BHIVA, DAIG, EACS, GESIDA & Polish Scientific AIDS Society

Statement on risk of COVID-19 for people living with HIV (PLWH)

Wednesday 5 August, 2020

COVID-19 & HIV

Case series of people living with HIV (PLWH) with COVID-19 have been published from China, Spain, Germany, Italy and the United States (1-15) with no clear evidence for a higher COVID-19 infection rate or different disease course in people with and without HIV. Of note, most case series of PLWH report a younger age in their study population than in HIV-negative hospitalised COVID-19 patients, but comparable rates of comorbidities.

In a cohort study from the United Kingdom a small potential increase in the risk of mortality among PLWH once hospitalised with COVID-19 was reported at the July 2020 BHIVA conference, albeit with no data around the risk of developing severe COVID-19 or hospitalisation among this cohort in the first place and no data on antiretroviral therapy (ART), viral load (VL) or CD4 count. [16].

More recently an analysis of risk factors for COVID-19 deaths in the Western Cape was presented at the virtual AIDS 2020 conference [17]. After adjusting for other risk factors, they found HIV increased a COVID-19 patient's death risk by a factor of 2.14 (95% CI 1.70;2.70), and active TB by a factor of 2.70 (95% CI 1.91.4.04). The larger prevalence of HIV in Africa permits study of higher participant numbers but there may be differences in baseline characteristics compared to populations from Western Europe or China with regard to other risk factors for mortality including age, concomitant comorbidities, obesity rate and socioeconomic status (the latter two were not captured in this data set).

Finally, in the Annals of Internal Medicine, Spanish researchers described the incidence of COVID-19 and risk of hospitalization among 77,590 PLWH receiving ART [18]. During a 3-month period, 236 PLWH were diagnosed with COVID-19, and 151 were hospitalized. The risk of hospitalization by NRTI treatment per 10,000 persons was lowest for TDF/FTC (10.5), while other NRTI strategies were similar (TAF/FTC 20.3, ABC/3TC 23.4, single or no NRTI 20.0) [14]; TDF/FTC recipients also had a lower overall incidence of infection and none died or were admitted to the intensive care unit . Noteworthy, PLWH remaining on TDF/FTC today are less likely to have some of the medical comorbidities associated with worse COVID-19 outcomes [19]. Older PLWH, in particular those with renal or cardiovascular disease, increasingly receive either TAF/FTC or just 3TC as NRTI backbone [19]. A recently published further analysis of the Spanish cohort suggests that confounding due to unmeasured clinical characteristics does not completely explain the association between TDF/FTC and a lower COVID-19 diagnosis and hospitalization [20]. Nevertheless, the somewhat diverse observations ranging from potentially improved outcome on TDF/FTC to two-fold increased mortality risk associated with HIV clearly underline the need for additional data from larger cohorts.

Current evidence indicates that the risk of severe COVID-19 illness increases with age, male gender and with certain chronic medical problems such as arterial hypertension, cardiovascular disease,

chronic lung disease, obesity and diabetes. Whether or not PLWH on treatment with a normal CD4 count and suppressed VL are at an increased risk of serious illness or death, many will have other conditions that increase their risk. Indeed, almost half PLWH in Europe are older than 50 years and chronic medical conditions, including cardiovascular and chronic lung disease, are more common in PLWH. As a risk factor for respiratory infections smoking cessation should be encouraged for all. Influenza and pneumococcal vaccinations should be kept up to date as recommended by BHIVA/EACS guidelines.

Despite the lack of evidence for an association between HIV surrogate markers and COVID-19 mortality in the Western Cape data, we continue to advise that immune suppression, indicated by a low CD4 (<200 cells/µL), or not receiving ART, should be considered a risk factor. Data in such PLWH is sparse as so far most COVID-19 patients with HIV have been on suppressive ART. For PLWH with low CD4 counts (<200 cells/µL), or who experience a CD4 decline during a COVID-19 infection, remember to initiate opportunistic infection (OI) prophylaxis. This is not aiming at preventing a more severe course of COVID-19 but rather complications through additional OIs. More information regarding recommendations for prophylaxis and treatment of specific opportunistic infections can be found in the BHIVA/EACS guidelines for HIV/AIDS.

