MPN HORIZONS 2021 LEARN, SHARE, GROW
VIRTUAL CONFERENCE
6th INTERNATIONAL CONFERENCE FOR ORGANIZATIONS REPRESENTING PEOPLE WITH MPN
MPN Advocates Network
Friday 12th November, 15:30 - 17:0

Covid-19 and MPN – What have we learned

Tiziano BARBUI
(tbarbui@fondazionefrom.it)

Clinical Research Foundation (FROM)
Ospedale Papa Giovanni XXIII
Bergamo, Italy

Bergamo was unfortunately the epicenter of the COVID-19 pandemic in Europe

In March 2020 more than 5.400 people have died in Bergamo province (1.2 million), **4.500 of which due to coronavirus.**

Pictures showing military vehicles carrying hundreds of coffins away, witnessing the tragedy all Bergamo people were experiencing.

MPN-COVID Study

- **MPN-COVID study** was launched by *European LeukemiaNet (ELN)* in March 2020.
- **Partecipating Centers** (n=38) from Italy, Spain, Germany, France, Croatia, Poland, England).
- After IRB approval, consecutive adult patients with **WHO-2016 diagnosed MPN with a positive PCR** from nasal swab, were included.
- The participating centres were asked to **report in an electronic case report form (e-CRF)** their consecutive MPN-COVID patients diagnosed since **15 February 15, 2020.**
- **Registration of new patients will continue until spring 2022**

COVID outcomes and MPN

At the outset of the COVID-19 pandemic in early 2020, scientists and clinicians faced a daunting list of desperately needed answers.
The best means for settling these questions was to conduct research on an unprecedented scale and at an accelerated pace".

Marion Renault, *Nature Medicine September 2021*

What questions have we addressed

- The **clinical epidemiology** during the acute phase in the first wave of the pandemic
- **Clinical sequelae** in patients who have passed the acute phase of the first wave
- Whether outcomes changed during the **subsequent waves**
- Whether drugs for MPN have affected the **effectiveness of vaccinations**

COVID outcomes and MPN

At the outset of the COVID-19 pandemic in early 2020, scientists and clinicians faced a daunting list of desperately needed answers.
The best means for settling these questions was to conduct research on an unprecedented scale and at an accelerated pace".

Marion Renault, *Nature Medicine September 2021*

What questions have we addressed

- The **clinical epidemiology** during the acute phase in the first wave of the pandemic
- **Clinical sequelae** in patients who have passed the acute phase
- Whether outcomes changed during the **subsequent waves**
- Whether drugs for MPN have affected the **effectiveness of vaccinations**

Patients n= 175

WHO	ET	PV	MF	pre-PMF
	N=59	N=57	N=39	N=23
Country, n (%)				
Italy	**22 (37.3%)**	**28 (49.1%)**	**16 (41.0%)**	**11 (47.8%)**
Spain	**33 (55.9%)**	**22 (38.6%)**	**15 (38.5%)**	**9 (39.1%)**
Other (France, UK,Poland Germany)	**4 (6.8%)**	**7 (12.3%)**	**8 (20.5%)**	**3 (13.0%)**
Sex, n (%)				
Male	29 (49.2%)	35 (61.4%)	26 (66.7%)	15 (65.2%)
Age, years, median (IQR)	56.8 (43.0-71.5)	61.8 (47.8-70.3)	65.7 (56.8-72.0)	67.9 (55.6-75.0)
JAK2, n (%)	33 (56.9%)	54 (97.4%)	21 (55.3%)	16 (76.2%)
CALR, n (%)	14 (34.1%)	0 (0.0%)	**12 (50.0%)**	2 (16.7%)
MPL, n (%)	4 (10.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Patients at COVID (n=175)

	ET	PV	MF	pre-PMF	Total
	N=51	N=46	N=60	N=18	N=175
Age, years, median (IQR)	72.0 (54.1-80.6)	70.0 (58.2-74.7)	70.9 (62.7-77.1)	78.8 (70.3-86.4)	71.0 (60.0-79.9)
Hospital	40 (78.4%)	32 (69.6%)	51 (85.0%)	12 (66.7%)	135 (77.1%)
Home	11 (21.6%)	14 (30.4%)	9 (15.0%)	6 (33.3%)	40 (22.9%)
COMORBIDITES, n (%)					
Hypertension	33 (66.0%)	27 (60.0%)	34 (57.6%)	10 (58.8%)	104 (60.8%)
Diabetes mellitus	4 (8.0%)	5 (10.9%)	12 (20.0%)	2 (12.5%)	23 (13.4%)

Cytoreductive drug for MPN at last follow-up

(months 1.5; Range 0.8-3.0 before COVID)

	Last fup pre-COVID
ET, n=51	
Hydroxyurea, n/N (%)	31/51 (60.8%)
Ruxolitinib, n/N (%)	2/51 (3.9%)
PV, n=46	
Hydroxyurea, n/N (%)	26/46 (56.5%)
Ruxolitinib, n/N (%)	8/46 (17.4%)
MF, n=60	
Hydroxyurea, n/N (%)	10/60 (16.7%)
Ruxolitinib, n/N (%)	**34/60 (56.7%)**
Pre-PMF, n=18	
Hydroxyurea, n/N (%)	12/18 (66.7%)
Ruxolitinb, n/N (%)	1/18 (5.6%)

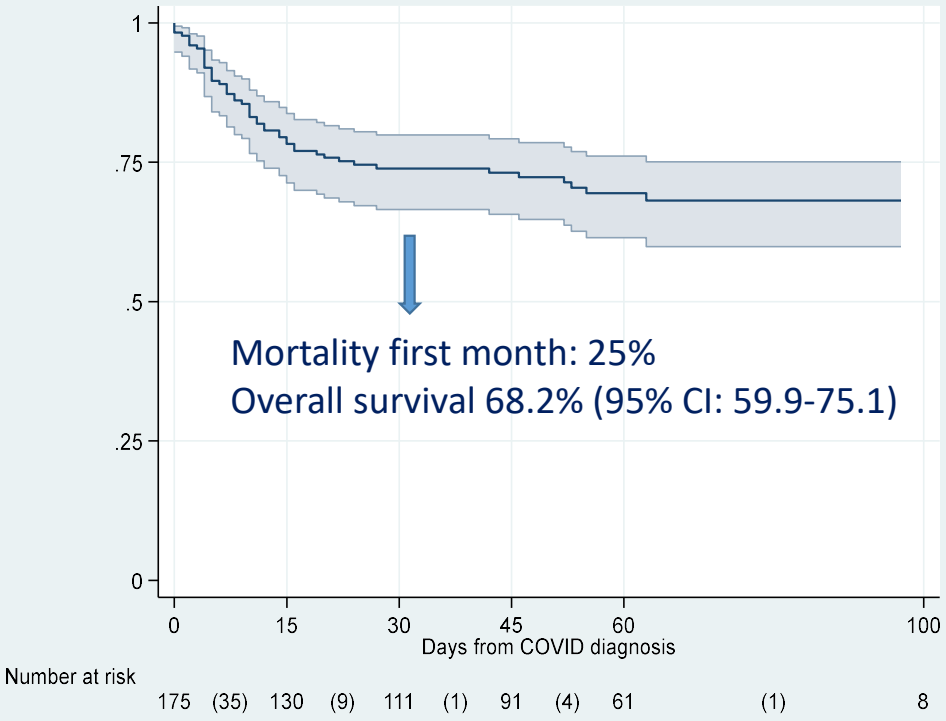
Interferon alfa and Anagrelide in 4 and 8 patients, respectively

Barbui T, et al Leukemia. 2021 Jan 7:1-9.

