12.0
NonICU	1	1	0			0	0		4.0
Type of AE									0.0
AKI	1	2	4	0		0	0		7.0
LFT	3	3		1		0	1		8.0
Rash	1	0		0		0	0		1.0
Other	0			0		0			0.0
Discontinued early	3	0		0		0			3.0
Nonconsistating FDA report	2	0		0		0			2.0

A more transparent and functional tracking system of remdesivir developed for Performance Manager



Examination of ethnic/race diversity





OMR Macro development to ensure data integrity and documentation

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Remdesivir EUA Allocation OMR Communication v080320
Title: Remdesivir EUA Allocation
Requires attending sig/cosig

DATE 08/03/20

Contacted by XXXXXXXXXX requesting allocation of remdesivir
for treatment of COVID-19 for this patient, LAST NAME, MRN.

Upon review of patient's condition:

Confirmed COVID+
[ ] NP swab PCR
    Date: 08/02/20

Hypoxic respiratory failure
[ ] O2 sat less than or equal to 94% on RA
[ ] Requires supplemental O2 to maintain O2
[ ] Requires oximizer therapy to maintain O2
[ ] Mechanical Ventilation and/or ECMO < 5 days
[ ] Mechanical Ventilation and/or ECMO 6-10 days

Renal function
[ ] estimated GFR (CG calculation) > 30 mL/min
[ ] estimated GFR < 30 mL/min, AKI requiring CRRT, benefit exceeds risk
(unstudied population, consider Nephrology consultation)
[ ] estimated GFR < 30 mL/min, AKI or CKD, benefit exceeds risk (unstudied
population, consider Nephrology consultation)

Liver function
[ ] ALT < 200 (5x ULN), no signs or symptoms of liver disease
[ ] ALT > 200 (5x ULN) or above normal accompanied by signs or symptoms of
liver disease or increasing bilirubin, alkaline phorphatase, or INR, benefit
exceeds risk (unstudied population)

Informed consent
[ ] Team notified regarding requirement for documented consent,
signed/cosigned by attending physician prior to administration

Based on these factors, patient meets criteria for remdesivir under emergency
use authorization as per BIDMC Guideline, and thus is approved for allocation
at this time.  The drug will not be dispensed until consent is documented in
CWS.

NOTE: Please order daily CBC w/diff, LFT panel (AST/ALT plus alk phos and
tbili), Scr for estimated CrCl by CG. If any significant adverse events not
detectable with routine labs, e.g., rash, please notify AST at 39244.
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FDA approves Remdesivir fully and it earns a brand name

FDA NEWS RELEASE

FDA Approves First Treatment for COVID-19

For Immediate Release:

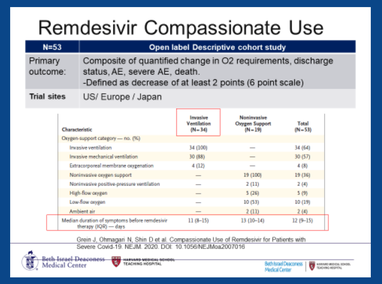
October 22, 2020

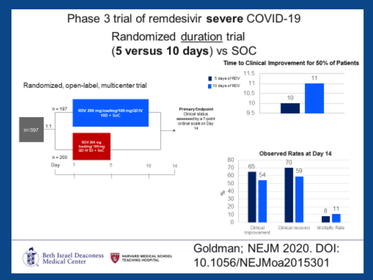
Español (/news-events/press-announcements/la-fda-aprueba-el-primer-tratamiento-para-el-covid-19)

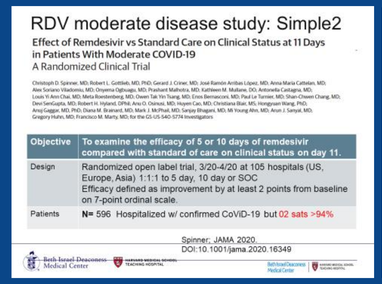
Today, the U.S. Food and Drug Administration approved (https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf) the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. Veklury is the first treatment for COVID-19 to receive FDA approval.

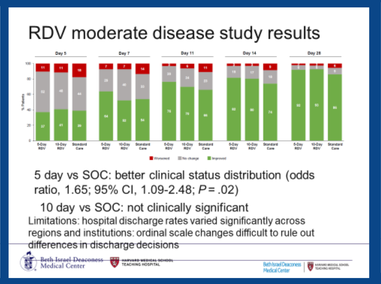
Approval is broadly permissive for inpatients with CoVID-19

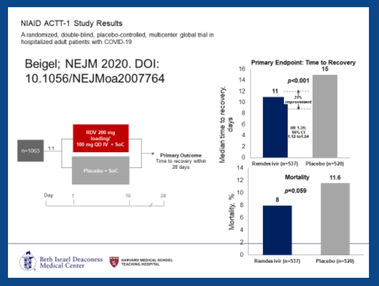
Stewardship group engages in a full review of remdesivir trial publications, local experience and FDA submission to present to treatment collaborative, local and system P&T











For more information, contact:

Christopher McCoy, PharmD cmccoy@bidmc.Harvard.edu Clinical Manager, Infectious Diseases Pharmacy, Antimicrobial Stewardship

