Patients

Webinars

EuroBloodNet

Risk and Course of COVID-19 in AA and PNH Patients, Including Vaccination Strategies

Speaker: Austin Kulasekararaj

Role : Consultant Haematologist

Institution: King’s College Hospital and King’s College London

Co-funded by
the Health Programme
of the European Union

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Content of the session

- COVID-19 and its impact on AA/PNH
- Impact of vaccination on AA and PNH
- Effectiveness of vaccine in AA and PNH
  - On treatment or not
  - 4th dose
- Effectiveness of anti-viral medications for AA/PNH patients

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COVID-19 vaccination antibody responses in patients with aplastic anaemia and paroxysmal nocturnal haemoglobinuria

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SARS-CoV-2 vaccination responses in PNH and Aplastic Anaemia Study

Study:	
Location:	
Inclusion:	
Exclusion:	

UNIVERSITY OF LEEDS

PNH National Service
LEEDS & LONDON

the aplastic anaemia trust

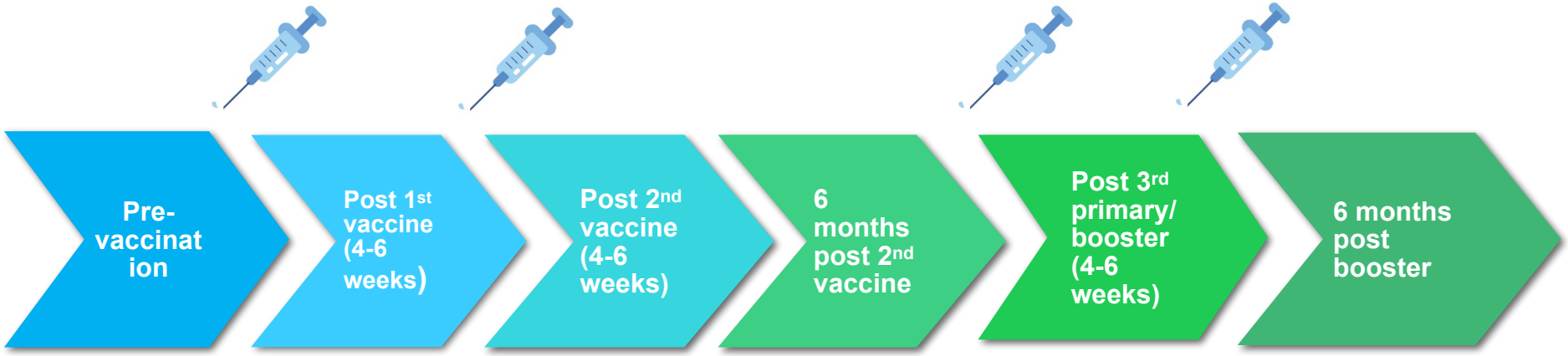
PNH RTB

NHS
The Leeds Teaching Hospitals
NHS Trust

Blood cancer UK

	Healthy volunteers	Classical PNH	AA/PNH overlap	AA	Significance *p* value
Number of subjects	45	76	53	42	
Age					
Mean (range)	44·8 (24-63)	53·8 (19-88)	55·2 (21-8-83)	56·4 (22-94)	
Median (IQR)	46·0 (36·5-54·5)	52·5 (41·24-65)	59 (39·5-72)	55 (44-70·5)	0·0045
Female, n (%)	33 (73·3%)	42 (55·3%)	22 (41·5%)	21 (50·0%)	0·015
Number of pre-vaccination samples analysed	17	12	8	1	
Interval (days) post first vaccination					
Median (IQR)	35·0 (30-47)	35 (29·25 – 40)	34 (29·5 – 41)	33·5 (29·5 – 52·25)	0·82
