Remdesivir reduces mortality in elderly patients 65+ years hospitalised for COVID-19 during Omicron

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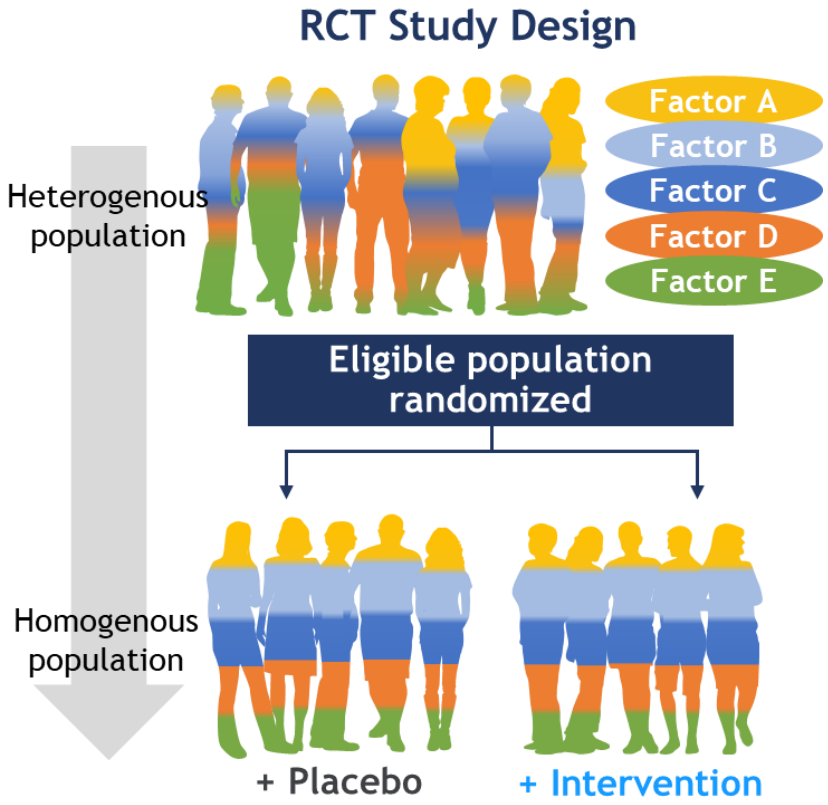
Key Findings

- In this study using real-world observational data, **remdesivir is associated with reduced mortality among elderly patients hospitalized for COVID-19** regardless of supplemental oxygen requirements upon admission and age groups
- This significant association was observed in the most recent Omicron pre-dominant era from December 2021 to April 2023

	Comparative Effectiveness Research studies (CERs)	Randomized Clinical Trials (RCTs)
Purpose	Establish effectiveness (clinical, economic, humanistic etc.)	Establish efficacy and safety
Setting	Real-world	Clinical
Design	Observational	Experimental/interventional
Variability/ heterogeneity	Designed to capture the **full heterogeneity** of patient populations managed in routine clinical practice, including patients with comorbidities who are taking other/multiple medications	Designed to control for as much variability as possible (eligibility criteria for study population, treatment administration, etc.) via randomization
Data quality	Variable - rely on data that is already being collected as part of routine clinical care, which can vary in quality and completeness	High - high-quality data using standardized protocols and rigorous quality control measures
External validity	**High**	**Low**
Sample size	**Generally larger than RCTs**	**Generally small**

RWE complements randomized controlled trials (RCTs)



RCTs considered 'gold standard', but[1-3]

- Not always feasible or ethical
- Costly, time consuming, and generally short follow-up
- Normally conducted done in specific populations and may not be generalizable to patients in actual clinical practice

RWE studies are not alternatives to RCTs, but rather support and complement them[1-4]

- Include populations more reflective of 'real-world' people with comorbidities and/or taking multiple medications
- FDA/EMA recognize the role of RWE in drug approval processes and post-authorization studies
- During public health crises, it is essential that RWE is of sufficient quality to inform clinical decision making real-time
- CERs are RWD studies that generate evidence to directly complement the findings of RCTs

1. Sherman, et al. N Engl J Med 2016; 375:2293-7.
2. Blonde, et al. Adv Ther 2018; 35:1763-74.
3. Read SH, et al. J Comp Eff Res 2021 Aug 31;10.2217/cer-2021-0179.
4. Public Law 114-255, 114th Congress. The 21st Century Cures Act. December 13, 2016.