Therapy in MPN patients for COVID (n=175)

	ET	PV	MF	pre-PMF	Total
	N=51	N=46	N=60	N=18	N=175
Need of respiratory support	**32 (62.7%)**	**22 (47.8%)**	**38 (64.4%)**	**11 (61.1%)**	**103 (59.2%)**
Not invasive	25 (49.0%)	18 (39.1%)	31 (52.5%)	9 (50.0%)	83 (47.7%)
Invasive	*7 (13.7%)*	*4 (8.7%)*	*7 (11.9%)*	*2 (11.1%)*	*20 (11.5%)*
Transfer to ICU	6 (11.8%)	4 (8.9%)	7 (12.1%)	2 (11.1%)	19 (11.0%)
Drugs , n (%)					
Hydroxychloroquine	34 (68.0%)	19 (41.3%)	38 (70.4%)	9 (56.3%)	100 (60.2%)
Antiviral	17 (34.0%)	11 (23.9%)	24 (44.4%)	5 (31.3%)	57 (34.3%)
Experimental	4 (8.0%)	6 (13.0%)	6 (10.7%)	3 (16.7%)	19 (11.2%)
Antithrombotic	**32 (64.0%)**	**18 (40.9%)**	**32 (57.1%)**	**11 (68.8%)**	**93 (56.0%)**
Heparin	32 (100.0%)	17 (94.4%)	29 (93.5%)	11 (100.0%)	89 (96.7%)
DOACs	0 (0.0%)	1 (5.6%)	1 (3.2%)	0 (0.0%)	2 (2.2%)
Warfarin	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (1.1%)

Overall Survival (n=175)



Mortality

- overall 28,6%
- ET 25%
- PV 19%
- **MF 48%**
- pre-MF 22%

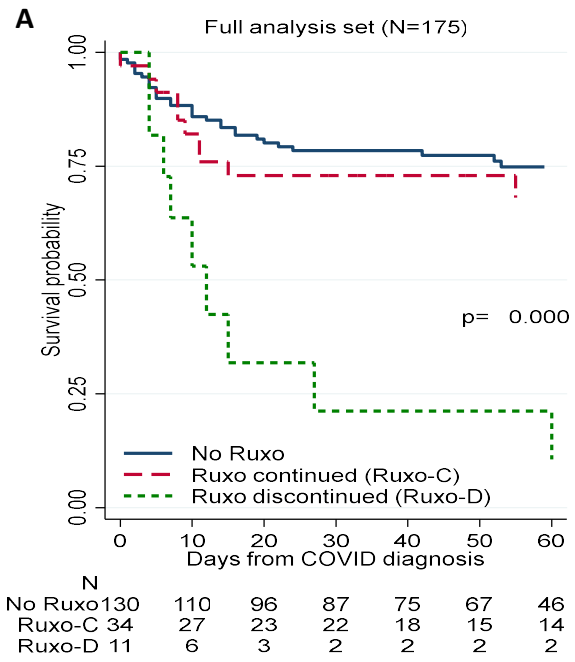
Causes of death

- Vascular 2%
- UNK 13%
- Pneumonia 33%
- MOF 42%
- Other 6%

MPN directed drugs at COVID acute phase and Survival

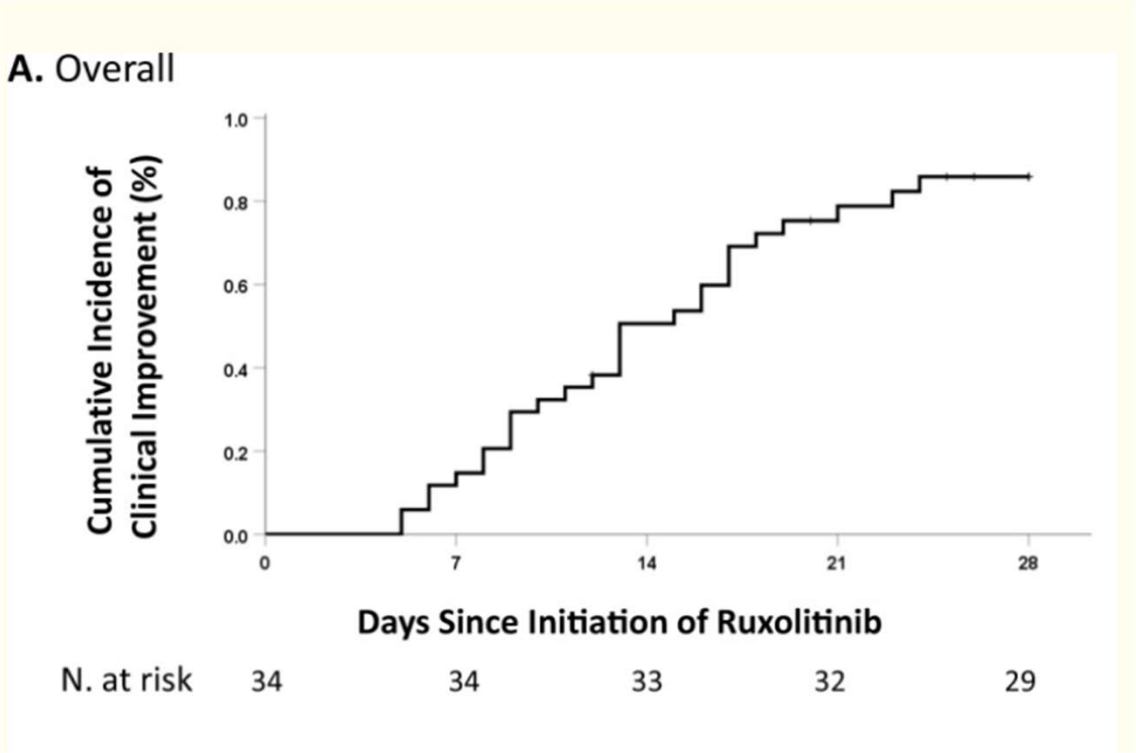
	Total N=175	Survivors N=125	Non survivors N=50	p-value
MPN drugs				
Hydroxyurea	79 (45.1%)	60 (48.0%)	19 (38.0%)	0.23
Discontinued after COVID-19 onset	9 (17.3%)	7 (21.2%)	2 (10.5%)	0.33
Ruxolitinib	45 (25.7%)	25 (20.0%)	20 (40.0%)	0.006
Discontinued after COVID-19 onset	11 (24.4%)	2 (8.0%)	9 (45.0%)	0.004
Interferon	4 (2.3%)	4 (3.2%)	0 (0.0%)	0.20
Anagrelide	8 (4.6%)	5 (4.0%)	3 (6.0%)	0.57
Other	5 (2.3%)	4 (3.2%)	1 (2.0%)	0.67

Kaplan Meier curves of survival stratified by use and discontinuation of Ruxo in the full analysis set



Multivariate Analysis	OR (95%CI)	p-value
Age > 70 yrs	2.28 (0.91-5.67)	**0.077**
Male sex	2.42 (1.04-5.65)	**0.040**
MF diagnosis	1.50 (0.57-3.89)	0.415
Chronic heart disease	2.58 (0.85-7.85)	**0.094**
Intensive care unit	13.0 (4.11-41.8)	**<.001**
Ruxo continued	2.14 (0.67-6.83)	0.199
Ruxo discontinued	19.3 (2.67-144)	**0.003**

Compassionate use of JAK1/2 inhibitor ruxolitinib for severe COVID19: a prospective observational study (non MPN patients)



Prospective, observational study in 34 patients with COVID-19. **Median age was 80.5 years,** and 85.3% had ≥ 2 comorbidities.
Median exposure time to ruxolitinib was 13 days, median dose intensity was 20 mg/day.

