Federal Agency for Medicines and Health Products
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DG Post/Pharmacovigilance

Summary Adverse Drug Reactions in Corona virus infection

The search was done in EudraVigilance[1] on the 24th of June 2020. It contains cases between **01/09/2019 and 24/06/2020** where the **indication 'coronavirus infections'** was mentioned.

The interpretation of these data should be done carefully :

- Overall, there is a large underreporting of adverse events;
- Among available cases in EudraVigilance, it is possible that not all Covid-cases are retrieved in this analysis based on our search terms (indication coronavirus infection). It is possible that in some cases the indication is not completed in the database;
- It concerns suspected associations, this is not a confirmation of a causal relation;
- It can't be concluded that some substances have more ADRs than others based on these figures. The usage and the period that the substance is on the market have to be taken into account and cannot be estimated at this stage.
- The number of adverse events will not always be the same as the number of individual cases. Some cases may report different adverse events.

The interpretation of the safety data should take into account the benefits for the products.

As of 24th of June 2020, 19 Belgian cases have been received (10 in EudraVigilance, 9 directly by the FAMHP) : 1 case with isavuconazole, 2 cases with itraconazole, 8 cases with hydroxychloroquine, 1 with lopinavir/ritonavir, 2 case with tocilizumab, 1 case with remdesivir , 3 cases with sarilumab and 1 case with combination of sarilumab and hydroxychloroquine.

The reported ADRs for Lopinavir/ritonavir, remdesivir and hydroxychloroquine are in line with their known safety profile.

More details are given in the following pages.

[1] The information in this document does not reflect any confirmation of a potential link between the medicine and the observed effect(s); the information in this document concerns suspected associations that reflect the reporter's observations and opinions. A scientific assessment of a cause-and-effect relationship between a medicine and an effect is part of the continuous monitoring of the benefits and risks of a medicine; the assessment takes into account many other factors, such as the medical condition and the medical history of the patient; the information may include known side effects already listed in the summary of product characteristics (SmPC) and the package leaflet; the number of suspected side effects in EudraVigilance should not serve as a basis for determining the likelihood of a side effect occurring. This is because the numbers need to be put into context with other factors, such as how many people take the medicine and how long the medicine has been on the market; each individual case in EudraVigilance refers generally to a single patient; however, more than one side effect may have been reported in a report. Therefore, the number of side effects will not always be the same as the number of individual cases; the side-effect reports in EudraVigilance do not represent all available information concerning the benefits and risks of a medicine and should not be used in isolation to make decisions regarding a patient's treatment regimen; other sources of information, including the product/prescribing information, should be consulted first. The authors are indebted to the national pharmacovigilance centres that contributed data to EudraVigilance database, maintained by the European Medicines Agency.

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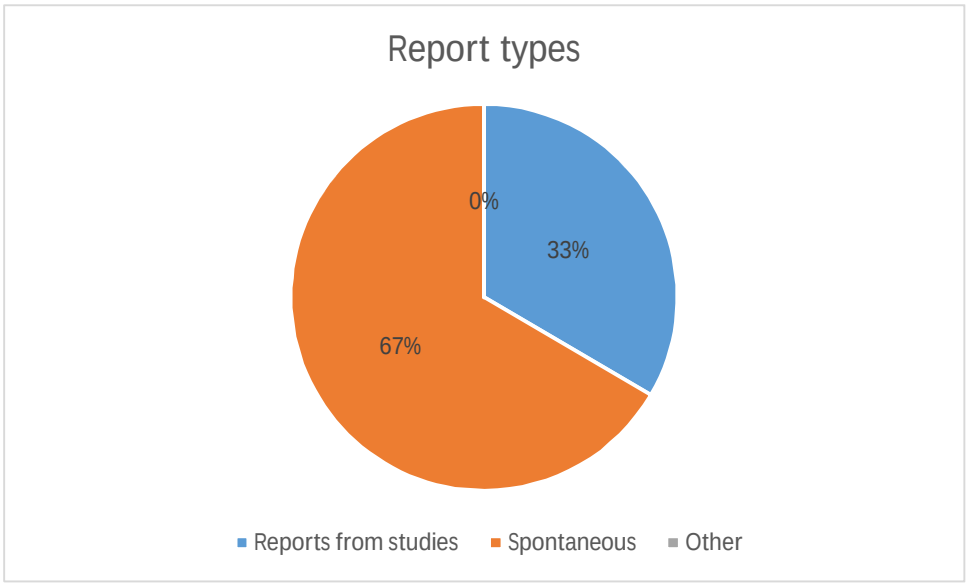
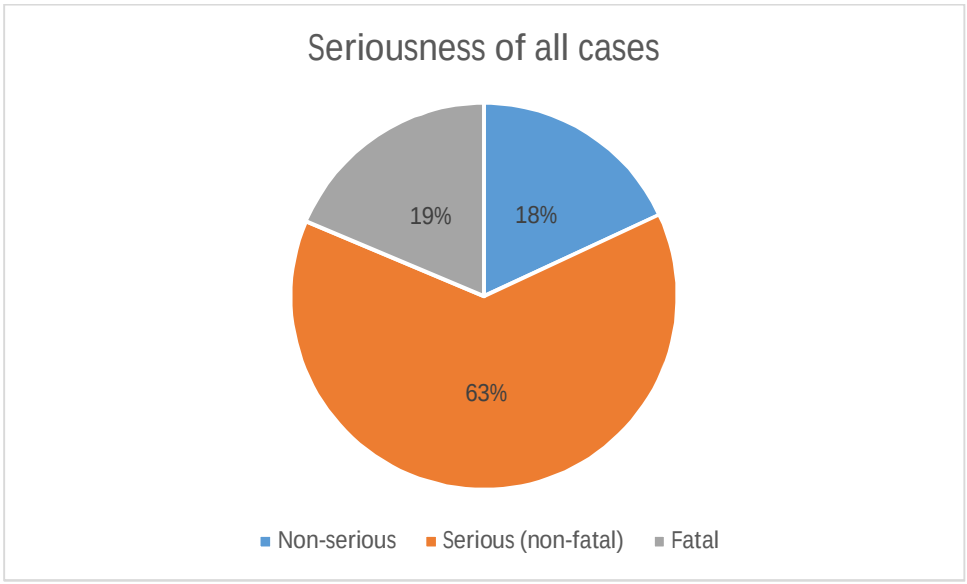
1. General information

2846 reports have been retrieved from EudraVigilance (up to the 24th of June 2020).

Report types :



Seriousness of the cases :



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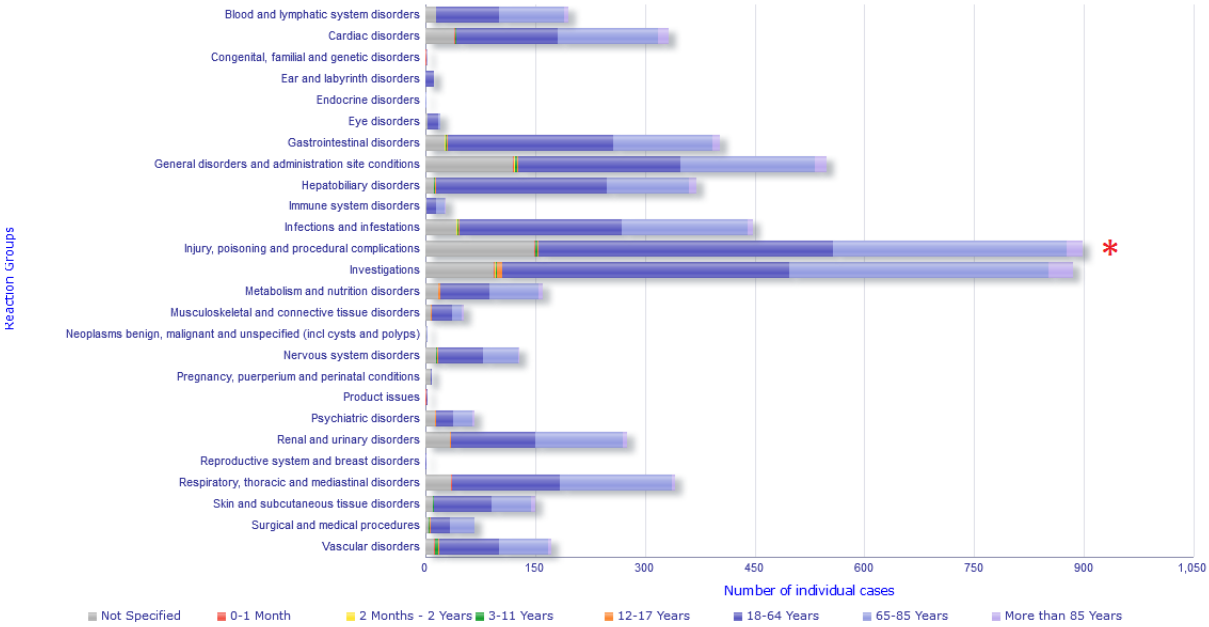
Age groups (per SOC) (for all cases)



* *The SOC Injury, poisoning and procedural complications contains in majority PTs in the context of 'off-label use'*

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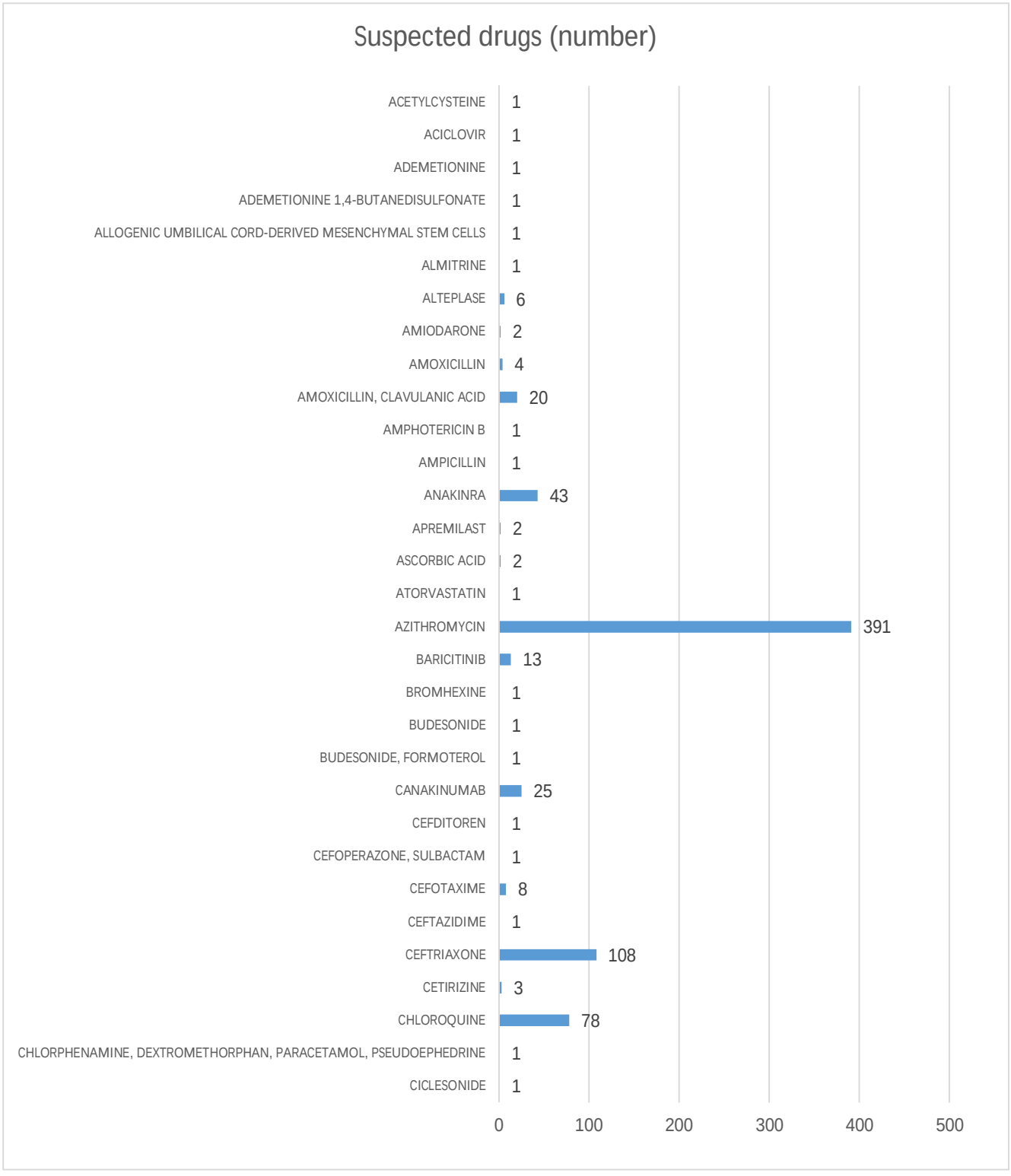
2. Suspected drugs



