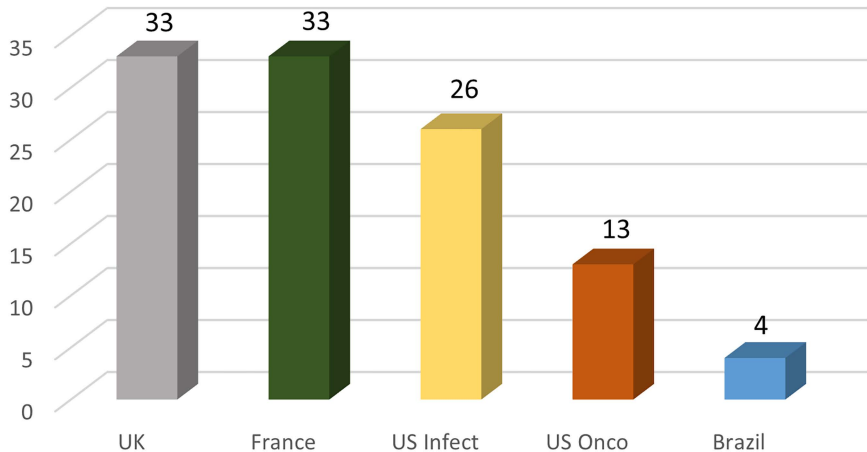
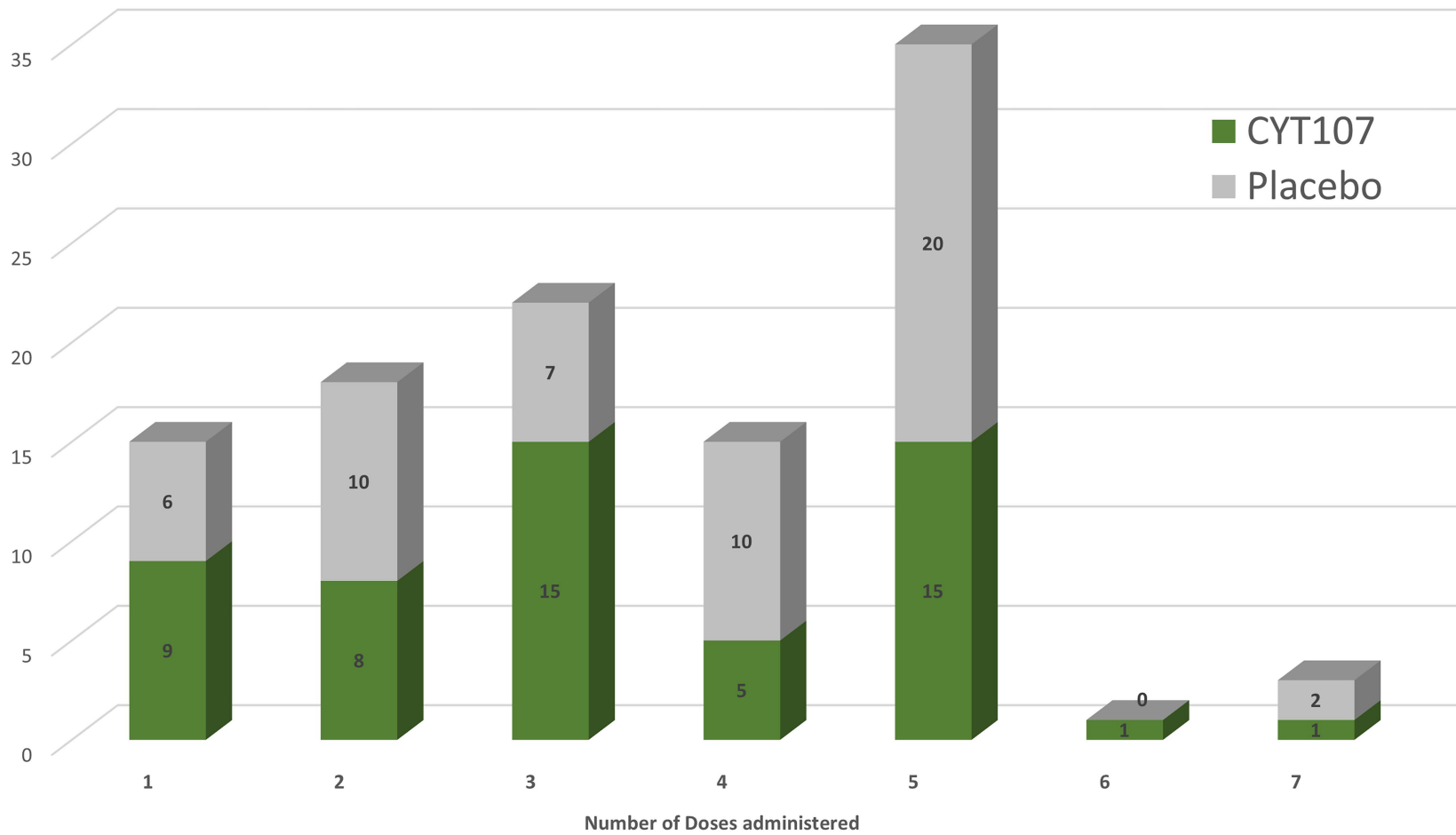