Study overview

To compare inpatient all-cause mortality in patients who were administered remdesivir (RDV) in the first two days of hospitalization vs. those not administered remdesivir during hospitalization among patients **65+years of age** and hospitalized **for COVID-19**

Patients 65+years of age and hospitalized for COVID-19 documented as the primary discharge diagnosis and flagged as "present-on-admission"

- **RDV in the first two days of hospitalization**
- **No RDV in the first two days of hospitalization**

Primary Endpoints

14-day in-hospital mortality
28-day in-hospital mortality

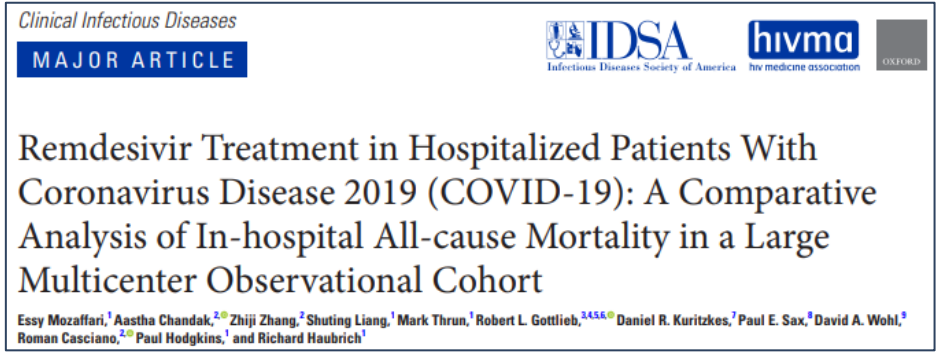
Inclusion criteria	✓	First admission to the hospital Dec 1, 2021-Apr 30, 2023 (Omicron pre-dominant period in US)
	✓	Age ≥65 years old
	✓	***Primary*** **discharge diagnosis of COVID-19** (ICD-10-CM: U07.1) flagged for being "present-on-admission"
Exclusion criteria	×	Pregnant
	×	Had incomplete/erroneous data fields
	×	Transferred from another hospital or hospice; Transferred to another hospital
	×	Admitted for elective procedures
	×	Discharged or died during the baseline period (first two days of hospitalization)

Data source:

PINC AI Healthcare Database (formerly Premier Healthcare Database)

- US hospital-based, service-level, all-payer (Commercial, Medicare, Medicaid, others) database
- Covers ~25% of all US hospitalizations from 48 states

Methodology published previously in peer-reviewed journals



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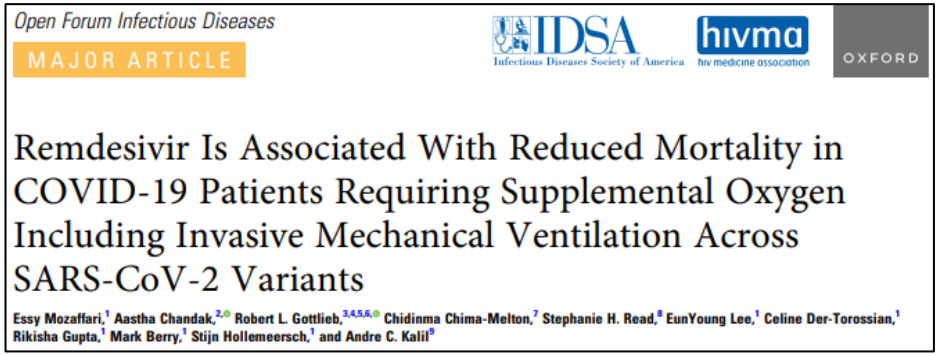
Remdesivir Treatment in Hospitalized Patients With Coronavirus Disease 2019 (COVID-19): A Comparative Analysis of In-hospital All-cause Mortality in a Large Multicenter Observational Cohort

