Remdesivir – a death protocol

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DATA SOURCE

Eudra-vigilance data for all medicines, substances, products and vaccines between 2017 and 2024. [500 Mb compressed].

Note :

- Single-line datafile has fields – “PATHOLOGY”, “DRUGS”, REACTION” . It has a one symptom per line.
- Multi-line datafile has fields – “PATHOLOGY”, “DRUG”, REACTION”. It has one record per line. Each record can have multiple symptoms.

- All fields should be converted to lower case before analysis, and all null rows removed.

Download link -
https://www.dropbox.com/scl/fi/phs3y74e3fytltuuv7otx/eudra.zip?rlkey=5hwm09juhwp7cmks6qx8uw17a&st=lhie7ev0&dl=0

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SYMPTOMS OF REMDESIVIR contents

METHOD

1. The multi-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports for Remdesivir where selected
5. The frequency of each unique symptom in the filtered records was counted.
6. Each symptom count was divided by the total number of symptoms (7734) to give the percentage of all symptoms for a particular symptom.

RESULTS

TABLE 1 : Symptoms of Remdesivir ordered by incidence.

SYMPTOM	FREQ	%
death	410	5.30
bradycardia	251	3.25
covid-19	241	3.12
alanine aminotransferase increased	216	2.79
acute kidney injury	200	2.59
transaminases increased	166	2.15
drug ineffective	158	2.04
off label use	157	2.03
renal impairment	130	1.68
aspartate aminotransferase increased	124	1.60
respiratory failure	112	1.45
covid-19 pneumonia	105	1.36
sinus bradycardia	99	1.28
liver function test increased	90	1.16
hepatic enzyme increased	89	1.15
hypertransaminasaemia	89	1.15
blood creatinine increased	84	1.09
hypotension	71	0.92
hepatic function abnormal	71	0.92
pneumonia	71	0.92
dyspnoea	66	0.85
renal failure	66	0.85
cardiac arrest	64	0.83
rash	59	0.76

It can be seen that almost all of the most common symptoms have to do with liver injury and kidney injury.

BIOMARKERS OF LIVER INJURY **contents**

Three liver enzymes

Alanine aminotransferase (ALT) is used in the assessment of liver disease (not a test of liver function). **Increased values indicate hepatocyte injury and leakage of intracellular enzymes, such as could occur in acute hepatitis, hepatic trauma, neoplasia (occasionally), and cirrhosis**.

https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/alanine-aminotransferase

Elevated transaminases : The most common causes of elevated transaminase levels are **nonalcoholic fatty liver disease and alcoholic liver disease**. Uncommon causes include drug-induced liver injury, hepatitis B and C, and hereditary hemochromatosis.

https://pubmed.ncbi.nlm.nih.gov/29431403/

Aspartate aminotransferases : High levels of AST in the blood may be a sign of **hepatitis, cirrhosis, mononucleosis, or other liver diseases**. High AST levels may also be a sign of heart problems or pancreatitis.

https://medlineplus.gov/lab-tests/ast-test/

Elevated liver enzymes **often are a sign of inflamed or damaged cells in the liver**. Inflamed or injured liver cells leak higher levels of certain chemicals into the bloodstream. These chemicals include liver enzymes that may appear higher than usual on blood tests.

https://www.mayoclinic.org/symptoms/elevated-liver-enzymes/basics/definition/sym-20050830

Remdesivir-associated hepatotoxicity has been observed as increased transaminases more than five times the upper limit of normal in hospitalized patients with COVID-19

https://www.mdpi.com/2813-0618/3/1/5

Studies have shown that many of these drugs could have adverse side-effects, including drug-induced liver injury—also known as DILI... https://www.mdpi.com/1648-9144/58/12/1848

Figure 2. COVID-19 medications that can cause DILI, the category in which they belong, the liver contraindications that exist, and the DILI patterns that they develop. Abbreviations used: NSAIDs—non-steroidal anti-inflammatory drugs; LMWH—low molecular weight heparins; LF—liver failure; ALT—alanine aminotransferase; ULN—upper limit of normal; FRP—favipiravir; AST—aspartate aminotransferase; ALP—alkaline phosphatase; MAFLD—metabolic associated fatty liver disease; NAFLD—non-alcoholic fatty liver disease. The arrow used in this figure signifies elevation of the mentioned biomarkers.

MEDICATION	TYPE	LIVER CONTRAINDICATIONS	DILI PATTERN
Systemic corticosteroids	systemic corticosteroids	caution in LF	hepatocellular / mixed
Remdesivir	antiviral drug	ALT>10 x ULN or ALT>5 x ULN + symptoms	hepatocellular
Lopinavir/ Ritonavir	antiviral drug	ALT>5 x ULN	hepatocellular
Favipiravir	antiviral drug	↑FRP, ALT, AST, ALP, total bilirubin levels	cholestatic + hepatocellular
Azithromycin	antibiotic	ALT>5 x ULN + dermal reactions	hepatocellular / mixed
Hydroxychloroquine	antimalarials	ALT elevation	-
Tocilizumab	monoclonal antibody	ALT>5 x ULN	hepatocellular
Sarilumab	monoclonal antibody	ALT>1.5 x ULN	hepatocellular
Paracetamol	antipyretic	MAFLD/NAFLD, alcoholic patients	hepatocellular
NSAIDs	NSAIDs	caution in LF, contradiciton in severe LF	hepatocellular

This table shows that –

Remdesivir induces an elevation of alanine aminotransferases (ALT) to more than 10 times the upper limit of normal – causing hepatocellular damage.

Ritonavir, otherwise known as Paxlovid, induces an elevation of ALT to more than 5 times the upper limit of normal – causing hepatocellular damage.

The highest incidence rate of DILI (Drug Induced Liver Injury) per 10,000 defined daily doses (DDD) was with remdesivir (992.7/10,000 DDD). while another study by Kaur et al. reported the first case of DILI caused by remdesivir in a newborn with COVID-19 - https://www.mdpi.com/2077-0383/10/19/4432

So the two main drugs used to combat COVID, both induce excessive liver injury.

