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Cohorte du PUT plasma convalescent dans la Covid19

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Utiliser le plasma ou sérum de patients convalescents pour guérir ou prévenir une maladie: A propos du 1er prix Nobel de Médecine en 1901

Adolf von Behring médecin allemand et premier lauréat du prix Nobel de physiologie ou de médecine en 1901 pour avoir découvert le sérum* de l'antitoxine de la diphtérie (1890) et du tétanos (1890) et démontré un transfert de l'immunité (avec Kitasato Shibasaburō, médecin japonais).

Par ailleurs :

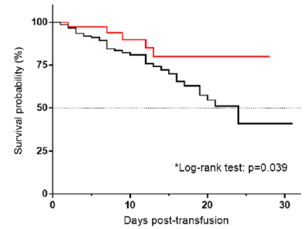
- Charles Richet: sérum anti staphylocoque (1888) sérum anti tuberculeux (1890)
- Albert Calmette: sérum antivenimeux (1890)
- Emile Roux: sérum antidiphtérique (1894)

** Le sérum: un plasma dépourvu de facteurs de la coagulation*

Convalescent plasma treatment of severe COVID-19: a propensity score–matched control study

Liu et al, Nature Medicine

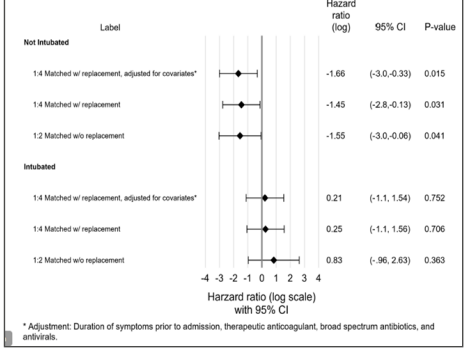
Figure 2. Survival Probability



1:4 Matched Controls	156	65	20	1
Convalescent Plasma Recipients	39	22	9	0

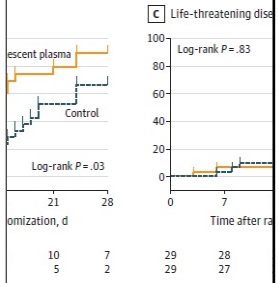
Numbers at Risk

Figure 3. Hazard ratios for in-hospital mortality



* Adjustment: Duration of symptoms prior to admission, therapeutic anticoagulant, broad spectrum antibiotics, and antivirals.

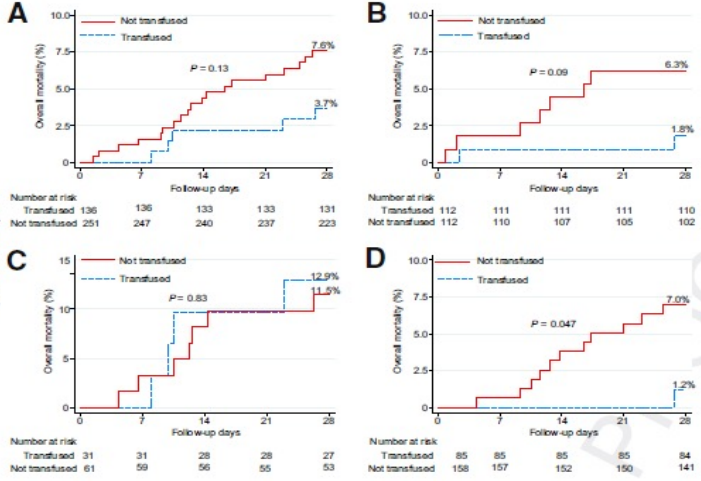
on Time to Clinical Improvement ening COVID-19



edian (IQR) follow-up times for the convalescent pl
l group, respectively, were 15 (10-28) days and 24 (
and 18.5 (11-26) days among those with severe CO
(15-28) days among those with life-threatening CO

Treatment of Coronavirus Disease 2019 Patients with Convalescent Plasma Reveals a Signal of Significantly Decreased Mortality

Joyner et al, JAMA Pathol, 2020



print & web 4C/FPO

Figure 2 Kaplan-Meier curves for mortality within 28 days post-day 0 for secondary matched cohorts. **A:** All secondary matched patients. **B:** Secondary matched patients transfused within 72 hours of admission. **C:** Secondary matched patients transfused >72 hours after admission. **D:** Secondary matched patients transfused within 72 hours of admission with plasma with anti—receptor binding domain IgG titer ≥1:1350.