The ongoing discussion about potential COVID-19 vertical transmission remains controversial. Although few case reports have claimed perinatal transmission several other large case series could not find any case of vertical transmission [21-25]. Pregnant women with critical COVID-19 who deliver during their disease course mostly deliver preterm via caesarean section [21]. Although the majority of mothers have been discharged without any major complications, severe maternal morbidity as a result of COVID-19 and perinatal deaths have been reported. Careful monitoring of pregnancies with COVID-19 and measures to prevent neonatal infection are warranted.

Existing national guidelines should be followed in terms of reducing risk for acquiring a COVID-19 infection and managing symptoms [26-29].

COVID-19 treatment: individual antiretrovirals (ARVs)

Expedited research and publication are welcomed with the caveat that results may be disseminated pre-publication and/or published without usual peer review. There is ongoing discussion and research around some ARVs which may have some activity against COVID-19. The first randomised clinical trial (RCT) with lopinavir-ritonavir (LPV/r) started a median of 13 days after symptom onset and demonstrated no benefit over standard care in 199 hospitalised adults with severe COVID-19 [30]. Since then the large UK RECOVERY trial, which to date has randomised almost 12,000 people hospitalised with COVID-19 to different therapeutic options, has stopped recruitment to the LPV/r arm after a review by Data Monitoring Committee revealed no benefit of LPV/r over standard of care in terms of mortality, ventilation requirement or length of stay [31]. There is no evidence to support the use of other ARVs, including PIs; indeed, structural analysis demonstrates no darunavir (DRV) binding to COVID-19 protease. Moreover, an Italian case series suggests boosted DRV does not prevent SARS-CoV-2 infection in PLWH or protect against worsening respiratory function, at least not at a dose of 800 mg daily [32].

Data regarding the activity of TDF against SARS CoV-2 is conflicting. In Silico data suggests that TDF/FTC may bind to SARS CoV-2 Nsp1 protein [33], an unreviewed study shows that TDF and TAF may inhibit the SARS-CoV-2 polymerase [34], one in vitro study supports antiviral activity of TDF/FTC [35] and an animal models suggest shortened duration of symptoms, and possibly infectiousness [36]. However, two studies have failed to demonstrate any in vitro activity of tenofovir aginst CoV-2 [37,38] so more data is required.

Currently a large randomised phase 3 placebo-controlled study in Spain using the HIV pre-exposure prophylaxis (PrEP) combination TDF/FTC and low-dose hydroxychloroquine (HCQ) as prophylaxis for COVID-19 in health workers is planned [39], but the clinical trial results have to be awaited to shed light on the usefulness of this PrEP strategy.

Currently no evidence is available to justify switching PLWH from their usual ART. Additionally, there is no evidence to support HIV-negative people taking ARVs outside the context of PrEP to prevent HIV acquisition – PrEP should be taken as directed and there is no current evidence that PrEP is effective against COVID-19.

CCR5-inhibitors, in particular maraviroc (MVC,) have also been suggested to have antiviral properties against SARS-CoV-2. Indeed, the binding pattern of MVC has suggested a strong binding to the pocket of SARS-CoV-2 main protease (Mpro) which could result in strong inhibition and prevention of infection [40]. MVC also binds in between the domain I and II where the substrate-binding site is located and forms a significant number of interactions to the critically important residues of SARS-CoV-2 Mpro [40]. Moreover, CCR5 antagonism prior to the 'second wave' of inflammatory mediator expression in SARS-CoV-2 may reverse lymphoid depletion and alter inflammatory cell trafficking, both increasing viral control capacity and dampening damage to lung tissue, respectively. Clinical trials are underway to establish whether one week of treatment with MVC, used at its approved dosage to treat HIV, is safe and tolerable in patients with SARS-CoV-2.

PRO 140 (leronlimab) is a humanized monoclonal antibody targeted against the CCR5 receptor found on human T lymphocytes under investigation as a potential HIV therapy. More recently, laboratory data from persons treated with leronlimab for COVID-19 infection has shown increases in the profoundly decreased CD8 T-lymphocyte percentages by Day 3, normalization of CD4/CD8 ratios, and resolving cytokine production including reduced IL-6 correlating with clinical improvement [41]. The current data suggests a trend toward the restoration of immune function by day 7. Restoration of the immune function is critical in COVID-19 patients to prevent other infections.

