Pharmacovigilance-based drug repurposing: The search for inverse signals via OpenVigil identifies putative drugs against viral respiratory infections

Ruwen Böhm1 | Claudia Bulin1 | Vicki Waetzig1 | Ingolf Cascorbi1 | Hans-Joachim Klein2 | Thomas Herdegen1

1Institute of Experimental and Clinical Pharmacology, University Hospital Schleswig-Holstein Campus Kiel, Germany
2Department of Computer Science, Kiel University, Germany

Correspondence
Ruwen Böhm, Institute of Experimental and Clinical Pharmacology, University Hospital Schleswig-Holstein Campus, Kiel, Germany.
Email: ruwen.boehm@pharmakologie.uni-kiel.de

Aims: Pharmacovigilance data are primarily used to identify adverse drug reactions by screening for disproportionate reporting, i.e. more reports of certain combinations of adverse events and drugs than expected. However, scanning for associations of drugs and adverse events that occur less frequently than expected provides hypotheses for drug repurposing, i.e. a known drug could be therapeutically beneficial for a new indication such as the coronavirus disease (COVID-19). As coronavirus-related adverse events are scarce in pharmacovigilance data prior to 2020, we searched for drugs suitable against similar viral diseases.

Methods: In this observational, retrospective, pharmacovigilance study, drugs associated with viral respiratory tract infections and/or diseases caused by RNA-viruses, which are phylogenetically similar to SARS-CoV-2, were extracted from the US FAERS pharmacovigilance data 2004Q1 to 2020Q2 using OpenVigil 2.1-MedDRA17, filtered for significant inverse associations (reporting odds ratio <1 and adjusted P < .05), checked for implausibility (e.g. only topically) or clinical infeasibility (e.g. strong cytotoxic effects), and categorised by their World Health Organization Anatomical Therapeutic Chemical classification code.

Results: A total of 126 drugs were identified. Anatomical Therapeutic Chemical clustering of the manually curated list of 112 candidate drugs revealed female sex hormones, antidiabetics, neuropharmacological sigma-receptor modulators, peptidase inhibitors, antiviral drugs, nicotinic acetylcholine receptor agonists and tyrosine kinase inhibitors as putatively antiviral.

Conclusion: Scanning for inverse signals in pharmacovigilance data provides new hypotheses for drug repurposing, theoretically for all indications. Concerning the treatment of viral respiratory infections, there are affirmative data for some candidate drugs; the remaining proposed candidate drugs without already known antiviral mechanism of action should stimulate further exploration.

KEYWORDS
coronavirus, COVID-19, drug repositioning, drug repurposing, influenza, pharmacovigilance
INTRODUCTION

The new coronavirus disease COVID-19 prompts for pharmacological treatments. Initially, drugs originally developed for Retroviridae such as HIV (lopinavir) and Filoviridae such as Ebola (remdesivir) were recommended. However, there are more druggable targets than viral proteases and polymerases. Since conventional drug development pipelines are time-consuming, various in silico procedures were instantly applied to accelerate the identification of potential candidate drugs.

There are 2 frequently utilized in silico techniques for drug repurposing. The first is using genetic expression data or bibliome to build a network of the viral and interacting human genome, transcriptome and/or proteome (interactome), to identify known drugs that either target these proteins or change the genetic expression profile. The second approach is to perform ligand docking on viral proteins or interacting human proteins, where applicable followed by interactome analysis. Furthermore, there are very few in vitro or in vivo approaches. Pharmacovigilance has rarely been used for drug repurposing.

Pharmacovigilance data consist of spontaneous reports of adverse events (AEs). Disproportionate reporting, i.e. a drug–event combination, is seen more frequently than expected, helps to estimate whether this AE happened at random or was caused by the drug, and could thus be considered a true adverse drug reaction (ADR). Pharmacovigilance is used since the late 1960s to detect new ADRs of existing and of new medicinal products on the market by national drug regulating authorities. Answering a call for freely available pharmacovigilance analysis tools, several open-accessible web-based search engines are now available (Table S1). Due to the nature and origin of the pharmacovigilance data, these tools should be used for hypothesis generation only.

Recently, pharmacovigilance data was also employed to generate hypotheses of new therapeutic applications for existing drugs using different approaches such as: (i) scanning for drugs associated with AEs that are the opposite of the disease of interest; (ii) scanning for drugs with an AE-profile, that is similar to that of drugs that are currently used against the disease; or (iii) scanning for inverse signals of drugs and AEs, that are similar to the disease.