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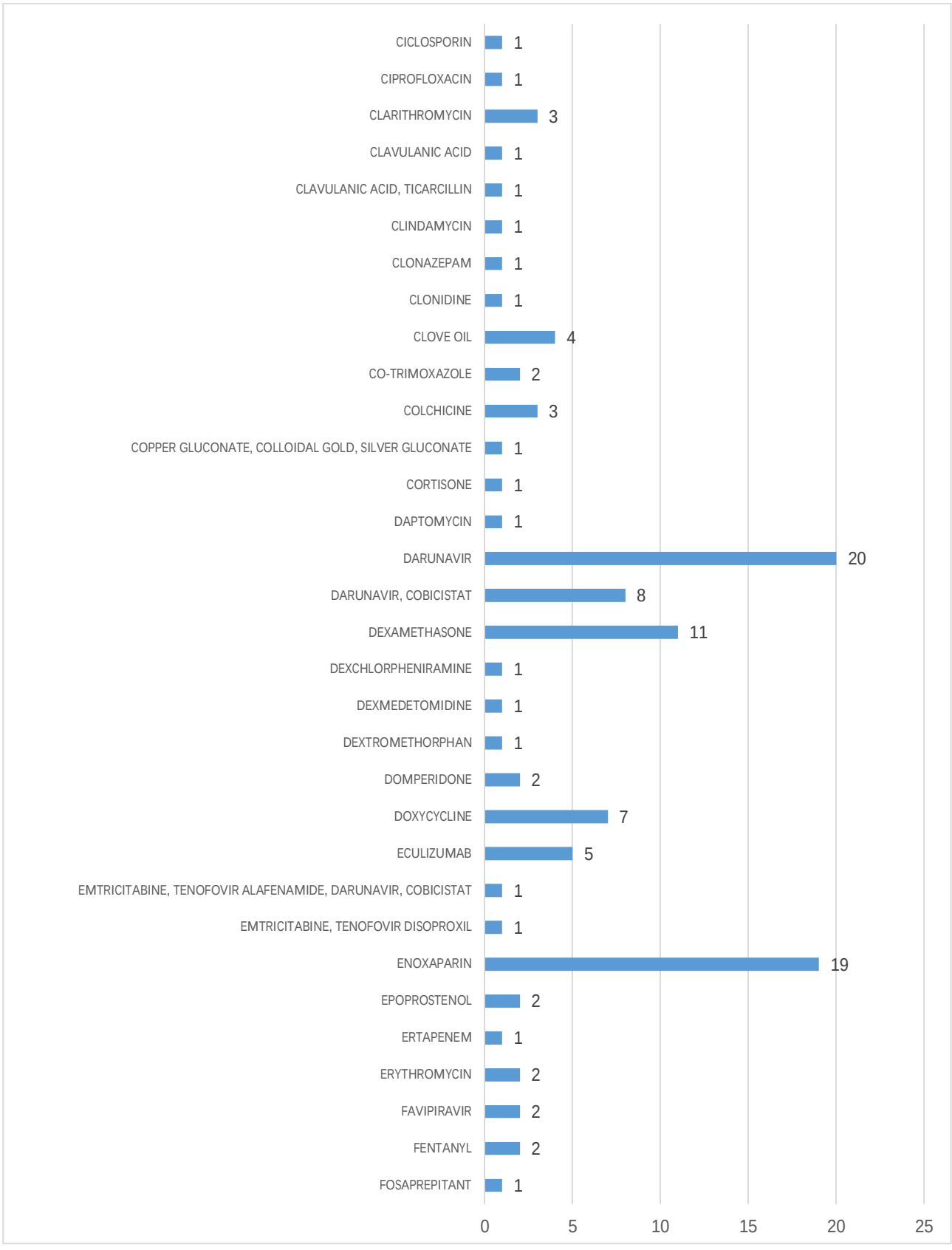

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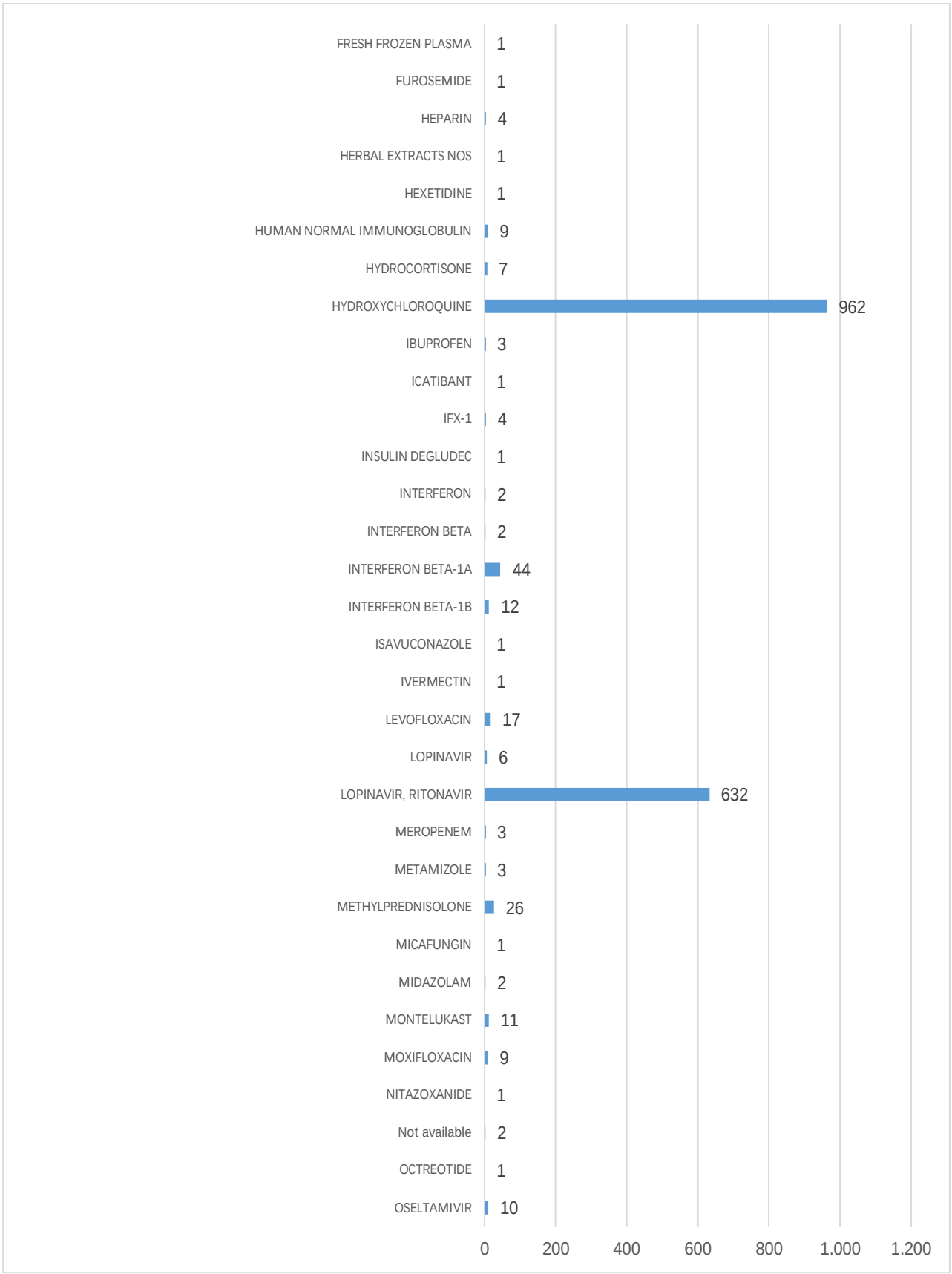

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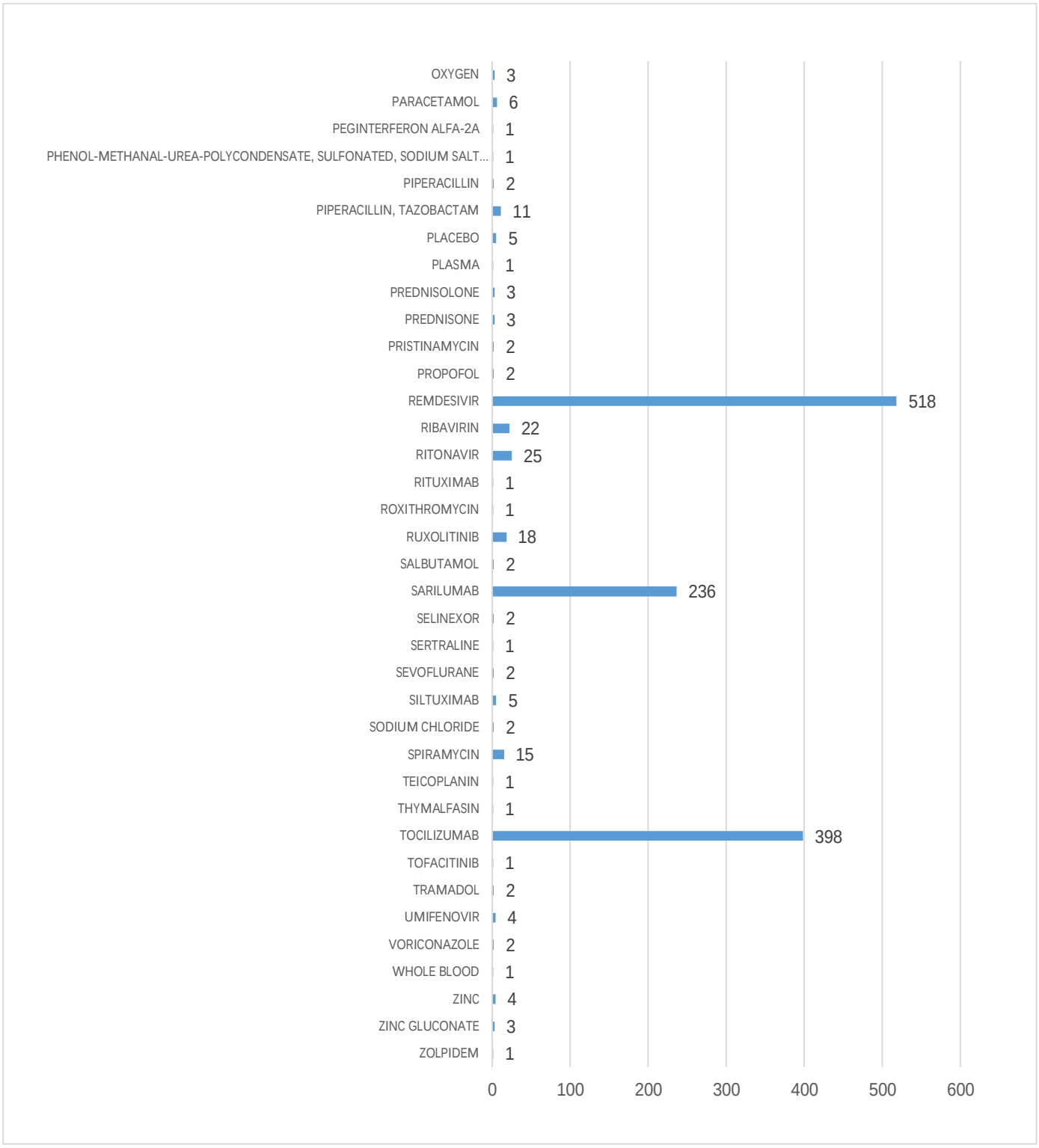
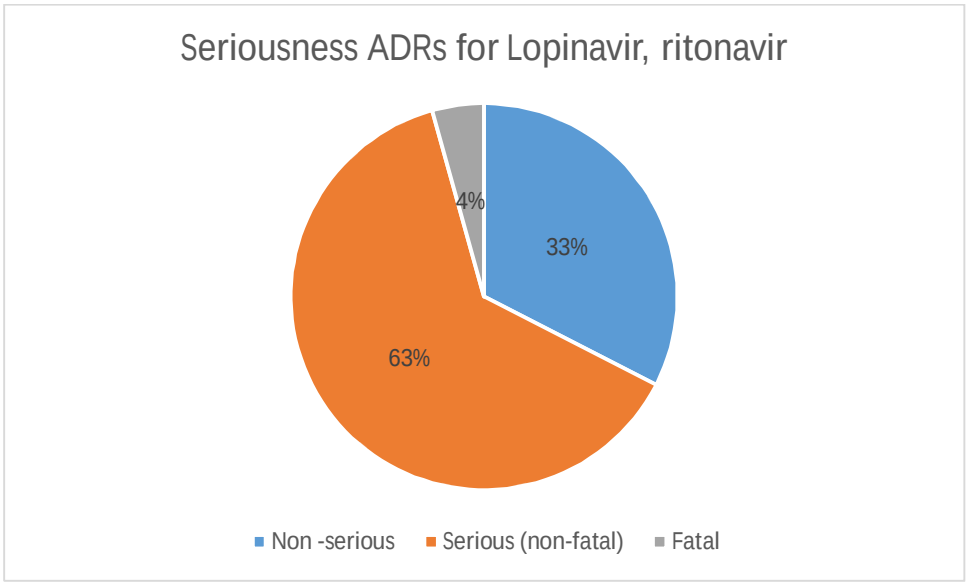