WHO Disproportionality Analysis **contents**

Prior studies found a strong association between administration of remdesivir and AKIs (Acute Kidney Injury) in COVID-19 patients. One comparative study examined the differential ARF/AKI (Acute Renal Failure/ Acute Kidney Injury) risk among COVID-19 patients treated with remdesivir or other antivirals such as hydroxychloroquine, lopinavir/ritonavir, and tocilizumab using data derived from WHO's post - marketing pharmacovigilance data (VigiBase) . This study discovered a 20-fold increase in the odds of reporting Acute renal failure as an adverse event after taking remdesivir (ROR = 20.3; 95% CI: 15.7-26.3) compared to users of the other antivirals

Gérard AO, Laurain A, Fresse A, Parassol N, Muzzone M, Rocher F, Esnault VLM, Drici MD. Remdesivir and Acute Renal Failure: A Potential Safety Signal From Disproportionality Analysis of the WHO Safety Database. Clin Pharmacol Ther. 2021 Apr;109(4):1021-1024. doi: 10.1002/cpt.2145. Epub 2021 Jan 16. Erratum in: Clin Pharmacol Ther. 2022 Jun;111(6):1343. PMID: 33340409

https://digitalcommons.usf.edu/cgi/viewcontent.cgi?article=11021&context=etd

Although there was no evidence of remdesivir related nephrotoxicity in Phase I clinical studies, dose-dependent kidney injury and/or reduced function was detected in the repeated dose toxicity studies of remdesivir in animals, which correlated with histopathology findings of renal tubular atrophy, basophilia and casts [3]. Grein et al. reported renal impairments, acute kidney injury and hematuria in 8 %, 6 % and 4 % of the remdesivir recipients, respectively [2]. A COVID-19 patient, who was treated by our team in Wuhan in March 2020, suffered from acute renal failure after using remdesivir. This case was also reported in a RCT in China [6]. Therefore, it is important to monitor kidney function during remdesivir treatment, particularly for those with pre-existing renal impairments or those receiving combination therapies with other nephrotoxins. Fan Q, Zhang B, Ma J, Zhang S. Safety profile of the antiviral drug remdesivir: An update. Biomed Pharmacother. 2020 Oct;130:110532. doi: 10.1016/j.biopha.2020.110532. Epub 2020 Jul 22. PMID: 32707440; PMCID: PMC7373689

https://www.researchgate.net/publication/343138058_Safety_profile_of_the_antiviral_drug_remdesivir_An_update/link/5f18734b45851515ef3e7438/download?_tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmxpY2F0aW9uIiwicGFnZSI6InB1YmxpY2F0aW9uIn19

WHO Disproportionality Analysis **contents**

To provide additional data, we performed a pharmacovigilance analysis on the World Health Organization global database of individual case safety reports, VigiBase (https://www.who-umc.org/vigibase/vigibase/). This database gathers spontaneous reports of suspected adverse drug reactions from >130 countries, which makes it a powerful tool to perform disproportionality analyses.[3] This approach, based on a case–noncase method, estimates whether an adverse event is differentially reported for a specific drug compared with other drugs. Among 1,565,117 reports registered from January 1st until August 30th, 2020, 5532 concerned COVID-19 patients and have been included in this study. Of them, 434 (7.8%) cases were related to kidney disorders, including 327 (5.9%) reported with remdesivir. In remdesivir kidney disorder cases, 217 (66.3%) patients were male, with a median age of 65 (interquartile range, 55–73) years (Supplementary Table S1). Remdesivir was discontinued early after kidney disorder onset, with a median treatment duration of 3 (interquartile range, 1–4) days. In the vast majority of cases (316 [96.6%]), no other drug was suspected in the onset of kidney disorders. Reactions were serious in 301 (92.0%) cases, with a fatal outcome for 15 (4.6%) patients. They were mainly AKI in 295 (90.2%) cases and tubular necrosis in 8 (2.4%) cases.

Compared with the use of chloroquine, hydroxychloroquine, dexamethasone, sarilumab, or tocilizumab, the use of remdesivir was associated with an increased reporting of kidney disorders (reporting odds ratio, 7.2; 95% confidence interval, 5.7–9.0)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7907730/

FAERS Disproportionality Analysis **contents**

The U.S. Food and Drug Administration (FDA) has stated that the prescription of remdesivir should be cautious for patients with estimated glomerular filtration rate (eGFR) < 30 (because remdesivir makes it worse) and some studies reported risk of adverse renal events. The available information on the renal safety profile for remdesivir is limited, thus we analyzed the renal and urinary adverse reactions attributed to remdesivir reported in a large open pharmacovigilance database. We obtained reports of remdesivir and other drugs used to treat COVID-19 (tocilizumab, hydroxychloroquine, lopinavir/ritonavir) registered by September 30 2020, from the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS). We analyzed the reporting odds ratios (RORs) for reports of adverse renal and urinary events for remdesivir and other drugs. We found 2,922 reports with remdesivir registered in FAERS for COVID-19. Among these, 493 renal and urinary adverse effects (16.9%) were reported. The most frequent events were acute kidney injury (338; 11.6%), renal impairment (86; 2.9%), and renal failure (53; 1.8%). Versus hydroxychloroquine, lopinavir/ritonavir, or tocilizumab, the use of remdesivir was associated with an increased chance of reporting renal and urinary disorders regardless of gender and age of patients (2.53; 95%CI: 2.10-3.06). The ROR remained significant when we restricted the analysis to hydroxychloroquine (4.31; 95%CI: 3.25-5.71) or tocilizumab (3.92; 95%CI: 2.51-6.12). Our results reinforce this already reported signal, emphasizing that it could be extremely useful for health professionals who prescribe this new antiviral to treat COVID-19, mainly knowing its low efficacy.

https://pubmed.ncbi.nlm.nih.gov/34787281/

COMPARISON WITH OTHER DRUGS contents

"transaminases increased"

Elevation of transaminases and increase of alanine aminotransferases are both biomarkers of liver injury.