Data of viral respiratory infections resembling COVID-19 and their sequelae (e.g. cytokine storm, elevated d-dimers or anosmia) are available within the American pharmacovigilance database, the Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). AEs are coded using terms in the Medical Dictionary for Regulatory Activities (MedDRA). We thus used OpenVigil 2 to scan FAERS data for inverse signals of AE high-level term (HLT) keywords related to the pathogenesis of COVID-19 as well as similar viral diseases (i.e. RNA-viruses, Figure S1) and their symptoms (i.e. respiratory manifestations) to detect already marketed drugs that could be repurposed for treatment of these viral infections. To our best knowledge, this pioneering drug discovery approach has not been applied to viral diseases before.

METHODS

We performed an observational, retrospective pharmacovigilance study in FAERS using OpenVigil 2 and scanned for inverse signals of existing drugs and AEs that are similar to the disease. Details on the methodology and study design decisions are available in the Supplemental Methods document.

2.1 Inverse signals

Reporting odds ratios (ROR) and their Benjamini–Hochberg corrected 95% confidence interval (ROR95CIadj) were used as measurements of...
disproportionality. The traditional signal concept, i.e. a drug and an AE are more frequently observed than expected (Figure S2), was reversed (ROR95CIadj < 1) to focus on less frequently observed than expected combinations of drugs and AEs. These inverse signals were used for generating hypotheses for new putative antiviral drugs.

### 2.2 Cleaning of FAERS data

The cleaning and mapping of drug names in FAERS was done by OpenVigil 2. We used an installation of OpenVigil-2.1-MedDRA containing 7,924,898 case reports of FAERS data from 2004Q1 to 2020Q2 for data extraction (Figure 1). This corresponds to approximately 67.5% of successfully imported reports.

### 2.3 Choice of MedDRA terms for diseases caused by Coronaviridae or similar viruses and search strategies

**Coronaviridae** provoke severe acute respiratory syndrome (SARS) or Middle Eastern respiratory syndrome (MERS). COVID-19, which is caused by the current pandemic SARS-CoV-2, manifests with an upper and sometimes a potentially deadly, highly inflammatory lower respiratory tract infection and hypercoagulation.

The family of **Coronaviridae** belongs to the phylum of single-stranded plus-orientated RNA viruses (Figure S1), such as **Flaviviridae** or **Faliciviridae**. SARS-CoV-2 is often compared to influenza virus concerning the air-borne way of transmission and its mortality. However, Influenza A (family **Orthomyxoviridae**), belongs to the phylum of single-stranded minus-orientated RNA viruses, which also encompasses the Ebola virus (**Filoviridae**).
Pharmacovigilance offers data of cases with viral infections, e.g. all the viral families mentioned above, and their respiratory manifestations are available as AEs in FAERS.

The MedDRA version 17 HLTs “viral upper respiratory tract infections” (38 436 cases), “viral lower respiratory tract infections” (2727 cases), “influenza viral infections” (34 814 cases), “parainfluenzae viral infections” (384 cases), “caliciviral infections” (494 cases), “flaviviral infections” (885 cases) and “astroviral infections” (5 cases) were combined resulting in 42 637 cases for analysis. Due to the large overlap of cases (and resulting inverse signals) for the different search terms, all cases were analysed together. Robustness analyses did not show a change in signals (Figures S3 and S4).

In addition, we extracted cases of sequelae to coronavirus infections, namely the preferred terms “fibrin d dimer increased” (999 cases), “cytokine storm” (118 cases) and the HLT “olfactory nerve disorders” (5776 cases).

MedDRA terms referring to coronavirus infection or disease were not considered as they are primarily used since 2020 only.

No ethics committee approval was needed for this publicly available and anonymized data source.

2.4 | Filtering criteria and sorting

The tables were filtered to include only drug-AEs pairs which fulfilled the criteria: (i) ≥30 cases; (ii) ROR <1; and (iii) ROR95CIadj <1.

2.5 | Robustness and confounding

Pharmacovigilance databases consist of spontaneous reports of varying quality and accuracy. Due to the nature of this collection, it is suitable for hypothesis generation only, not for proof. Pitfalls are described in caveat documents of the agencies providing the data and good pharmacovigilance practice guidelines have been proposed.13

For our application, a good specificity is the most important premise. Subgroup analyses were completed to document the robustness of the signals (Figures S3 and S4).