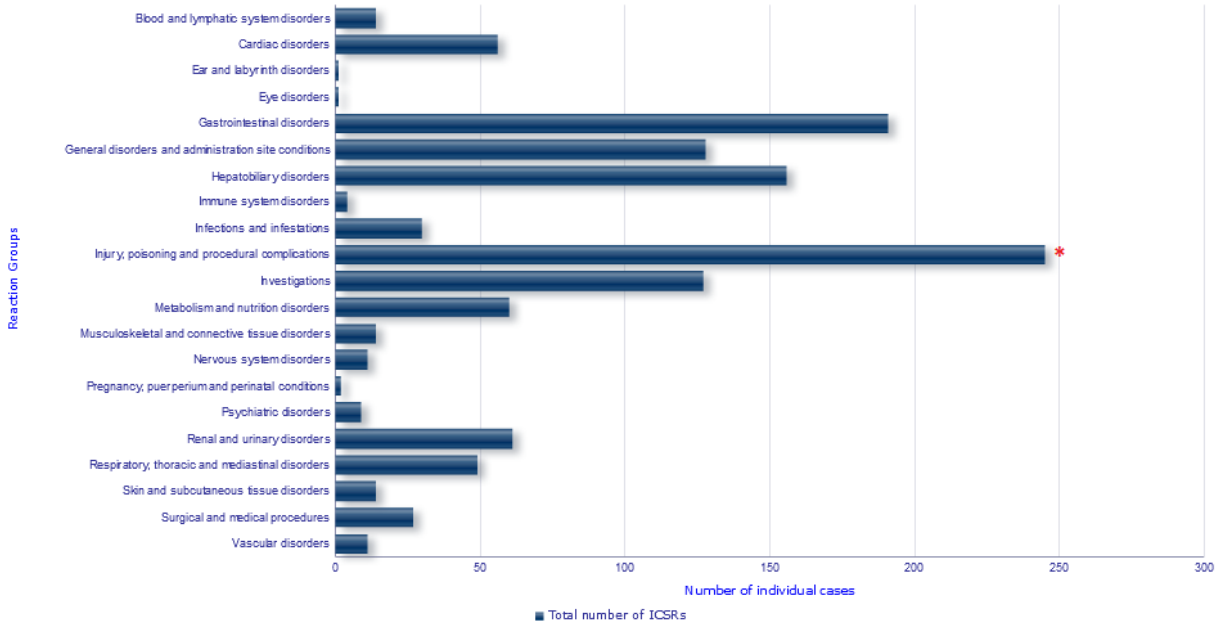
For the following medicinal products, the cases were explored a bit more in detail : Lopinavir/ritonavir, remdesivir and hydroxychloroquine.

2.1 Lopinavir, ritonavir

Seriousness ADRs for Lopinavir, ritonavir (632 cases in total)



Number of individual cases by reaction SOC



* *The SOC Injury, poisoning and procedural complications contains in majority PTs in the context of 'off-label use'*

The following PTs are listed in the 4 SOCs with the most reported PTs apart from the SOC Injury, poisoning and procedural complications.

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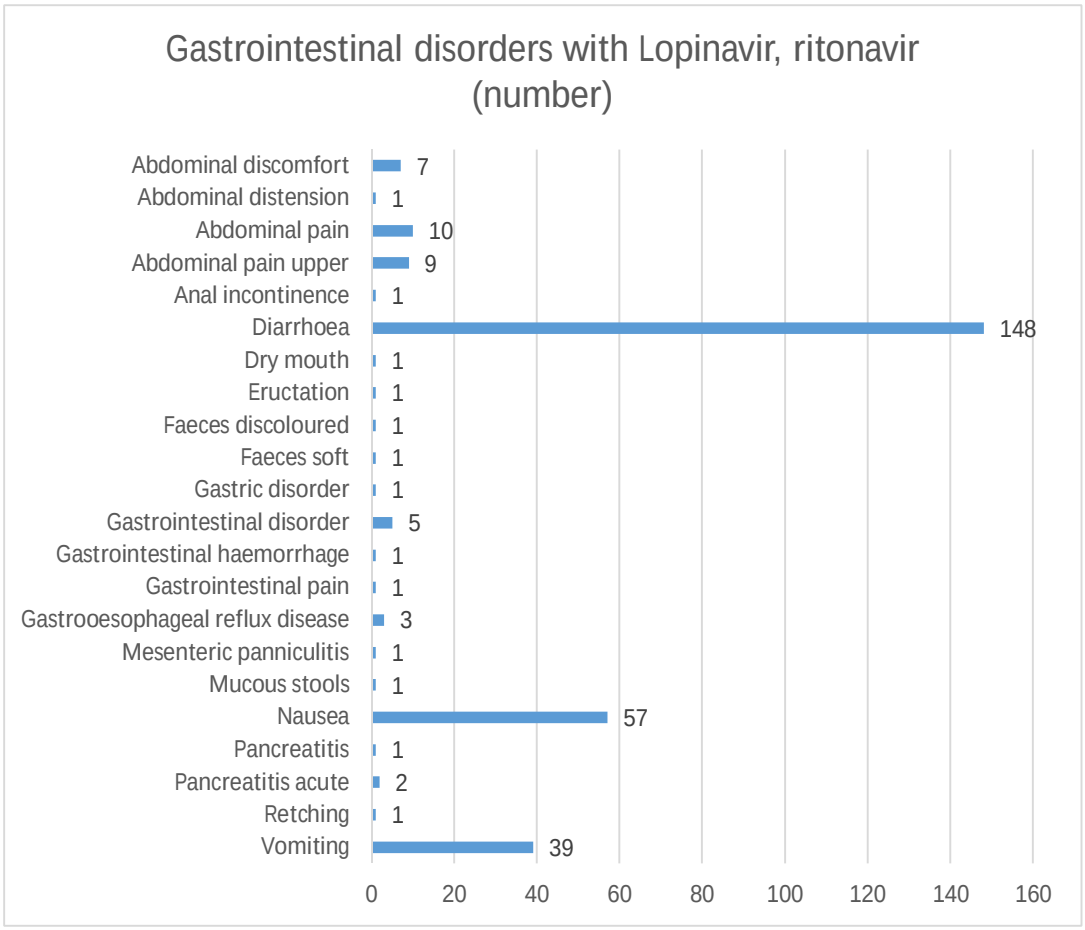
PTs in the SOC Gastrointestinal disorders



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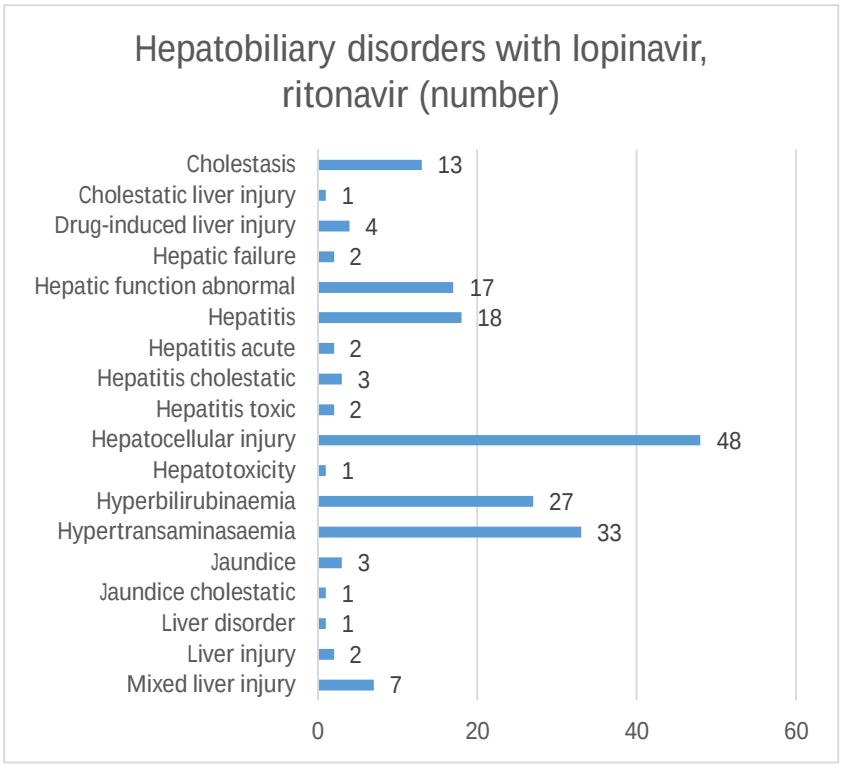
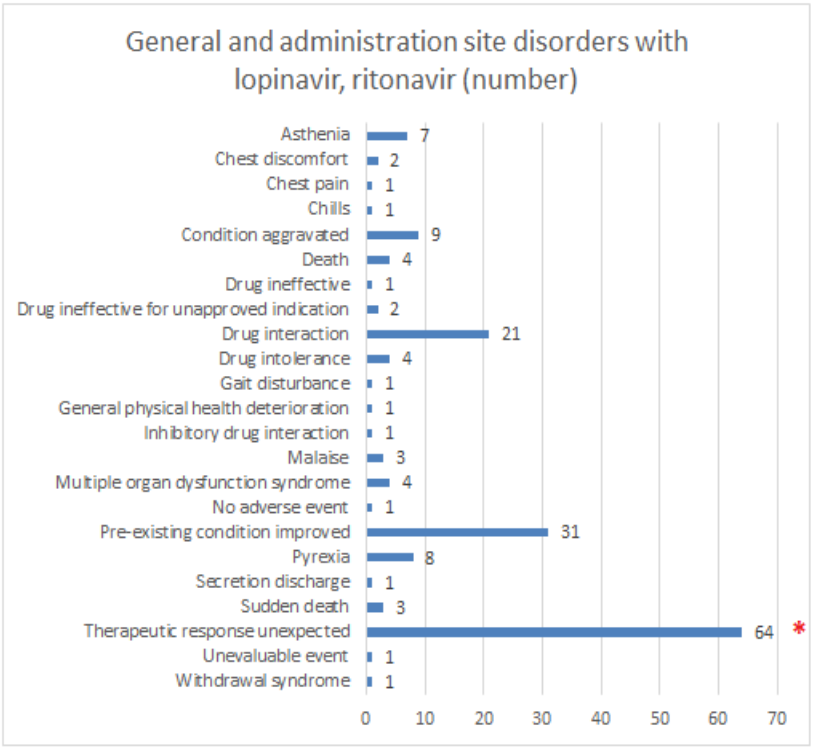
PTs in the SOC hepatobiliary disorders



PTs in the SOC General and administration site disorders



* 'Therapeutic response unexpected' should be interpreted in the context of off-label use where 'unexpected therapeutic benefit/need' was reported in the cases.

