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#### ABNORMALITIES OF THE IMMUNE SYSTEM IN CANCER PATIENTS



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BEATING CANCER IS IN OUR BLOOD.

# Immunodeficiency in Individuals with Leukemia and Lymphoma

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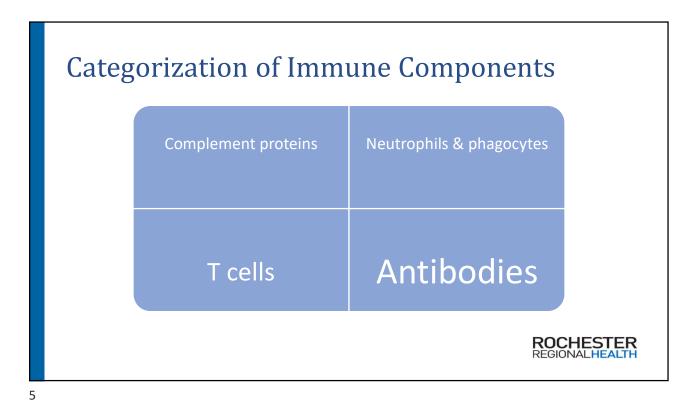
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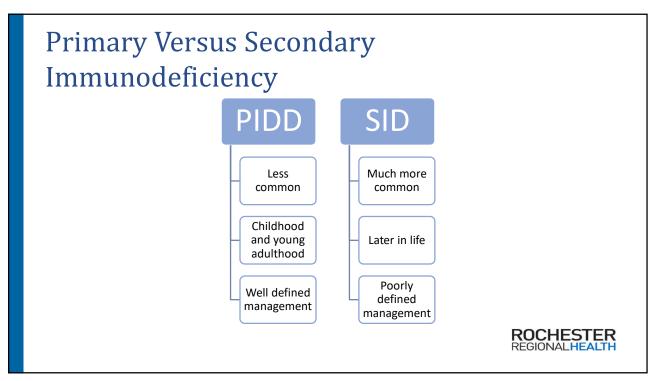
## Outline

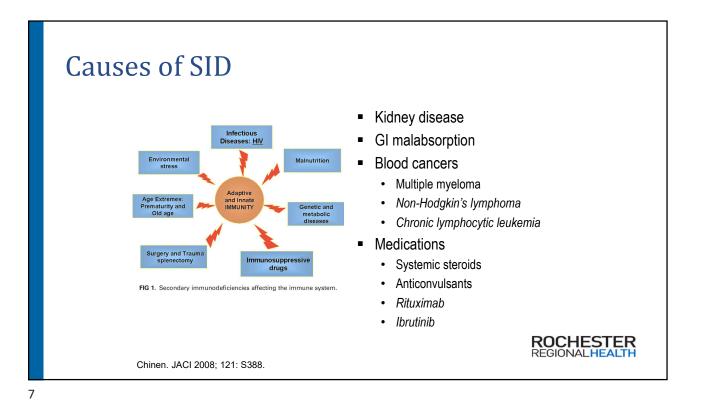
- Background of immunodeficiency
- Proposed evaluation of immunodeficiency
- Therapeutic options for immunodeficiency

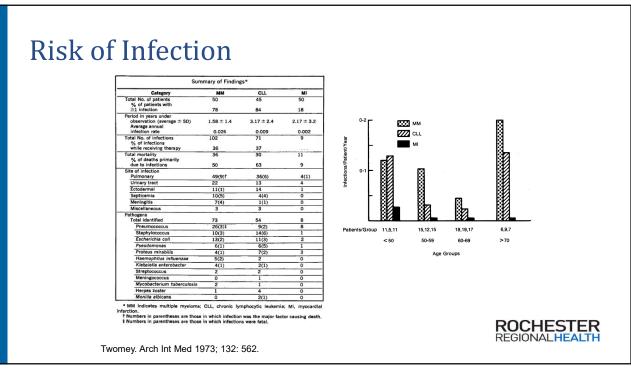
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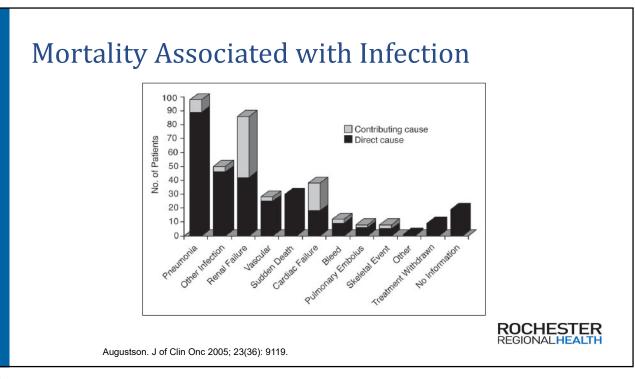
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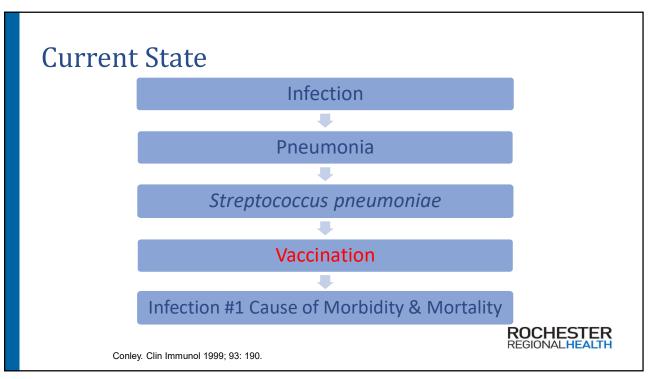