But how does this level of liver injury compare with all the other 25,000 drugs in Eudra-vigilance? To answer this I took one symptom – "transaminases increased" – and counted the frequency of this symptom in all other drugs.

METHOD

1. The single-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports were selected where REACTION = "transaminases increased"
5. The frequency of reports for each drug was counted
6. Each report count was divided by the total number of reports for each drug to give the percentage of reports.

RESULTS

TABLE 2 : All drugs ordered by incidence of "transaminases increased"

DRUG	FREQ	TOT	%
ESMYA [ULIPRISTAL ACETATE]	106	1482	7.15
[FLUVASTATIN, FLUVASTATIN SODIUM]	96	1484	6.47
TRABECTEDIN [TRABECTEDIN]	19	299	6.35
[PYRAZINAMIDE]	49	786	6.23
OFEV 150 MG SOFT CAPSULES [NINTEDANIB]	13	229	5.68
MULTAQ 400 MG FILM-COATED TABLETS [DRONEDARONE]	14	264	5.30
VEKLURY [REMDESIVIR]	106	2268	4.67
[ROSUVASTATIN CALCIUM]	92	1998	4.60
YONDELIS [TRABECTEDIN]	52	1133	4.59
[FLUVASTATIN SODIUM]	125	3013	4.15
[ISONIAZID]	69	1822	3.79
REMDESIVIR [REMDESIVIR]	57	1511	3.77
VFEND 200 MG FILM-COATED TABLETS [VORICONAZOLE]	15	416	3.61
[CEFTRIAXONE, CEFTRIAXONE DISODIUM, CEFTRIAXONE DISODIUM SALT HEMIHEPTAHYDRATE, CEFTRIAXONE SODIUM, CEFTRIAXONE, LIDOCAINE HYDROCHLORIDE]	14	405	3.46
IRINOTECAN HYDROCHLORIDE TRIHYDRATE [IRINOTECAN HYDROCHLORIDE TRIHYDRATE]	12	355	3.38

[DISULFIRAM]	44	1341	3.28
STOCRIN [EFAVIRENZ]	11	342	3.22
PAZOPANIB [PAZOPANIB]	58	1866	3.11
OLYSIO 150 MG HARD CAPSULES [SIMEPREVIR]	10	325	3.08
[ATORVASTATIN CALCIUM]	20	698	2.87
PACLITAXEL ALBUMIN-BOUND [PACLITAXEL ALBUMIN-BOUND]	11	397	2.77
[CEFOPERAZONE SODIUM, SULBACTAM SODIUM, CEFOPERAZONE, SULBACTAM]	38	1399	2.72
[PARACETAMOL]	43	1662	2.59
KALETRA 200 MG/50 MG FILM-COATED TABLETS [LOPINAVIR, RITONAVIR]	23	890	2.58
KIVEXA [ABACAVIR SULFATE, LAMIVUDINE, ABACAVIR, LAMIVUDINE]	19	739	2.57
[ETHAMBUTOL, ETHAMBUTOL HYDROCHLORIDE]	67	2676	2.50
[ATORVASTATIN, ATORVASTATIN CALCIUM, ATORVASTATIN CALCIUM TRIHYDRATE]	65	2786	2.33
EUCREAS [METFORMIN HYDROCHLORIDE, VILDAGLIPTIN]	35	1511	2.32
[PITAVASTATIN]	12	519	2.31
TAMIFLU 75 MG HARD CAPSULE [OSELTAMIVIR]	13	584	2.23
KISQALI [RIBOCICLIB]	97	4429	2.19
MULTAQ [DRONEDARONE]	86	3928	2.19

Remdesivir has a high incidence of reports where transaminases are increased – about 5%

Paxlovid (Ritonavir) has about half that incidence – about 2.5%

Tamiflu has about the same incidence as Paxlovid.

Other drugs belonging to the Remdesivir family are shown shaded in grey. These drugs are all ANTI-RETRO VIRAL DRUGS. In Table 2 they include –

REMDESIVIR (Veklury)

SIMEPREVIR

LOPINAVIR

RITONAVIR (Paxlovid)

ABACAVIR

OSELTAMIVIR (Tamiflu)

COMPARISON WITH OTHER DRUGS contents

"hepatic enzyme increased"

Elevation of hepatic enzyme is a biomarker of liver injury.

> *If you've ever had a liver function test as part of an annual physical, you may know that the exam screens for certain biomarkers, like liver enzymes in the blood. If these substances are found to be elevated,* ***it may mean that you have a liver disease or have been exposed to some medications or environmental toxins****.*
>
> *https://www.pfizer.com/news/articles/in_search_of_a_better_biomarker_why_studying_liver_enzymes_matters_for_drug_safety*

METHOD

1. The single-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports were selected where REACTION = "hepatic enzyme increased"
5. The frequency of reports for each drug was counted
6. Each report count was divided by the total number of reports for each drug to give the percentage of reports.

RESULTS

TABLE 3 : All drugs ordered by incidence of "hepatic enzyme increased"

DRUG	FREQ	TOT	%
ABACAVIR SULFATE [ABACAVIR SULFATE]	1029	2040	50.44118
APREPITANT [APREPITANT]	285	841	33.88823
ABACAVIR SULFATE, LAMIVUDINE [ABACAVIR SULFATE, LAMIVUDINE]	245	901	27.19201
APREMILAST [APREMILAST]	154	770	20
ABATACEPT [ABATACEPT]	615	3922	15.68078
ACLIDINIUM BROMIDE [ACLIDINIUM BROMIDE]	78	524	14.8855
ARAVA [LEFLUNOMIDE]	4242	30951	13.70553
ADALIMUMAB [ADALIMUMAB]	2113	16216	13.03034
[FLUTAMIDE]	139	1101	12.62489
[ANHYDROUS PAMIDRONATE DISODIUM, PAMIDRONATE DISODIUM]	12	100	12
ORENCIA [ABATACEPT]	42	403	10.42184
APTIVUS [TIPRANAVIR]	17	171	9.94152
AMPRENAVIR [AMPRENAVIR]	11	111	9.90991
ABACAVIR, LAMIVUDINE [ABACAVIR, LAMIVUDINE]	22	257	8.560311