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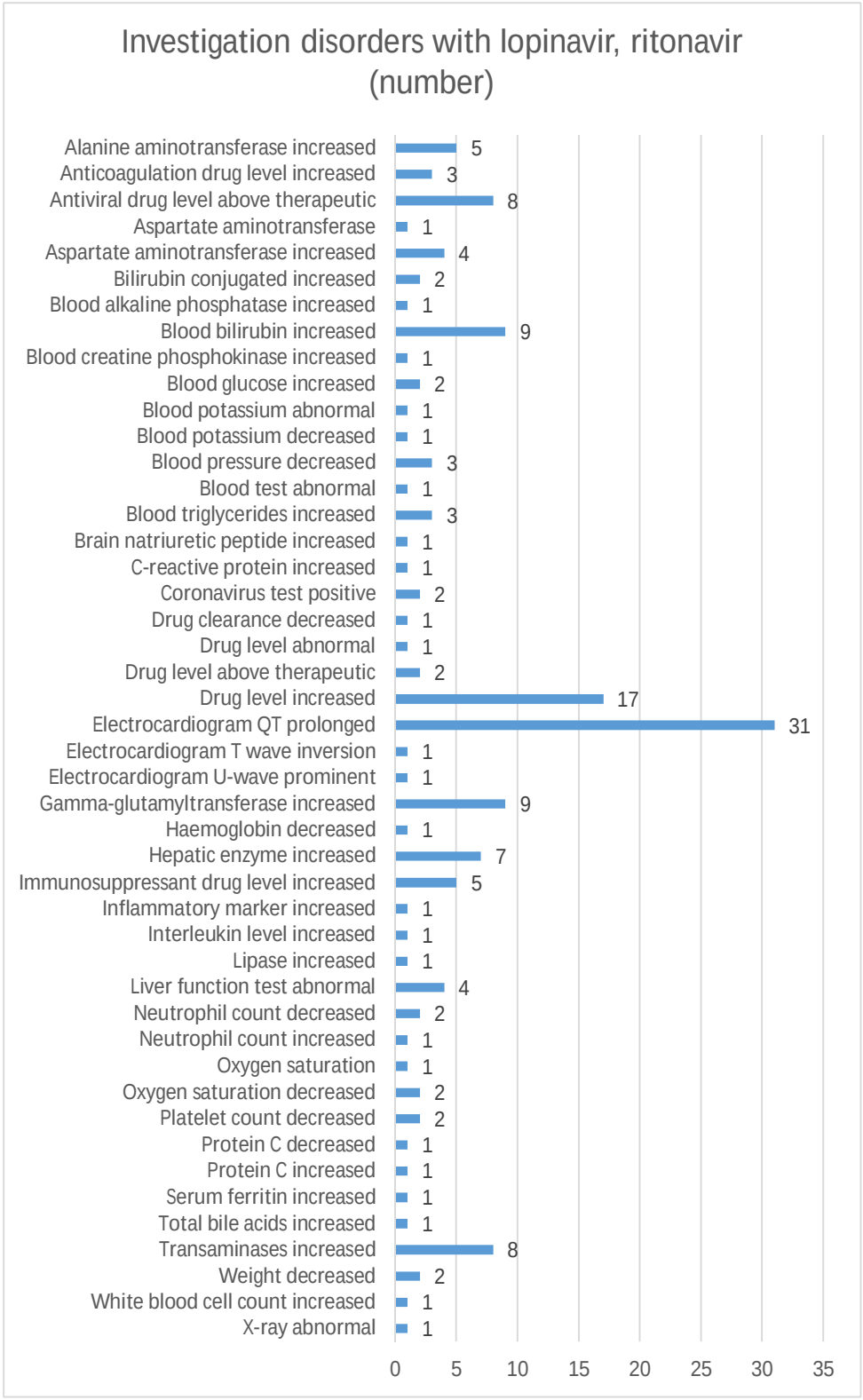
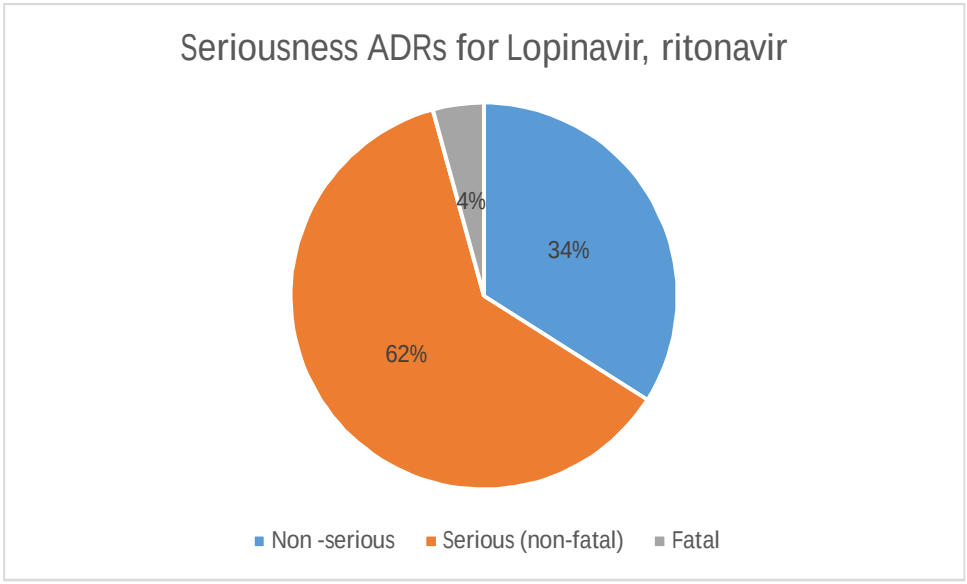
PTs in the SOC Investigations

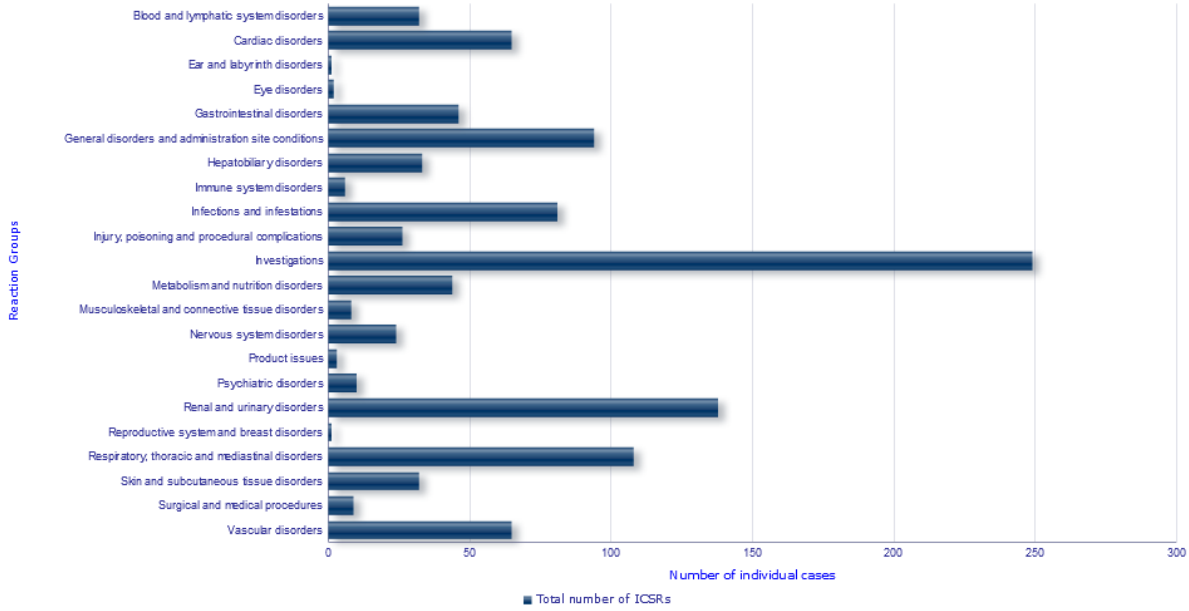


2.2 Remdesivir

Seriousness ADRs for remdesivir (518 cases in total)



Number of individual cases by reaction SOC



The following PTs are listed in the 4 SOCs with the most reported PTs.

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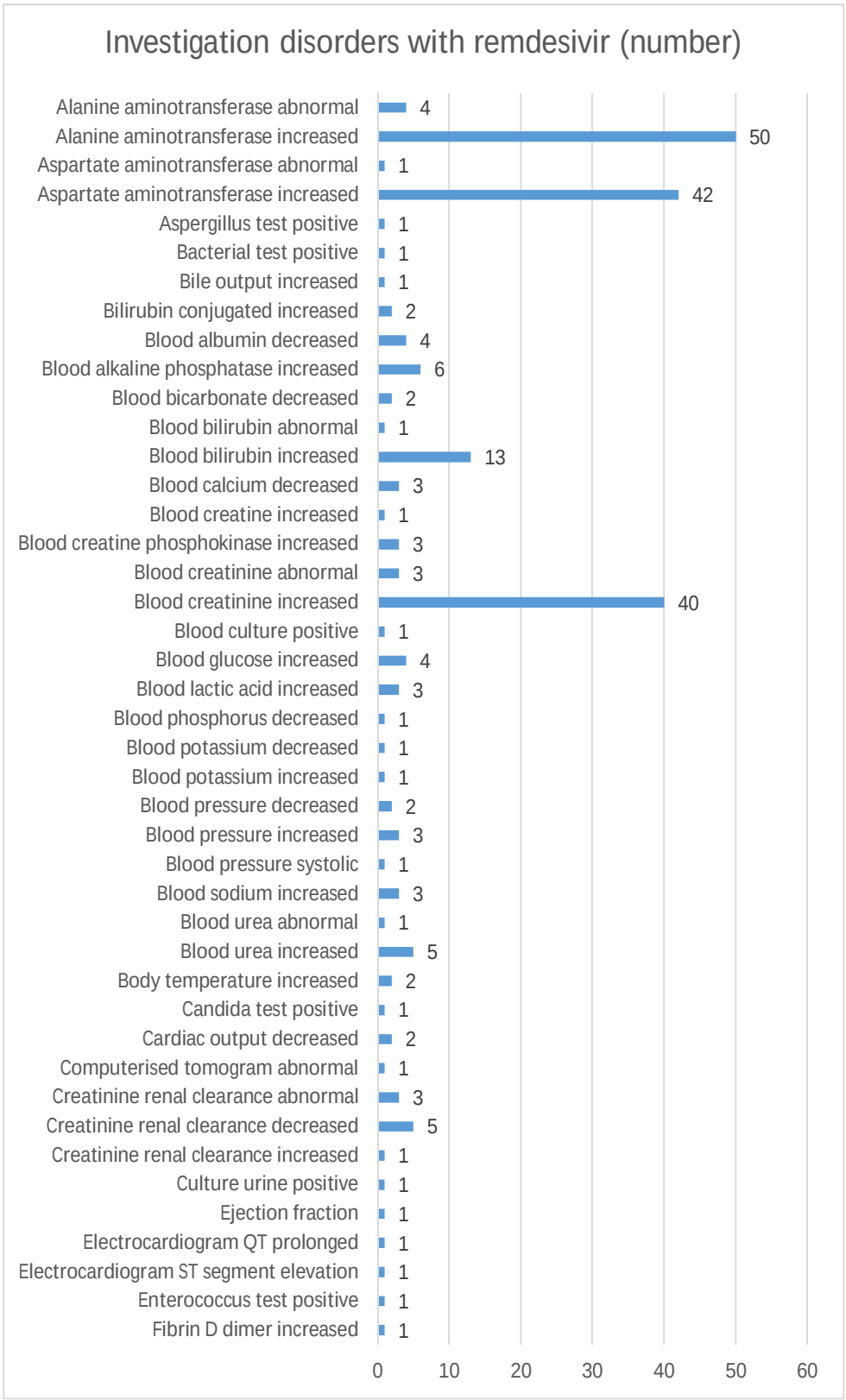
PTs in the SOC Investigations