COVID-19 treatment: other options

A case series on HCQ , with or without azithromycin, was not able to demonstrate a clear clinical benefit, despite in vitro inhibition of SARS-CoV-2, due to methodological issues [42]; although the same group postulated an infection control benefit of more rapid viral clearance there was a lack of control arm for comparison [43]. One small RCT demonstrated trends for reduced time to clinical recovery and short-term radiological improvement for HCQ [44], though another showed no benefit in terms of viral clearance, clinical or radiological endpoints [45]. A recently published retrospective analysis of patients hospitalised with confirmed SARSCoV-2 infection in all US Veterans Health Administration medical centres found no evidence that use of HCQ, with or without azithromycin, reduced the risk of mechanical ventilation and even found an association of increased overall mortality in patients treated with HCQ alone [46]. Subsequently, two further observational studies

showed no impact of HCQ, azithromycin, or both, on in-hospital mortality and/or intubation rates [47,48]. Finally, the Recovery trial, stopped its HCQ arm due to "no evidence of benefit" [49] based on 28-day mortality rates of 25.7% and 23.5% in the HCQ and usual care arms, respectively. In addition to lack of efficacy, the study has flagged important safety concerns including cardiac arrhythmias on HCQ or chloroquine and methaemoglobinaemia on HCQ [50].

The first successfully licensed drug for COVID-19 treatment is remdesivir, originally developed for Ebola therapy, which has broad in vitro antiviral activity against SARS-CoV-2 [51]. First cases from the expanded access program using remdesivir for COVID-19 patients suggested potential clinical benefit [52]. The first RCT from China demonstrated that remdesivir was not associated with statistically significant clinical benefits in adults with severe COVID-19 [52], indeed remdesivir was stopped early in 18 (12%) patients because of adverse effects, compared with 4 (5%) in the control group [53]. Of note, the study was stopped early due to low patient enrolment which may limit its power. Finally, data on remdesivir from the Adaptive COVID-19 Treatment Trial (ACTT) was presented, in which 1,063 hospitalised patients with advanced COVID-19 and lung involvement who were randomised to remdesivir recovered faster than similar patients who received placebo, with a median recovery time to 11 days and 15 days, respectively [54]. Results also suggested a survival benefit, with a mortality rate of 8.0% for the group receiving remdesivir versus 11.6% for the placebo group (p=0.059) [54]. Meanwhile the SIMPLE study showed that a five-day dosing duration of remdesivir led to "similar improvement in clinical status" as the 10-day treatment course being evaluated in the NIAID study and other ongoing trials [55]. An expansion phase of the SIMPLE study has been added and will enrol an additional 5,600 patients, including patients on mechanical ventilation.

A further agent under investigation for COVID-19 treatment is famotidine. Following the observation of lower mortality amongst hospitalised COVID-19 patients on famotidine [56], a small single-arm study described improved patient reported outcomes in non-hospitalised COVID-19 patients starting famotidine [57]. Retrospective chart data patients hospitalized with COVID-19 in New York showed that famotidine use was associated with a reduced risk of clinical deterioration leading to intubation or death [57]. A RCT is currently underway to determine whether famotidine can improve clinical outcomes in hospitalized COVID-19 patients (NCT04370262).

A recent study reported that ivermectin was successfully used in vitro for the treatment of SARS-CoV-2 in experimentally infected cells [58]. It has been emphasized however, that the laboratory results showing efficacy of ivermectin to reduce viral loads in laboratory cultures, at dosage levels far beyond those approved by the FDA for treatment of parasitic diseases in humans, are not sufficient to indicate that ivermectin will be of clinical benefit to reduce viral loads in COVID-19 patients. Chaccour et al. caution against using in vitro findings as more than a qualitative indicator of potential efficacy and emphasize that due diligence and regulatory review are needed before testing ivermectin in COVID-19 [59].

Finally, first data from a meta-analysis of trials from Iran studying the therapeutic effects of the HCV direct acting antivirals sofosbuvir and daclatasvir have been presented at the AIDS 2020 virtual conference suggesting a potential mortality benefit from this treatment intervention [60]. Not all included data was derived from RCTs, and the overall number of treated patients was low; larger studies are currently underway.