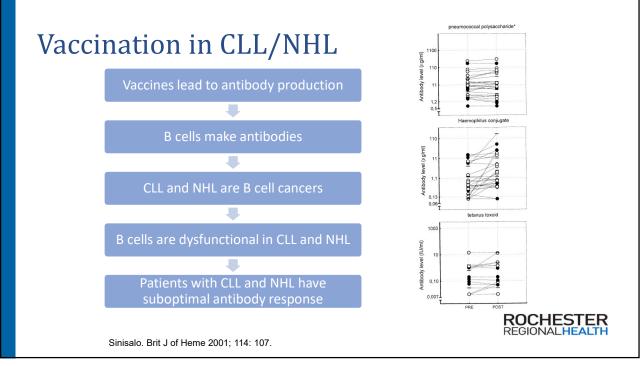


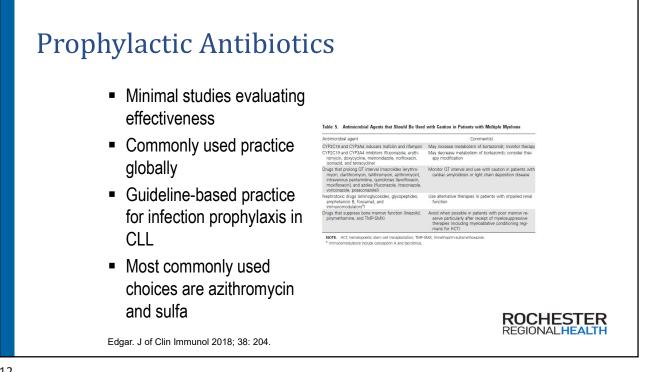


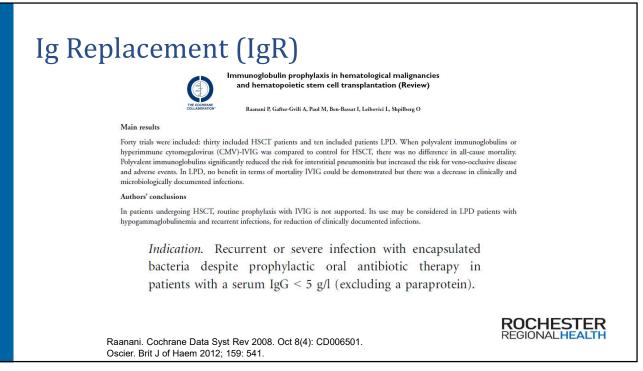




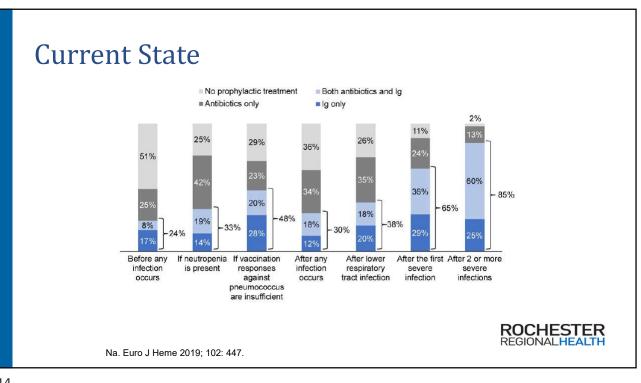


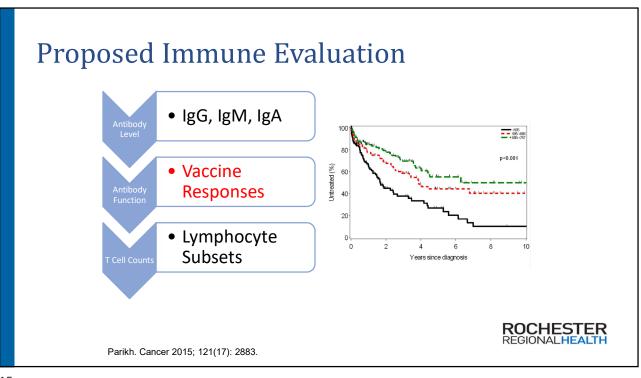


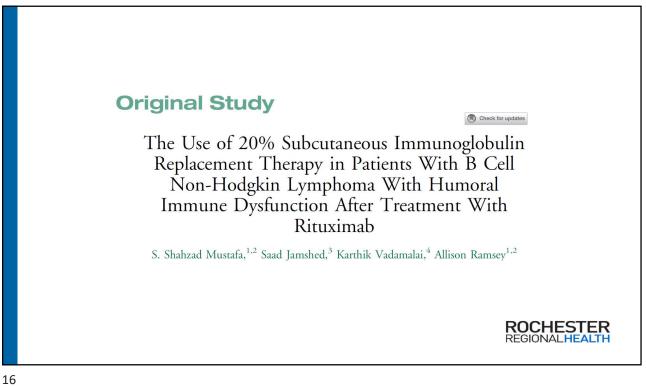




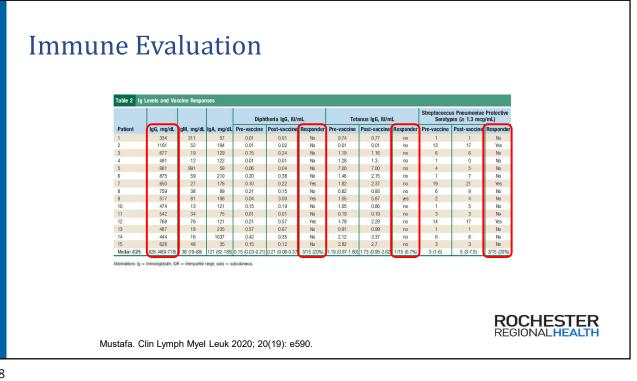








#### Demographics Table 1 Demographics Time Since Diagnosis, Time Since Rituximab, No. Cycles of Rituximab Concurrent Patient Age, y Gender Diagnosis mos mos Chemotherapy 71 М Lymphoplasmatic lymphoma 49 20 Bendamustine 1 2 81 M Follicular lymphoma 93 15 11 Bendamustine Diffuse large B cell lymphoma 3 66 F 10 6 7 CHOP 4 73 Diffuse large B cell lymphoma 10 CHOP 6 Bendamustine 5 Marginal zone lymphoma 66 F 16 3 13 14 CHOP Diffuse large B cell lymphoma М 6 48 6 13 CHOP 7 77 М Follicular lymphoma 6 9 8 73 М Mantle cell lymphoma 45 14 13 Bendamustine 9 72 F Follicular lymphoma 26 24 None 4 10 47 Follicular lymphoma 70 18 11 Bendamustine 11 79 F Diffuse large B cell lymphoma 13 6 8 CHOP 12 76 M Diffuse large B cell lymphoma 20 6 16 CHOP 13 63 М 194 Bendamustine Follicular lymphoma 30 9 14 68 Μ Lymphoplasmatic lymphoma 18 9 3 Bendamustine 15 58 F 12 Bendamustine Follicular lymphoma 6 Abbreviations: CHOP = cyclophosphamide, doxorubicin, vincristine, and prednisone; F = female; M = male. **ROCHESTER** REGIONALHEALTH Mustafa. Clin Lymph Myel Leuk 2020; 20(19): e590.