Essy Mozaffari,[1] Aastha Chandak,[2] Zhiji Zhang,[2] Shuting Liang,[1] Mark Thrun,[1] Robert L. Gottlieb,[3,4,5,6] Daniel R. Kuritzkes,[7] Paul E. Sax,[8] David A. Wohl,[9] Roman Casciano,[2] Paul Hodgkins,[1] and Richard Haubrich[1]



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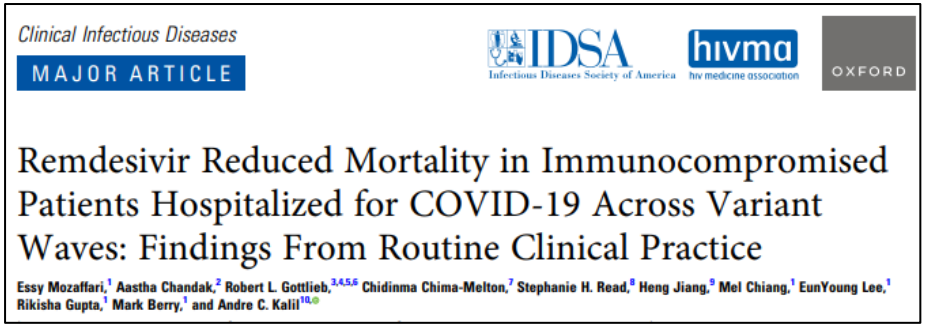
Remdesivir Is Associated With Reduced Mortality in COVID-19 Patients Requiring Supplemental Oxygen Including Invasive Mechanical Ventilation Across SARS-CoV-2 Variants

Essy Mozaffari,[1] Aastha Chandak,[2] Robert L. Gottlieb,[3,4,5,6] Chidinma Chima-Melton,[7] Stephanie H. Read,[8] EunYoung Lee,[1] Celine Der-Torossian,[1] Rikisha Gupta,[1] Mark Berry,[1] Stijn Hollemeersch,[1] and Andre C. Kalil[9]



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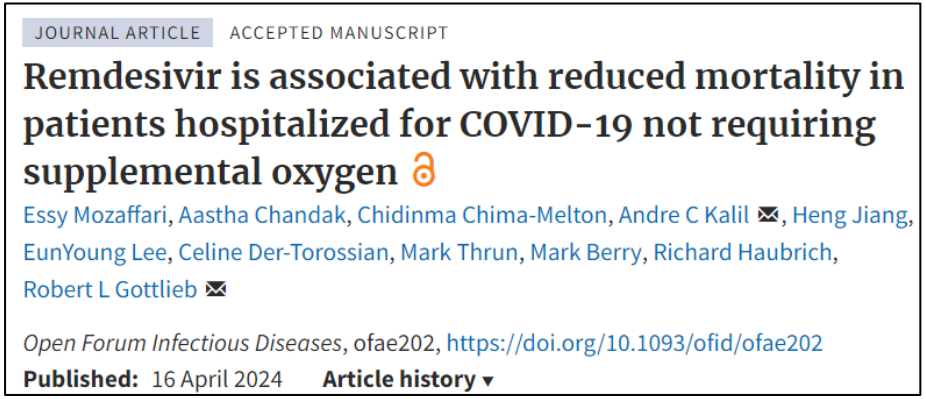
Remdesivir Reduced Mortality in Immunocompromised Patients Hospitalized for COVID-19 Across Variant Waves: Findings From Routine Clinical Practice

Essy Mozaffari,[1] Aastha Chandak,[2] Robert L. Gottlieb,[3,4,5,6] Chidinma Chima-Melton,[7] Stephanie H. Read,[8] Heng Jiang,[9] Mel Chiang,[1] EunYoung Lee,[1] Rikisha Gupta,[1] Mark Berry,[1] and Andre C. Kalil[10]



JOURNAL ARTICLE · ACCEPTED MANUSCRIPT

Remdesivir is associated with reduced mortality in patients hospitalized for COVID-19 not requiring supplemental oxygen

Essy Mozaffari, Aastha Chandak, Chidinma Chima-Melton, Andre C Kalil ✉, Heng Jiang, EunYoung Lee, Celine Der-Torossian, Mark Thrun, Mark Berry, Richard Haubrich, Robert L Gottlieb ✉