Overall survival by day 28 was 94.1%.

Vannucchi et al, Leukemia, 2020

Cumulative incidence of thrombosis in ET versus PV/MF.

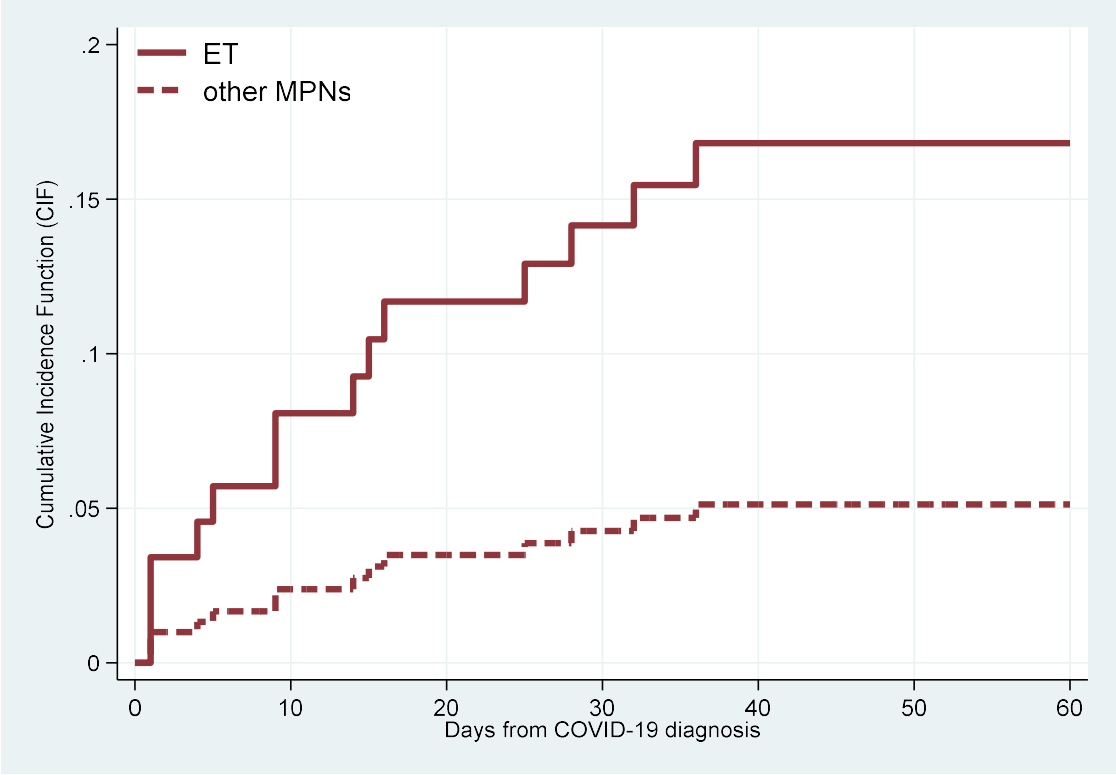


Figure illustrates the **remarkable difference in the CIF of thrombosis in patients with ET** compared with the other MPN phenotypes.

CIF of arterial/VTE
in ET ……. 17%
in PV/MF…. 5%

Of note is the **rapid steepness of the curve** starting from the first hours after hospitalization and reaching the peak after 30 days

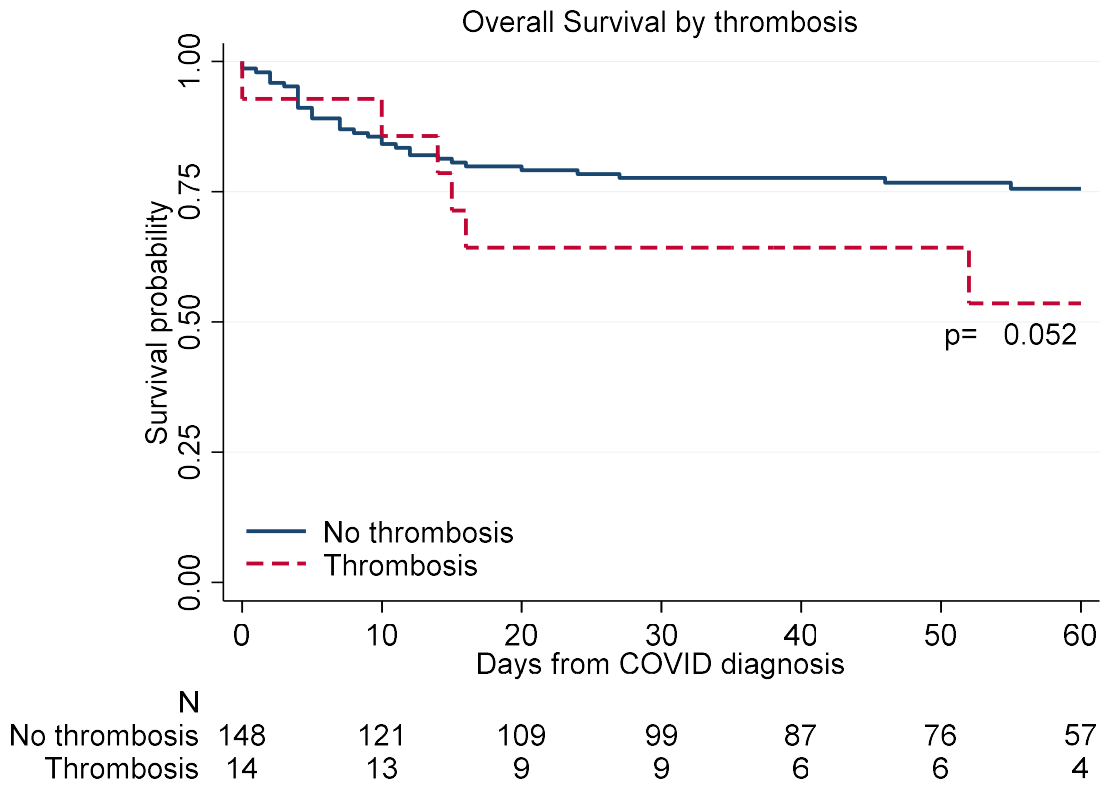
Characteristics of ET and PV/MF were similar in terms of sex, age, driver mutations and prior history of thrombosis

	Total	ET	PV/MF	p
	N=162	N=48	N=114	
Sex, n (%)				0.29
Female	66 (40.7%)	23 (47.9%)	43 (37.7%)	
Male	96 (59.3%)	25 (52.1%)	71 (62.3%)	
Age (years), median (IQR)	70.6 (60.0-79.9)	71.6 (53.9-80.3)	70.3 (60.9-79.7)	0.70
<60 years, n (%)	40 (24.8%)	15 (31.3%)	25 (22.1%)	0.35
60-70 years, n (%)	36 (22.4%)	8 (16.7%)	28 (24.8%)	
>70 years, n (%)	85 (52.8%)	25 (52.1%)	60 (53.1%)	
JAK2V617F, n (%)	112 (70.9%)	27 (57.4%)	85 (76.6%)	0.016
CALR, n (%)	26 (29.5%)	13 (39.4%)	13 (23.6%)	0.12
MPL, n (%)	5 (6.0%)	2 (6.9%)	3 (5.6%)	0.81
Previous thrombosis, n (%)	23 (14.4%)	8 (16.7%)	15 (13.4%)	0.59
Previous bleeding, n (%)	12 (7.5%)	4 (8.3%)	8 (7.1%)	0.79

ET vs PV/MF presented at COVID-19 with higher platelet number but comparable inflammatory tests and coagulation pattern