REBIF [INTERFERON BETA-1A]	28	362	7.734807
ANTIBIOTICS [NOT AVAILABLE]	11	165	6.666667
ALOXI [PALONOSETRON, PALONOSETRON HYDROCHLORIDE]	22	331	6.646526
[FLUVASTATIN SODIUM]	184	3013	6.10687
[CEFTRIAXONE, CEFTRIAXONE DISODIUM, CEFTRIAXONE DISODIUM SALT HEMIHEPTAHYDRATE, CEFTRIAXONE SODIUM, CEFTRIAXONE, LIDOCAINE HYDROCHLORIDE]	24	405	5.925926
[PERAZINE, PERAZINE DIMALONATE]	12	212	5.660377
[CEFTRIAXONE, CEFTRIAXONE SODIUM, CEFTRIAXONE, LIDOCAINE HYDROCHLORIDE]	13	232	5.603448
DELAMANID [DELAMANID]	60	1084	5.535055
CEFUROXIME SODIUM [CEFUROXIME SODIUM]	14	259	5.405405
ERELZI [ETANERCEPT, ETANERCEPT, HYDROCHLOROTHIAZIDE]	13	242	5.371901
ACLASTA [ZOLEDRONIC ACID, ZOLEDRONIC ACID MONOHYDRATE]	17	324	5.246914
KETEK [TELITHROMYCIN]	11	210	5.238095
LEFLUNOMIDE [LEFLUNOMIDE]	79	1576	5.01269
TYGACIL [TIGECYCLINE]	10	201	4.975124
[ATORVASTATIN CALCIUM]	33	698	4.727794
ESMYA [ULIPRISTAL ACETATE]	68	1482	4.588394
[FLUVASTATIN, FLUVASTATIN SODIUM]	66	1484	4.447439
AGOMELATINE [AGOMELATINE]	11	248	4.435484
ENBREL [ETANERCEPT]	325	7868	4.130656
[ROSUVASTATIN CALCIUM]	82	1998	4.104104
LYSODREN [MITOTANE]	11	283	3.886926
[HEPATITIS B SURFACE ANTIGEN, HEPATITIS A VACCINE	43	1127	3.815439
REMDESIVIR [REMDESIVIR]	55	1511	3.639974
TERIFLUNOMIDE [TERIFLUNOMIDE]	16	467	3.426124
TWINRIX ADULT [ALUMINIUM PHOSPHATE, HEPATITIS A VIRUS	92	2814	3.269367
VIRAMUNE [NEVIRAPINE]	33	1030	3.203883
[VORICONAZOLE]	10	320	3.125
[TERBINAFINE, TERBINAFINE HYDROCHLORIDE]	311	10123	3.072212
[ISONIAZID]	52	1822	2.854007
EPIDYOLEX [CANNABIDIOL]	11	401	2.743142
LUMYKRAS [SOTORASIB]	15	548	2.737226
ABACAVIR [ABACAVIR]	66	2412	2.736318
[CEFOPERAZONE SODIUM, SULBACTAM SODIUM, CEFOPERAZONE, SULBACTAM]	38	1399	2.716226
[ATORVASTATIN, ATORVASTATIN CALCIUM, ATORVASTATIN CALCIUM TRIHYDRATE]	75	2786	2.692032
MYCAMINE [MICAFUNGIN, MICAFUNGIN SODIUM]	21	782	2.685422

ZIAGEN [ABACAVIR, ABACAVIR SULFATE]	13	485	2.680412
CELSENTRI [MARAVIROC]	15	579	2.590674
TAMIFLU 75 MG HARD CAPSULE [OSELTAMIVIR]	15	584	2.568493

Remdesivir has a high incidence of reports where transaminases are increased – about 3.63%

Paxlovid (Ritonavir) has about half that incidence – about 1.4%

Tamiflu has an incidence of 2.5%.

Other drugs belonging to the Remdesivir family are shown shaded in grey. They include –

ABACAVIR

TIPRANAVIR

AMPRENAVIR

REMDESIVIR (Veklury)

OSELTAMIVIR (Tamiflu)

RITONAVIR (Paxlovid)

Note that out of all drugs in Eudra-vigilance, Abacavir has the highest incidence of hepatic enzyme increased.

WHAT ARE ANTI-RETRO-VIRAL DRUGS ? **contents**

Remdesivir belongs to a family of drugs called ANTI-RETROVIRAL drugs – they are used to treat HIV. A full list of these drugs can be found here - https://en.wikipedia.org/wiki/List_of_antiviral_drugs

Antiretroviral Drug	For Treating
Abacavir	HIV
Acyclovir (Aciclovir)	Herpes Simplex, chickenpox,[2] varicella zoster virus
Adefovir	Hepatitis B[3]
Amantadine	Influenza
Ampligen	Avian Influenza
Amprenavir (Agenerase)	HIV
Atazanavir	HIV
Atripla (Efavirenz/emtricitabine/tenofovir)	HIV
Baloxavir marboxil (Xofluza)[4]	Influenza A/B
Biktarvy (Bictegravir/emtricitabine/tenofovir alafenamide)	HIV
Boceprevir	Hepatitis C genotype 1[5]
Bulevirtide	Hepatitis D/B
Cidofovir	AIDS
Cobicistat (Tybost)[6]	HIV
Combivir (Lamivudine/Zidovudine)	HIV
Daclatasvir (Daklinza)	Hepatitis C
Darunavir	HIV
Delavirdine	HIV
Descovy (Emtricitabine/tenofovir alafenamide)	Hepatitis B
Didanosine	HIV
Docosanol	Herpes Simplex
Dolutegravir	HIV
Doravirine (Pifeltro)[7]	HIV
Edoxudine	Herpes Simplex
Efavirenz	HIV
Elvitegravir	HIV
Emtricitabine	HIV
Enfuvirtide	HIV
Ensitrelvir	COVID-19
Entecavir	HIV
Etravirine (Intelence)[8]	HIV
Famciclovir	Herpes Zoster
Fomivirsen	AIDS
Fosamprenavir	HIV
Foscarnet	Herpes
Ganciclovir (Cytovene)[9]	Cytomegalovirus (CMV)[10]
Ibacitabine	Herpes labialis
Ibalizumab (Trogarzo)[11]	HIV
Idoxuridine	Herpes
Imiquimod	Genital wart, Basal cell carcinoma, Actinic keratosis
Indinavir	HIV
Inosine pranobex	Herpes Simplex
Lamivudine	HIV

