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Key Remdesivir Resistance Mutations in SARS-CoV-2 Using GISAID Data (2020-2024)

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BACKGROUND

The emergence of remdesivir (RDV) resistance mutations poses a potential challenge in treating SARS-CoV-2 infections, especially as the virus continues to evolve globally. GISAID[1] data provides an extensive resource for tracking such mutations. This study aims to investigate the **temporal trends and incidence rates of RDV resistance-associated mutations**, specifically those conferring a **>2.5-fold reduction** in susceptibility, to understand their prevalence and patterns over time.

METHODS

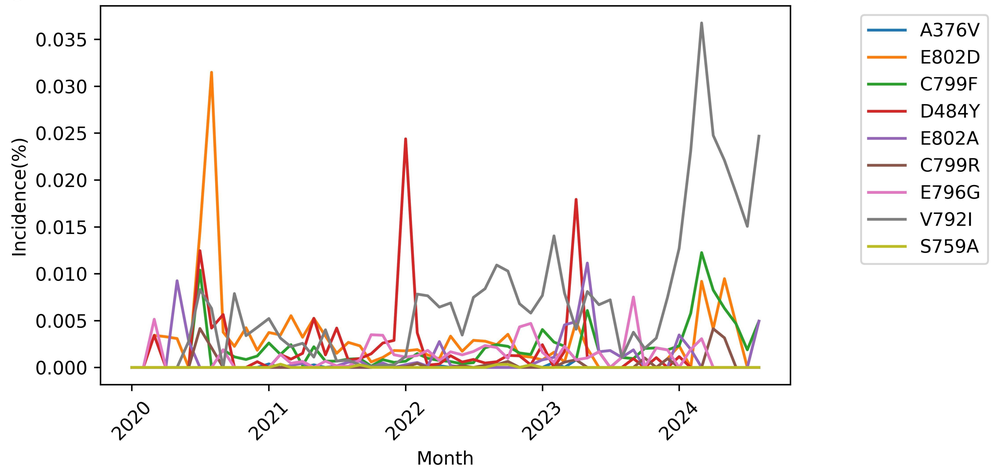
Genomic surveillance data from GISAID, covering the period from January 2020 to August 2024, were analyzed. The focus was on nine mutations associated with RDV resistance which confers > 2.5-fold reduction in susceptibility per **The Stanford Coronavirus Resistance Database (CoV-RDB)**[2]: A376V, E802D, C799F, D484Y, E802A, C799R, E796G, V792I, and S759A (Table). Monthly incidence rates were calculated by dividing the number of samples carrying each mutation by the total number of samples sequenced each month. Descriptive statistics were used to summarize trends, and the mean, standard deviation, and quartiles of the incidence rates were calculated to characterize mutation frequency patterns over time.

Mutation	RDV: fold	Ref.
A376V	12.6	PMID: **39699245**
D484Y	3.1	PMID: **36972312**
S759A	2.6	PMID: **35482820**
V792I	2.6	PMID: **35482820**
E796G	2.8	PMID: **36972312**
C799F	3.4	PMID: **36972312**, PMID: **35482820**
C799R	2.8	PMID: **35482820**
E802A	3	PMID: **35301314**, PMID: **34534263**
E802D	6	PMID: **35301314**, PMID: **34534263**

Table. RdRP inhibitor resistance mutations conferring > 2.5 fold reduction in RDV susceptibility

GISAID surveillance data (2020-2024) reveals that **high-level remdesivir** resistance remains **exceptionally rare**, with the most common mutation (**V792I**) peaking at only **0.037%** incidence.

Figure. Incidence of RDV Mutations Conferring > 2.5 fold Reduction in Susceptibility Over Time



RESULTS

The mutation with the highest peak incidence was **V792I**, with a **maximum of 0.0367%** of total sequenced samples in one month. **E802D** also demonstrated a significant peak incidence of **0.0315%**. Mutations such as **C799F**, **D484Y**, and **C799R** exhibited lower but consistent incidences, with means ranging from 0.0020% to 0.0031%. Notably, **A376V** and **S759A** exhibited very low incidence rates, with means of 0.00007% and 0.00003%, respectively, indicating rare occurrences. The data showed periodic surges in certain mutations, particularly **E802D** and **V792I**, which could indicate selective pressures or shifts in viral fitness during the study period (Fig).

CONCLUSIONS

The study highlights that while **RDV resistance mutations remain relatively rare**, specific mutations such as **E802D** and **V792I** have demonstrated transient increases in prevalence. This suggests **potential adaptive advantages in certain populations or during specific time frames**. Continued genomic surveillance is critical to monitor these mutations, assess their clinical significance, and guide therapeutic strategies for SARS-CoV-2 treatment, especially in the context of antiviral resistance. Further research should explore the underlying mechanisms driving these periodic surges and evaluate the clinical implications of RDV resistance in treatment outcomes.

References

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2. Tzou PL, Tao K, Pond SLK, Shafer RW. **Coronavirus Resistance Database (CoV-RDB): SARS-CoV-2 susceptibility to monoclonal antibodies, convalescent plasma, and plasma from vaccinated persons.** PLOS ONE. 2022 Mar 9;17(3):e0261045. doi: 10.1371/journal.pone.0261045

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