Open Forum Infectious Diseases, ofae202, https://doi.org/10.1093/ofid/ofae202

Published: 16 April 2024 **Article history** ▾

Methodology published previously in peer-reviewed journals

Propensity score (PS) matching approach was used to balance the two groups

PS Calculation

- Calculate the PS through logistic regression – 4 separate models (baseline supplemental oxygen requirements)

Matching

- 1:1 preferential within-hospital matching with replacement (forced matched on age group, baseline supplemental oxygen requirements, admission month group)
- Matched pair of patients were excluded if discharged within 3 days of RDV initiation

Balance checks

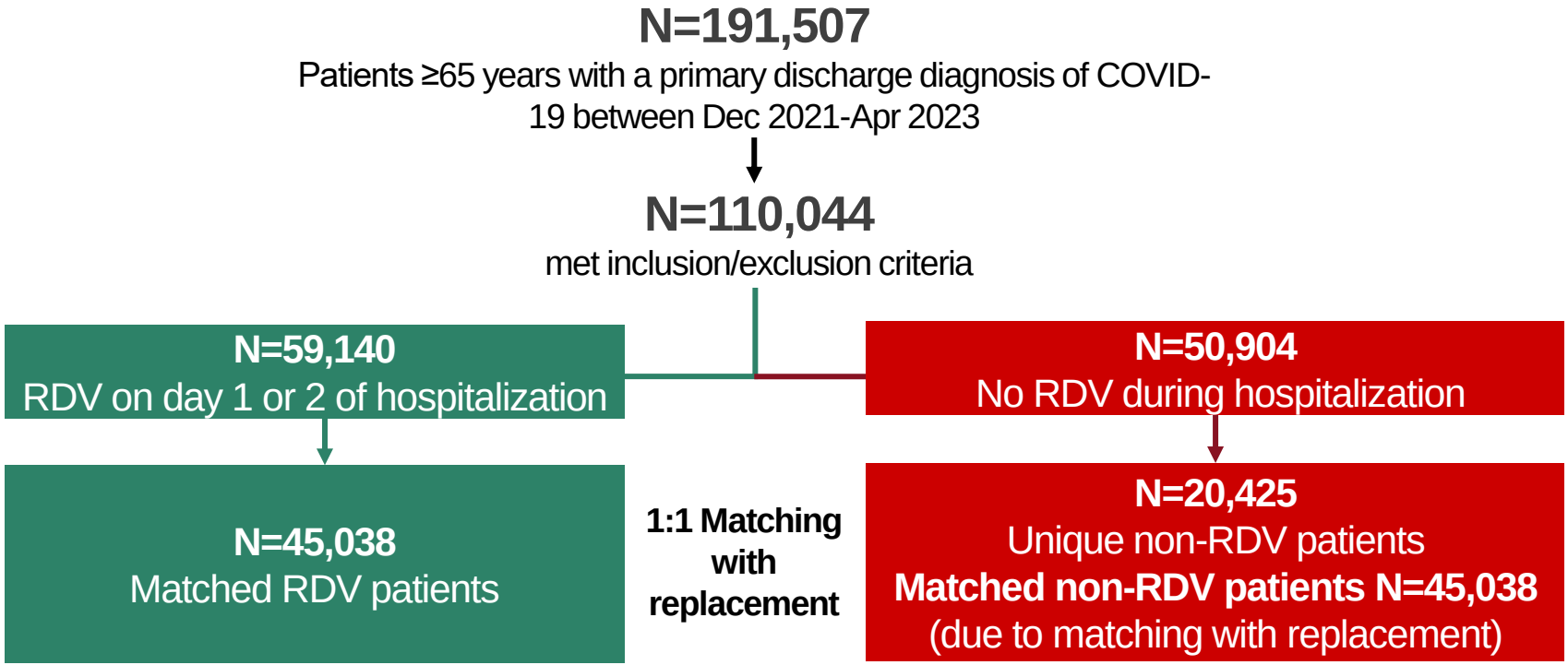
- Examine the distribution of the BL characteristics (covariates)
- Standardized difference* to compare balance between treatment groups

Outcome assessment

- Crude mortality rates in the matched cohort
- Adjusted Cox proportional hazards model in the matched cohort to examine time to 14- and 28-day mortality