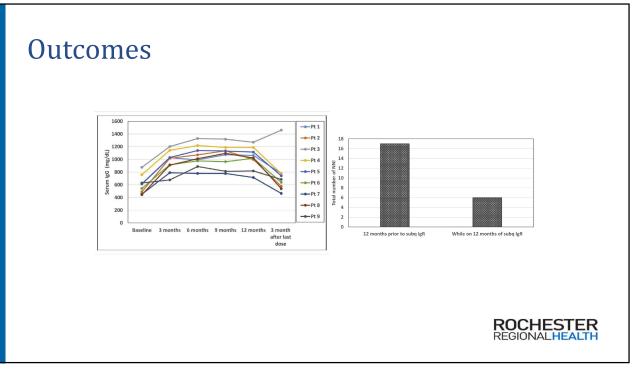
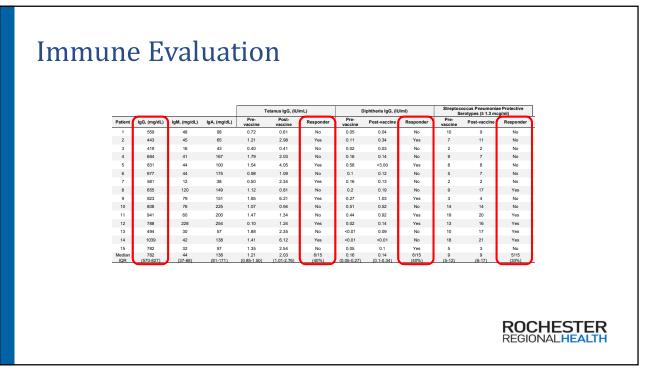
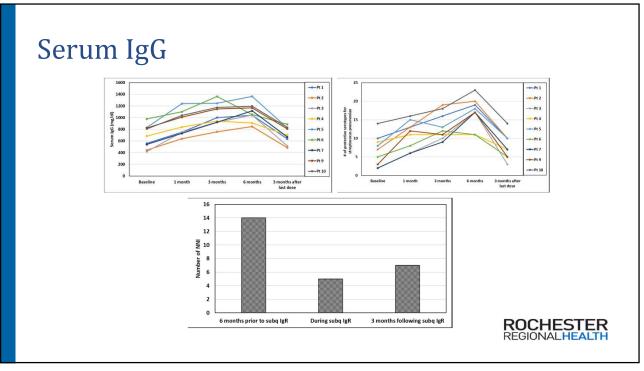




Table 1.	Dem	ograp	hics.			
Patient	Age	Sex	Time since diagnosis (years)	NNI treated with antibiotics (previous 6 months)	Current treatment	Previous treatment
1	68	М	14.6	5	Ibrutinib	Fludarabine + rituximab in 2011, rituximab in 2013, bendamustine + cyclophosphamide in 2014
2	75	F	8.3	3	None	None
3	76	М	18.4	1	None	None
4	68	М	20.4	2	None	None
5	66	F	1.8	0	None	None
6	68	М	15.8	0	None	Radiation to tonsil bed
7	71	М	0.5	2	None	None
8	70	М	23.0	0	None	Fludarabine 2003–1013, fludarabine + cyclophosphamide + rituximab 2012–2013
9	56	M	1.8	0	None	None
10	69	М	0.3	1	None	None
11	75	М	3.4	0	None	None
12	79	М	4.3	1	None	None
13	62	М	4.4	2	None	None
14	86	М	4.3	0	None	None
15	53	М	4.7	0	None	Vincristine + cyclophosphamide + rituximab 2012-2013, bendamustine + rituximab 2014-2015, ublituximab + umbralisib 2019





## SCIg Replacement

Patient	Weight (kg)	Weekly Dose (g)	Weekly Dose (g/kg/week)	# of sites (average)	Infusion time (min) (average)	Pre-medication regimen	Adverse events
1	91	12	0.133	2.5	55	None	None
2	78	10	0.129	2.5	64	None	None
3	88	12	0.137	3	56	None	None
4	103	12	0.117	2.5	57	None	None
5	84	11	0.131	2.5	63	None	None
6	137	18	0.132	3	64	None	None
7	85	11	0.130	2.5	64	None	None
8	104	13	0.126	2.5	56	Diphenhydramine, acetaminophen	Fatigue
9	88	11	0.125	2	62	None	None
10	86	11	0.127	2	59	None	None
Median IQR	88 (85-100)	11.5 (11-12)	0.12 (0.12-0.13)	2.5	61 (56-64)		

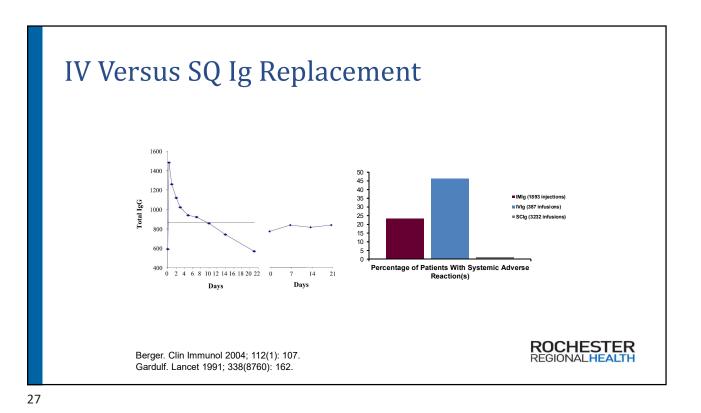
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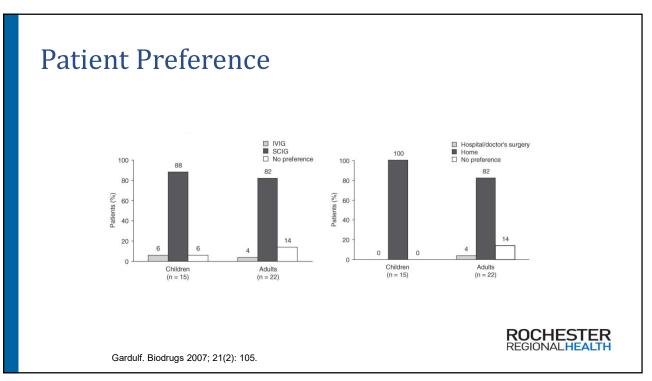
## Ig Replacement