ansm

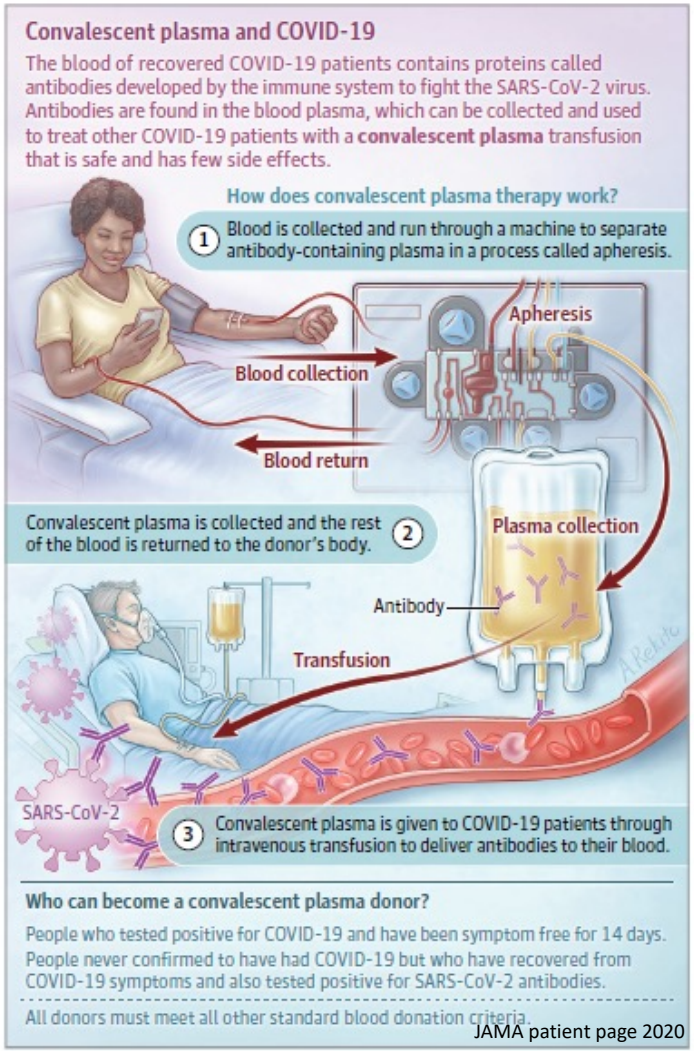
Agence nationale de sécurité du médicament et des produits de santé

PROTOCOLE D'UTILISATION THERAPEUTIQUE

24 avril 2020

Plasma convalescent COVID-19

Infection par le coronavirus SARS-CoV-2 (maladie COVID-19)



JAMA patient page 2020

Convalescent donor selection

Standard eligibility criteria, including a delay of 14 days since COVID-19 symptoms resolution (fever, dyspnea)

Apheresis : standard procedure, 650 ml

Frequency : up to 3 times with a minimum of 15 days interval (per standard regulation)

Donor qualification:

Neutralizing activity titer >= 1/40 and/or Euroimmun Elisa ratio > 5,6

Plasma:

Pathogen reduced (Intercept) and cryopreserved for use as:

- Convalescent plasma (neutralizing titer >= 1/40)
- Standard plasma (neutralizing titer < 1/40)

From 07/04 to 12/06:

- 2869 plasma donations (apheresis, 3 units / donation), among which 563 PlasmaCoV2 donations
- 64 to 55% qualified donations (76% among PCR+ donors)
- 4700 qualified convalescent plasma units (200 to 220 ml/unit)

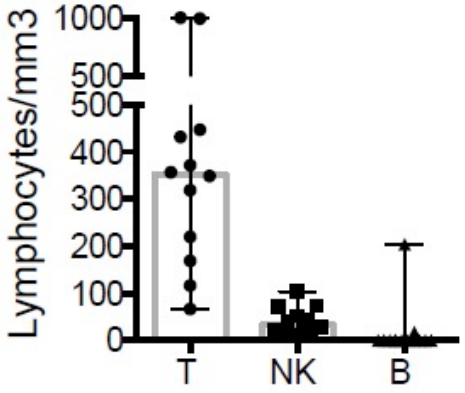
Reinitiation of CCP collection **since 26/10**: 100 to 200 plasmapheresis / week with a focus on B, AB CCP donors)