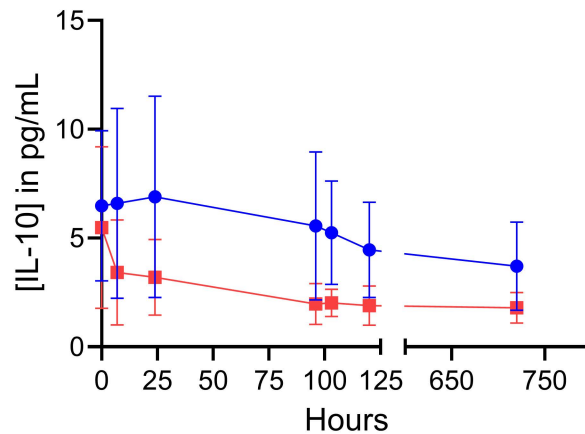
Total enrolled patients=109



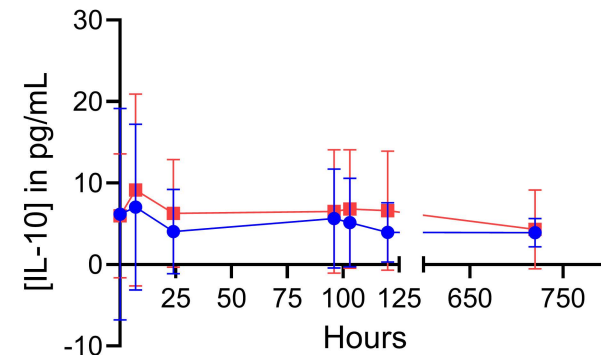
Distribution of patients per #doses received