- Decreases rate of infections
- Decreased antibiotic dependence
- Decreased hospitalizations
- Does NOT prevent additional cancer
- Routes of administration
  - IM versus IV versus SQ

Busse PJ. JACI 2002; 109: 1001.







## IV Versus SQ Pros and Cons

#### Advantages of Intravenous

Ability to administer large doses Infrequent dosing \*

#### Disadvantages of Intravenous

Need for IV access Increased risk of adverse reactions Large variations in IgG levels Increased use of medical resources

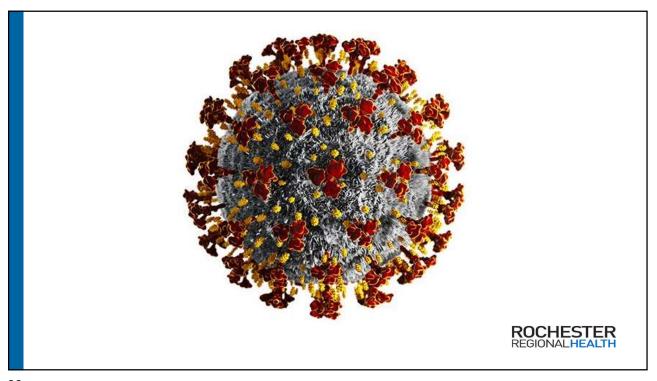
#### Advantages of Subcutaneous

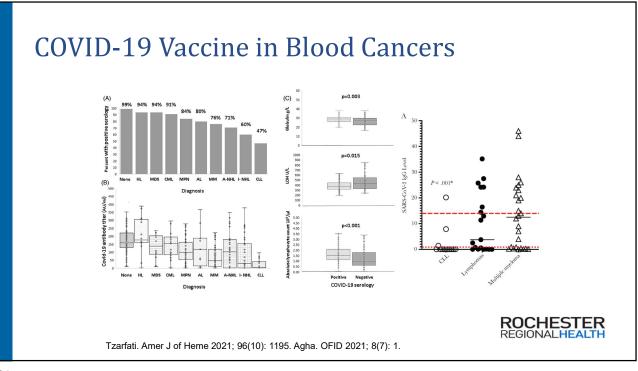
No need for IV access Decreased risk of adverse reactions Consistent levels of IgG Increased patient autonomy

#### Disadvantages of Subcutaneous

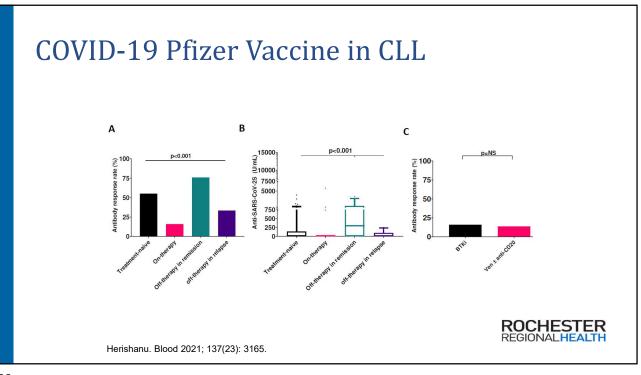
Historically more frequent dosing \* May apply to small amount of patients