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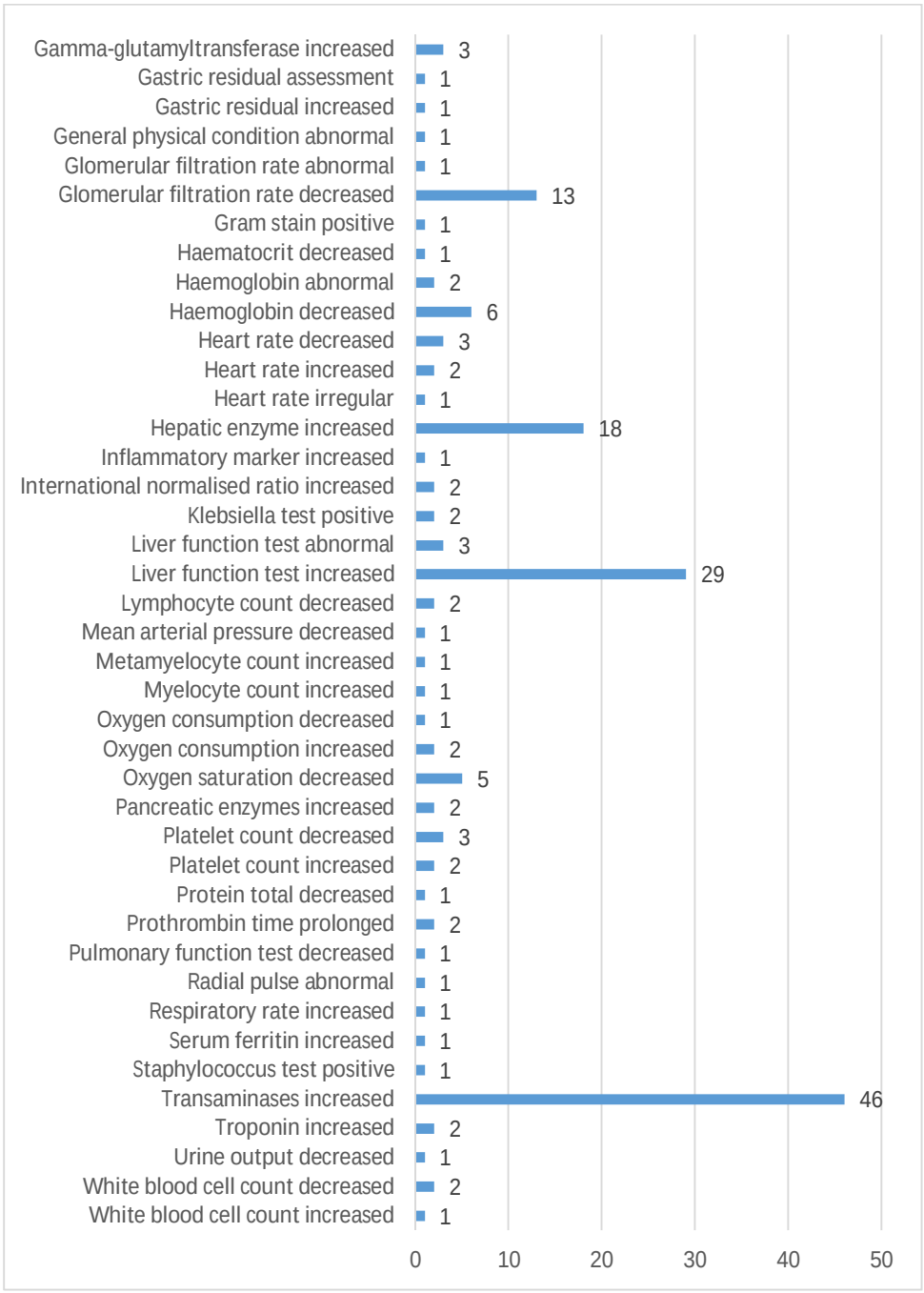

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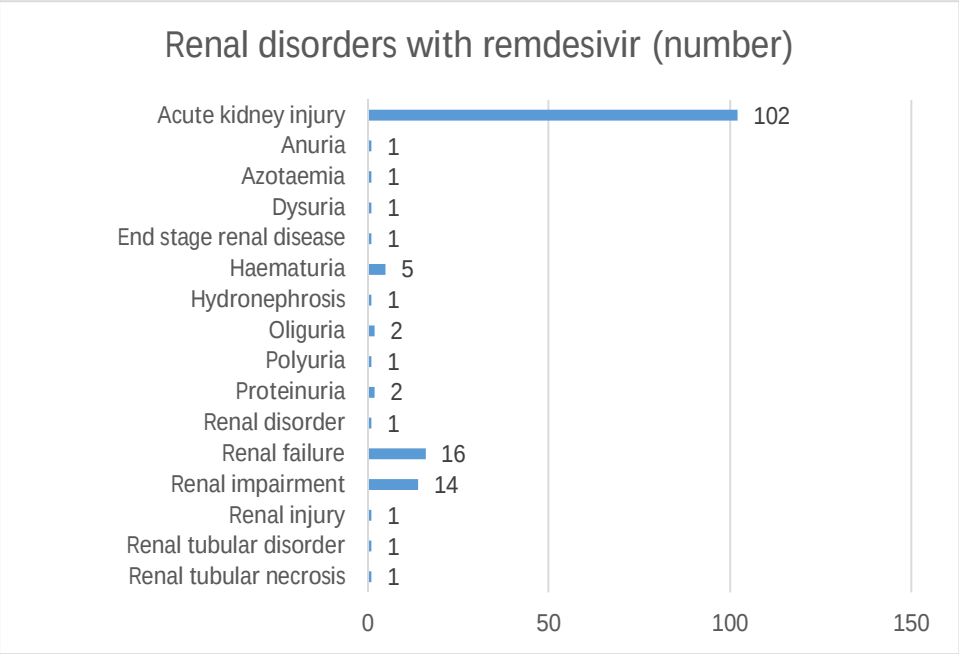
PTs in the SOC Renal and urinary disorders



In total 138 patients experienced renal disorders while on remdesivir treatment. Several patients had pre-existing renal conditions or other risk factors. These data should be interpreted with caution since liver and kidneys can be damaged in patients with COVID-19[2,3].

The percentage of the renal cases in the total of ADR cases with remdesivir was calculated and compared with the percentages for lopinavir/ritonavir and HCQ (to account for the possible influence of Covid-19 itself) :

- Remdesivir : 138 / 518 = **26.6 %**
- Lopinavir/ritonavir : 61 / 632= **9.7 %**
- Hydroxychloroquine : 36 / 962= **3.7 %**

There're a lot more renal cases reported with remdesivir than with the other 2 products.

[2] Rismanaf A, Zarei S. Liver and Kidney Injuries in COVID-19 and Their effects on Drug Therapy; a Letter to Editor. Arch Acad Emerg Med. 2020;8(1): e17
[3] Ronco and Reis. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol. 2020.

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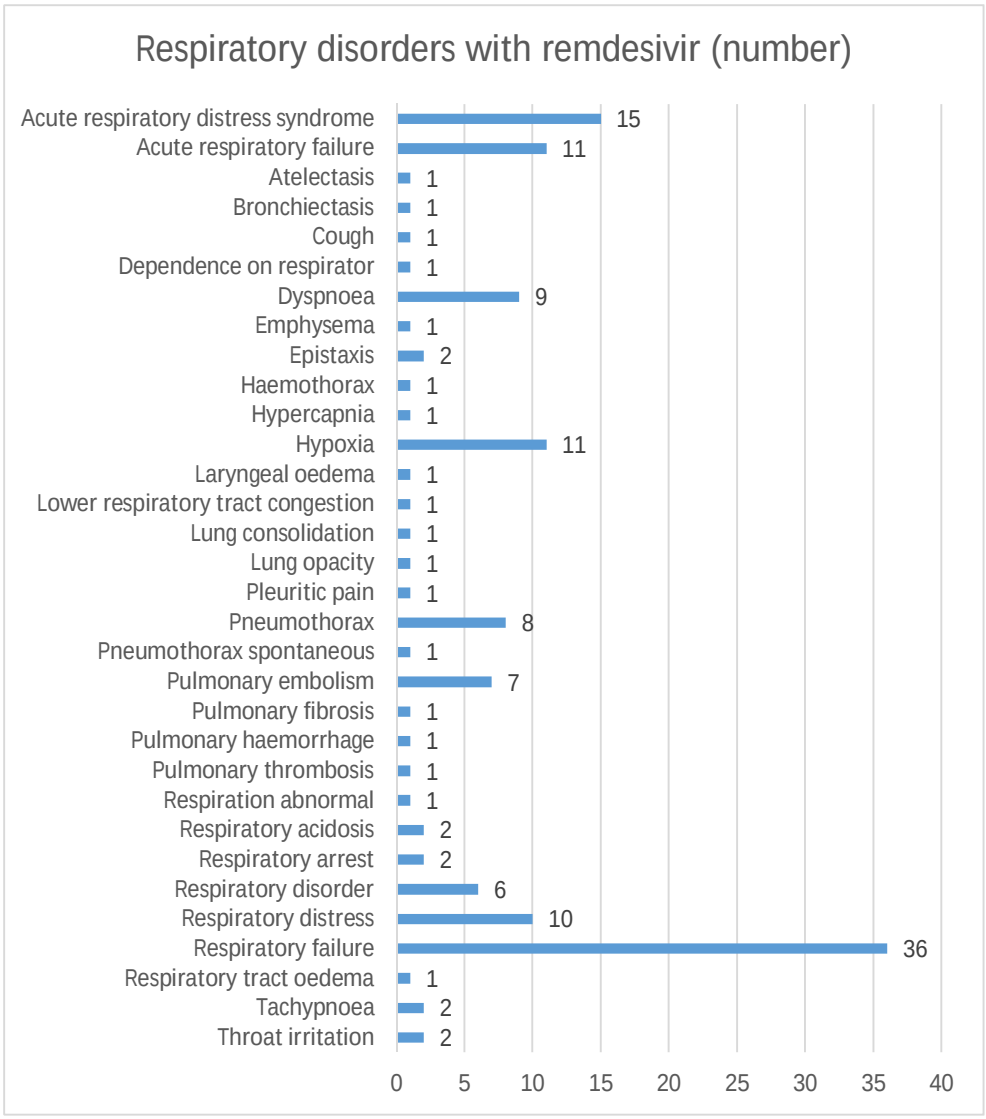
PTs in the SOC Respiratory, thoracic and mediastinal disorders



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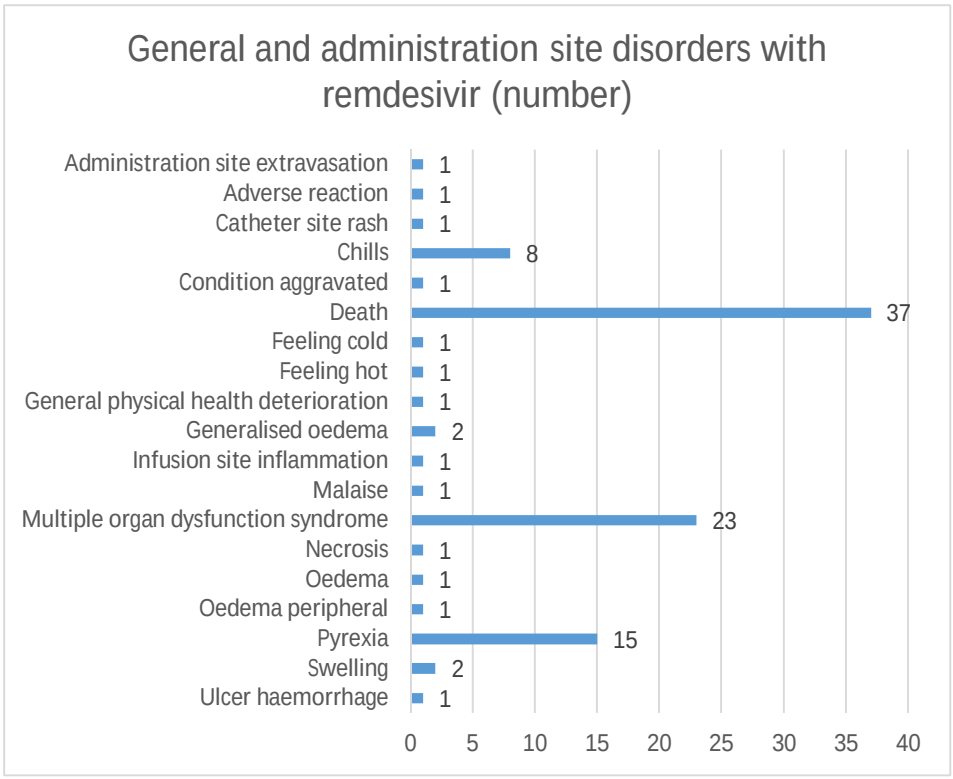
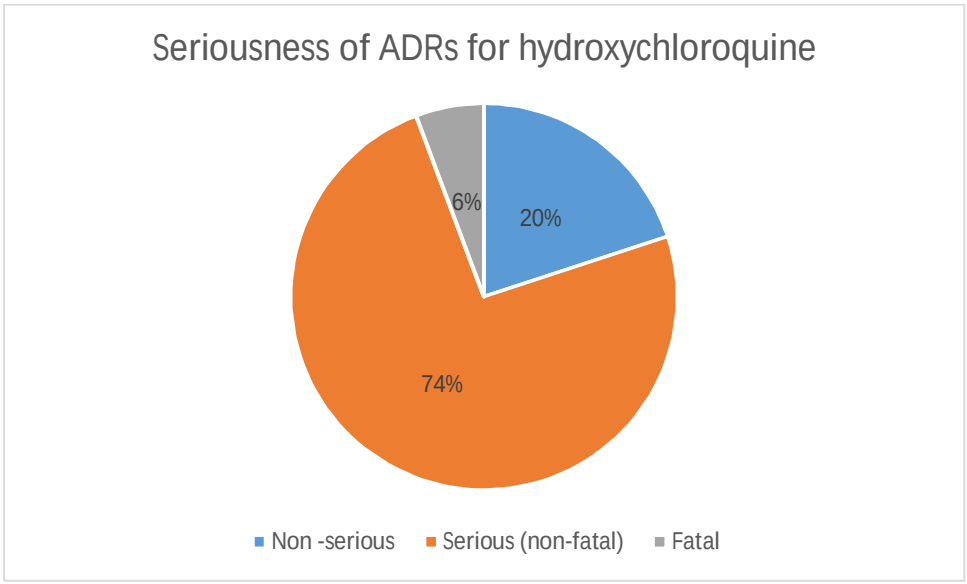
PTs in the SOC General and administration site disorders