2.6 | Semantic taxonomy enrichment and clustering by Anatomical Therapeutic Chemical classification

Drugs were taxonomically enriched by categorizing them by their World Health Organization Anatomical Therapeutic Chemical (ATC) classification code, which is a descriptive key with 5 levels. This allows clustering of drugs using the 4 higher levels of the code.

2.7 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in http://www.guidetopharmacology.org, and are permanently archived in the Concise Guide to PHARMACOLOGY 2019/20.14,15

2.8 | Comparison to other drug repurposing approaches

We searched in PubMed, Google Scholar and CURE ID (https://cure.ncats.io/) for other publications using a combination of the keywords “drug repurposing”, “drug repositioning” and “viral infection”, “covid-19”, “corona” and present the overlap of these candidates with our data.

3 | RESULTS

We used OpenVigil 2 to extract signals of drugs that were inversely associated with AE indicative for either RNA-viral infections or respiratory manifestations.

In total, 126 drugs fulfilled the search criteria. The list was further pruned: calcium was excluded as it represents both an active substance and a (not necessarily active) counter-ion. Cytotoxics (e.g. *cisplatin*) were removed because of their detrimental action on the patient. Drugs that are topically used (e.g. *timolol* eye drops) were removed as they might have no systemic action. Finally, drugs that are already known not to be effective against viral infections or even promote the disease (e.g. *carbidopa* and *levodopa*,16 *anastrozole*, *testosterone*17), were not considered.

This manual, data-driven curation of the list and the removal of clinically infeasible drugs resulted in a list of 112 candidate drugs.

All data (raw and postprocessed) are available as spreadsheet files from the OpenVigil website. As an example, the 5 most statistically significant candidate drugs against viral respiratory infections are shown in Figure 2.

All 112 curated candidate drugs were categorised according to their ATC classification code and visualized in Figure 3 and supp. Figure S5.

Mechanisms of established or hypothesised antiviral or immunomodulatory activities and their references are presented in Table S3 and Figure 4.

For the sequelae such as cytokine storm, thrombosis and anosmia, only the latter could be analysed. We found 11 candidate drugs to be effective against olfactory disorders (Figure S6).

An overview of current drug repurposing strategies against COVID-19 is presented in Table S3.
3.1 Review of selected candidate drugs

3.1.1 Antidiabetics

Antidiabetic drugs of different classes were detected as potentially beneficial for the treatment of viral diseases.

**Metformin** increases interferon production and impairs hepatitis B virus protein production, possibly because of its mitochondria-impairing action. Inhalation is considered an appropriate route of administration to target the lower respiratory tract. Inhalative metformin has previously been tested for its application against cancer.

Glitazones such as *rosiglitazone* have previously been shown to impair viral replication. Glitazones might either act via their antidiabetic target, the peroxisome proliferator-activated receptor-γ, regulating T-cell activity, or by inhibiting viral transfer using solute carriers.

Insulins are the first-choice agent in diabetic critically ill COVID-19 patients. It remains to be elucidated whether insulins have an additional beneficial effect beyond glucose control. Hyperglycaemia is an independent risk factor of mortality.

A recent review on endocrinological drugs against COVID-19 further proposes gliflozins, glitides and dipeptidyl peptidase 4 (DDP4) inhibitors as beneficial in COVID-19.

Another in silico drug repurposing study based on data of the SARS-CoV-2 proteome detected the antipsychotic *haloperidol* (ROR 0.2, see supplemental material) as a candidate drug. Haloperidol binds to sigma nonopioid intracellular receptor 1, which might interfere with the viral protein nonstructural protein 6, a part of the **CoV replicase polyprotein 1a**. Binding of sigma-receptors is a common property of antipsychotics and opioids. The latter might explain the abundance of opioid drugs in our findings.

The antipsychotic *aripiprazole*, which has a quinolone moiety, was identified as a putative anti-influenza drug using a structure-based approach, since it is supposed to interfere with viral RNA polymerases. Gyrase inhibiting antibiotics such as *levofloxacin* and *ciprofloxacin* (proposed candidate drugs) have a central quinolone moiety, too. Since the **CoV RNA-dependent RNA polymerase** is fundamentally different from all other viruses, it remains to be elucidated whether these inhibitors work with SARS-CoV-2. A ligand-docking study suggests that ciprofloxacin and moxifloxacin could also inhibit the viral **CoV 3C-like (main) protease** (see below).