The full results from these trials, as well as other ongoing clinical trials especially in early COVID-19 disease, are eagerly awaited. A list of currently ongoing or planned COVID-19 studies in PLWH can be found under:https://www.clinicaltrials.gov/ct2/results?term=hiv+covid&Search=Search

Maintaining HIV care during the COVID-19 pandemic

Implementation of quarantine, social distancing, and community containment measures have reduced access to routine HIV testing, which challenges completion of UNAIDS' first 90-90-90 target globally [61]. Moreover, timely linkage to HIV care as well as ART continuation, will be hindered during the COVID-19 pandemic, as physicians from HIV-clinics are sharing HIV care and COVID-19 care duties as recently demonstrated from the Euro Guidelines in Central and Eastern Europe (ECEE) Network Group for more than 50% of clinics in central and Eastern Europe [62]. In many countries with high COVID-19 case load there is a need to prepare for operating under minimal medical resources with the aim to secure retention on ART. Non-governmental organisations are needed to second medical efforts to ensure the continuity of ART deliverance for treatment and prevention.

COVID-19 data collection & resources

A COVID-19 drug interactions website (www.covid19-druginteractions.org) has been developed for the experimental drugs being trialed to treat COVID-19 in different parts of the world. EACS and BHIVA are happy to announce that they have agreed to financially support this very useful website. A useful Spanish interaction resource can be found under: http://www.interaccionesvih.com/docs/Interacciones%20importantes%20con%20Kaletra%20e%20Hidroxicloroquina_20%20marzo%202020_COVID.pdf.

We would like to highlight three resources for reporting COVID-19 cases:

- The NEAT ID Foundation has developed a 'data dashboard' to monitor COVID-19 case numbers, hospitalisations and mortality in people with HIV and/or hepatitis at European and country level. The data will be available for public viewing via www.NEAT-ID.org and if your centre has not signed up, you can do so via this link.
- The Lean European Open Survey on SARS-CoV-2 Infected Patients (LEOSS) launched by the German Society for Infectious Diseases (DGI) and ESCMID's Emerging Infections Task Force (EITaF) an open register based on anonymous questionnaires and they are keen to collaborate with other registries. See https://leoss.net, contact them by email at info@leoss.net and the register can be accessed here https://leoss.net/statistics
- EASL is supporting a registry which can be found under the following link https://www.covid-hep.net/

The coronavirus outbreak is rapidly evolving. EACS, BHIVA, DAIG, GESIDA and the Polish Scientific AIDS Society will continue to share any updates to specific guidance for PLWH. Wishing you all well. Stay healthy.