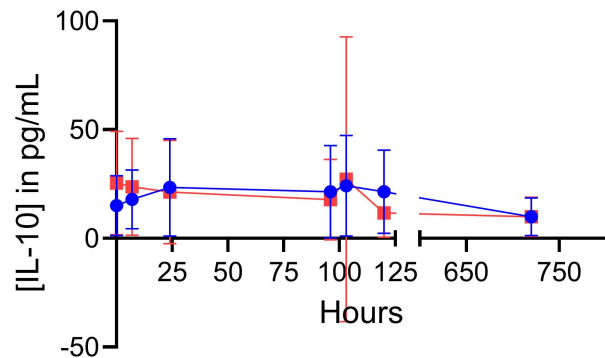
IL-10 US



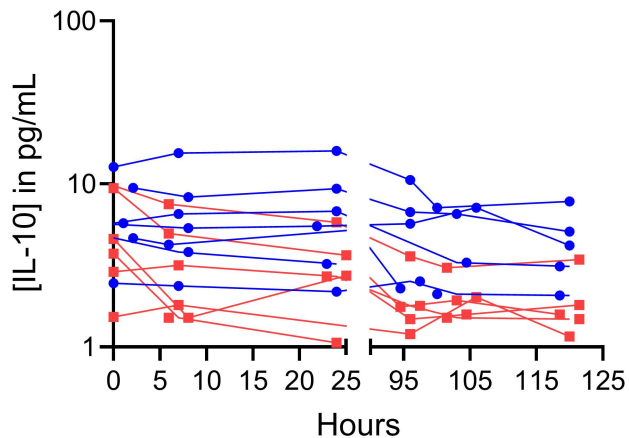
IL-10 UK



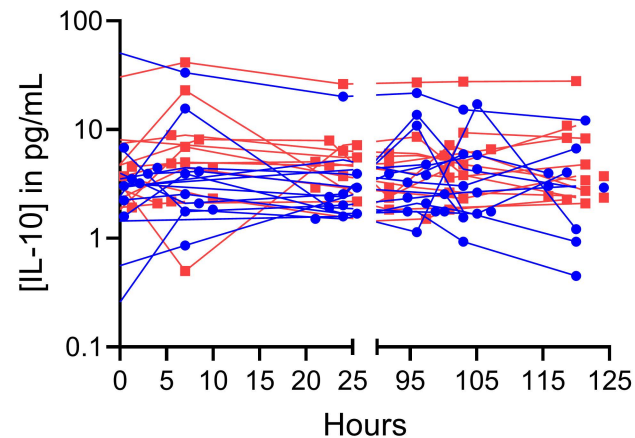
IL-10 FR



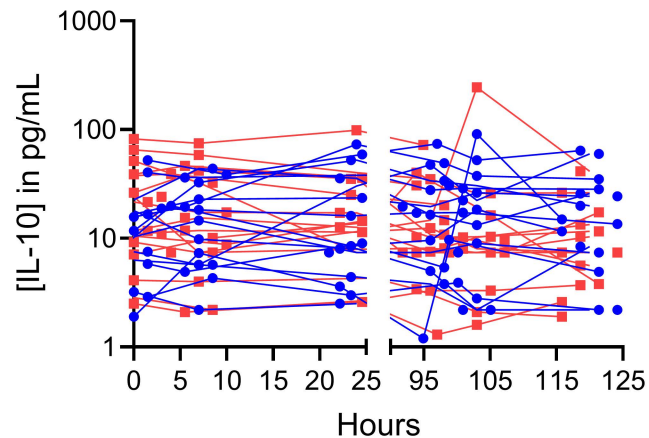
IL-10 US D0-D3



IL-10 UK D0-D3

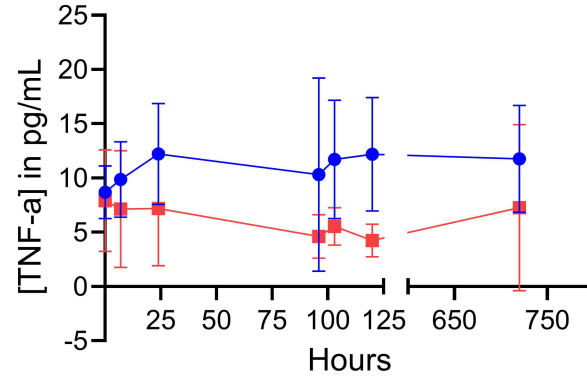


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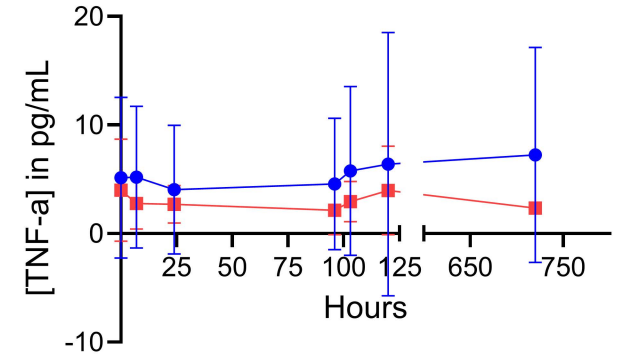