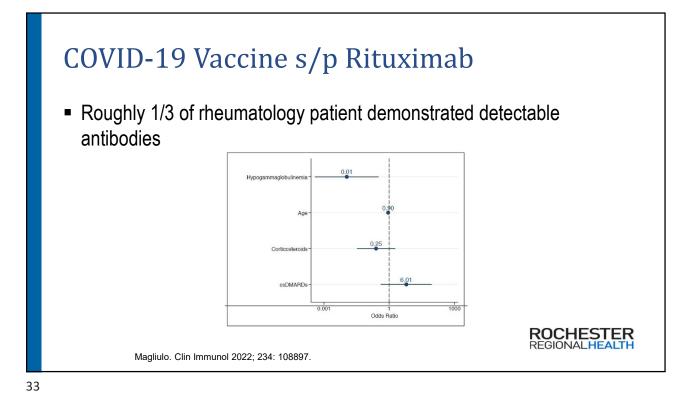


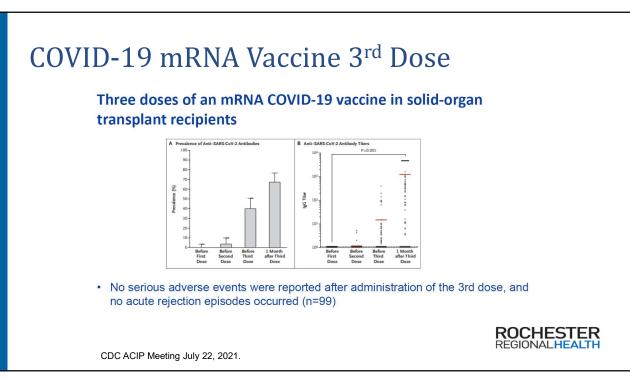


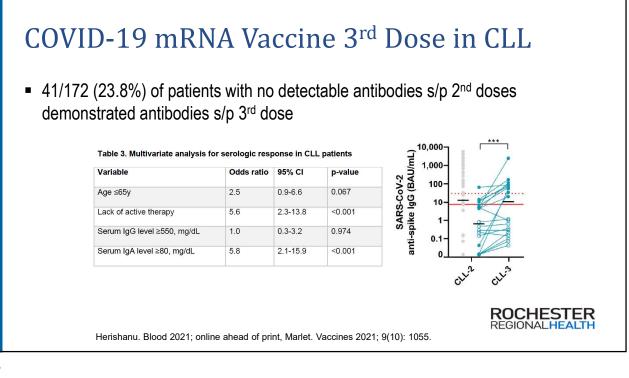




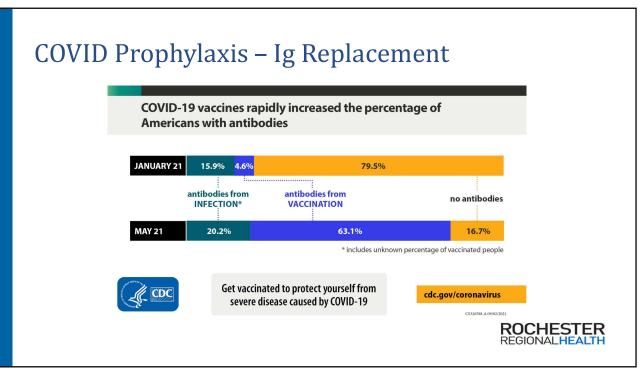


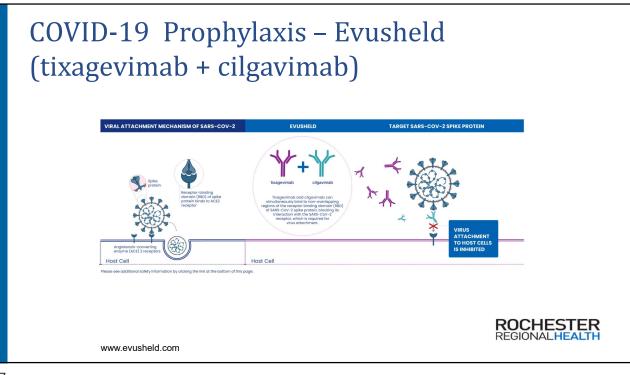


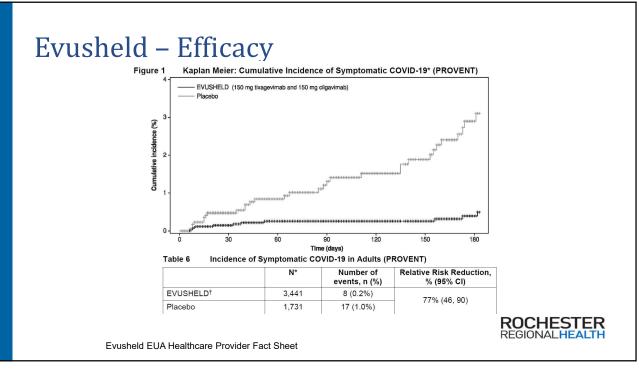












## Evusheld – Adverse Events

#### Cardiac SAEs Regardless of Causality in PROVENT with Onset Prior to Day 183 Table 3 Using the Median 6-Month Data Cut-off Date

	EVUSHELD N= 3,461	Placebo N= 1,736
Subjects with any cardiac SAE*	22 (0.6%)	3 (0.2%)
SAEs related to coronary artery disease or myocardial ischemia <sup>†</sup>	10 (0.3%)	2 (0.1%)
Myocardial infarctions <sup>‡</sup>	8 (0.2%)	1 (0.1%)
SAEs related to cardiac failure <sup>§a</sup>	6 (0.2%)	1 (0.1%)
SAEs related to an arrhythmia <sup>¶</sup>	4 (0.1%)	1 (0.1%)
Other (cardiomegaly, cardiomyopathy, and cardio-respiratory arrest)	3 (0.1%)	0