Number of post first vaccine samples analysed	41	68	41	22	
Interval (days) post second vaccination					
Median (IQR)	31·5 (28·0-38·0)	38·0 (30·0-49·0)	36·0 (31·0 – 50·0)	55·0 (38·5 – 70·75)	<0·0001
Number of post second vaccine samples analysed	42	71	47	38	
Complement inhibitor therapy, n (%)	n/a	74 (97·4%)	47 (88·7%)	0	
Previous ATG, *n* (%)	n/a	0	34 (64·1%)	29 (69·0%)	
If ATG, >12 m ago (%)	n/a	n/a	100	100	
Previous alemtuzumab, n (%)	n/a	0	2 (3·8%)	1 (2·4%)	
Previous ciclosporin/tacrolimus therapy, n (%)	n/a	4 (5·3%)	43 (81·1%)	39 (92·9%)	
Current ciclosporin/tacrolimus therapy, n (%)	n/a	0	20 (37·7 %)	19 (45·2 %)	
Total subjects in cohort, n, by vaccine type					<0·001
Follow up time, days, median (IQR)	n/a	407 (402·8 – 415)	406 (402·5 – 410)	409 (401·3 – 416·5)	
ChAdOx1-S, n (%)	14 (31·1%)	54 (71·1%)	34 (64·2%)	24 (57·1%)	
Total BNT162b2, n (%)	30 (66·7%)	22 (28·9%)	16 (30·2%)	18 (42·9%)	
Data unavailable, n (%)	1 (2·22%)	0	3 (5·7%)	0	
Post first vaccine samples analysed, n, by vaccine type					++
ChAdOx1-S, n (%)	14 (31·1%)	47 (69·1%)	28 (68·3%)	15 (68·2%)	
BNT162b2, n (%	28 (68·3%)	21 (30·9%)	12 (29·3%)	7 (31·8%)	
Data unavailable, n (%)	0	0	1 (2·4%)	0	
Post second vaccine samples analysed, n, by vaccine type					
ChAdOx1-S, n (%)	13 (31·0%)	48 (67·6 %)	31 (66·0%)	22 (57·9%)	
BNT162b2, n (%)	28 (66·7%)	23 (32·4%)	16 (34·0%)	16 (42·1%)	
Data unavailable, n (%)	1 (2·3%)	0	0	0	

Design



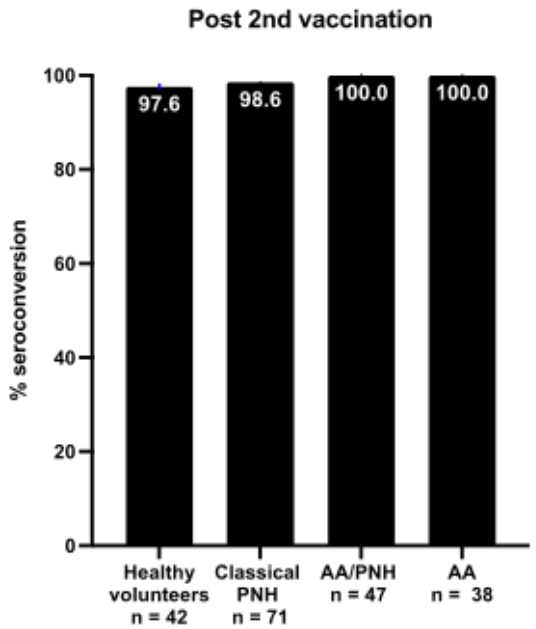
Serum

- Humoral immune response (IgG/A/M)
- Virus neutralisation assay (Francis Crick Institute)
- Total immunoglobulin