Variables	Total	ET	Other MPNs	p
	N=162	N=48	N=114	
White blood cells, x10^9/L	6.6 (4.7-10.3)	6.5 (4.7-9.2)	6.7 (4.7-10.5)	0.73
Lymphocytes, x10^9/L	0.9 (0.6-1.6)	1.0 (0.6-1.6)	0.8 (0.5-1.6)	0.29
Neutrophils, x10^9/L	4.8 (3.2-7.8)	4.6 (2.5-6.8)	4.9 (3.4-7.9)	0.54
Monocytes, x10^9/L	0.4 (0.3-0.7)	0.4 (0.3-0.5)	0.4 (0.3-0.7)	0.41
Platelets, x10^9/L	**250.5** (151.0-397.5)	**359.0** (208.0-458.0)	**229.0** (121.0-328.0)	**0.012**
Neutrophils/lymphocytes ratio	5.2 (3.4-9.0)	4.6 (3.0-7.4)	5.6 (3.6-9.9)	0.11
Platelets/lymphocytes ratio	292.1 (172.3-450.0)	306.6 (248.7-457.8)	276.4 (147.4-414.0)	0.23
C-Reactive Protein, mg/dL	73.8 (23.0-156.8)	72.5 (31.9-161.5)	75.0 (17.5-148.5)	0.71
Fibrinogen, mg/dL	473.0 (276.5-598.5)	422.0 (267.0-529.0)	499.0 (330.0-617.0)	0.26
D-Dimer, ng/mL	660.0 (282.0-1655.0)	458.5 (223.5-2008.5)	789.0 (337.0-1504.0)	0.72
INR	1.2 (1.0-1.3)	1.1 (1.0-1.3)	1.2 (1.1-1.3)	0.52

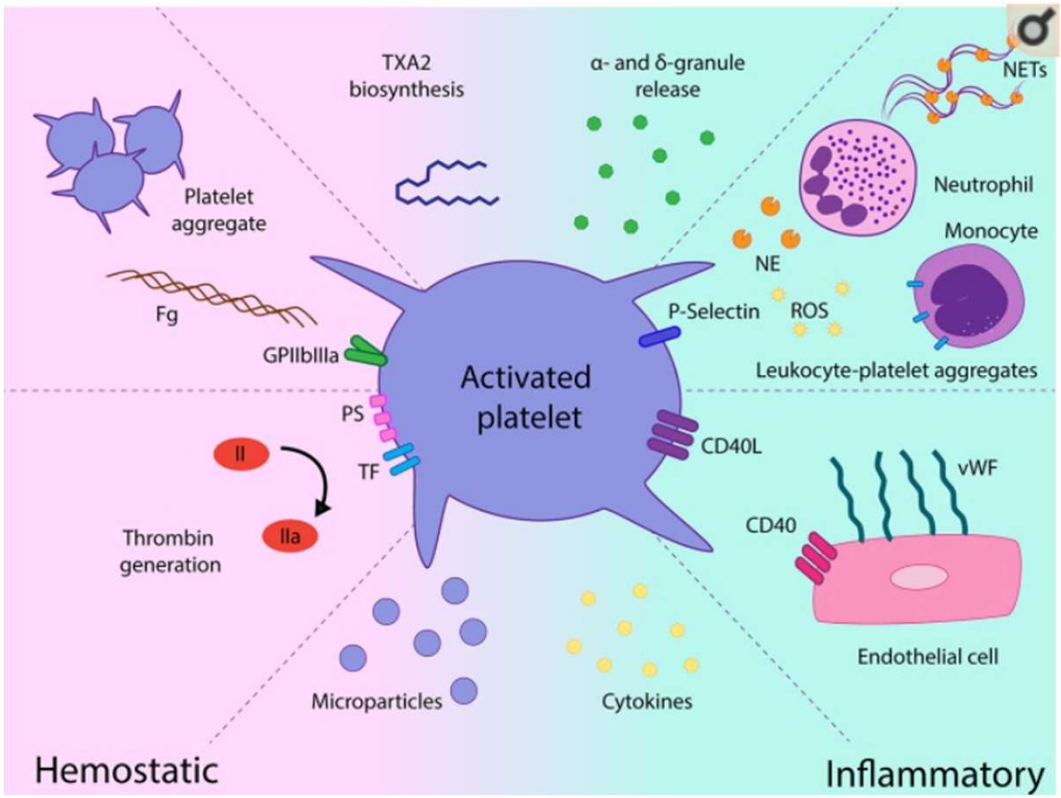
Thrombosis in ET patients has un impact on survival



Note that among the 11 deaths that occurred in ET patients, **pneumonia was more frequent (n=6, 55%)** than in PV (n=2/6, 33%) and MF (n=6/21, 29%)

and a **non significant trend (p=0.06) for fatalities due to MOF** in ET (n=5/11, 45%) and PV (n=3/6, 50%)

Platelets as Mediators of Thromboinflammation in Chronic MPN



Triggers of platelet activation in chronic myeloproliferative neoplasms (MPN).

A. Intrinsic abnormalities derived from the MPN clone,

- such as JAK2-dependent hyperactivation of signaling pathways
- and hyperreactive newly-formed platelets

B. extrinsic signals driven by enhanced interaction with activated leukocytes and endothelial cells

- soluble mediators, including classical platelet agonists, such as thrombin generated by the hypercoagulable state
- and inflammatory factors may all converge to trigger platelet activation in MPN.

Front Immunol. 2019; 10: 1373

Clin Trial GOV

The potential protective effect of antiplatelet agents in hospitalized patients with COVID-19 is being evaluated in RCTs.

- REMAP-CAP (A Randomized, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia) is planning to randomize 7,100 patients to receive multiple therapeutic interventions, including an anticoagulant arm and an antiplatelet agent arm evaluating aspirin and the P2Y12 inhibitors clopidogrel, ticagrelor or prasugrel.
- PEAC (Protective Effect of Aspirin on COVID-19 Patients; NCT04365309) aims to test the efficacy of aspirin in shortening clinical recovery time.
- RECOVERY (Randomized Evaluation of COVID-19 Therapy) is looking at the impact of aspirin on all-cause mortality among hospitalized patients is also under evaluation. This is the largest adaptive platform RCT for COVID-19 with 20,000 participants.
- RESIST (CTRI/2020/07/026791) aims to evaluate the role of aspirin plus atorvastatin in clinical deterioration in 800 hospitalized patients with COVID-19.
- CAM-COVID-19 evaluates the impact of a higher dose of aspirin (325 mg 4 times a day) along with colchicine and montelukast on inflammatory markers such as high-sensitivity C-reactive protein in 34 patients.
- PARTISAN (Prasugrel in Severe COVID-19 Pneumonia; NCT04445623) will be comparing the effect of prasugrel versus placebo among 128 patients with COVID-19 on the primary outcome of improved oxygenation

COVID outcomes and MPN

At the outset of the COVID-19 pandemic in early 2020, scientists and clinicians faced a daunting list of desperately needed answers.
The best means for settling these questions was to conduct research on an unprecedented scale and at an accelerated pace".