Letermovir (Prevymis)[12]	Cytomegalovirus (CMV)
Lopinavir	HIV
Loviride	HIV
Maraviroc	HIV
Methisazone	Smallpox
Molnupiravir	COVID-19
Moroxydine	Influenza
Nelfinavir	HIV
Nevirapine	HIV
Nirmatrelvir/ritonavir (Paxlovid)	COVID-19
Nitazoxanide	Broad-spectrum antiviral
Norvir	HIV
Oseltamivir (Tamiflu)[13]	Influenza
Penciclovir	Herpes
Peramivir (Rapivab)[14]	Influenza
Pleconaril	Picornavirus
Podophyllotoxin	Genital wart
Raltegravir	HIV
Remdesivir	COVID-19
Ribavirin	Hepatitis C[15]
Rilpivirine (Edurant)[16]	HIV
Rimantadine	Influenza A
Ritonavir	HIV
Saquinavir	HIV
Simeprevir (Olysio)	Hepatitis C
Sofosbuvir	Hepatitis C[17]
Stavudine	HIV
Taribavirin (Viramidine)	Hepatitis Syndromes in which Ribavirin is active[18]
Telaprevir	Hepatitis C
Telbivudine (Tyzeka)	Hepatitis B
Tenofovir alafenamide	Hepatitis B
Tenofovir disoproxil	Hepatitis B, HIV[19]
Tipranavir	HIV
Trifluridine	Eyes related Herpes
Trizivir	HIV
Tromantadine	Herpes Simplex
Truvada	HIV
Umifenovir	Influenza
Umifenovir (Arbidol)	Influenza
Valaciclovir (Valtrex)[20]	Herpes Simplex/Zoster
Valganciclovir (Valcyte)[21]	Cytomegalovirus (CMV)
Vicriviroc	HIV-1
Vidarabine	Herpes Simplex, Varicella Zoster
Zalcitabine	HIV
Zanamivir (Relenza)[22]	Influenza A, Influenza B
Zidovudine	HIV[23]

COMPARISON WITH OTHER DRUGS contents

"renal" symptoms

"Renal" means "Kidney"

METHOD

1. The single-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports were selected where REACTION = "renal"
5. The frequency of reports for each drug was counted
6. Each report count was divided by the total number of reports for each drug to give the percentage of reports.

RESULTS

TABLE 4 : All drugs ordered by incidence of "renal" symptoms

DRUG	FREQ	TOT	%
ATRIPLA [EMTRICITABINE, EFAVIRENZ, TENOFOVIR DISOPROXIL, EMTRICITABINE, EFAVIRENZ, TENOFOVIR DISOPROXIL FUMARATE]	37831	58696	64.45
TRUVADA [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE]	18354	31035	59.14
STRIBILD [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE, COBICISTAT, ELVITEGRAVIR]	4453	9031	49.31
TRUVADA [EMTRICITABINE, TENOFOVIR DISOPROXIL, EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE]	1612	3486	46.24
[ACEBUTOLOL HYDROCHLORIDE]	173	386	44.82
STRIBILD [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE, COBICISTAT, ELVITEGRAVIR, EMTRICITABINE, TENOFOVIR DISOPROXIL, COBICISTAT, ELVITEGRAVIR]	484	1107	43.72
HEPSERA TABLETS [ADEFOVIR DIPIVOXIL]	52	136	38.24
VIREAD [TENOFOVIR DISOPROXIL, TENOFOVIR DISOPROXIL FUMARATE]	1477	4168	35.44
TENOFOVIR DISOPROXIL FUMARATE [TENOFOVIR DISOPROXIL FUMARATE]	323	954	33.86
[ESOMEPRAZOLE MAGNESIUM]	51	177	28.81
EPIVIR FILM-COATED TABLETS [LAMIVUDINE]	26	102	25.49
[LOXOPROFEN, LOXOPROFEN SODIUM]	30	122	24.59
TRUVADA 200 MG/245 MG FILM-COATED TABLETS [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE]	138	564	24.47

What is noticeable is the extreme prevalence of drugs with a similar name to Remdesivir. This family of drugs appears to be associated with very high levels of renal toxicity = kidney disorder.

All of these drugs belong to the Remdesivir family and are called ANTI-RETRO-VIRAL drugs – they ae used to treat HIV.

Tenofovir	Abacavir	Epivir
Adefovir	Valaciclovir	Dolutegravir
Cidofovir	Aciclovir	Ganciclovir
Indinavir	Norvir	Remdesivir
Atazanavir	Raltegravir	
Ritonavir	Entecavir	
Lopinavir		

One of these drugs – Ritonavir – is otherwise known as Paxlovid. We are told –

> ***Paxlovid, an oral antiviral pill that can be taken at home, is the go-to treatment for COVID-19***. *If you are at high risk for severe disease from COVID, and you take it within the first five days of experiencing symptoms, it will lower your risk of getting so sick that you need to be hospitalized*.
>
> *https://www.yalemedicine.org/news/13-things-to-know-paxlovid-covid-19*

Ritonavir has an incidence of 17.57% in Table 4 (not shown – table truncated)

Remdesivir has an incidence of 6.35% in Table 4 (not shown – table truncated)

As noted in TABLE 1, one of the highest ranking symptoms for Remdesivir is “acute kidney injury”. Whilst Remdesivir is being prescribed in hospitals, Ritonavir is being recommended as the at-home remedy!