Blue=CYT107  
Red=Placebo

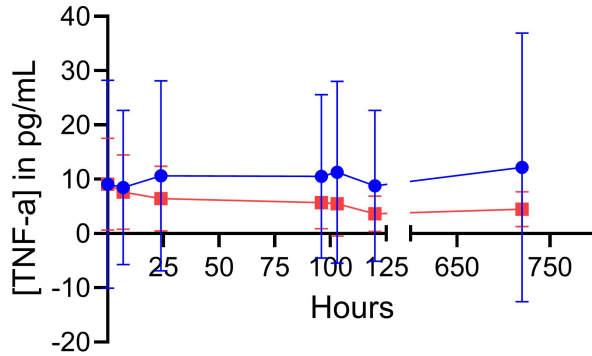
TNF-a US



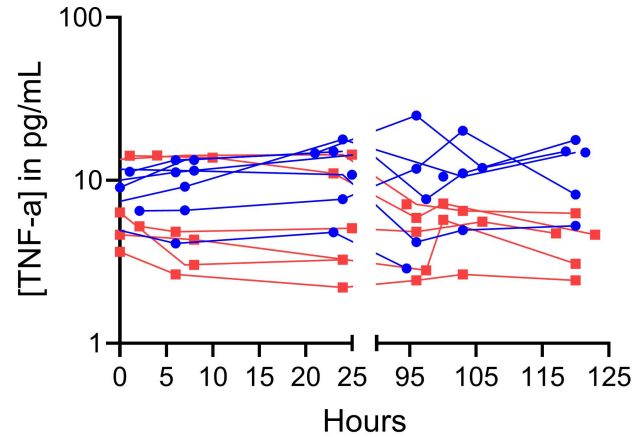
TNF-a UK



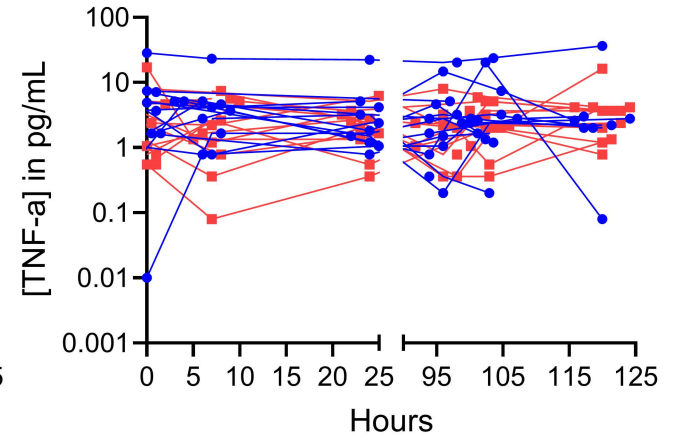
TNF-a FR



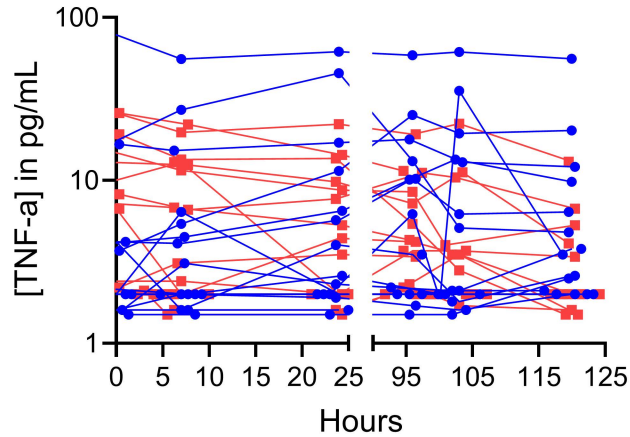
TNF-a US D0-D3



TNF-a UK D0-D3



TNF-a FR D0-D3



Blue=CYT107  
Red=Placebo

Supplemental Table 1:

|                      | All Patients |             |         | Anti-Virals  |             |         | No Anti-Virals |              |         |
|----------------------|--------------|-------------|---------|--------------|-------------|---------|----------------|--------------|---------|
|                      | CYT107       | Placebo     | p-value | CYT107       | Placebo     | p-value | CYT107         | Placebo      | p-value |
| Baseline WBC         | 9.39 (0.56)  | 9.98 (0.75) | 0.9719  | 10.10 (0.82) | 9.50 (1.09) | 0.2892  | 8.29 (0.60)    | 10.61 (0.97) | 0.0955  |
| Baseline Neutrophils | 8.42 (0.56)  | 8.65 (0.72) | 0.8364  | 8.87 (0.78)  | 8.30 (0.99) | 0.2892  | 7.71 (0.76)    | 9.13 (1.05)  | 0.2598  |
| Baseline Monocytes   | 0.45 (0.08)  | 0.44 (0.05) | 0.6600  | 0.48 (0.06)  | 0.49 (0.07) | 0.7556  | 0.40 (0.06)    | 0.37 (0.04)  | 0.8660  |
| Baseline Lymphocytes | 0.61 (0.03)  | 0.51 (0.03) | 0.0160  | 0.61 (0.03)  | 0.53 (0.3)  | 0.1105  | 0.610 (0.05)   | 0.49 (0.04)  | 0.0663  |

Reported values are k/cumm<sup>3</sup> and represent the mean (Standard Error of the Mean) of the relevant study populations. P-values are derived from the Mann-Whitney test. Abbreviations: WBC-White Blood Cells

Supplemental Table 2:

| Pts<br>number                     | Average<br>Duration of<br>antiviral<br>Treatment(days) | SD    | Confid Interval |  | MEDIAN | p-value |
|-----------------------------------|--------------------------------------------------------|-------|-----------------|--|--------|---------|
|                                   |                                                        |       | ±               |  |        |         |
| REMDESIVIR + CYT107 =<br>31       | 5,32                                                   | 3,44  | ± 6,88          |  | 5      | P=0,095 |
| REMDESIVIR + PBO = 27             | 9,37                                                   | 12,76 | ± 25,52         |  | 5      |         |
| ACICLOVIR analogs + CYT107<br>= 6 | 31,3                                                   | 21,2  | ± 42,4          |  | 45     | P=0,44  |
| ACICLOVIR analogs + PBO =<br>11   | 23,64                                                  | 18,2  | ± 36,4          |  | 26     |         |

Supplemental Table 3:

| Treatment<br>Subject Number | Primary Cause Of Death              | Related<br>PI assessment | Related<br>PhV final assessment |
|-----------------------------|-------------------------------------|--------------------------|---------------------------------|
| CYT107                      | Pulmonary fibrosis                  | Not related              | No reasonable possibility       |
| CYT107                      | Pulmonary air leakage               | Unlikely to be related   | No reasonable possibility       |
| CYT107                      | Coronavirus pneumonia               | Unlikely to be related   | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related              | No reasonable possibility       |
| CYT107                      | COVID-19 pneumonia                  | Unlikely to be related   | No reasonable possibility       |
| CYT107                      | Acute respiratory failure           | Not related              | No reasonable possibility       |
| CYT107                      | Septic shock                        | Not related              | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related              | No reasonable possibility       |
| CYT107                      | Shock                               | Not related              | No reasonable possibility       |
| CYT107                      | Respiratory failure                 | Not related              | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related              | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Unlikely to be related   | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related              | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related              | No reasonable possibility       |