Marion Renault, *Nature Medicine September 2021*

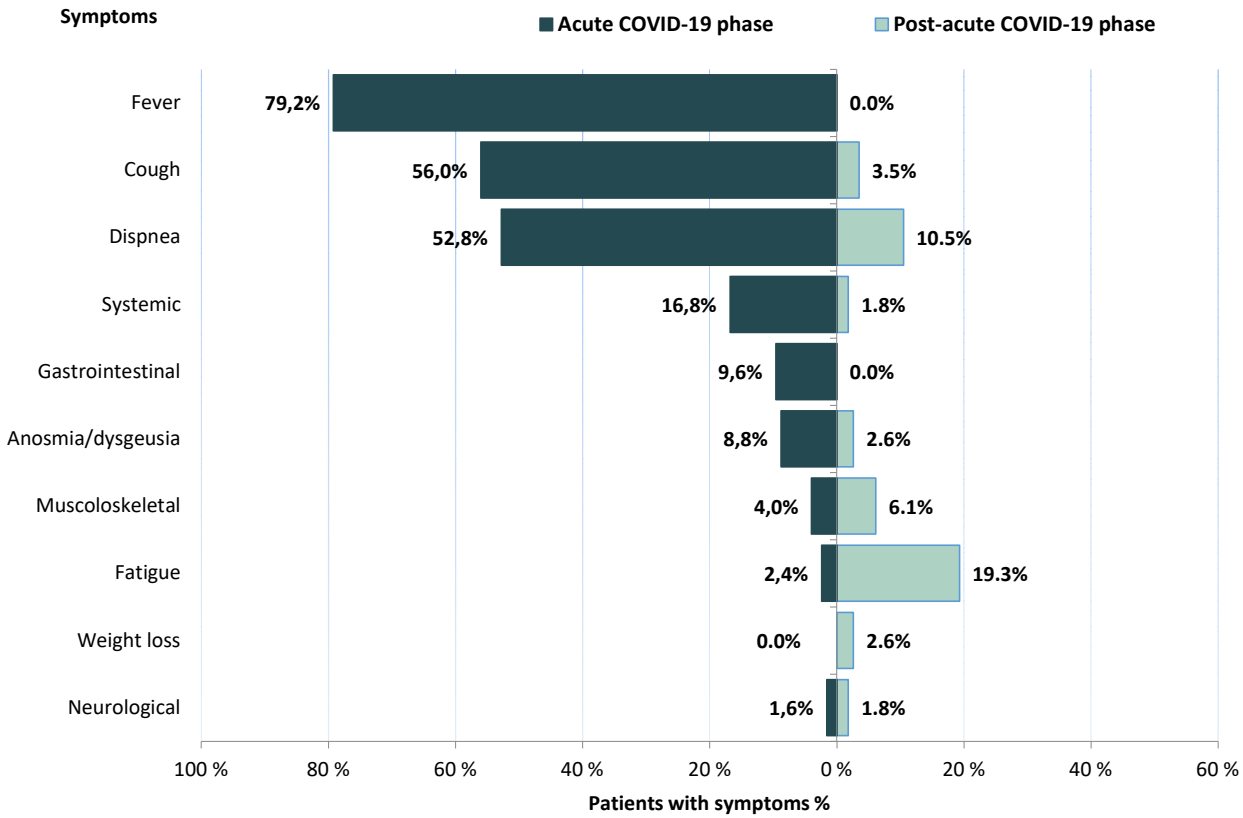
What questions have we addressed

- The **clinical epidemiology** during the acute phase in the first wave of the pandemic
- **Clinical sequelae** in patients who have passed the acute phase
- Whether outcomes changed during the **subsequent waves**
- Whether drugs for MPN have affected the **effectiveness of vaccinations**

Persistent Symptoms in Patients After Acute COVID-19

N=125, MPN-COVID cohort

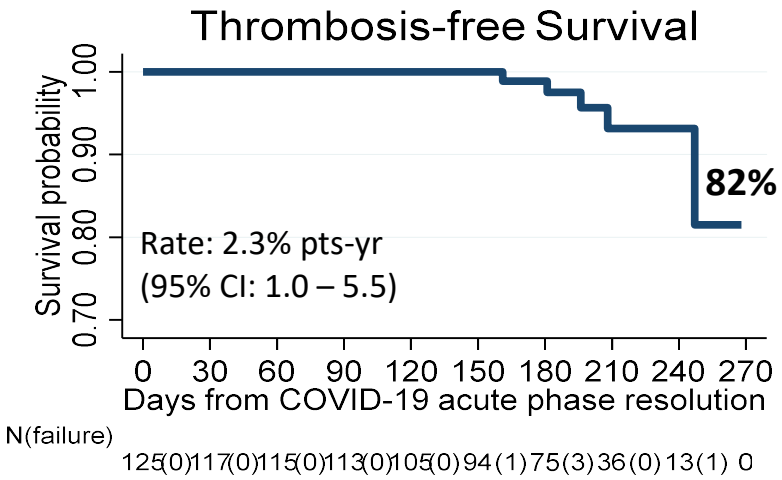
Persistent symptoms
32.1%

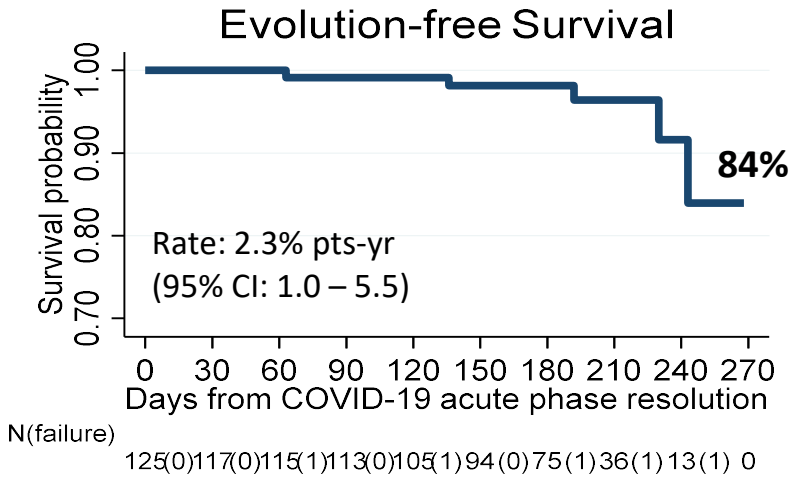


Barbui T et al, unpublished

MPN-COVID major outcomes in post-acute COVID-19 phase

Median fup: 185 days (IQR: 150-215)

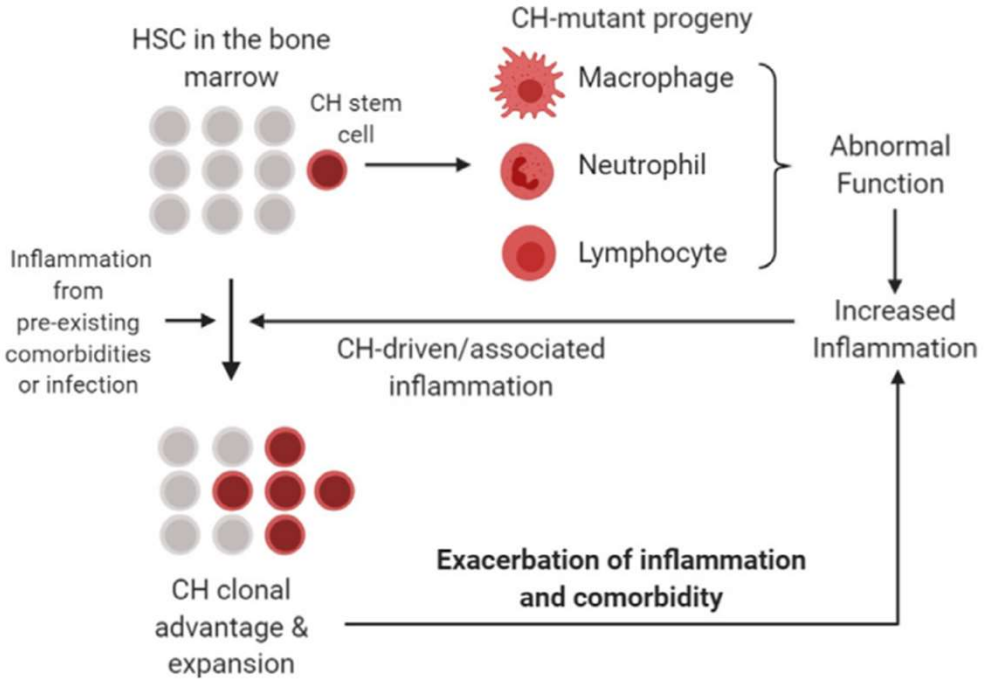




THROMBOSIS (N=5)	Fatal	MPN/age	Cyto treat	Anticoag
Intestinal ischemia	Yes	MF/71.7	No	No
Splenic infarction	No	MF/72.3	Ruxolitinb	No
DVT (legs) + PE	No	ET/61.5	Ruxolitinib	No
Acute myocardial infarction	No	PV/80.6	Hydroxyurea	No
Pheripheral arterial thrombosis	No	MF/75.4	Ruxolitinb	Yes