For further information please contact info@eacsociety.org or bhiva@bhiva.org

References

1. Blanco JL, Ambrosioni J, Garcia F, Martínez E, Soriano A, Mallolas J, Miro JM; COVID-19 in HIV Investigators. COVID-19 in patients with HIV: clinical case series. Lancet HIV. 2020 Apr 15. pii: S2352-3018(20)30111-9.
2. Härter G, Spinner CD, Roider J, Bickel M, Krznaric I, Grunwald S, Schabaz F, Gillor D, Postel N, Mueller MC, Müller M, Römer K, Schewe K, Hoffmann C. COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients. Infection. 2020 May 11. doi: 10.1007/s15010-020-01438-z. [Epub ahead of print]
3. Guo W, Ming F, Dong Y et al. A Survey for COVID-19 among HIV/AIDS Patients in Two Districts of Wuhan, China. Preprint research paper, The Lancet, 2020.
4. Wu Q, Chen T, Zhang H. Recovery from COVID-19 in two patients with coexisted HIV infection. J Med Virol. 2020 May 13. doi: 10.1002/jmv.26006. [Epub ahead of print]
5. Karmen-Tuohy S, Carlucci PM, Zacharioudakis IM, Zervou FN, Rebick G, Klein E, Reich J, Jones S, Rahimian J. Outcomes among HIV-positive patients hospitalized with COVID-19. medRxiv. https://www.medrxiv.org/content/10.1101/2020.05.07.20094797v1 (This preprint report has not been peer-reviewed.)
6. Gervasoni C, Meraviglia P, Riva A, Giacomelli A, Oreni L, Minisci D, Atzori C, Ridolfo A, Cattaneo D. Clinical features and outcomes of HIV patients with coronavirus disease 2019. Clin Infect Dis. 2020 May 14. pii: ciaa579. doi: 10.1093/cid/ciaa579. [Epub ahead of print]
7. Siegel K, Swartz T, Golden E et al. Covid-19 and People with HIV Infection: Outcomes for Hospitalized Patients in New York City. Clinical Infectious Diseases published 28th June 2020
8. Shalev N, Scherer M, LaSota ED, et al. Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19 [published online ahead of print, 2020 May 30]. Clin Infect Dis. 2020;ciaa635.
9. Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfected patients in The Bronx, New York city [published online ahead of print, 2020 May 28]. J Med Virol. 2020;10.1002/jmv.26077.
10. Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort [published online ahead of print, 2020 May 28]. Lancet HIV. 2020;S2352-3018(20)30164-8.
11. Ridgway JP, Schmitt J, Friedman E, et al. HIV Care Continuum and COVID-19 Outcomes Among People Living with HIV During the COVID-19 Pandemic, Chicago, IL [published online ahead of print, 2020 May 7]. AIDS Behav. 2020;1-3.
12. Patel VV, et al. Clinical outcomes by HIV serostatus, CD4 count, and viral suppression among people hospitalized with COVID-19 in the Bronx, New York. AIDS 2020: Virtual; July 6-10, 2020. Abst. OABLB0102
13. Park LS, et al. COVID-19 in the largest US HIV cohort. AIDS 2020: Virtual; July 6-10, 2020. Abst. LBPEC23
14. Lee MJ, et al. Comparative outcomes in hospital admissions with COVID-19 in people living with HIV and people living without HIV: A retrospective study. AIDS 2020: Virtual; July 6-10, 2020. Abst. LBPEB09.
15. Post F, et al. Black ethnicity is a risk factor for hospitalization with COVID-19 in people with HIV. AIDS 2020: Virtual; July 6-10, 2020. Abst. LB
16. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, Holden KA, Read JM, Dondelinger F, Carson G, Merson L, Lee J, Plotkin D, Sigfrid L, Halpin S, Jackson C, Gamble C,

Horby PW, Nguyen-Van-Tam JS, Ho A, Russell CD, Dunning J, Openshaw PJ, Baillie JK, Semple MG; ISARIC4C investigators. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ. 2020 May 22;369:m1985. doi: 10.1136/bmj.m1985.

17. Davies MA et al. COVID-19 mortality in people with HIV or tuberculosis: Results from the Western Cape Province, South Africa. AIDS 2020: Virtual; July 6-10, 2020. Abst OAXLB0106
18. Del Amo J, Polo R, Moreno S, et al. Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy: A Cohort Study [published online ahead of print, 2020 Jun 26]. Ann Intern Med. 2020;10.7326/M20-3689.
19. https://blogs.jwatch.org/hiv-id-observations/index.php/is-covid-19-different-in-people-with-hiv/2020/06/28/
20. del Amo J et al. Antiretrovirals and risk of COVID-19 diagnosis and hospitalization in HIV-positive persons. Epidemiology 2020 (in print)
21. Zeng L, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. JAMA Pediatr 2020; DOI: 10.1001/jamapediatrics.2020.0878.
22. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. Am J Perinatol. 2020 Apr 18. doi: 10.1055/s-0040-1710050. [Epub ahead of print]
23. Zamaniyan M, Ebadi A, Aghajanpoor Mir S, Rahmani Z, Haghshenas M, Azizi S. Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. Prenat Diagn. 2020 Apr 17. doi: 10.1002/pd.5713. [Epub ahead of print]
24. Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, Penfield CA, Roman AS, DeBolt CA, Stone JL, Bianco A, Kern-Goldberger AR, Hirshberg A, Srinivas SK, Jayakumaran JS, Brandt JS, Anastasio H, Birsner M, O'Brien DS, Sedev HM, Dolin CD, Schnettler WT, Suhag A, Ahluwalia S, Navathe RS, Khalifeh A, Anderson K, Berghella V. Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study. Am J Obstet Gynecol MFM. 2020 May 8:100134. doi: 10.1016/j.ajogmf.2020.100134. [Epub ahead of print]
25. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand. 2020;99(7):823-829. doi:10.1111/aogs.13867
26. www.rki.de
27. https://www.cdc.gov/coronavirus/2019-ncov/index.html
28. https://www.gov.uk/government/collections/wuhan-novel-coronavirus).
29. https://seimc.org/contenidos/documentoscientificos/recomendaciones/seimc-rc-2020-RecomendacionesInmunodeprimidos_SARS-COV-2.pdf
30. Cao B, Wang Y, Wen D et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med 2020; doi: 10.1056/NEJMoa2001282.
31. https://www.recoverytrial.net/news/no-clinical-benefit-from-use-of-lopinavir-ritonavir-in-hospitalised-covid-19-patients-studied-in-recovery; accessed 20th July 2020.
32. Riva A, Conti F, Bernacchia D, et al. Darunavir does not prevent SARS-CoV-2 infection in HIV patients. Pharmacol Res, in press 2020.
33. Wu C, Liu Y, Yang Y et al. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharm Sin B. 2020 Feb 27. doi: 10.1016/j.apsb.2020.02.008