CORIPLASM-ID: évaluation du plasma convalescent chez les immunodéprimés covid19, preuve de concept

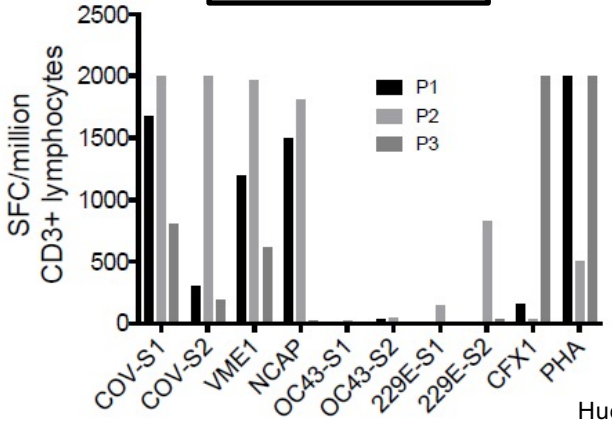
Description : profil immunologique des 17 patients

- Hypogammaglobulinémie profonde (médiane 3,5g/L)
- Absence de lymphocytes B circulants pour 16 patients
- Une réponse cellulaire T effective et spécifique

Immunophénotypage lymphocytaire



ELISPOT (N=3)

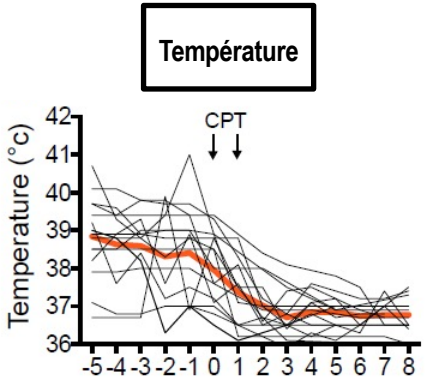


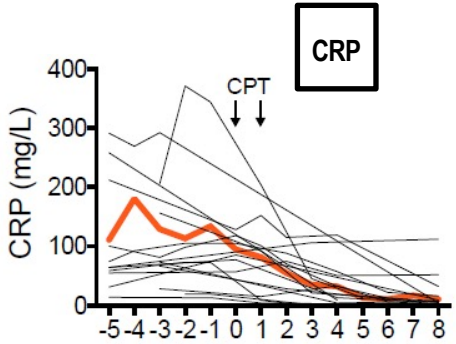
Hueso, Blood 2020

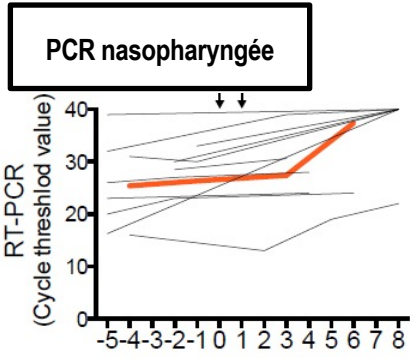
CORIPLASM-ID: évaluation du plasma convalescent chez les immunodéprimés covid19, preuve de concept

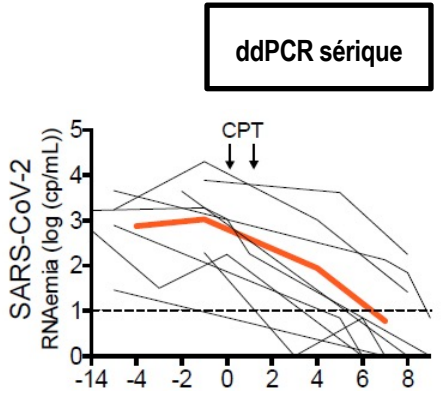
- Aucun effet indésirable rapporté

- Bénéfice clinique :
  - Apyrexie dans les 48h pour tous les patients
  - 10 patients sous oxygénothérapie : sevrage sous 5 [1-45] après la transfusion
  - 2 patients sous ventilation mécanique :
    1 décès (J7, PAVM)
    1 sevrage de la ventilation mécanique avec sevrage de l'O2 à J14.
  - Sur les 16 patients vivants à J15, tous déclarés asymptomatiques