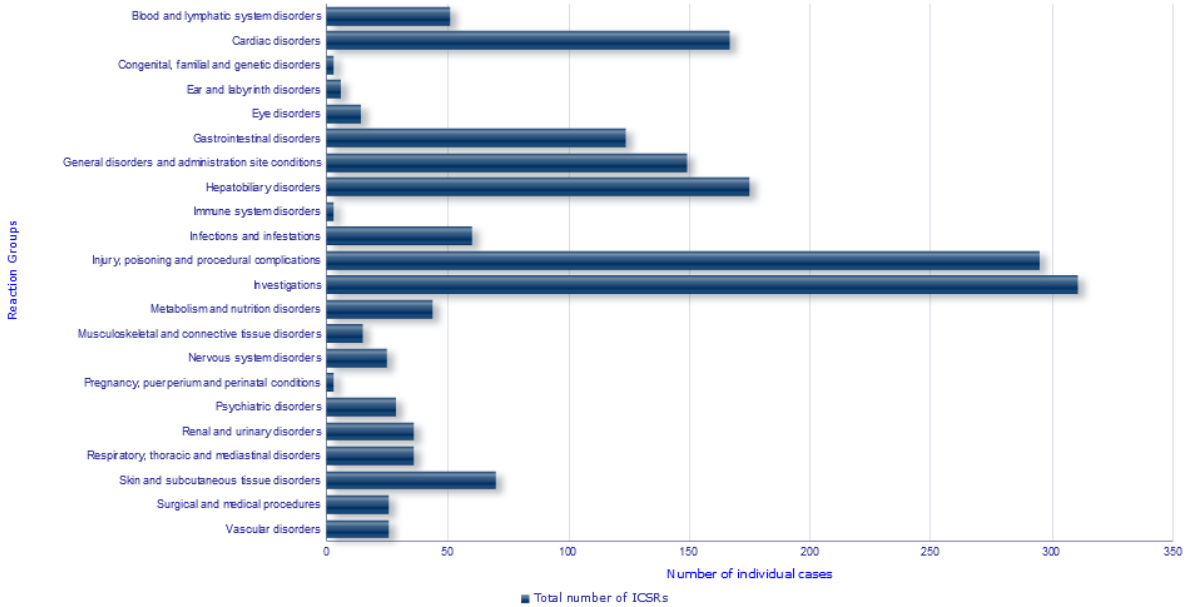


2.3 Hydroxychloroquine

Seriousness ADRs for hydroxychloroquine (962 cases in total)



Number of individual cases by reaction SOC



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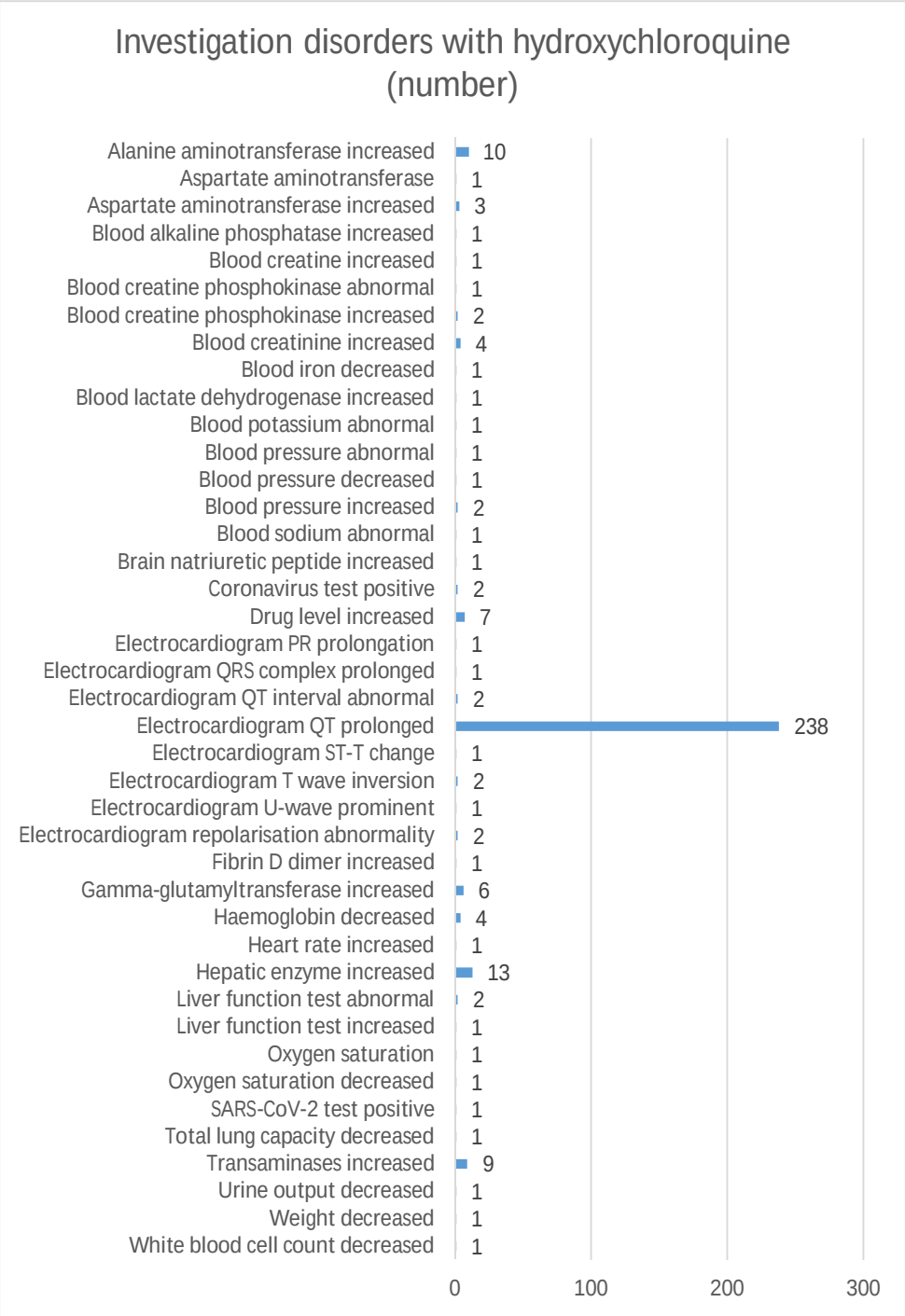
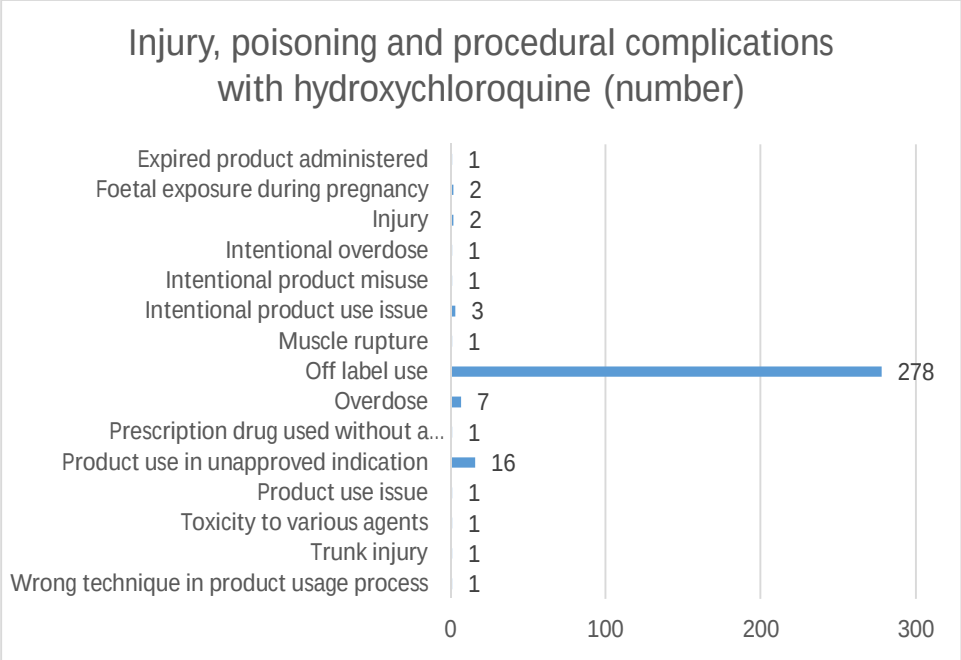
PTs in the SOC Investigations



In total 238 patients experienced Electrocardiogram QT prolonged while on hydroxychloroquine treatment. The majority of these cases present confounding factors as it mainly concern patients with underlying diseases or co-medication. These data are in line with the updated BE

recommendations for hydroxychloroquine treatment of Covid-19. For more details on patient managing, especially patients with long QT, we refer to recent publication from Wu and al.[4].

PTs in the SOC Injury, poisoning and procedural complications



[4] Wu C-I, Postema PG, Arbelo E, Behr ER, Bezzina CR, Napolitano C, Robyns T, Probst V, Schulze-Bahr E, Remme CA, Wilde AAM, SARS-CoV-2, COVID-19 and inherited arrhythmia syndromes, Heart Rhythm (2020), doi: https://doi.org/10.1016/j.hrthm.2020.03.024.