Beth Israel Lahey Health

Beth Israel Deaconess Medical Center

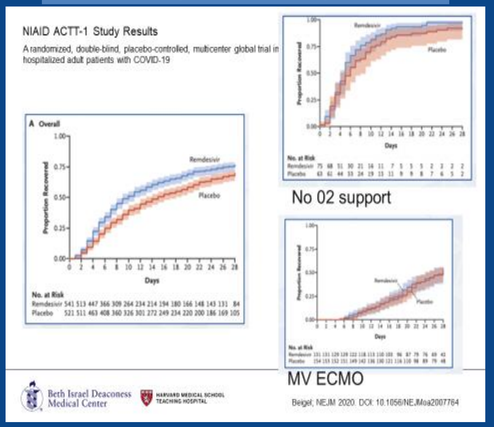
Remdesivir: From research to Emergency Use to FDA approval and Stewardship

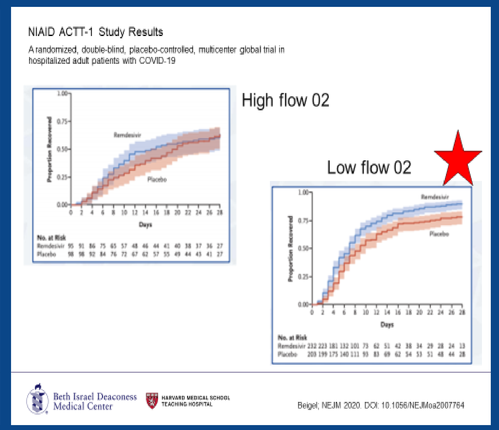
Christopher McCoy, Ryan Chapin, Jamie LeVash, Julius Yang, Katy Stephenson, Howard Seth Gold.

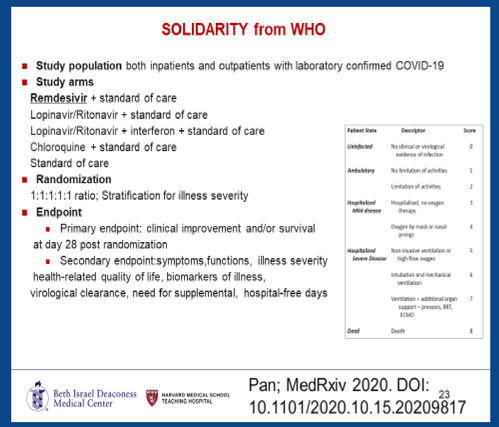
Department of Pharmacy, Division of Infectious Diseases, Division of Health Care Quality, Beth Israel Deaconess Medical Center

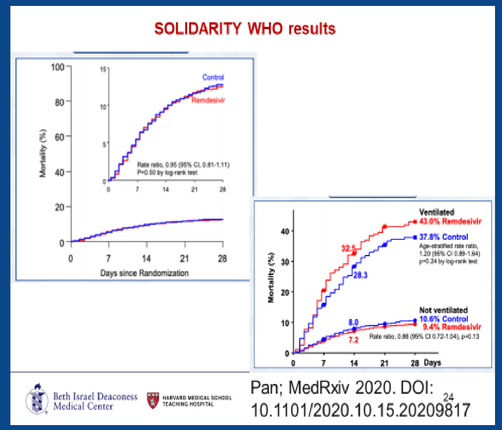
Results and progress

Formulary Review: Study Details

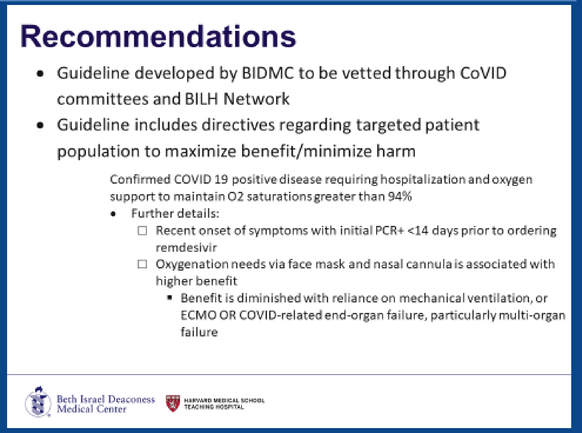








Final recommendations for approval with restrictions



Remdesivir Stewardship across the Network

High utilization at low volume hospitals

	Week 1	Week 2
AJH	172	135
BIDMC	1890	1827
BIDMIL	69	46
BIDNED	75	39
BIDPLY	488	445
LAHEY	793	744
MAH	289	184
Northeast	529	445
WIN	336	301
Total	4641	4166

High demand and utilization necessitated network shifts of supply

Lessons Learned

- Fielding the “in time” trajectory of drug research, compassionate use access, expanded use access and translation of published experience to best practice requires collaboration and human resources to avoid unintended consequences and optimize efficiency.
- Education, intensive tracking and communication are key to meeting regulatory compliance and optimizing care
- Open discussion and collaboration during an acute stressful surge allows for more transparent decision making and engagement

Next Steps

- Use the experience from remdesivir to build upon future Emergency Use Guidance
- Continue to steward remdesivir to gain benefit in the early infection stage of viral replication
- Optimize Stewardship resources for the network to build upon experience and higher level controls

For more information, contact:

Christopher McCoy, PharmD cmccoy@bidmc.Harvard.edu Clinical Manager, Infectious Diseases Pharmacy, Antimicrobial Stewardship