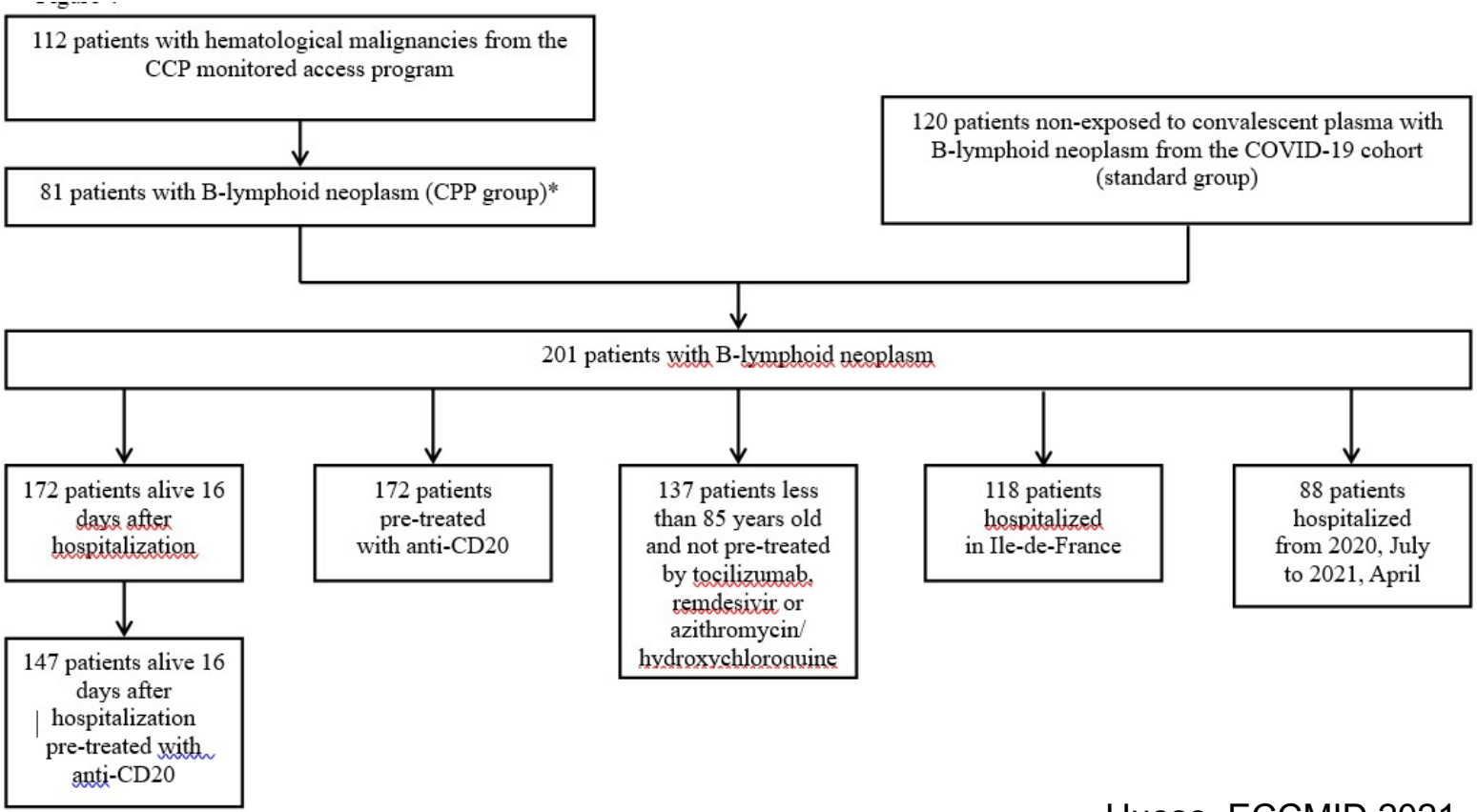






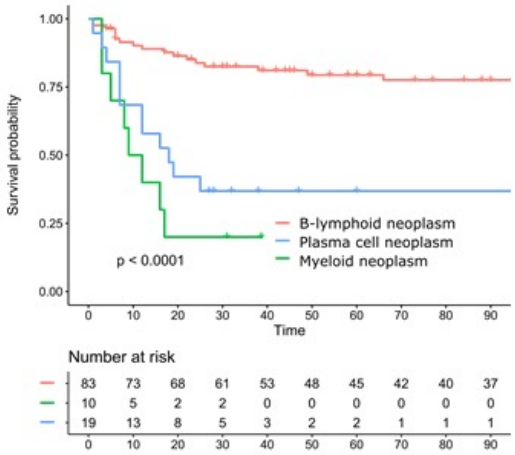
Hueso, Blood 2020

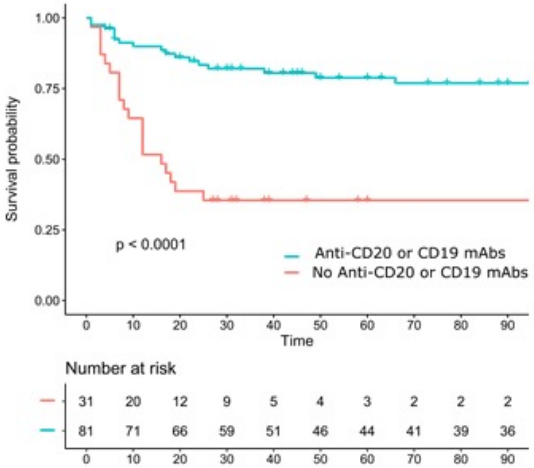
HEMOPLASM: cohorte exposé/non exposé avec score de propension – Evaluation du plasma convalescent dans les hémopathies malignes

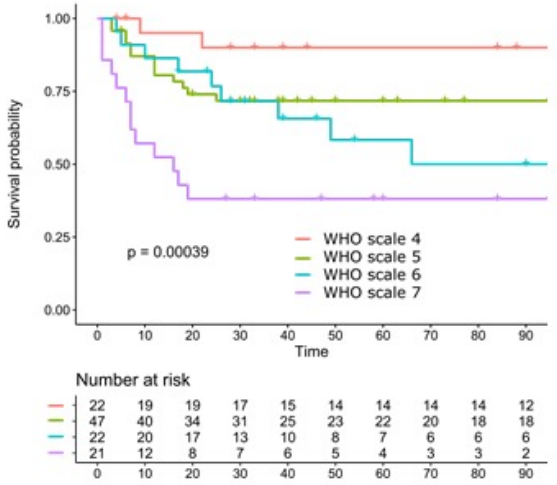


Hueso, ECCMID 2021