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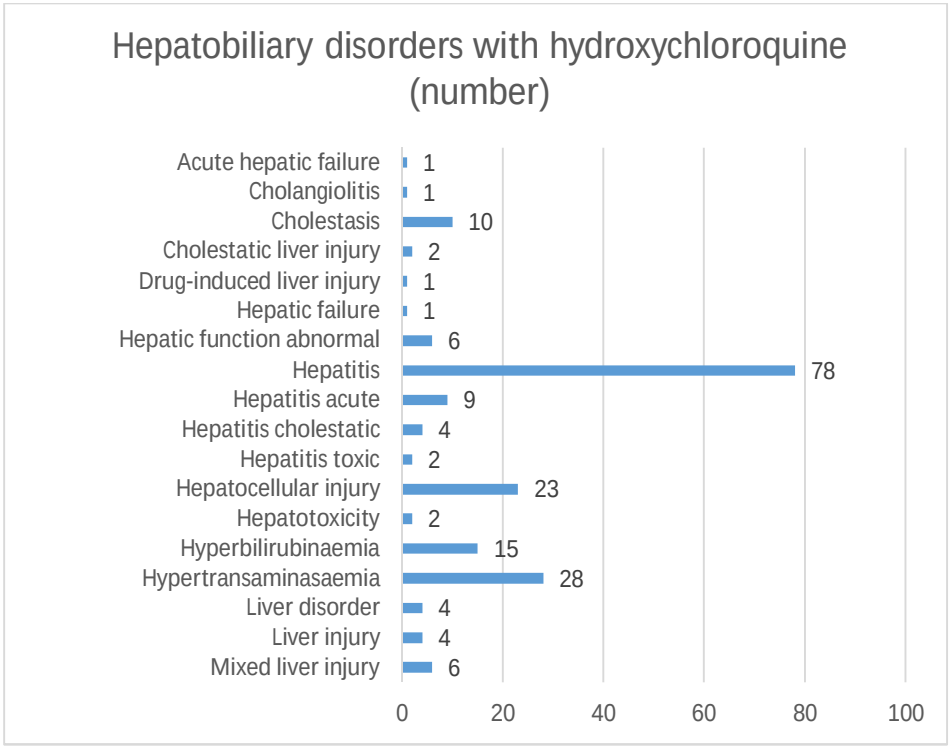
PTs in the SOC Hepatobiliary disorders



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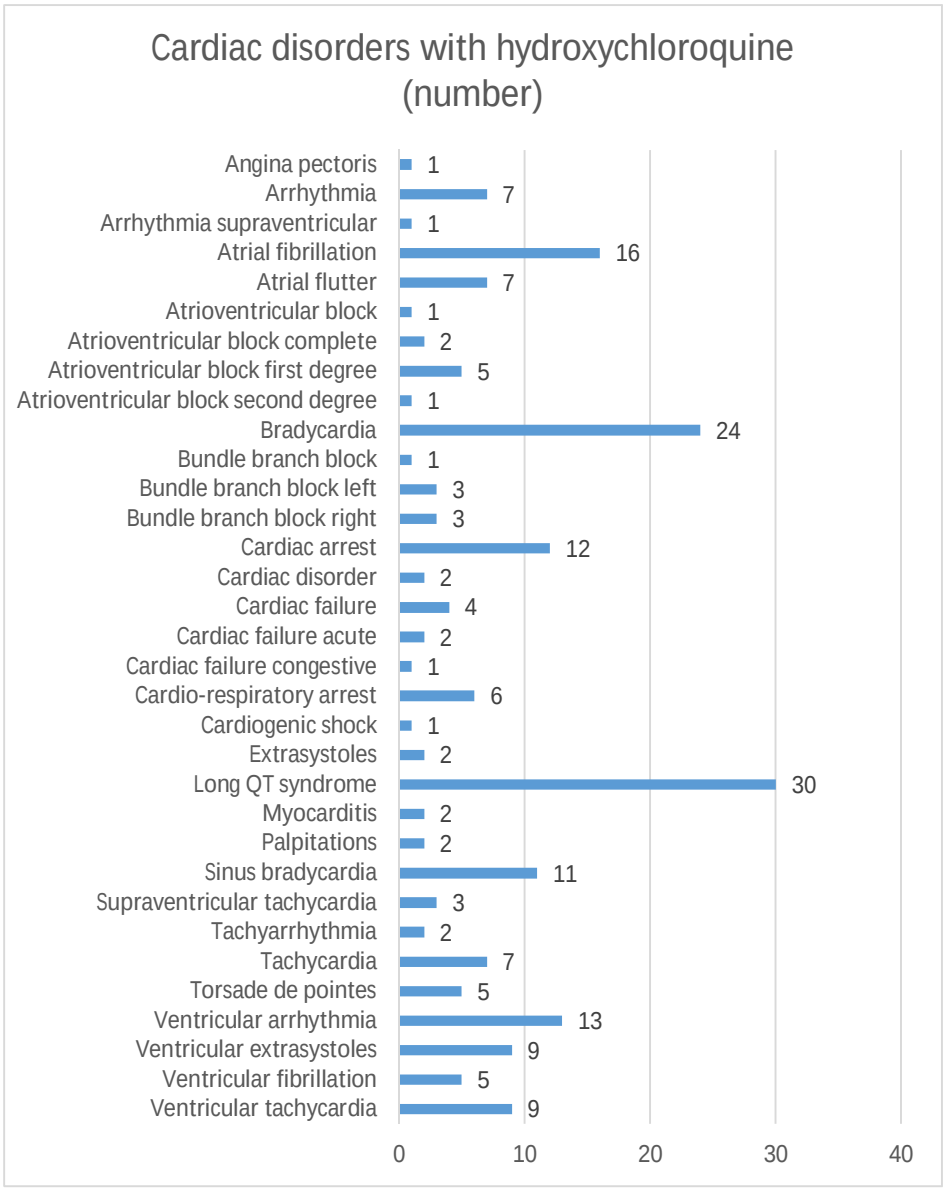
PTs in the SOC Cardiac disorders



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2.4 Belgian Cases

Isavuconazole

Case with isavuconazole (fatal outcome)

On an unspecified date, the patient started therapy with Cresemba (isavuconazole sulfate) at a dose of 200mg (one vial) for Coronavirus infection. On a unspecified date, the patient died due to an unknown reason. The patient's medical history and concomitant medication details were not provided.

No further information is available. Because of the limited information, no conclusions can be drawn.

Hydroxychloroquine

Case of rhabdomyolysis with hydroxychloroquine :

50 year old male patient (100kg, 190cm, BMI 27,7) was treated with hydroxychloroquine from 29/3 to 31/3 (D1 : 2x200mg BID, D2-D3 : 200mg). Concomitant medications are : Haldol IV (1 ampoule 5mg/ml), Paracemol IV (1g/100ml), Fraxiparine (3800IE SC), Dafalgan Forte (1g), Morfine (half ampoule 10mg/ml).

He developed massive rhabdomyolysis. The following CK's were reported : 29/3 : 13195 U/L, 30/3 : 23452 U/L, 31/3 : 33265 U/L, 1/4 : 65726 U/L, 2/4 : 168224 U/L, 3/4 : 257224 U/L, 4/4 (peak) : 714028 U/L, 5/4 : 540021 U/L, 6/4 : 34120 U/L.

Hydroxychloroquine was withdrawn on 31/3. The patient is recovering. Follow-up information was received stating that the patient already had rhabdomyolysis at admission but the rhabdomyolysis aggravated during hospitalisation at the ICU.

In EudraVigilance 4 other cases of rhabdomyolysis with hydroxychloroquine have been reported in the treatment of Covid-19.

Recently there was a publication describing rhabdomyolysis as potential late complication with Covid-19[5].

Case of haemolysis with hydroxychloroquine :

A 32 year old male patient presented signs of haemolysis two days after the start of hydrochloroquine treatment. The hemoglobin level at nadir was 7.1 g/dL. The patient received a transfusion of red blood cells and folic acid. Treatment with hydroxychloroquine was continued as per Sciensano guidelines (5 days total treatment). The patient was able to leave the hospital but maintained a certain degree of anaemia upon discharge. In this patient, a biological examination revealed a

[5] Jin M, Tong Q. Rhabdomyolysis as potential late complication associated with 2019 novel coronavirus disease. Emerg Infect Dis. 2020 Jul [date cited]. https://doi.org/10.3201/eid2607.200445

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deficiency in G6PD, suggesting that hydroxychloroquine may have promoted hemolysis in this context.

Case of acute kidney injury and haemolysis due to G6PD deficiency with hydroxychloroquine

A 65 old male with diabetes type 2 and hypertension experienced haemolysis due to G6PD-deficiency with acute kidney insufficiency while treated with hydroxychloroquine for Covid-19. The patient was treated with hydroxychloroquine from 19/3 to 23/3 at a dosage of 400 mg every 12h for day 1 and then 200 mg every 12h for 4 days. The concomitant medications were Clarithromycine, Januvia, Metformine, Zanidip and Augmentin. On 23/3 the patient experienced haemolysis due to G6PD-deficiency with acute kidney insufficiency. The patient was treated with CVVH (continuous venous-venous hemofiltration) at the intensive care and recovered after 7 weeks.

5 other cases of haemolysis with hydroxychloroquine in the indication coronavirus infection have been introduced into EudraVigilance. In total, 3 of these reports mention G6DP deficiency. In addition, an article was found in the scientific literature describing a case of severe haemolytic crisis in a patient with G6PD deficiency, initiated by severe Covid-19 infection and hydroxychloroquine use[6].

Case of QT increased with Hydroxychloroquine – olanzapine – trazodone

A 83 year old female with atrial fibrillation, pulmonary embolism, arterial hypertension and diabetes in the medical history, experienced QT prolongation)while treated with hydroxychloroquine (7/04 : 2x 400 mg, from 08/04 to 10/04 5 doses de 200 mg in total), olanzapine (started 7/04) and trazodone (home medication). Concomitant medication : Clexane, Algostase, Contramal, L-thyroxine, Movicol, Perindopril and Prolopa 125 mg. On 10/04 the patient had a QT=730ms. Treatment with hydroxychloroquine was withdrawn and treatment with trazodone and risperidone was suspended 11/04 and 12/04. The QT interval decreased to 460 ms on 11/04 and 450ms on 12/04. Blood analysis showed that he had hypokalaemia on 09/04 for which she received potassium supplementation.

Case of QT prolongation with hydroxychloroquine

A 66 year old male patient was treated with hydroxychloroquine and experienced QTc prolongation (450 msec). The treatment with hydroxychloroquine was withdrawn. The evolution and the concomitant medication are not known.

Case of tachycardia, dizziness and cardiac pain with hydroxychloroquine

A 39 year old female patient experienced tachycardia, dizziness and cardiac pain two days after start of treatment with Plaquenil (200 mg, twice a day) for Covid-19. Plaquenil was started on 15-APR-2020 and stopped on 20-APR-2020. The events did not resolve. Concomitant medication included: Befact Forte, C-Will, folic acid, paracetamol and Levorichter30.

[6] Beauverd et al. COVID-19 Infection and Treatment With Hydroxychloroquine Cause Severe Haemolysis Crisis in a Patient With glucose-6-phosphate Dehydrogenase Deficiency. Eur J Haematol. 2020 Apr 23

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QT prolongation is a listed adverse drug reaction for hydroxychloroquine in the product information of Plaquenil.

Case of neuropsychiatric symptoms and suicide attempt with hydroxychloroquine

The case was received from a consumer via social media. The patient's past medical history, medical treatment(s), concomitant medication(s) and family history were not provided. On an unknown date, the patient started taking hydroxychloroquine sulphate (dose, route, frequency, strength, formulation, batch number: unknown) for Covid-19. On an unknown date and after unknown latency, the patient had a suicide attempt and neuropsychiatric disorders that appeared mainly during the first days of treatment, at high doses.

Psychiatric disorders (psychosis, suicidal behaviour) are listed in the product information of Plaquenil.

Case of pancytopenia with hydroxychloroquine, eusaprim and axicabtagene ciloleucel

A 26 old female patient with refractory primary mediastinal large B-cell lymphoma was treated with axicabtagene ciloleucel on 16-Sept-19. Concomitant medications included CERAZETTE, FRAXODI, PANTOMED, ZOVIRAX, NEUPOGEN, EUSAPRIM, DAFALGAN, FOLAVIT, XARELTO, and PRIVIGEN. Co-Suspect drug included PRIVIGEN, PLAQUENIL, and EUSAPRIM. Beginning in MAR-2020 (5 weeks prior to admission), the patient had experienced dry cough, rhinorrhea, myalgia, headache, and anosmia. Beginning in APR-2020 ("after 2 weeks"), the patient experienced dyspnea with effort and fever of up to 38 degrees C. Beginning in late APR-2020 ("this week"), the patient experienced dyspnea with orthopnea, and fever peaks to a maximum of 39.7 degrees 7, with night sweats. On 25-APR-2020, the patient was hospitalized due to experiencing COVID-19. On admission, in addition to progressive leukopenia, the patient also experienced neutropenia and anemia; the patient experienced the onset of serious Pancytopenia. Treatment medications included IVIGLOB-EX, ROCEPHIN, ASPEGIC, PARACETAMOL, PLAQUENIL, ZITROMAX. On 26-APR-2020 the patient received Plaquenil which was discontinued after 1 day, due to pancytopenia (specified as "pre-existing condition"). Treatment included NEULASTA with good effect: normalization of platelets and white blood cells. On 28-APR-2020, PRIVIGEN was administered for known Hypogammaglobulinaemia. One hour after onset, the patient had a sudden onset of fever, up to 42 degrees C, with malaise and hypotension up to 80/40 mmHg. Initial treatment included PLASMALYTE, and PRIVIGEN was discontinued. On 29-APR-2020, the patient was transferred to the intensive unit (ICU) with consideration of the high fever, persistent hypotension despite adequate filling and tachycardia up to 170 bpm; the reporter clarified the event was related to specific event of Allergic reaction on Privigen. The patient had no prior drug allergies. Treatment included PETHIDINE. The patient remained in the ICU until 30-APR-2020; treatment with ROCEPHINE ended. Rapid favorable evolution with supportive therapy, the day after the patient returned to the COVID unit. Tryptase was not increased. The outcome of Allergic reaction on Privigen was resolved. On 04-MAY-2020, due to persistent fever with peaks to 40.9 degrees C, a computed tomography (CT) was performed, showing: newly emerged large lung consolidations in the upper left lobe and dorsolateral in the lower right lob. Furthermore, a newly developed nodular peribron chovascular consolidation central due to the lower right lobe. On 10-MAY-2020, the patient started treatment with REMDESIVIR and convalescent PLASMA. She became afebrile 2 days after start

combined therapy (RDV and convalescent PLASMA). On 18-MAY-2020, the patient was discharged from the hospital; she had "no oxygen shortage" at discharge. The patient was to remain in home isolation. The outcome of Pancytopenia was considered to be resolved.