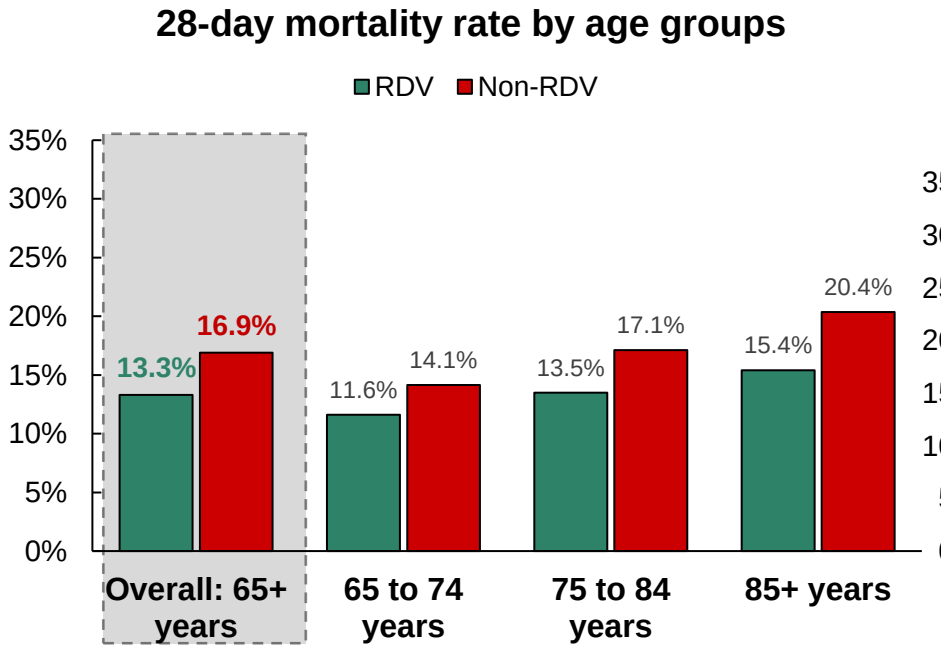
BL: baseline; PS: propensity score; RDV: remdesivir; NSOc: No supplementary oxygen charges; LFO: Low Flow Oxygen; HFO/NIV: High Flow Oxygen; IMV/ECMO: Invasive Mechanical Ventilation / Extracorporeal Membrane Oxygenation
*Standardized difference is the difference in mean (mean RDV – mean control) divided by the standard deviation of the groups

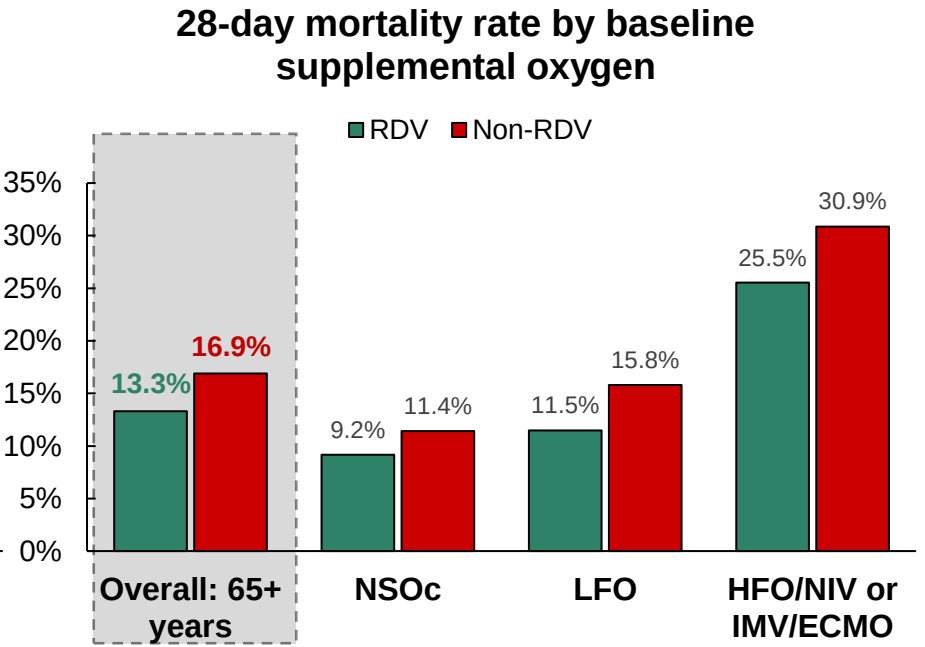
Patient Disposition



Since matching with replacement technique was used, 1 non-RDV patient could be matched multiple times to different RDV patients