HEMOPLASM: cohorte exposé/non exposé avec score de propension – Evaluation du plasma convalescent dans les hémopathies malignes







➔ Meilleur pronostic si hémopathies lympoïdes B, utilisation d'antiCD19-20, transfusé tôt

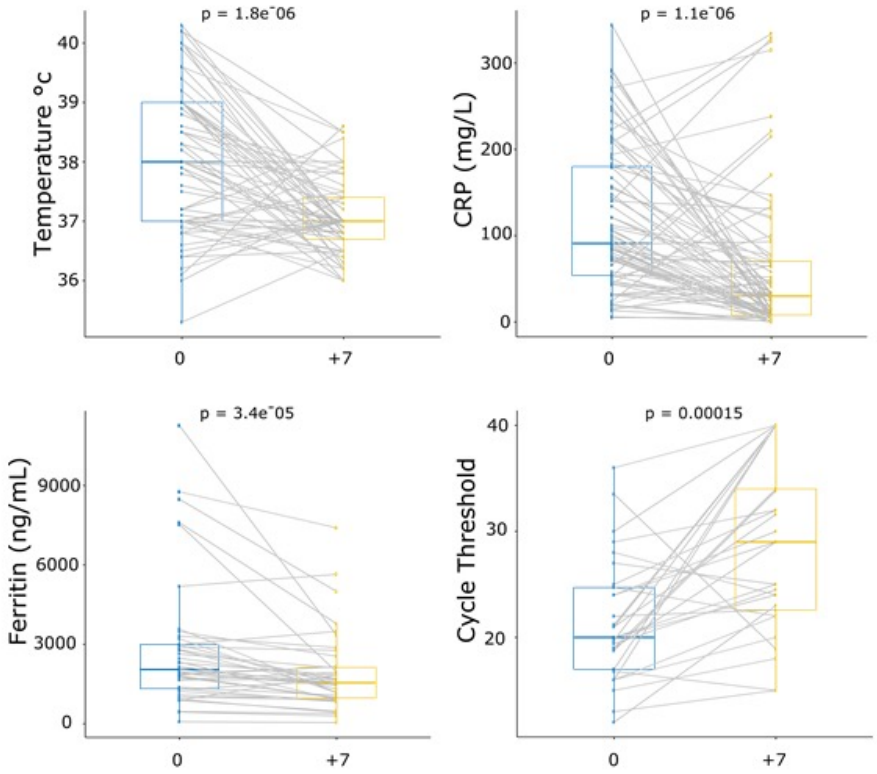
HEMOPLASM: cohorte exposé/non exposé avec score de propension – Evaluation du plasma convalescent dans les hémopathies malignes