34. Jockusch S, Tao C, Li X, Anderson TK, Chien M, Kumar S, et al. Triphosphates of the Two Components in DESCOVY and TRUVADA are Inhibitors of the SARS-CoV-2 Polymerase. bioRxiv 2020; 22:826–8.

35. Clososki GC et al. Tenofovir Disoproxil Fumarate: New Chemical Developments and Encouraging in vitro Biological results for SARS-CoV-2. J Braz Chem Soc 2020; 31: 1552-1556 https://clinicaltrials.gov/ct2/show/NCT04334928; accessed 26th April 2020

36. Park SJ, Yu KM, Kim YI, et al. Antiviral efficacies of FDA-approved drugs against SARS-CoV-2 infection in ferrets. mBio. 2020;11. [PMID: 32444382] doi:10.1128/mBio.01114-20

37. Choy K-T, Wong AY-L, Kaewpreedee P, Sia SF, Chen D, Hui KPY, Chu DKW, Chan MCW, Cheung PP-H, Huang X, Peiris M, Yen H-L. 2020. Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. Antiviral Res 178:104786.

38. Xie X, Muruato AE, Zhang X et al. A nanoluciferase SARS-CoV-2 for rapid neutralization testing and screening of anti-infective drugs for COVID-19. bioRxiv 2020.06.22.165712; doi: https://doi.org/10.1101/2020.06.22.165712

39. Shamsi A, Mohammad T, Anwar S, et al. Glecaprevir and Maraviroc are high-affinity inhibitors of SARS-CoV-2 main protease: possible implication in COVID-19 therapy. Biosci Rep. 2020;40(6):BSR20201256.

40. Manuscript Describes How CytoDyn's Leronlimab Disrupts CCL5/RANTES-CCR5 Pathway, Thereby Restoring Immune Homeostasis, Reducing Plasma Viral Load, Reversing Hyper Immune Activation and Inflammation in Critical COVID-19 Patients [news release]. Vancouver, WA: CytoDyn; May 6, 2020. LINK. Accessed May 8, 2020.

41. Gautret P et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study. Int J Antimicrob Agents. 2020 Mar 20:105949. doi:10.1016/j.ijantimicag.2020.105949.

42. https://www.mediterranee-infection.com/wp-content/uploads/2020/03/COVID-IHU-2-1.pdf; accessed 31st March 2020

43. Chen Z, Hu J, Zhang Z et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. medRxiv 2020.03.22.20040758; doi: https://doi.org/10.1101/2020.03.22.20040758

44. Chen J, Liu D, Li L et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). J Zhejiang Univ. 2020; Mar. (DOI 10.3785/j.issn. 1008-9292.2020.03.03

45. Magagnoli J, Narendran S, Pereira F, Cummings TH, Hardin JW, Sutton SS, Ambati J. Outcomes of Hydroxychloroquine Usage in United States Veterans Hospitalized with COVID-19. Med. 2020 Jun 5. doi: 10.1016/j.medj.2020.06.001. Epub ahead of print. PMCID: PMC7274588.