EVOLUTION (N=5)	Fatal	MPN/age	Cyto treat	MPN dis duration
AML	Yes	MF/49.3	Hydroxyurea	5.9 years
AML	No	ET/78.3	Hydroxyurea	6.0 years
AML	No	Pre-PMF/ 82.1	Hydroxyurea	3.8 years
Non-Hodgkin lymphoma	No	ET/60.0	No	8.6 years
Progression of Parotid Carcinoma	Yes	MF/77.3	Ruxolitinb	21.7 years

Clonal hematopoiesis (HCH) and inflammation are partners in leukemogenesis and comorbidity



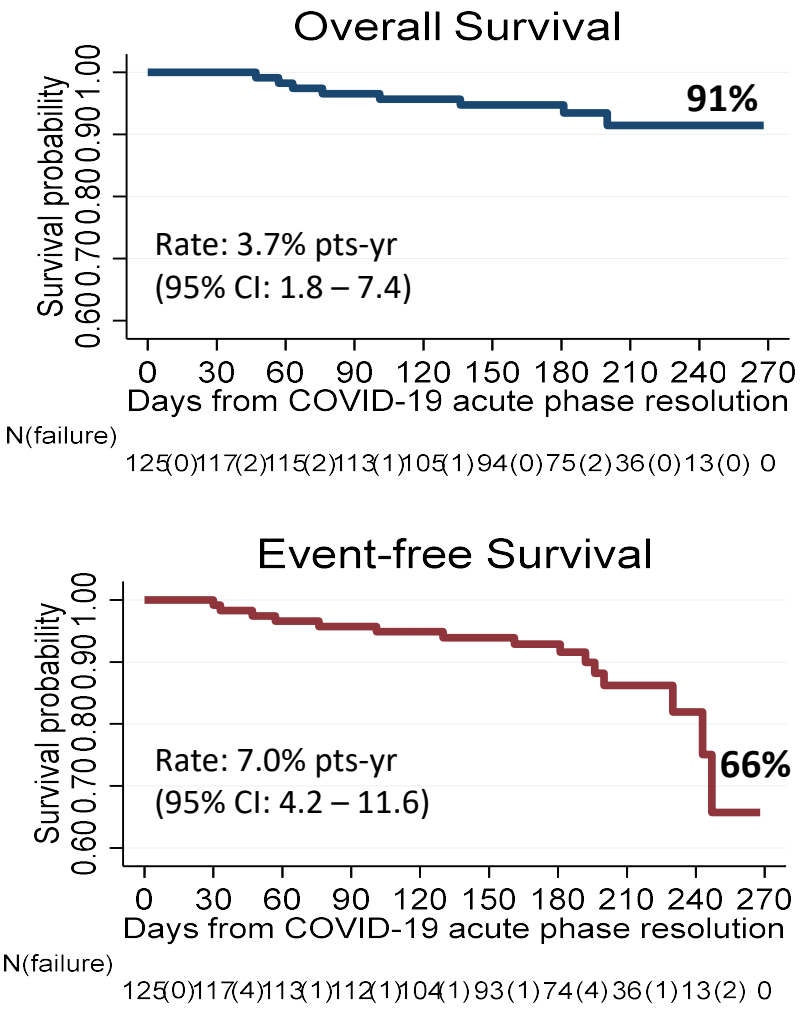
Proposed relationship between clonal hematopoiesis and inflammation.

- Macrophages, monocytes, and lymphocytes arising from the clone have a hyper-inflammatory phenotype.
- **Inflammation from CH or other sources such as infection or pre-existing comorbidities provides favorable conditions for the clone to expand.**

- Increased production of hyper-inflammatory leukocytes exacerbates the systemic inflammation, **which contributes to cardiovascular comorbidities to further clonal expansion and disease progression.**

Cook EK, Luo M, Rauh MJ. Experimental Hematology. 2020.

MPN-COVID major outcomes in post-acute COVID-19 phase



Median fup: 185 days (IQR: 150-215)

DEATHS (N=8) Causes	MPN/Age	Cyto treat	MPN dis duration
AML	MF/49.3	Hydroxyurea	5.9 years
Progression of solid cancer (parotid)	MF/77.3	Ruxolitinb	21.7 years
Progression of solid cancer (lung)	MF/80.9	unk	10.9 years
Multi Organ Failure	ET/85.7	Hydroxyurea	5.8 years
Thrombosis	MF/71.7	No	10.2 years
Heart failure	MF/82.4	unk	24.7 years
Heart failure	Pre-PMF/88.7	No	8.8 years
Unknown	ET/87.0	unk	0.8 years

COVID outcomes and MPN

At the outset of the COVID-19 pandemic in early 2020, scientists and clinicians faced a daunting list of desperately needed answers.
The best means for settling these questions was to conduct research on an unprecedented scale and at an accelerated pace".

Marion Renault, *Nature Medicine September 2021*

What questions have we addressed

- The **clinical epidemiology** during the acute phase in the first wave of the pandemic
- **Clinical sequelae** in patients who have passed the acute phase
- Whether outcomes changed during the **subsequent waves**
- Whether drugs for MPN have affected the **effectiveness of vaccinations**

Second *Versus* First Wave of COVID-19 in Patients with MPN

Tiziano Barbui[1*], Alessandra Iurlo, MD, PhD[2*], Arianna Masciulli, PhD[1*], Alessandra Carobbio, BSc[1*], Arianna Ghirardi, BSc[1*], Greta Carioli, PhD[1*], Marta Sobas, MD PhD[3*], Elena Maria Elli, MD[4*], Elisa Rumi, MD[5*], Valerio De Stefano, MD[6*], Francesca Lunghi, MD[7*], Monia Marchetti, MD[8*], Rosa Daffini, MD[9*], Mercedes Gasior Kabat, MD[10*], Beatriz Cuevas, MD[11*], Laura Maria Fox, MD[12*], Marcio Andrade, MD, PhD[13*], Francesca Palandri, MD, PhD[14*], Paola Guglielmelli, MD, PhD[15], Giulia Benevolo, MD[16*], Claire Harrison, DM, FRCP, FRCPath[17], Maria Angeles Foncillas, MD[18*], Massimiliano Bonifacio, MD[19*], Alberto Alvarez-Larran, MD[20*], Jean-Jacques Kiladjian, MD[21], Estefanía Bolaños, MD[22*], Andrea Patriarca, MD[23*], Keina Quiroz, MD[24*], Martin Griesshammer, MD, PhD[25*], Valentín Garcia Gutierrez, MD, PhD[26], Alberto Marin Sanchez, MD[27*], Elena Magro, MD[28*], Marco Ruggeri, MD[29], Juan Carlos Hernandez Boluda, MD[30*], Santiago Osorio, MD[31*], Gonzalo Carreño Gomez-Tarragona, MD[32*], Miguel Sagüés, MD[33*], Rajko Kusec, MD, PhD[34*], Begoña Navas, MD[35*], Anna Angona, MD[36*], Blanca Xicoy, MD[37*], Emma Lopez Abadia, MD[38*], Steffen Koschmieder, MD[39], Daniele Cattaneo, MD[2,40*], Cristina Bucelli, MD[2*], Edyta Cichocka, MD PhD[41*], Anna Masternak, MD[42*], Fabrizio Cavalca, MD[4*], Oscar Borsani, MD[5*], Silvia Betti, MD, PhD[6*], Marta Bellini, MD[43*], Natalia Curto-Garcia, MD[17*], Alessandro Rambaldi, MD[40,43] and Alessandro Maria Vannucchi, MD[15]