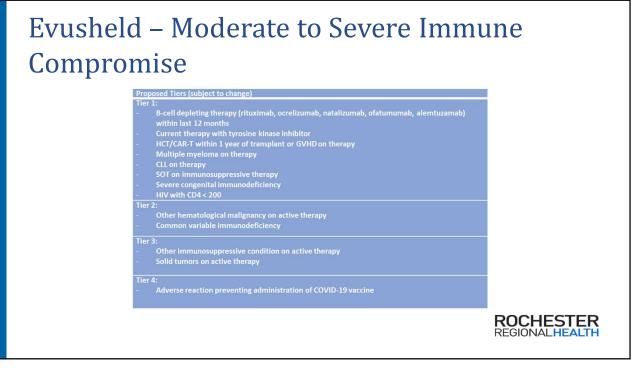
Cardio-respiratory arrest)
\* One EVUSHELD recipient and one placebo recipient had two cardiac SAEs each.
\* Includes the preferred terms angina pectoris, coronary artery disease, arterioscierosis, troponin increased, acute myocardial infarction,

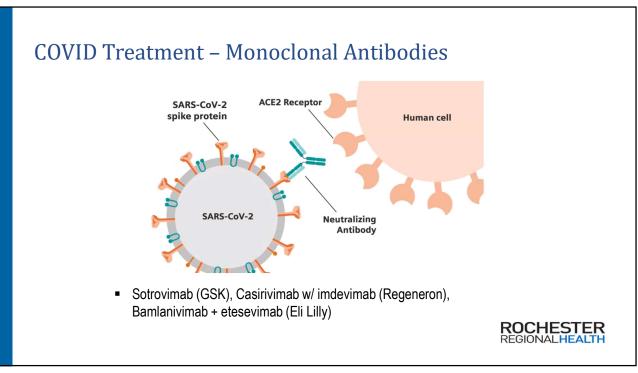
and myocardial infarction. <sup>1</sup>Includes the preferred terms acute myocardial infarction, myocardial infarction, and troponin increased (with a discharge diagnosis of myocardial infarction). <sup>9</sup>Includes the preferred terms cardiac failure congestive, acute left ventricular failure, cardiac failure, and cardiac failure acute.

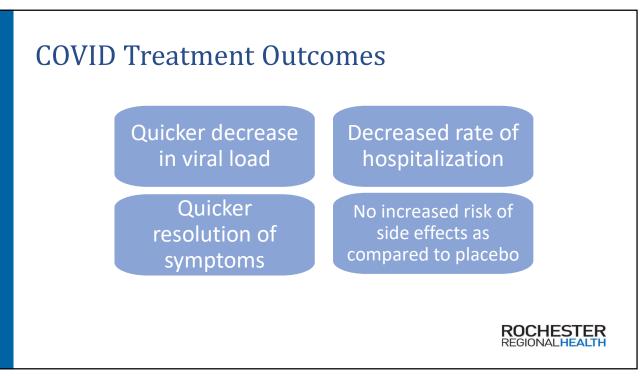
<sup>1</sup> Includes the preferred terms atrial fibrillation, arrhythmia, paroxysmal atrioventricular block, and heart rate irregular.



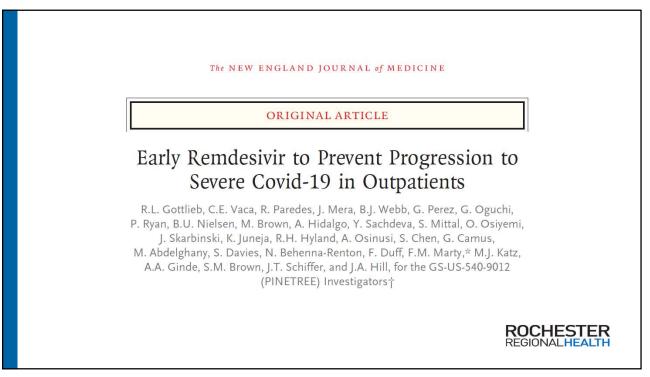
Evusheld EUA Healthcare Provider Fact Sheet







# Eligible Patients for MABs Treatment of mild to moderate OVID-19 in adults and pediatrics (≥ 12 years) with positive results for SARS-CoV-2 testing and are at high risk for progressing to severe COVID-19 • Hospitalized due to COVID-19 • Who require oxygen therapy due to COVID-19 • Require an increase in baseline oxygen flow rate due to COVID-19 • Require an increase in baseline oxygen flow rate due to COVID-19