COMPARISON WITH OTHER DRUGS contents

"kidney disease" symptoms

METHOD

1. The single-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports were selected where REACTION = "kidney"
5. The frequency of reports for each drug was counted
6. Each report count was divided by the total number of reports for each drug to give the percentage of reports.

RESULTS

TABLE 5 : All drugs ordered by incidence of "kidney" symptoms

DRUG	FREQ	TOT	%
TRUVADA [EMTRICITABINE, TENOFOVIR DISOPROXIL, EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE]	1689	3486	48.45
STRIBILD [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE, COBICISTAT, ELVITEGRAVIR, EMTRICITABINE, TENOFOVIR DISOPROXIL, COBICISTAT, ELVITEGRAVIR]	477	1107	43.09
TRUVADA [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE]	13160	31035	42.40
ATRIPLA [EMTRICITABINE, EFAVIRENZ, TENOFOVIR DISOPROXIL, EMTRICITABINE, EFAVIRENZ, TENOFOVIR DISOPROXIL FUMARATE]	24802	58696	42.26
TENOFOVIR DISOPROXIL [TENOFOVIR DISOPROXIL]	115	278	41.37
INVOKANA [CANAGLIFLOZIN]	901	2184	41.25
[LOXOPROFEN, LOXOPROFEN SODIUM]	48	122	39.34
STRIBILD [EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE, COBICISTAT, ELVITEGRAVIR]	3329	9031	36.86
[DICLOFENAC, DICLOFENAC DIETHYLAMINE, DICLOFENAC SODIUM]	82	224	36.61
[GENTAMICIN]	180	500	36.00
[OLMESARTAN MEDOXOMIL, AMLODIPINE BESILATE]	192	551	34.85
APROVEL 75 MG TABLETS [IRBESARTAN]	54	169	31.95
[OLMESARTAN MEDOXOMIL, HYDROCHLOROTHIAZIDE, AMLODIPINE BESILATE]	90	290	31.03

[PIPERACILLIN, TAZOBACTAM]	130	431	30.16
[ESOMEPRAZOLE MAGNESIUM]	53	177	29.94

Once again, there is a prevalence of drugs belonging to the Remdesivir family of anti-retro-virus drugs.

Paxlovid (Ritonivir) has an incidence of 11 %

Remdesivir has an incidence of 6.3 %

Tamiflu has an incidence of 1.3 %

"nephr" symptoms

These include symptoms related to nephritis and other nephropathies.

METHOD

1. The single-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports were selected where REACTION = "nephr"
5. The frequency of reports for each drug was counted
6. Each report count was divided by the total number of reports for each drug to give the percentage of reports.

RESULTS

TABLE 6 : All drugs ordered by incidence of "nephr" symptoms

DRUG	FREQ	TOT	%
[GADODIAMIDE, GADODIAMIDE HYDRATE]	484	653	74.12
OPTIMARK [GADOVERSETAMIDE]	1733	2438	71.08
CONTRAST MEDIA [NOT AVAILABLE]	76	114	66.67
[GADODIAMIDE]	772	1399	55.18
REYATAZ HARD CAPSULES [ATAZANAVIR, ATAZANAVIR SULFATE]	43	191	22.51
[VANCOMYCIN HYDROCHLORIDE]	493	2241	22.00
CRIXIVAN [INDINAVIR, INDINAVIR SULFATE]	421	2037	20.67
REYATAZ 300 MG HARD CAPSULES [ATAZANAVIR, ATAZANAVIR SULFATE]	39	190	20.53
BASILIXIMAB [BASILIXIMAB]	161	993	16.21
[ESOMEPRAZOLE MAGNESIUM]	28	177	15.82
SIMULECT [BASILIXIMAB]	16	102	15.69
CIDOFOVIR [ANHYDROUS CIDOFOVIR, CIDOFOVIR]	38	269	14.13
CRIXIVAN 400 MG HARD CAPSULES [INDINAVIR, INDINAVIR SULFATE]	17	123	13.82
[PENICILLAMINE]	54	394	13.71
BELIMUMAB [BELIMUMAB]	60	468	12.82
BOTULINUM TOXIN TYPE A [BOTULINUM TOXIN TYPE A]	164	1280	12.81
[LITHIUM]	349	2782	12.54
DOLUTEGRAVIR [DOLUTEGRAVIR]	107	858	12.47
CIDOFOVIR [CIDOFOVIR]	19	154	12.34
[HYDRALAZINE]	84	723	11.62
REYATAZ [ATAZANAVIR, ATAZANAVIR SULFATE]	200	1739	11.50

Drugs belonging to the family of anti-retro-virals are strongly represented in the higher ranks of this table.

- Remdesivir has an incidence of 9%
- Ritonavir, the active ingredient in Paxlovid, has an incidence of 4.88%
- Oseltamivir, the active ingredient in Tamiflu, has an incidence of 0.3%

Taking antiretroviral medications (ARVs) used to treat HIV infections or related health issues can also cause kidney disease. Kidney problems can lead to ESRD or kidney failure.

https://www.iapac.org/fact-sheet/hiv-and-kidney-disease/

HIV positive people are typically treated with Antiretroviral therapy (ART) using the above drugs, and this has been found to cause chronic kidney disease (CKD) 3 x more than for those not taking ART.

https://www.aidsmap.com/news/jun-2018/kidney-function-declines-faster-men-hiv-treatment-their-hiv-negative-peers