Accepted as **Oral presentation** at the 63rd ASH Annual Meeting and Exposition

- *Session Name:* ***634. Myeloproliferative Syndromes: Clinical and Epidemiological: Transplantation, COVID-19 and Biology Insights***
- *Session Date:* ***Saturday, December 11, 2021***
- *Session Time: 4:00 PM - 5:30 PM*
- *Presentation Time:* ***4:30 PM***
- *Room: Georgia World Congress Center, B312-B314*

First vs Second wave of COVID-19 in MPN

Summary

- This is **the largest analysis of MPN patients with COVID-19 in the period subsequent to first wave** of coronavirus pandemic that was characterized by conditions of exceptional lethality.
- Compared to the first, the **second wave recorded a lower severity of acute infection**, likely due (at least in part) to vaccinations, earlier diagnosis, and a positive influence of previous studies and subsequent recommendations.
- The impact on survival of **Ruxolitinib discontinuation and the greater vulnerability of ET** in **developing venous thrombosis** have been confirmed calling for specific antithrombotic prophylaxis studies.
- Our commitment is now to describe post-COVID events in a broader case series and to investigate to what extent vaccinations influence the frequency and severity of COVID-19 in MPN.

COVID outcomes and MPN

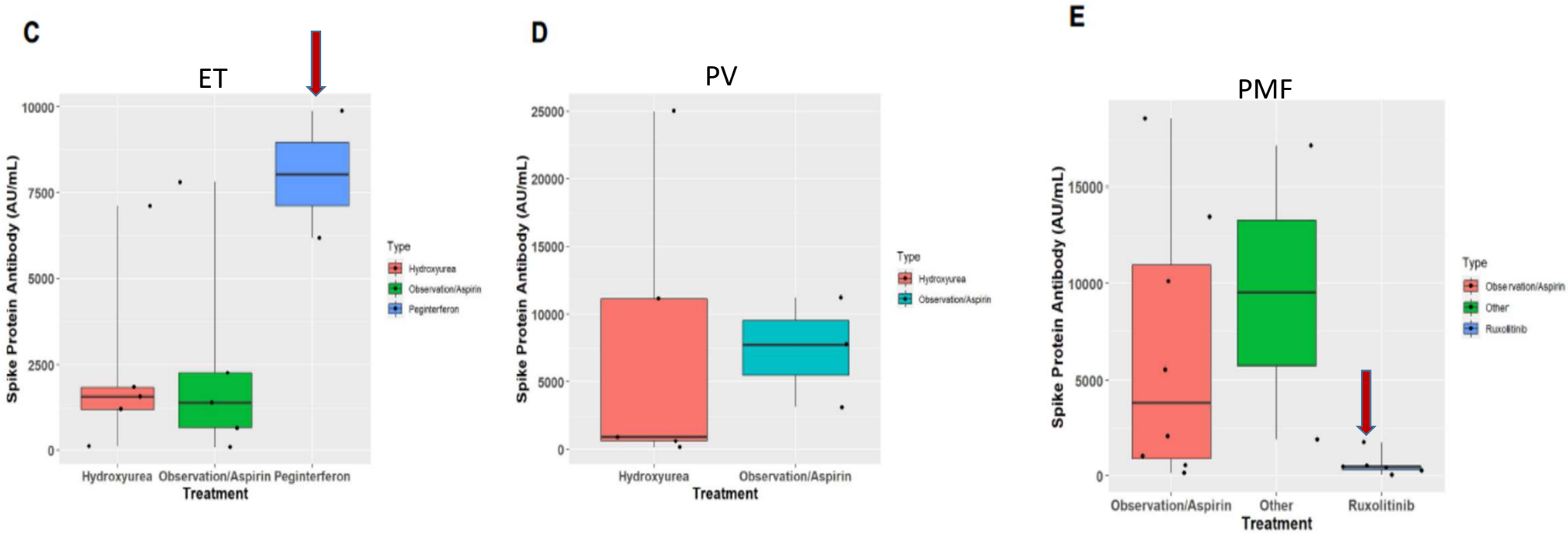
At the outset of the COVID-19 pandemic in early 2020, scientists and clinicians faced a daunting list of desperately needed answers.
The best means for settling these questions was to conduct research on an unprecedented scale and at an accelerated pace".

Marion Renault, *Nature Medicine September 2021*

What questions have we addressed

- The **clinical epidemiology** during the acute phase in the first wave of the pandemic
- **Clinical sequelae** in patients who have passed the acute phase
- Whether outcomes changed during the **subsequent waves**
- Whether drugs for MPN have affected the **effectiveness of vaccinations**

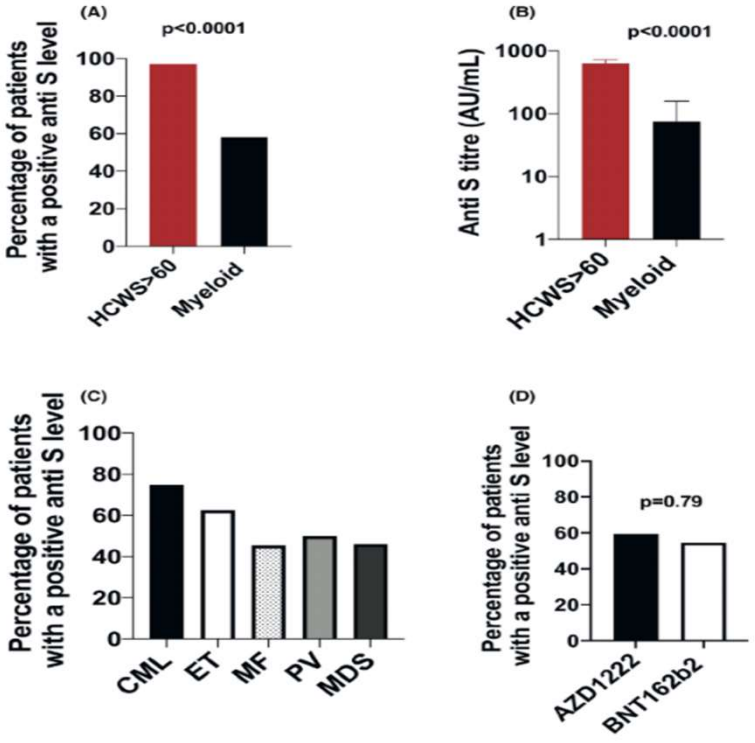
Serum Antibody Response in Patients with ET, PV and PMF Following Vaccination with SARS-CoV-2 Spike Protein messenger RNA (mRNA) vaccines