| Treatment<br>Subject Number | Primary Cause Of Death              | Related<br>PI assessment     | Related<br>PhV final assessment |
|-----------------------------|-------------------------------------|------------------------------|---------------------------------|
| CYT107                      | Acute Respiratory failure           | Unlikely to be related       | No reasonable possibility       |
|                             | Pneumonia                           | Unlikely to be related       | No reasonable possibility       |
| CYT107                      | Cardiac arrest                      | Not related                  | No reasonable possibility       |
| CYT107                      | Multiple organ dysfunction syndrome | Not related                  | No reasonable possibility       |
| CYT107                      | Acute Respiratory failure           | Not related                  | No reasonable possibility       |
| Placebo                     | Pulmonary fibrosis                  | Not related                  | No reasonable possibility       |
| Placebo                     | Respiratory arrest                  | Not related                  | No reasonable possibility       |
| Placebo                     | Hemorrhagic stroke                  | Not related                  | No reasonable possibility       |
| Placebo                     | Acute respiratory distress syndrome | Not related                  | No reasonable possibility       |
|                             | Pulmonary fibrosis                  | Unlikely to be related       | No reasonable possibility       |
| Placebo                     | Respiratory Failure                 | Unlikely to be related       | Not related                     |
|                             | Cardiac arrest                      | Potentially-Possibly related | No reasonable possibility       |
| Placebo                     | Multiple organ dysfunction syndrome | Unlikely to be related       | No reasonable possibility       |



| Treatment<br>Subject Number | Primary Cause Of Death                                            | Related<br>PI assessment                                                                                 | Related<br>PhV final assessment                                            |
|-----------------------------|-------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Placebo                     | Shock hemorrhagic                                                 | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Hypoxia                                                           | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Pneumonia                                                         | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | COVID-19 pneumonia                                                | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Multiple organ dysfunction syndrome                               | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Multiple organ dysfunction syndrome                               | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Multiple organ dysfunction syndrome                               | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Cardiac arrest                                                    | Not related                                                                                              | No reasonable possibility                                                  |
| Placebo                     | Acute respiratory failure<br><br>Shock<br><br>Acute kidney injury | Unlikely to be related<br><br>Potentially-possibly<br>related<br><br><br>Potentially-possibly<br>related | Not related<br><br>No reasonable possibility<br><br>Reasonable possibility |
| Placebo                     | Respiratory failure                                               | Potentially-possibly<br>related                                                                          | No reasonable possibility                                                  |

## SUPPLEMENTAL METHODS

### INCLUSION CRITERIA

In order to be eligible to participate in this Study, an individual must meet all of the following criteria:

1. A written, signed informed consent, or emergency oral consent, by the patient or the patient's legally authorized representative, and the anticipated ability for participant to be re-consented in the future for ongoing Study participation
2. Men and women aged  $\geq 25 - 80$  (included) years of age
3. Hospitalized patients with one absolute lymphocyte count (ALC)  $\leq 1000$  cells/mm<sup>3</sup> collected at baseline or no more than 72 hours before baseline
4. Hospitalized patients with hypoxemia requiring oxygen therapy at  $\geq 2$ L per minute nasal cannula or greater to keep saturations  $>90\%$ , non-invasive positive pressure ventilation (e.g., BIPAP) for respiratory failure
5. Confirmed infection with COVID-19 by any acceptable test available/utilized at each site
6. Willingness and ability to practice contraception regardless of the gender of the patient during 5 month after last drug exposure

The **co-morbidities** affecting a COVID-19 patient should be recorded (Obesity, diabetes, hypertension, and chemotherapies or immunotherapies for cancer which were completed more than 3 months ago. Patients with these co-morbidities are eligible for the Study and are **included** (except for BMI $>40$ ).

As we anticipate more frequent use of new anti-viral drugs in the coming weeks the administration of such drugs should be recorded. Patients who have received or are receiving such drugs for COVID-19 are eligible for the Study and these patients are **included**. As we anticipate ongoing use and testing of **anti-inflammatory drugs** in the coming weeks, the administration of such drugs should also be recorded. Patients who have received or are receiving such drugs for COVID-19 are eligible for the Study and are **included**, although treatment with such drugs should preferably be minimized.

For Patients receiving any agent with immune suppressive effects, **such as** steroids and/or anti-IL6R treatments like Tocilizumab or Sarilumab or anti-IL-1 treatment like Anakinra, these agents should preferably be minimized, **but do not prevent from enrollment**. Recent data from the RECOVERY study showing a benefit in patients with a CRP (C-reactive protein)  $\geq 75$  mg/L.

### EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this Study:

1. Pregnancy or breast feeding
2. ALT and/or AST  $> 5 \times$  ULN
3. Known, active auto-immune disease;
4. Ongoing cancer treatment with chemotherapy / immunotherapy or any cancer therapy within last 3 months and/or ongoing
5. Patients with past history of Solid Organ transplant
6. Active tuberculosis, uncontrolled active HBV or HCV infection, HIV with positive viral load

7. Patients whose respiratory condition is showing significant deterioration as indicated by:
  - a. Requirement for a persistent or sustained increase in inspired oxygen concentrations of 20% or more over the past 24 hours to maintain SpO<sub>2</sub> at greater than or equal to 88% (this 20 % limit does not apply to O<sub>2</sub> delivered by nasal canula)
  - b. need for invasive mechanical ventilation
8. Patients with chronic kidney dialysis
9. Patients with a SOFA score  $\geq 9$  at baseline
10. Patients with a BMI > 40
11. Patients with baseline Rockwood Clinical Frailty Scale  $\geq 6$  at Hospital admission (*assessed as patient or proxy 4-week recall of chronic health and frailty status prior to COVID infection*)
12. Patients showing a recent increase of the NEWS2 score by more than 6 points during the screening/ baseline period
13. Patients under guardianship

#### **ONCOLOGY COHORT – INCLUSION CRITERIA**

In order to be eligible to participate in this Study, an individual must meet all of the following criteria:

1. A written, signed informed consent, or emergency oral consent, by the patient or the patient's legally authorized representative, and the anticipated ability for participant to be re-consented in the future for ongoing Study participation
2. Patients receiving active or recent chemotherapy or immunotherapy (within 6 months) for cancer (and/or)
3. Patients who have received hematopoietic stem cell transplantation (for a diagnosis other than lymphoma) within the past 1 year (and/or)
4. Patients who received CAR-T cell therapy within the past 1 year (but not within last 30 days- see also exclusion criteria number 6 & 7) (and/or)
5. Patients receiving hormonal therapy for cancer (and/or)
6. Patients who have undergone surgery or radiotherapy for cancer within the past 6 months (or)
7. Patients with newly diagnosed (biopsy proven) malignancy who have not yet received cancer treatment but get COVID pneumonia in the interim (Incl. Criteria 11)
8. Men and women aged  $\geq 25 - 80$  (included) years of age
9. Hospitalized patients with one absolute lymphocyte count (ALC)  $\leq 1000$  cells/mm<sup>3</sup> collected at baseline or no more than 72h before baseline. (Baseline time is decided by the investigator independently of the initial hospitalization time) From this time point the investigator may choose to further postpone the commencement of IL-7 (CYT107) treatment according to patient's clinical status.
10. Hospitalized patients with hypoxemia requiring oxygen therapy at  $\geq 2$ L per minute nasal cannula or greater to keep saturations >90%, non-invasive positive pressure ventilation (e.g., BIPAP) for respiratory failure or patients intubated/ventilated for respiratory failure
11. Confirmed infection with COVID-19 by any acceptable test available/utilized at each site
12. Willingness and ability to practice contraception regardless of the gender of the patient during 5 months after last drug exposure

The **co-morbidities** affecting a COVID-19 patient should be recorded (Obesity, diabetes, hypertension, and chemotherapies or immunotherapies for cancer which were completed more than 3 months ago). Patients with these co-morbidities are eligible for the Study and are **included** (except for BMI>40).

As we anticipate more frequent use of new anti-viral drugs in the coming weeks the administration of such drugs should be recorded. Patients who have received or are receiving such drugs for COVID-19 are eligible for the Study and these patients are **included**.

As we anticipate ongoing use and testing of **anti-inflammatory drugs** in the coming weeks, the administration of such drugs should also be recorded. Patients who have received or are receiving such drugs for COVID-19 are eligible for the Study and are **included**, although treatment with such drugs should preferably be minimized.

For Patients receiving any agent with immune suppressive effects, **such as** steroids and/or anti-IL6R treatments like Tocilizumab or Sarilumab or anti-IL-1 treatment like Anakinra, these agents **do not prevent from enrollment**. Recent data from the RECOVERY study showing a benefit in patients with a CRP (C-reactive protein)  $\geq 75$  mg/L.