Among patients 65+ years hospitalized for COVID-19, **lower mortality rates** were observed for RDV-treated patients across **all baseline supplemental oxygen** requirements and across **all age groups**





LFO, low-flow oxygen; HFO/NIV, high-flow oxygen/non-invasive ventilation; IMV/ECMO, invasive mechanical ventilation/extracorporeal membrane oxygenation; NSOc, no supplemental oxygen charges; RDV, remdesivir

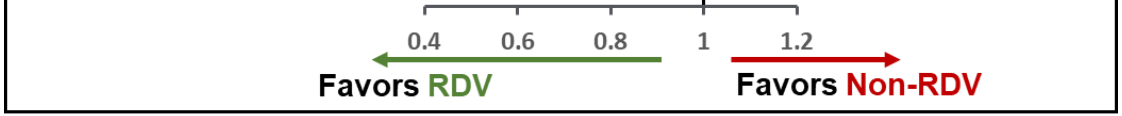
Among elderly patients hospitalized for COVID-19, RDV was associated with a **significantly lower mortality risk** compared to non-RDV across **all age groups above 65+years**

	N	aHR [95% CI]	P value
14-day mortality			
Overall: 65+ years	90076	0.74 [0.70 - 0.79]	<.0001
65 to 74 years	32524	0.77 [0.68 - 0.87]	<.0001
75 to 84 years	33908	0.75 [0.68 - 0.82]	<.0001
85+ years	23644	0.72 [0.66 - 0.80]	<.0001
28-day mortality			
Overall: 65+ years	90076	0.77 [0.73 - 0.81]	<.0001
65 to 74 years	32524	0.81 [0.73 - 0.89]	<.0001
75 to 84 years	33908	0.76 [0.71 - 0.83]	<.0001
85+ years	23644	0.74 [0.68 - 0.81]	<.0001

Note: Estimates adjusted for age, admission month, hospital ward upon admission (ICU vs. general ward), and baseline treatments (anticoagulants, convalescent plasma, corticosteroids, baricitinib, tocilizumab)
aHR, adjusted hazard ratio; CI, confidence interval; RDV, remdesivir

Among elderly patients hospitalized for COVID-19, RDV was associated with a **significantly lower mortality risk** compared to non-RDV across **all baseline supplemental oxygen requirements**

	N	aHR [95% CI]	P value
14-day mortality			
Overall	90076	0.74 [0.70 - 0.79]	<.0001
NSOc	41682	0.77 [0.70 - 0.85]	<.0001
LFO	29750	0.67 [0.60 - 0.75]	<.0001
HFO/NIV or IMV/ECMO	18644	0.77 [0.70 - 0.85]	<.0001
28-day mortality			
Overall	90076	0.77 [0.73 - 0.81]	<.0001
NSOc	41682	0.79 [0.72 - 0.86]	<.0001
LFO	29750	0.70 [0.64 - 0.77]	<.0001
HFO/NIV or IMV/ECMO	18644	0.79 [0.73 - 0.86]	<.0001



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Conclusions

- The elderly patient population remains vulnerable to severe manifestations of COVID-19 infection, with age being the strongest risk factor for severe COVID-19 outcomes[1]
  - These patients typically have a high comorbidity burden and polypharmacy[2]
- In the Omicron predominant COVID-19 era, initiation of RDV in elderly patients hospitalized for COVID-19 was associated with lower risk of mortality
  - These findings were consistent across baseline supplemental oxygen requirements and age groups
- Remdesivir is indicated to reduce mortality among the high-risk elderly patient population hospitalized for COVID-19

1. CDC (2023) Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals. Available: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html. [Accessed 10 April 2024].
2. Rahman, Sayeeda, et al (2020). The double burden of the COVID-19 pandemic and polypharmacy on geriatric population–public health implications. *Therapeutics and clinical risk management*, 16, 1007–1022

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- All authors contributed to and approved the presentation

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