T

Tenofovir, one of the most effective and commonly prescribed antiretroviral medications for HIV/AIDS, is associated with a significant risk of kidney damage and chronic kidney disease that increases over time, according to a study of more than 10,000 patients led by researchers at the San Francisco VA Medical Center (SFVAMC) and the University of California, San Francisco (UCSF)

https://www.ucsf.edu/news/2012/02/98532/tenofovir-leading-hiv-medication-linked-risk-kidney-damage

Antiretroviral therapy can contribute to renal dysfunction directly by inducing acute tubular necrosis, acute interstitial nephritis, crystal nephropathy, and renal tubular disorders or indirectly via drug interactions.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157198/

Drug-induced kidney injury is a major side effect in clinical practice, frequently leading to acute renal failure (ARF). It accounts for more than 2% to 15% of cases of ARF in patients admitted to the hospital or in the intensive care unit, respectively. The exact frequency of nephrotoxicity induced by antiviral drugs is difficult to determine. Antiviral drugs cause renal failure through a variety of mechanisms. Direct renal tubular toxicity has been described with a number of new medications with unique effects on epithelial cells of the kidney. These include cidofovir, adefovir dipivoxil, and tenofovir, as well as acyclovir. Additionally, crystal deposition in the kidney may promote the development of renal failure. Several different drugs have been described to induce crystal nephropathy, including acyclovir and the protease inhibitor indinavir. Renal injury associated with antiviral drugs involves diverse processes having effects on the renal transporters, as well as on tubule cells.

https://www.ajkd.org/article/S0272-6386(05)00253-2/abstract

SYMPTOMS OF RITONAVIR (active ingredient in Paxlovid) contents

METHOD

1. The multi-line data file was used.
2. All records where the REACTION is null were removed.
3. All records where the DRUG is null were removed.
4. All reports for Ritonavir (Paxlovid) where selected
5. The frequency of each unique symptom in the filtered records was counted.
6. Each symptom count was divided by the total number of symptoms (46,435) to give the percentage of all symptoms for a particular symptom.

RESULTS

TABLE : Symptoms of Ritonavir (active ingredient in Paxlovid) ordered by incidence.

SYMPTOM	FREQ	%
diarrhoea	1324	2.85
drug interaction	1248	2.69
off label use	1162	2.50
nausea	747	1.61
vomiting	639	1.38
acute kidney injury	627	1.35
osteonecrosis	562	1.21
renal failure	489	1.05
osteoporosis	441	0.95
pyrexia	428	0.92
bone density decreased	404	0.87
foetal exposure during pregnancy	403	0.87
renal injury	398	0.86
anaemia	358	0.77
bone loss	357	0.77
rash	338	0.73
skeletal injury	337	0.73
hepatic cytolysis	330	0.71
cushing's syndrome	327	0.70
jaundice	294	0.63
asthenia	289	0.62
multiple fractures	273	0.59
headache	265	0.57
electrocardiogram qt prolonged	255	0.55
chronic kidney disease	254	0.55
abdominal pain	243	0.52
hypertriglyceridaemia	238	0.51
fatigue	236	0.51

Severe hepatotoxicity was observed in 31 (10.4%) of 298 patients (95% confidence interval [CI], 7.2%-14.4%). Ritonavir use was associated with a higher incidence of toxicity (30%; 95% CI, 17.9%-44.6%)

https://jamanetwork.com/journals/jama/fullarticle/192258

As mentioned earlier, Paxlovid contains the medication ritonavir. Ritonavir is known to contribute to liver damage. This side effect is more likely to happen in people who already have liver problems.

https://www.goodrx.com/paxlovid/known-side-effects

Tamiflu/oseltamivir phosphate (OP), an anti-influenza drug, has a highly doubted safety especially after many cases of abnormal behaviour and deaths reported after being used. Such controversy was also locally and globally generated, especially after being heavily used in COVID-19 treatment protocol. This study was designed to evaluate the effect of three different doses of OP on the liver and kidneys of male adult albino rats through histological approaches, measuring their DNA integrity and biochemical analyses. Different doses of Tamiflu applied to humans were converted to rats, then observed their effects on the liver and kidneys. Rats were divided into four groups. G1: considered as control group. The rest of the three treated groups were received the same calculated dose of Tamiflu (6.75 mg/kg b.w.) in three different durations. G2, G3 and G4 represented the animals orally received OP, in which the rats received OP twice for 5 consecutive days, once for 10 and 45 days, respectively.

Our data showed numerous deleterious necrotic and fibrotic histopathological changes in the liver, and kidneys; as well as necrotic DNA smears, by using electrophoresis, in OP-treated rats of G2 and G4. In addition, OP significantly increased the serum cellular hepatic/renal toxicity markers (ALT, AST, ALP, GGT, indirect bilirubin, urea, creatinine, uric acid, & Na^+). Also, it showed a reduction in the levels of serum total protein, albumin and K^+ ions in rats of G2 and G4 compared with G1. In G3, OP treatment did not significantly alter hepatic/renal histological, DNA integrity and biochemical analyses in rats.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8787452/

FAERS Disproportionality Analysis 2 **contents**

The primary suspected drugs related to AKI (acute kidney injury) in more than half of the reports (75.60%, 127/168) were four common anti-COVID-19 drugs (remdesivir, tocilizumab, hydroxychloroquine, and lopinavir/ritonavir). Compared with other drugs in the same time window, remdesivir and lopinavir/ritonavir were associated with an increased risk of AKI in all COVID-19 patients (ROR: 3.97, 95% CI: 3.51–4.50; ROR: 4.02, 95% CI: 3.11–5.19, respectively). In COVID-19 patients with DM, remdesivir was significantly associated with AKI (ROR: 5.65, 95% CI: 4.06–7.87)

https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2022.833679/full

BNPV Disproportionate Analysis **contents**

228 reports after administration of Paxlovid : The main reported unexpected adverse drug reaction (ADRs) were high blood pressure (*n* = 7), confusion (*n* = 5), acute kidney injuries (AKI, *n* = 7) and various skin reactions (*n* = 22)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9990891/