**Valproic acid**, which is known to inhibit the human histone deacetylase 2 (HDAC2), is proposed to interfere with the coronavirus nonstructural protein 5, part of the **CoV replicase polyprotein 1a**.

Selective serotonin reuptake inhibitor-type and other antidepressants are predicted candidate drugs and were shown to be associated with lower fatality.

Nicotinergics could inhibit viral entry and inflammation by modulating various cholinergic pathways.

3.1.2 Neuro-psychiatrics as sigma-receptor modulators and replicase inhibitors

Antipsychotics, antihistaminergics and GABA-ergics have previously been hypothesized as potentially anti-inflammatory in inflammatory bowel disease using a similar approach.

3.1.3 Hydroxychloroquine

The sigma-receptor agonists *chloroquine* and *hydroxychloroquine* were not found to be beneficial, but a risk factor in our data (Spreadsheet S1: ROR 1.8 [95%-CI 1.1–3.0] for HLTs viral...
upper/lower respiratory tract infection and influenza). This is in line with clinical trials that reported that there were no beneficial effects of hydroxychloroquine concerning mortality or stay duration but a trend towards higher mortality (hazard ratio 1.11)\textsuperscript{38} and no effect in postexposure prophylaxis.\textsuperscript{39}

3.1.4 | Viral protease inhibitors

Viral proteases are needed to cleave the viral proteins. HIV antivirals are well known protease inhibitors. Docking studies suggest that sartans, valproic acid and statins such as simvastatin might

\textbf{FIGURE 3}  Sunburst plot of curated candidate drugs grouped by Anatomical Therapeutic Chemical (ATC) classification. Candidate drugs are grouped according to their ATC classification code. The inner circle shows the first level of the code, the anatomical main group (e.g. G stands for Genitourinary system and sex hormones). The middle circle shows the grouping according to level 3, therapeutic/pharmacological subgroup. The outer circle shows individual drugs belonging to the group. The width of each slice is the relative inverse reporting odds ratio. The larger the slice, the more disproportionate the signal. An effect size cannot be estimated from this (cf. the weaknesses of the ATC classification system in the discussion section)
also inhibit the CoV 3C-like (main) protease. Another docking study suggests quinolones as ligands.33

3.1.5 | Exopeptidase inhibitors

**Coronaviridae** causing MERS and SARS enter cells by binding to certain exopeptidases such as angiotensin-converting enzyme 2 (ACE2) and dipeptidyl peptidase 4 (DPP4).40 Apparently, SARS-CoV-2 is primarily dependent on the transmembrane serine protease 2 (TMPRSS2) and ACE2.2,41

Initially, it was hypothesized that patients treated with ACE-inhibitors (ACEi) might be at greater risk for severe COVID-19, since ACEi compensatory mechanisms increase the expression of ACE2.42 Two studies based on in-patient data denied the influence of ACEi and sartans on COVID-19.43,44 OpenVigil detected the ACEi ramipril and the AT1-receptor antagonist olmesartan as candidate drugs. In addition, irbesartan is a possible anti-COVID-19 candidate drug predicted by proteome analysis.34

ACE2 is increased in patients with diabetes mellitus or vascular diseases45. This could explain both the higher susceptibility of these patients for SARS-CoV-2, as well as the occurrence of antidiabetics and antihypertensives among our candidate drugs. However, with regard to ACEi or sartans, higher expression levels of ACE2 are not generally predictive for infectivity or a bad prognosis of COVID-19.

A dysregulated immune response and a hypercoagulable state further complicates the situation for patients with diabetes.46

Heparins such as enoxaparin and oxazolidinones such as rivaroxaban and other inhibitors of factor Xa were detected as signals. Factor Xa is a serine protease that cleaves the coronavirus spike-protein, so the virus can enter the cells.47 Factor Xa is also needed by other viruses for the cleavage of certain viral proteins.48,49 Inhalative heparin is proposed for prophylaxis and treatment of COVID-19.50 Beyond this special antiviral mechanism, all inhibitors of coagulation were hypothesized to be beneficial against the thrombotic events occurring in COVID-19.

**Sitagliptin**, a DPP4-inhibitor, was previously tested against SARS and MERS. The negative results might reflect the different binding sites of virus and drug.51 Furthermore, and in contrast to MERS and SARS, DPP4 appears not to be a relevant exopeptidase for SARS-CoV-2.