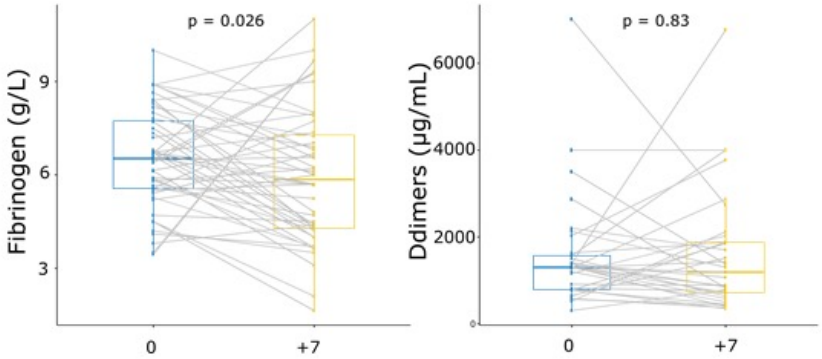
Table 4: Estimation of hazard ratio (HR) of death associated with plasma therapy and its 95% confidence interval (CI)

	Crude association		Adjusted association		Adjusted association including sex		IPW		IPW including sex	
Analysed population	HR of death associated with plasma therapy [95%CI]	p-value	HR of death associated with plasma therapy [95%CI]	p-value	HR of death associated with plasma therapy [95%CI]	p-value	HR of death associated with plasma therapy [95%CI]	p-value	HR of death associated with plasma therapy [95%CI]	p-value
16 day- anti-cd20 population	0.47 [0.16;1.3]	0.157	0.33 [0.11;0.99]	0.049			**0.37 [0.20;0.69]**	**0.002**		
Overall population	0.45 [0.26;0.79]	0.005	0.46 [0.26;0.84]	0.012	0.45 [0.25;0.83]	0.010	0.50 [0.34;0.72]	<0.001	0.48 [0.33;0.69]	<0.001
RCT-like population	0.54 [0.29;1.0]	0.064	0.58 [0.29;1.2]	0.117			0.57 [0.37;0.89]	0.014		
Wave 2-4 population	0.44 [0.20;0.97]	0.042	0.50 [0.23;1.1]	0.083			0.60 [0.35;1.0]	0.069		
IdF population	0.40 [0.17;0.95]	0.039	0.39 [0.16;0.96]	0.040			0.40 [0.24;0.67]	<0.001		
16 day- population	0.55 [0.19;1.6]	0.263	0.46 [0.15;1.4]	0.165			0.43 [0.23;0.78]	<0.001		
Anti-CD20 population	0.37 [0.21;0.65]	<0.001	0.32 [0.17;0.60]	<0.001			0.39 [0.26;0.58]	<0.001		

Adjusted associations and IPW models were controlled for age (<65 years vs. ≥65 years), arterial hypertension or diabetes or body mass index>25kg/m² (yes vs. not) and corticotherapy (yes vs. not). IdF: Ile-de-France, IPW: inverse probability of convalescent plasma exposure weighting, RCT: randomized controlled trial

HEMOPLASM: cohorte exposé/non exposé avec score de propension – Evaluation du plasma convalescent dans les hémopathies malignes





Hueso, ECCMID 2021

En conclusion

- Efficacité du plasma convalescent covid19 dans les hémopathies malignes, en particulier lymphoïdes B
- Facteurs associés à un bon pronostic : antécédent de traitement par rituximab, stade précoce, (femme)
- Comme pour les mAbs, la sérologie neg. est également associée à un meilleur pronostic