### **Oncology Cohort – Exclusion Criteria**

An individual who meets any of the following criteria will be excluded from participation in this Study:

1. Pregnancy or breast feeding;
2. ALT and/or AST  $> 5 \times$  ULN
3. Known, active auto-immune disease;
4. Patients with a history of lymphoid malignancy, with the exception of patients with B-cell lymphomas
5. Patients with any malignancy that is present at time of enrollment where treating physician expects life expectancy due to the underlying malignancy to be less than 6 months
6. Patients who received CAR-T cell therapy within the past 30 days or with unresolved cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS)
7. Patients with unresolved grade  $\geq 2$  toxicities from prior chemotherapy, immunotherapy, or CAR-T cell therapy
8. Patients with past history of Solid Organ transplant.
9. Active tuberculosis, uncontrolled active HBV or HCV infection, HIV with positive viral load.
10. Hospitalized Patients whose respiratory condition is showing significant deterioration as indicated by:  
requirement for a persistent or sustained increase in inspired oxygen concentrations of 20% or more over the past 24 hours to maintain SpO<sub>2</sub> at greater than or equal to 88% (this 20 % limit does not apply to O<sub>2</sub> delivered by nasal canula)
11. Patients with chronic kidney dialysis
12. Patients with a SOFA score  $\geq 9$  at baseline
13. Patients with a BMI  $> 40$
14. Patients showing a recent increase of the NEWS2 score by more than 6 points during the screening/ baseline period
15. Patients with hospital admission Rockwood Clinical Frailty Scale  $\geq 6$  (*assessed as patient or proxy 4-week recall of chronic health and frailty status prior to COVID infection*)
16. Patients under guardianship

*Members of the Data Safety Monitoring Board:* Dr. Steve Opal, Dr. Elliott Crouser, Dr. Philippe Eggimann, Dr. Peter Pickkers.

*Members of the Secondary Infection Adjudication Committee –*

-United States and Brazil: Dr. John Mazuski, Dr. Brian Fuller, Dr. Isaiah Turnbull

-France and United Kingdom: Dr. Bruno Abraham, Dr. Marc Clavel, Dr. Valerie Gissot.

## **Name of Site or Practice Participating in ILIAD 7 Trial of CYT107 in COVID-19**

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**France:** Bruno FRANCOIS & Thomas DAIX, CENTRE HOSPITALIER UNIVRSITAIRE DE LIMOGES; Pierre-Francois DEQUIN, HOPITAL BRETONNEAU; Jean-Paul MIRA, HOPITAL COCHIN-APHP; Laurent ARGAUD & Thomas RIMMELE, HOPITAL EDOUARD HERRIOT; Gregoire MULLER, CENTRE HOSPITALIER REGIONAL D'ORLEANS; Christophe GUITTON, CENTRE HOSPITALIER LE MANS; Jerome ROUSTAN, CENTRE HOSPITALIER MONTAUBAN

**United States:** Richard HOTCHKISS, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE; Scott BRAKENRIDGE & Phil EFRON, UNIVERISTY OF FLORIDA – GAINESVILLE; Vidula VACHHARAJANI, CLEVELAND CLINIC; Stephen KUPERBERG & Sadia ABBASI, RENAISSANCE SCHOOL OF MEDICINE AT STONY BROOK; Jag SUNDERRAM, RUTGERS ROBERT WOOD JOHNSON MEDICAL SCHOOL; David SRIKER, MISSOURI BAPTIST MEDICAL CENTER ST LOUIS; Ken REMY, UH CLEVELAND MEDICAL CENTER; Robert J. MARTIN & James BOSANQUET & Nitin ANAND, MISSOURI BAPTIST MEDICAL CENTER ST LOUIS; Marcel VAN DEN BRINK, MEMORIAL SLOAN KETTERING CENTER/ CITY OF HOPE; Stephen M. PASTORES, MEMORIAL SLOAN KETTERING CANCER CENTER; Christina GUTIERREZ & Yee CASSIAN, MD ANDERSON

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