Haematological changes (ex. medular aplasian anaemia, agranulocytosis, thrombocytopenia) are listed for hydroxychloroquine.

Lopinavir, ritonavir

Case of pancreatitis with lopinavir,ritonavir (Kaletra®):

A 49 year old male patient with arterial hypertension, dyslipidaemia and rheumatoid polyarthritis in the medical history was treated with Kaletra (3 tablets, 2x/day) from 31/3 to 8/4 for Covid-19. Concomitant medication : Glucose+vit B1 and vit B6, Pantomed IV 40 MG 1x / day, Riastap 1g from 07 to 08/04, Calcium gluconate, Propolipid 1% 50 ML /day, Adrénaline 10 mg / 24h, Dobutrex 250 mg / 24h, Noradrénaline 8mg 1amp every 3h, Rocuronium 500 mg every 10h, Circadin tablet 1/day Corsodyl, Plaquenil. On 07/04 he developed an acute pancreatitis. Treatment with Kaletra was withdrawn. The patient is recovering.

Pancreatitis has been listed in the product information of Kaletra. In addition the following warning/precaution is given : *"Cases of pancreatitis have been reported in patients receiving Kaletra, including those who developed hypertriglyceridaemia. In most of these cases patients have had a prior history of pancreatitis and/or concurrent therapy with other medicinal products associated with pancreatitis. Marked triglyceride elevation is a risk factor for development of pancreatitis. Patients with advanced HIV disease may be at risk of elevated triglycerides and pancreatitis. Pancreatitis should be considered if clinical symptoms (nausea, vomiting, abdominal pain) or abnormalities in laboratory values (such as increased serum lipase or amylase values) suggestive of pancreatitis should occur. Patients who exhibit these signs or symptoms should be evaluated and Kaletra therapy should be suspended if a diagnosis of pancreatitis is made (see section 4.8)."*

Tocilizumab

Case of anaphylactic shock with tocilizumab (fatal outcome)

An 73 year old female with Type 2 diabetes, obesisty and arterial hypertension in the medical history was treated with RoActemra (600mg dans 100ml de NaCl 0.9%) on 5/04 for ARDS related with confirmed Covid-19. 15 minutes after the start of treatment, the anaphylactic shock occurred. Treatment with RoActemra was withdrawn and the patient was treated with Solu-Medrol SAB 40mg IV, d'adrénaline Sterop and an increase of the Levophed doses, followed by the administration of Alburex 20% and d'Hartmann/Ringer lactate 500ml. The adverse events have slightly improved after the administration of these products but after approximately one hour, the symptoms reappeared. Concomitant medication : Cordarone 300mg IV (4/04) and then 200mg PO (via sonde) starting 5/04, Diprivan TCI IV since 28/03, Lasix 20mg IV since 30/03, Losec Mups 20mg PO (sonde) since 30/03, Clexane SC 40mg since 28/03 then Clexane 80mg SC since 2/04/2020, Plaquenil PO administered from 27/03 to 1/04/2020 (2x 400mg on 24h then 2x200mg during 4 days), Tamiflu 75mg PO form 27/03 to

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1/04/2020 (75mg 2x/day), Ultiva IV since 28/03, Levophed IV since 28/03, Tracrium IV since 30/03 switch to Nimbex starting 3/04, Humuline Regular SC starting 30/03, Midazolam IV starting 4/04, Dexdor IV starting 1/04, Rocephine 2g IV starting 28/03 until 3/04/2020 then stop and start Piperacilline/tazobactam 4g Fresenius. The patient did not recover and passed away on 06/04.

Anaphylaxis is listed in the product information of RoActemra.

Case of ischaemic colitis with tocilizumab (fatal outcome)

A 81 old female patient with abdominal aneurysm, renal transplant, coronary bypass and cardiac valve replacement in the medical history was hospitalised since 28/3 for serious Covid-19 related Acute respiratory distress syndrome (ARDS) which needed intubation, face-down ventilation and curarisation. Her biology showed signs of a cytokine storm. Therefore she received a single dose of tocilizumab on 1/4. The ARDS was improving under treatment of tocilizumab, antibiotics and corticosteroids. On 17/4 melena appeared. The patient had several gastrointestinal surgeries between 26/4 and 10/5 with final left and transverse colectomy. Analysis showed an ischemic colitis. Despite the improvement of her respiratory status and extubation on 15/5, the patient remained very asthenic. It was decided not to re-intubate. She passed away on 25/5 because of recurrent respiratory distress. According to the reporter possible explanation for the occurrence of ischaemic colitis are the abdominal aneurysm in her medical history, Covid-19, the use of corticosteroids to treat the ARDS and also tocilizumab.

Ischaemic colitis is not listed in the product information of RoActemra. No other cases of ischaemic colitis are found in EudraVigilance in the treatment of Covid-19. In the literature, we found a case-report of cecal necrosis[7] occurring in a patient treated for 5 months with tocilizumab for rheumatoid arthritis. We also found a case-report of mesenteric ischemia[8] in a patient with Covid-19 (without treatment mentioned for Covid-19).

Itraconazole

Case of nausea with itraconazole

A 83 old male patient was treated with itraconazole 200mg, 3x/day from 5/4 to 7/4. On 7/4 the patient experienced nausea. The treatment with itraconazole was withdrawn and the patient was recovering.

Case of blurred vision with itraconazole

A 87 year old patient received itraconazole on 29/3 (dose and frequency not reported). Concomitant medications included hydroxychloroquine. On 30/3 the patient experienced blurred vision. Treatment with itraconazole was withdrawn. The outcome of the adverse reaction was not reported.

[7] Avci et al. Is Tocilizumab A Risk Factor for Lower Gastrointestinal Perforations? Isolated Cecal Necrosis: A Rare Case Report. Turk J Colorectal Dis 2020;30:60-63
[8] Azouz et al. Systemic arterial thrombosis and acute mesenteric ischemia in a patient with COVID-19. Intensive Care Med. 2020 May 18;1-2.

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Nausea and blurred vision are listed in the product information of Sporanox.

Remdesivir

Case of hyperkalaemia, dysuria, stomach upset and oedema with remdesivir

On 23-APR-2020, a 55 year old male patient received REMDESIVIR for treatment of Covid-19. Current conditions : Covid-19, hypertension, diabetes mellitus type 2, sleep apnoea syndrome, hyperlipidaemia and stenosis in the medical history. Concomitant medications : NORADRENALINE, KETALAR, FENTANYL, DIPRIVAN, MEROPENEM, METHYLPREDNISOLON, ESMERON, EXACYL, DIAMOX, PANTOMED, HYGROTON, HYDROXYCHLOROQUINE, INSULINE, CLEXANE, BURINEX, ASPEGIC, PARACETAMOL, ACTRAPID, PRIMPERAN, DORMICUM, SUFENTA, LASIX, METFORMAX. On 25-APR-2020, the patient experienced OEDEMAE. On 25-APR-2020, the patient experienced AN INCREASED STOMACH RESIDUE. On 25-APR-2020, the patient experienced HYPERKALEMIA. On 24-APR-2020, the patient experienced HYPERKALEMIA. On 23-APR-2020, the patient experienced DYSURIA. No laboratory/diagnostic tests were reported. The action taken with REMDESIVIR was Drug Discontinued. The outcome was recovered.

Sarilumab

3 cases of off-label use with sarilumab (1 with fatal outcome)

The first case involves a 47 years old male patient. On an unknown date, the patient started taking sarilumab for Cytokine release Syndrome in life threatening Covid-19 Pneumonia. He experienced oxygen deficiency and an urgent situation request for the treatment of a Covid-19 patient with Kevzara with the use of medical device sarilumab autoinjector. The patient's past medical history, medical treatment(s) and family history were not provided. Concomitant medications included hydroxychloroquine sulfate (Plaquenil) and azithromycin. The outcome is unknown.

The second case involves a 54 years old female patient. The patient's past medical history included mammo carcinoma for which the patient received curative treatment. The patient was admitted to corona cohort of hospital and received all the intensive supportive care but was not improving as expected. Patient had all the signs of a severe cytokine release syndrome with a high risk of Multiorgan failure and lethality. It was further stated that risk of non-treatment was higher than the risk of treatment of Kevzara. On an unknown date, the patient started taking sarilumab for cytokine release syndrome in a patient with life threatening Covid-19 pneumonia via sarilumab autoinjector. Concomitant medications included hydroxychloroquine sulfate (plaquenil); and azithromycine. On unknown date, patient experienced spectacular decline in crp (latency-unknown). Corrective treatment-not reported.

The third case involves a 62 years old male patient who was having off label use with sarilumab (Kevzara) for suffering of a severe Covid-19 bilateral pneumonia and life threatening respiratory conditions and died of respiratory failure secondary to SARS-COV2. The patient's past medical history included kidney transplant on 10-Feb-2020 with Renal function correct and stable. The regiment of immunosuppressors had been adapted considering the need of an adequate T cell immune response

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against the viral replication. At the time of the event, the patient had ongoing Bilateral pneumonitis-SARS at Covid-19 since 01-Apr-2020, Acute respiratory distress syndrome with severe hypoxemia. The patient was currently with a breathing support consisting of a continuous positive airway pressure with high fraction of inspired oxygen (FiO2 60%), Hypertension, Type 2 diabetes mellitus, Diabetic neuropathy. Concomitant medications included hydroxychloroquine sulfate (Plaquenil). On 24-Apr-2020, the patient started treatment with sarilumab 400 mg via IV route for severe Covid-19 bilateral pneumonia and life- threatening respiratory conditions via sarilumab autoinjector. On 07-May-2020, the patient died of respiratory failure secondary to SARS-COV2.

Sarilumab and hydroxychloroquine

Case with sarilumab in combination with hydroxychloroquine (fatal outcome)

The case involves an elderly patient approximately 83 years old male who died after treatment with Kevzara (with autoinjector) and Plaquenil (both suspected) after an urgent situation request for the treatment of Covid-19. The patient had an extensive medical history including ongoing type 2 diabetes and high blood pressure. It was reported that severe SARS-CoV2 pneumonia was proven by RT-PCR on 24-April-2020 requiring Optiflow ventilation. Start of symptoms included inappetence, asthenia and confusion on 21-Apr-2020, admission occurred on 26-Apr-2020. On 27-Apr-2020, the patient started taking Plaquenil 200 mg capsule at a dose of 2 DF twice daily orally for a severe SARS-Cov2 pneumonia. On 28-Apr-2020 Plaquenil dosage was changed to 1 DF BID. On 29-Apr-2020, the patient started taking sarilumab 200mg/1.14 ml injection at a dose of 400 mg subcutaneously in 100 ml of 0.9% NaCl delivered via sarilumab autoinjector for a severe SARS-Cov2 pneumonia and as anti IL6. On 29-Apr-2020 Plaquenil dosage was last administered at 1 DF twice daily. Treatment with Kevzara was stopped on 30-Apr-2020.
The patient had aggravation of pulmonary failure on an unknown date. Life expectancy was of more than 48 Hours. The patient died of it and COVID-19 pneumonia on 01-May-2020. According to the notifier, death was not related to sarilumab. No autopsy was performed.
Concomitant medications included: azithromycin from 26-Apr-2020 to 01-May-2020, cefuroxime from 26-Apr-2020 to 29-Apr-2020, Asaflow, Clexane (start date: 26-Apr-2020), Clopidogrel, Contramal, Cymbalta, ciproxine, Coversyl, Dafalgan Forte, Inderal, Haldol, Lantus, midazolam, mirtazapine, morphine HCl, Novorapid, paracetamol, perindopril, Pantomed, Remergon, NaCl, Sildenafil Sandoz, simvastatin, tamsulosin, Zocor.