Re-read these hospital reports of 2020. What caused the rise in people needing dialysis?
https://edition.cnn.com/2020/04/17/health/coronavirus-kidney-dialysis-need/index.html

Summary contents

1. When we look at Remdesivir on its own, the most frequent symptoms are all to do with liver injury and kidney injury
2. When we compare Remdesivir with all other drugs for a biomarker of liver injury (increased transaminases), we find that Remdesivir occurs in the top 0.03 % - only 1 in 3000 drugs are associated with such an incidence.
3. Remdesivir belongs to a family of drugs that consistently elevate hepatic enzyme – a biomarker for liver disease.
4. Remdesivir belongs to a family of drugs strongly associated with symptoms of kidney disease identified by keywords -
    - "renal" / "kidney"
    - "kidney disease".
    - "nethropathy", "nephritis"
    - "proteinuria"
    - "fluid retention"
8. Tamiflu, a weaker member of the Remdesivir family, still causes significant renal and hepatic disorder.
9. The family of drugs to which Remdesivir belongs are ANTI-RETRO-VIRAL drugs, used to treat HIV, HEPATITUS and INFLUENZA.

Conclusion contents

Anti-retro-viral drugs used in hospitals and at home as a preventative measure, increase the incidence of acute kidney injury. It is therefore probable that many of the kidney and liver injuries occurring during the COVID "pandemic" may be due to the protocols and prophylactics used – Remdesivir, Paxlovid, Tamiflu.

People were not adequately warned of this danger – and instead were encouraged to follow "the Science", trading their liver and kidney function for "safety" from a disease that generated no excess mortality in 2020.

The processes by which we detoxify the body are metabolism (liver) and excretion (kidneys). Impairment of liver and kidney function prevents detoxification resulting in persistence of toxins and poisoning. This will have produced a host of debilitating symptoms.

The anti-retro-viral drugs are also used to treat HIV and may be responsible for a leading cause of death among HIV infected people – namely kidney and liver failure.
https://academic.oup.com/cid/article/50/10/1387/377418,
https://onlinelibrary.wiley.com/doi/pdf/10.1111/hiv.12937

40 years ago we had the HIV "epidemic", managed by Dr Fauci. 40 years later we have the Covid "pandemic" managed by the same person – applying the same drugs used against HIV – with the same devastating effects on kidney and liver function.

Appendix A **contents**

REMDESIVIR EMERGENCY USE AUTHORIZATION – suspicious circumstances

https://www.science.org/content/article/very-very-bad-look-remdesivir-first-fda-approved-covid-19-drug

APPENDIX B **contents**

Remdesivir Trials

1. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

A randomized multi-intervention trial was later conducted during the EVD outbreak in the DRC. 18 Patients of any age, including pregnant women, were eligible for enrolment if they tested positive for EBOV. Patients received standard supportive care along with an assignment to one of four treatment arms in a 1:1:1:1 ratio. Study treatments included ZMapp (a triple monoclonal antibody), MAb114 (a single human monoclonal antibody derived from an Ebola survivor), REGN-EB3 (a mixture of three human immunoglobulin G1 [IgG1] monoclonal antibodies), and intravenous remdesivir. Remdesivir was administered at a dose of 200 mg on day 1, followed by 100 mg daily for 9–13 days. Weight-based doses were used for paediatric patients.

The primary outcome was mortality at day 28.

Nearly 700 patients had been randomized when an interim analysis led to early cessation of the trial. The data and safety monitoring board found higher mortality in the ZMapp and remdesivir groups compared to the MAb114 and REGN-EB3 groups. Further, the REGN-EB3 group had met a prespecified threshold for efficacy.

A total of 673 patients were included in the final analysis. The mean age of enrolled patients was 29 years and 56% of patients were women (6% of whom were pregnant). At day 28, mortality rates were:

Remdesivir (53.1%),

ZMapp (49.7%),

MAb114 (35.1%),

REGN-EB3 (33.5%).

For Remdesivir, 85 and 29% of patients with high- and low-viral loads at baseline died, respectively.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10680050/

https://archive.ph/7WwFH#selection-5071.188-5071.253

https://carterheavyindustries.wordpress.com/2021/09/21/fauci-remdesivir/

2. *Compassionate Use of Remdesivir for Patients with Severe Covid-19*

Very small sample. Not clear what caused remission – since no control group – did ventilation help or did they recover spontaneously ? Would more have recovered without Remdesivit?

APPENDIX C contents

Python Code for Reading the Data

1. Getting frequency of each symptom of Remdesivir

```
import pandas as pd
pd.set_option('display.max_rows', None)

Total = pd.read_csv(r"C:\Users\User\Downloads\drug-results\total-singleline-12-06-2024.csv")

Total.head()
```

```
Total = Total.fillna("Empty")
```

```
#Total["DRUG"] = Total["DRUG"].str.lower()

filtered = Total[Total["DRUGS"].str.contains("REMDESIVIR")]
filtered.shape
```

```
result = filtered['REACTION'].value_counts().reset_index().rename(columns={"DRUG1": "Count", 0: "TOTAL RECORDS"})
result.head()
```

```
result.to_csv(r"C:\Users\User\Downloads\drug-results\remdesivir.csv")
```

2. Comparing Remdesivir with all other drugs for frequency of the symptom “transaminases increased”

```
import pandas as pd
pd.set_option('display.max_rows', None)

Total = pd.read_csv(r"C:\Users\User\Downloads\drug-results\total-singleline-12-06-2024.csv")

Total.head()
```

```
Total = Total.fillna("Empty")
```

```
Total["REACTION"] = Total["REACTION"].str.lower()

filtered = Total[Total["REACTION"].str.contains("transaminases increased")]
filtered.head(100)
```

```
filtered.shape
```

```
result = filtered['DRUGS'].value_counts().reset_index().rename(columns={"DRUG1": "Count", 0: "TOTAL RECORDS"})

result.head(100)
```

```
result.to_csv(r"C:\Users\User\Downloads\drug-results\transaminases-increased.csv")
```