3.1.6 | Kinase inhibitors

Inhibition of intracellular kinases that regulate cell viability and immune reactions appears as a new concept for treatment of COVID-19: the candidate drugs erlotinib and sunitinib have previously been proposed to treat dengue fever, possibly by inhibition of intracellular kinases that regulate trafficking of viruses.52 Imatinib

**FIGURE 4** Selection of antiviral pathways of the candidate drugs identified with our pharmacovigilance-based approach. ACE: angiotensin converting enzyme; AMPK: AMP-activated protein kinase; DPP: dipeptidyl peptidase; ER: endoplasmic reticulum; Factor Xa: coagulation factor X activated; GA: Golgi apparatus; NSP: nonstructural protein; PP1A/B: viral polyproteins 1A/1B; TMPRSS2: transmembrane protease serine subtype 2
could inhibit the fusion of coronaviruses with the cell, maybe due to a putative ABL proto-oncogene 2, nonreceptor tyrosine kinase–TMPRSS2-pathway or by interfering with actin dynamics needed for cell–virus fusion.

3.1.7 | Hormones

Male sex is a major risk factor. Androgens enhance the expression of TMPRSS2 and–at least in rats–ACE2. We have identified leuproide, finasteride, enzalutamide and abiraterone as potentially beneficial. The signal for testosterone might be caused by confounding, i.e. a male patient with a lack of testosterone getting replacement therapy. There is evidence that testosterone is an infection-promoting agent. 17β-oestradiol can attenuate viral diseases but apparently only in patients with low endogenous oestradiol.

In addition to the putative gestagen effect, drospirenone is also a mineralocorticoid-receptor antagonist. This antagonism is considered anti-inflammatory. Surprisingly, we could not detect a beneficial but rather a detrimental signal for the mineralocorticoid-receptor antagonist spironolactone.

3.1.8 | Various

Nicotinic acid (niacin) and its derivatives are implicated in boosting anti-viral defenses. The well-known pleiotropic effects of statins could mitigate inflammation.

Proton pump inhibitors (PPIs) such as lansoprazole possess an intrinsic antiviral effect. However, PPIs were not effective against flaviviridae, which are similar to coronaviridae. In addition, the antiviral effect will probably be countered by the increased susceptibility to bacteria and viruses due to the effect of PPIs on gastric pH and the gastrointestinal antimicrobial barrier. The gastrointestinal tract is a route of infections for MERS-CoV infections and possibly for SARS-CoV-2 as well, so risk–benefit ratio is unclear.

The various antibodies detected could be confounded by the very special situation of the patients (e.g. hospitalized treatment and thus less risk of airborne infections). Since some of the antibodies modulate inflammatory pathways, we have not removed them from curated list. We could not detect leads for confounding within our data.

3.2 | Candidate drugs against anosmia

Eleven candidate drugs against anosmia fulfilled our filtering criteria (Figure S6). The largest group consisted of various immunomodulatory drugs, the majority targeting tumour necrosis factor shed form such as etanercept. There is 1 case report in which the late onset of anosmia was attributed to the usage of etanercept. Etanercept is effective in an olfactory inflammation mouse model.

The candidate drug quetiapine was also beneficial in a mouse model.

3.3 | Candidate drugs without known or proposed antiviral mechanism

For some candidate drugs no affirmative data could be found in the literature. This absence of evidence must not be misinterpreted as an evidence of absence of any mechanism. In contrast, this should stimulate further research to elucidate these disproportionality signals.

4 | DISCUSSION

We used OpenVigil 2 and statistical constraints to extract statistically strong inverse signals of drugs associated with AEs indicating viral respiratory diseases. The results were further manually pruned to exclude clinically infeasible drugs; 112 candidate drugs remained.

All reports in pharmacovigilance databases are biased by technical limitations as explained later on and by the nature of spontaneous reporting: the reports represent only a small proportion of the real-world situation. The healthy part of the population is not known and thus all calculations of observed/expected disproportionality are performed against the background of all other drugs and all other events. AEs are expected to be underreported by 1:1.1 to 1:100, dependent on their seriousness and whether an ADR was already well known and presented in scientific or lay media. Data on SARS-CoV-2 becomes available, albeit in a biased way: e.g. reporting of AEs of the anti-influenza drug oseltamivir spiked during 2009 (A/H1N1, swine flu), 2016 (A/H5N8, avian flu) and 2018 (A/H3N2; Figure S7). This selective reporting over time introduces bias into the data.

Since inverse signals are undesigned byproducts of pharmacovigilance analyses, their meaning and limits are debated. However, they have been used convincingly before.

