# The response to Convalescent-Plasma in COVID-19 induced ARDS does not differ across immunological sub-phenotypes

# Immunological sub-phenotypes and response to Convalescent-Plasma (CP) in COVID-19 induced ARDS (C-ARDS): a hierarchical cluster analysis


**Benoît Misset (1), Anh Diep Nguyet (1), Axelle Bertrand (1), Michael Piagnerelli (2), Eric Hoste (3), Isabelle Michaux (4), Elisabeth De Waele (5), Alexander Dumoulin (6), Philippe G Jorens (7), Emmanuel van der Hauwaert (8), Frédéric Vallot (9), Walter Swinnen (10), Nicolas De Schryver (11), Nathalie de Mey (12), Nathalie Layios (1), Jean-Baptiste Mesland (13), Sébastien Robinet (1), Etienne Cavalier (1), Anne-Françoise Donneau (1), Michel Moutschen (1), Pierre-François Laterre (13,14)**

**(1)** Intensive care, Biostatistics, Biology and Infectious diseases, Liege;

**(2 to 14)** Intensive care; (2) ULB Charleroi, (3) UZ Gent, (4) UCL Namur, (5) VUB Jette, (6) AZ Delta Roeselare, (7) UZ Antwerp, (8) Imelda Bonheiden, (9) GH Tournai, (10) Sint Blasius GH Dendermonde, (11) Saint Pierre Ottignies, (12) OLV Aalst, (13) UCL Brussels, (14) Mons; **All** in Belgium

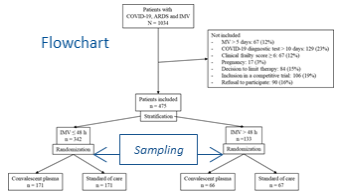

## INTRODUCTION

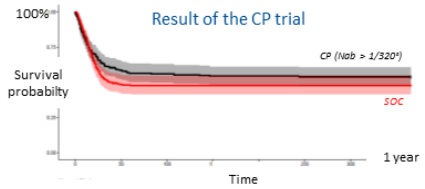
The CONFIDENT trial tested the effect of passive immunization with plasma collected from convalescents and high titers of neutralizing antibodies may reduce mortality in patients with COVID-19 associated ARDS when administered early after the introduction of IMV. It demonstrated a 9.7% reduction in day-28 mortality (p=0.03) (*Misset, New Engl J Med, 2023 in press*).

As the immunological response to COVID-19 is likely heterogeneous across patients, we hypothesized that immunologically similar **COVID-19 clusters might differ in their responses** to convalescent-plasma treatment.

## METHODS

- Secondary analysis of the CONFIDENT trial
- **Inclusion criteria** : Adult, Frailty scale < 6, SARS-CoV-2 pneumonia, **IMV <5 days** (stratification at 48h)
- **Intervention :** 2 x 250 mL bags of CP with **NAb > 1/320°**
- Control : standard care (SC)




- **Sampling at the time of inclusion** (in 13/17 centers having accepted the secondary part of the trial).
- **Multiplex Luminex** technique (ELISA combined with flow cytometry)
- **20 cytokines, chemokines and cell adhesion markers**.
- Descriptive statistics (median [IQR]), **hierarchical cluster analysis and search for association between the identified clusters and CP effect on day-28 mortality**.

## CONCLUSIONS

In a cohort of patients with COVID-associated ARDS included in a convalescent plasma trial, we identified 4 sub-phenotypes based on their immune response associated with different clinical profiles. The response to convalescent plasma as assessed by the day-28 mortality was not different between the 4 sub-phenotypes.


## FUNDING

KCE (Belgian federal agency) 2020, 1-0-1 AXA 2021, Liège University 2021



## CONTACT INFORMATION

*benoit.misset@chuliege.be*

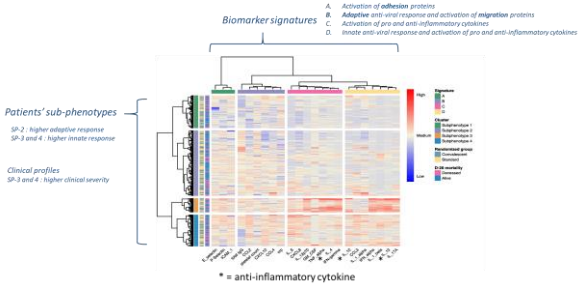

## RESULTS

### Population

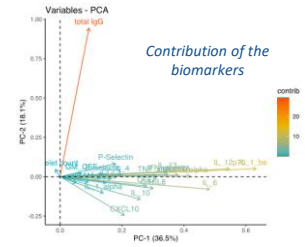
*Similar to the total trial population (n=475)*

| Patients, n | 391 |
|---|---|
| Age, y | 64 [56-72] |
| BMI, kg/m² | 30,0 [26,4-34,5] |
| APACHE II | 13 [9-17] |
| SOFA | 6 [4-8] |
| PaO2/FiO2 | 120 [90-160] |
| Steroids | 375 (95,9%) |
| Group (CP/SC) | 196 / 195 |
| Inclusion IMV < 48h | 299 (76,5%) |

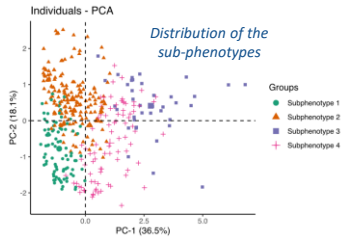
### Hierarchical clustering



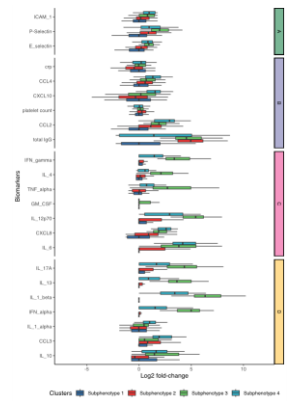

### Principal component analysis 1




### Principal component analysis 2




### Biomarkers by sub-phenotypes



### Effect of CP/SC by sub-phenotypes

| Groups | Odds ratio (95%CI) | p.value |
|---|---|---|
| All | 0.816 (0.542 - 1.228) | 0.329 |
| Subphenotype 1 | 0.719 (0.304 - 1.700) | 0.451 |
| Subphenotype 2 | 0.846 (0.454 - 1.579) | 0.600 |
| Subphenotype 3 | 0.667 (0.184 - 2.410) | 0.537 |
| Subphenotype 4 | 0.900 (0.384 - 2.110) | 0.808 |