Katrin E. Kozak1 , Linda Ouyang1 , Andriy Derkach3 , Alexandra Sherman1 , Susan J. McCall1 , Christopher Famulare4 , Jordan Chervin4 , Ryan J. Daley1 , Sejal Morjaria2 , Michael J. Maruo1* , Raajit K. Rampal1,4

Serological responses >14 days after a single dose of BNT162b2 or AZD1222 vaccine in HCWs *(healthcare workers)* with no clinical or laboratory evidence of past COVID-19 exposure

- CML, n = 12; **ET,** n = 17; **MF/Pre-fibrotic** MF, n = 7; **PV,** n = 11 and MDS, n = 13



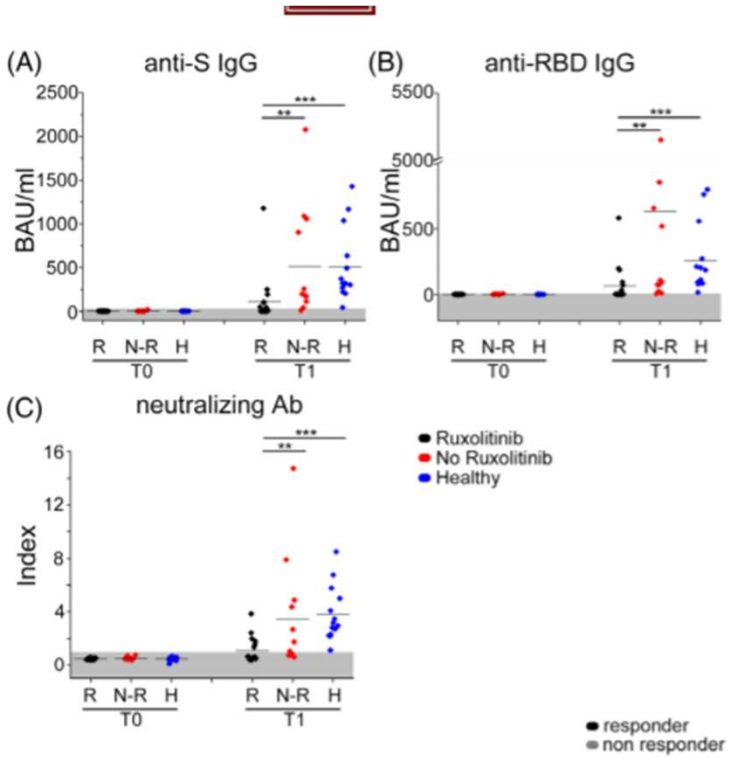
- Peg-IFN .....Highest response rates (88%, or 7/8 patients)
  Ruxolitinib... (MF n = 1; ET n = 1; PV n = 2) None
  HU..... (4/11 patients (36%)
  None .....seroconverted 65% (11/17)

- **The suboptimal responses observed here to the first vaccine dose highlight an unexpected and potentially important immuno-compromise in this patient group.**

- Further study with longer-term follow-up is required to determine responses to **booster vaccine doses**, and whether the observation of reduced seroconversion following first vaccine dose will be associated with higher rates of COVID-19 infection.

Onima Chowdhur et al, BJH, *Correspondence* 2021

Impaired response to first SARS-CoV-2 dose vaccination in myeloproliferative neoplasm patients receiving ruxolitinib



In summary, these findings, with the limitation of the small number of subjects included, **make a strong and urgent argument for an impaired early response to SARS-CoV-2 vaccine in patients receiving ruxolitinib.**

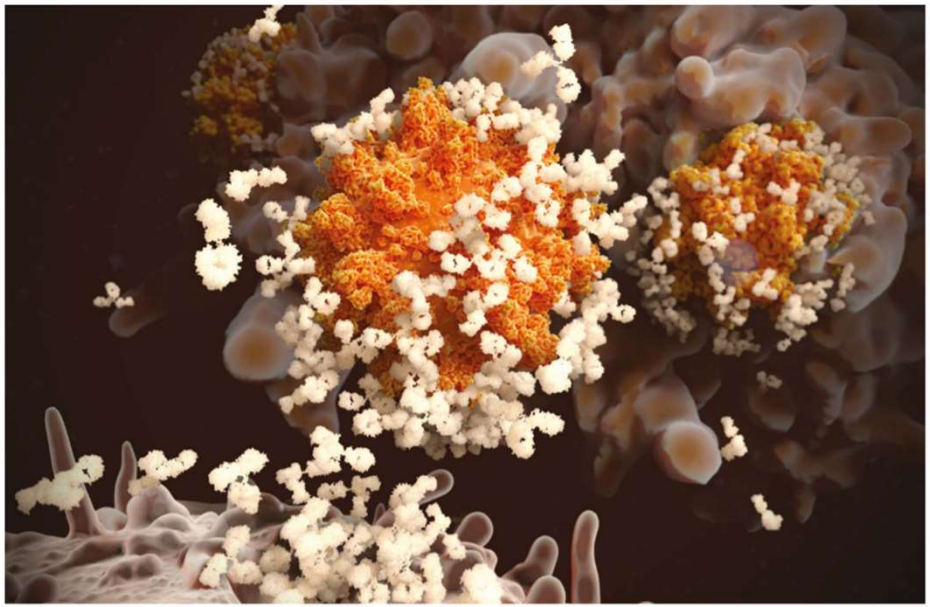
Further and future studies are needed to address **whether such unresponsive status persists after the second dose of vaccine,** as suggested by a study performed **in Israel, where the rate of seropositivity (anti-S1/ S2 IgG) after complete vaccination in patients with MPN was 42% for those using JAKi.**

Paola Guglielmelli et al, AJH July 2021 ,

What are the current recommendations for providing a third vaccination dose in immunocompromised individuals

- On August 12, the FDA amended the EUAs for both the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine to **allow for the use of an additional dose of the same vaccine in certain immunocompromised individuals,** specifically, solid organ transplant recipients or those who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.
- On August 13, the CDC vaccine advisory panel endorsed the FDA recommendation.
- ASH recommends the third dose in immunocompromise patients **including those on Ruxolitinib**

Good news for our MPN patients who recovered from COVID-19



LIAN GAERTNER/SPL

Researchers are investigating enhanced immunity to SARS-CoV-2 in people who are vaccinated after recovering from COVID-19.

COVID SUPER-IMMUNITY: ONE OF THE PANDEMIC'S GREAT PUZZLES

Why do people who have previously recovered from COVID-19 have a stronger immune response after being vaccinated than those who have never been infected?

Those who had recovered from COVID-19 months **before receiving their jabs harboured antibodies capable of defanging the mutant spike,** which displays much more resistance to immune attack than does any known naturally occurring variant.

These peoples' antibodies even blocked other types of coronavirus. "It's very likely they will be effective against any future variant that SARS-CoV-2 throws against them,"

By Ewen Callaway Nature | Vol 598 | 21 October 2021

Conclusion

- In this multicenter European study, we described a relatively large MPN series of 175 patients with MPN and COVID-19, **collected under conditions of exceptional COVID-19 lethality, from February to June 2020,** and report estimates and risk factors of mortality.
- An unexpected result of this study was the association between **Ruxolitinib discontinuation and and overall mortality.**
- In patients with PV and MF, the rate of VTE was 4.8% and 5.4%, respectively, overall similar to that reported in non-MPN acutely ill medical patients with COVID-19 admitted in regular wards. Conversely, **the rate of VTE was higher in ET**

Next questions:

- **Confirm the results** relating to the acute phase of the first wave of COVID-19 (Feb-May / 2020)
- Describe **clinical epidemiology in the second wave of infection**
- Describe **vaccination results**