The FAERS pharmacovigilance data are dirty, i.e. they include reports with nonunderstandable drug names. OpenVigil 2 employs a mapping logic based on the external drug databases Drugbank.ca and drugs@FDA, and loads only fully understandable reports (complete case analysis). Approximately, 67.5% of all available FDA case reports could be completely imported into OpenVigil 2. It is unclear whether discarding not fully understandable reports introduces bias to the analysis. Exploration of common incomprehensible drug names revealed no qualitative influence on our results. We suggest that other, available case approaches (e.g. used by openFDA/OpenVigilFDDA) are inferior, as the size of the complement (noncases) is likely to be overestimated and, consequently, more inverse signals generated. Therefore, we consider complete case analysis superior for the application of drug repurposing, since this needs a high specificity.

The ATC system has substantial flaws: a substance can have >1 ATC classification code, depending on the route of application and the intended indication. Level 3 and 4 are diffusely mixing therapeutic, chemical and pharmacological categories. Thus, group sizes are
arbitrary. Subgroups containing the letter X contain substances with different mechanisms of action and/or chemical structures. A better approach could be to build a multidimensional space based on quantitative data, e.g., affinities of substances to different targets (e.g., by using CMap, Drugbank etc., cf. Table S3), and to detecting clusters within. This could be a method that is superior to 1- or few-dimensional qualitative classification systems such as ATC, the Kyoto Encyclopedia of Genes and Genomes, or the National Drug File—Reference Terminology.

The data do not allow to distinguish whether a candidate drug can prevent or ameliorate the condition. Furthermore, the effect size is not known and cannot be derived from the ROR. Some case reports feature data on drug dosage, treatment duration, AE severity or outcome (e.g., dead) but mostly this information is not available. Thus, the potential benefit cannot be estimated solely based on pharmacovigilance data. Importantly, dosage recommendations cannot be derived.

Especially in viral diseases such as COVID-19, the different treatment goals, i.e., post- or pre-exposition prophylaxis, treatment of mildly or severely ill patients, early or late stage of the disease,17 curative or palliative treatment intention, need to be distinguished and suitable drugs for each need to be identified. This cannot be done with pharmacovigilance data only.

Drug repurposing using pharmacovigilance data is a rather new application. We have currently limited knowledge how on to translate results to bedside and which pitfalls, such as confounding, to avoid and how to avoid them.

Using drugs in a new way of application, i.e., targeting directly the inflammatory tissue by inhalation, introduces new challenges. With exception maybe for metformin and interferons, which are used inhalatively, the safety of these applications needs to be proven in clinical trials.

Using pharmacovigilance for drug repurposing is an approach that is fundamentally different to all other methodologies currently employed. Interestingly, while the same drug might be proposed by different drug repurposing techniques, the theorized target and mode of action might differ.

5 | OUTLOOK

Pharmacovigilance-based drug repurposing is a novel strategy not related to ligand docking or omics- and network-based approaches. Besides developing new antiviral strategies, this approach can be used for other indications.9 Curating the results is the biggest challenge: can a substance be effective at all and, if so, by which mechanism, and at what time in the course of the disease should it be used?

We have identified a plethora of candidate drugs. However, more preclinical and clinical trials are necessary to evaluate these hypotheses. Candidate drugs that were not explainable by our research should stimulate further research. The raw data and the results presented here might guide and thus accelerate these trials with educated guesses.

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COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

H.J.K. developed OpenVigil 2. R.B. performed the data extraction. C.B. cleaned and annotated the data. V.W. and T.H. postprocessed the signals. I.C. gave conceptional advice. All authors contributed to writing the manuscript.

CODE AVAILABILITY

OpenVigil 2 can be downloaded as executable and source from https://openvigil.sf.net under the GNU General Public License v2.

DATA AVAILABILITY STATEMENT

All data are included in the supplemental material and at the OpenVigil website at http://openvigil.pharmacology.uni-kiel.de/data/Supplement_tab01_Candidate_drugs_viral_respiratory.ods http://openvigil.pharmacology.uni-kiel.de/data/Supplement_tab02_Candidate_drugs_sequelae.ods and at OSF at https://osf.io/gv258/

ORCID

Ruwen Böhm https://orcid.org/0000-0003-1007-3011
Vicki Waetzig https://orcid.org/0000-0001-6690-5281
Ingolf Cascorbi https://orcid.org/0000-0002-2182-9534
Thomas Herdegen https://orcid.org/0000-0001-8502-6207

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