#### **Remdesivir for Outpatient COVID** Table 2. Efficacy Calculated with the Use of a Cox Proportional-Hazards Model with Baseline Stratification Factors as Covariates.\*\* Hazard Ratio (95% CI) Remdesivir Placebo End Point (N=279) (N = 283) P Value Primary efficacy end point Covid-19–related hospitalization or death from any cause by day 28 — no. (%)† 2 (0.7) 15 (5.3) 0.13 (0.03 to 0.59) 0.008 Secondary efficacy end points Covid-19-related hospitalization or death from any cause by day 14 — no. (%) 2 (0.7) 15 (5.3) 0.13 (0.03 to 0.59) Covid-19-related medically attended visit or death from any cause — no./total no. (%)‡ Day 14 2/246 (0.8) 20/252 (7.9) 0.10 (0.02 to 0.43) 4/246 (1.6) Day 28 21/252 (8.3) 0.19 (0.07 to 0.56) Death from any cause by day 28 — no. 0 0 NC Hospitalization for any cause by day 28 — no. (%)§ 0.28 (0.10 to 0.75) 5 (1.8) 18 (6.4) **ROCHESTER** REGIONALHEALTH

Gottlieb. NEJM 2021; Online ahead of print.

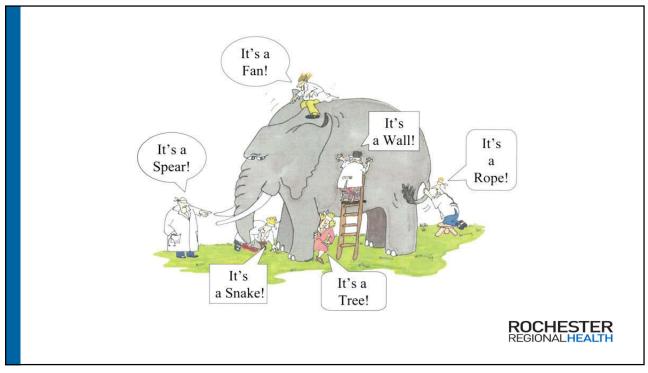
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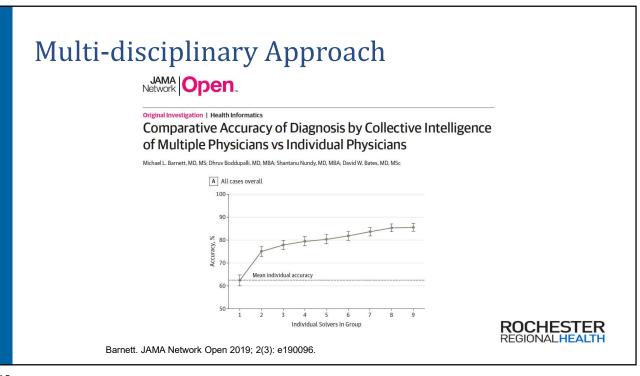
# COVID-19 Treatment – Oral Antivirals

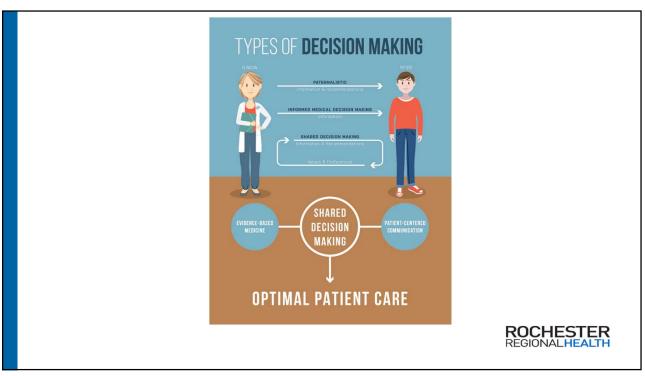
Treatment of mild to moderate COVID-19 in adults and pediatrics (≥ 12 years) with positive results for SARS-CoV-2 testing and are at high risk for progressing to severe COVID-19 and/or hospitalization.

## Paxlovid (nirmetrelvir + ritonavir)

- Consider drug-drug interactions
- Molnupiravir
  - Contraindicated in pregnancy or in individuals who may become pregnant







## Summary

- Individuals with blood cancers have immune dysfunction and should be routinely evaluated
- Infections are the #1 cause of complications in patients with blood cancers
- Vaccines are recommended but response is often suboptimal
- Additional strategies to decrease infectious complications should be considered on a case by case basis
- COVID pandemic poses increased risk to individuals with CLL

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# Thank You

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