46. Rosenberg ES, Dufort EM, Udo T, Wilberschied LA, Kumar J, Tesoriero J, et al. Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State. JAMA 2020; :1–10.

47. Geleris J, Sun Y, Platt J, Zucker J , Baldwin M, Hripcsak G, Labella A, Manson D, Kubin C, Barr RG, Sobieszczyk ME, Schluger NW. Observational Study of Hydroxychloroquine in Hospitalized Patients With Covid-19. N Engl J Med 2020 May 7; NEJMoa2012410. doi: 10.1056/NEJMoa2012410. Online ahead of print

48. RECOVERY trial statement. Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on hydroxychloroquine. (5 June 2020). https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf

49. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/OSE%20Review_Hydroxychloroquine-Cholorquine%20-%2019May2020_Redacted.pdf; accessed 20th July 2020

50. Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020 Mar;30(3):269-271.

51. Grein J, Ohmagari N, Shin D, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. N Engl J Med. 2020 Apr 10. doi:10.1056/NEJMoa2007016. [Epub ahead of print]

52. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020; Published online April 29, 2020

53. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh M, Ruiz-Palacios GM, Benfield T, Fätkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, and Lane HC, for the ACTT-1 Study Group Members. Remdesivir for the Treatment of Covid-19 — Preliminary Report. N Engl J Med 2020, published on May 22, 2020, DOI: 10.1056/NEJMoa2007764

54. Goldman JD et al. for the GS-US-540-5773 Investigators. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. N Engl J Medicine 2020; DOI: 10.1056/NEJMoa2015301

55. Freedberg DE, Conigliaro J, Sobieszczyk M, et al. Famotidine use is associated with improved clinical outcomes in hospitalized COVID-19 patients: a retrospective cohort study. medRxiv 2020.

56. Janowitz T, Gablenz E, Pattinson D, Wang TC, Conigliaro J, Tracey K, Tuveson D. Famotidine use and quantitative symptom tracking for COVID-19 in non-hospitalised patients: a case series. Gut. 2020 Jun 4:gutjnl-2020-321852. doi: 10.1136/gutjnl-2020-321852. Epub ahead of print. PMID: 32499303; PMCID: PMC7299656.

57. Freedberg DE, Conigliaro J, Wang TC, Tracey KJ, Callahan MV, Abrams JA; Famotidine Research Group Famotidine Research Group, Sobieszczyk ME, Markowitz DD, Gupta A, O'Donnell MR, Li J, Tuveson DA, Jin Z, Turner WC, Landry DW. Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study. Gastroenterology. 2020 May 22:S0016-5085(20)34706-5. doi: 10.1053/j.gastro.2020.05.053. Epub ahead of print. PMID: 32446698; PMCID: PMC7242191.

58. Caly L, Druce JD, Catton MG, Jans DA. The FDA-approved drug ivermectin inhibits the replication of SARSCoV-2 in vitro. Antiviral research, 2020.

59. Chaccour C, Hammann F, Ramón-García S, Rabinovich NR. Ivermectin and COVID-19: Keeping Rigor in Times of Urgency. Am J Trop Med Hyg. 2020;102(6):1156-1157.

60. Sadeghi A, et al. IAS COVID-19 Conference: Virtual; July 10-11, 2020

61. Jiang H, Zhou Y, Tang W. Maintaining HIV care during the COVID-19 pandemic. Lancet HIV. 2020 May;7(5):e308-e309. doi: 10.1016/S2352-3018(20)30105-3. Epub 2020 Apr 6.

62. Kowalska JD, Skrzat-Klapaczyńska A, Bursa D, Balayan T, Begovac J, Chkhartishvili N, Gokengin D, Harxhi A, Jilich D, Jevtovic D, Kase K, Lakatos B, Matulionyte R, Mulabdic V, Nagit A, Papadopoulos A, Stefanovic M, Vassilenko A, Vasylyev M, Yancheva N, Yurin O, Horban A; ECEE Network Group. HIV care in times of the COVID-19 crisis - where are we now in Central and Eastern Europe? Int J Infect Dis. 2020 May 10. pii: S1201-9712(20)30319-2.