Mononuclear cells

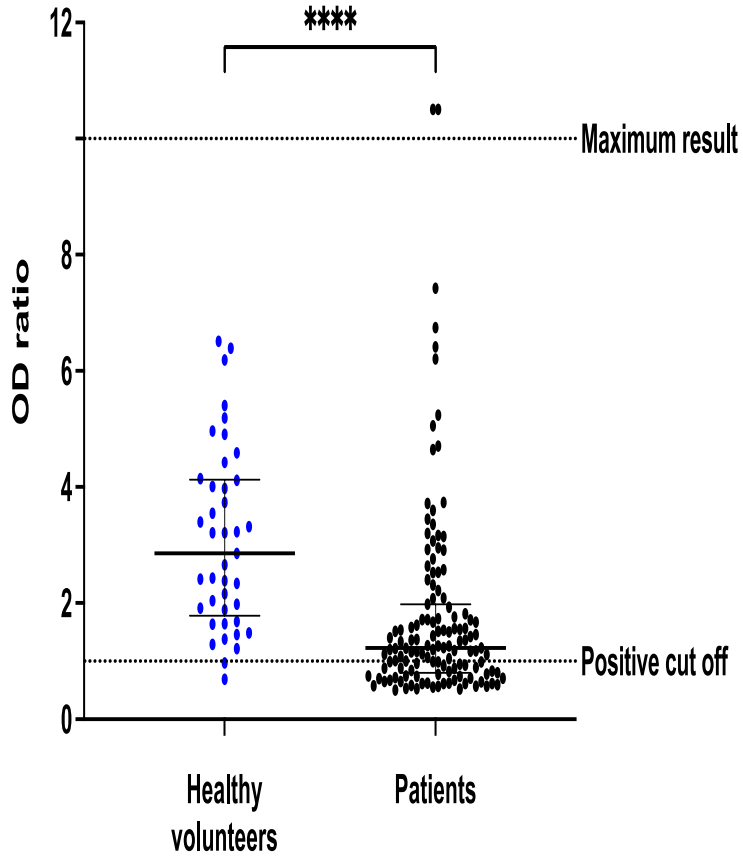
- Viable MNC cryopreserved
- T-cell IFN-γ release assay

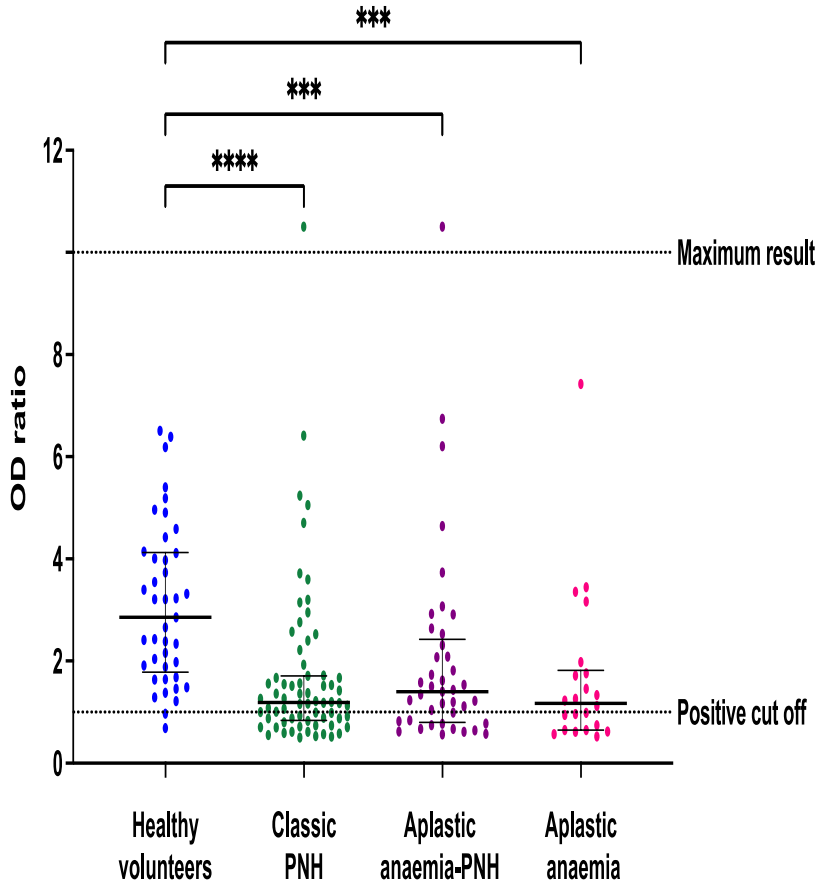
- >1000 serum and MNC samples collected over 6 timepoints from 272 subjects (227 patients and 45 healthy volunteers)

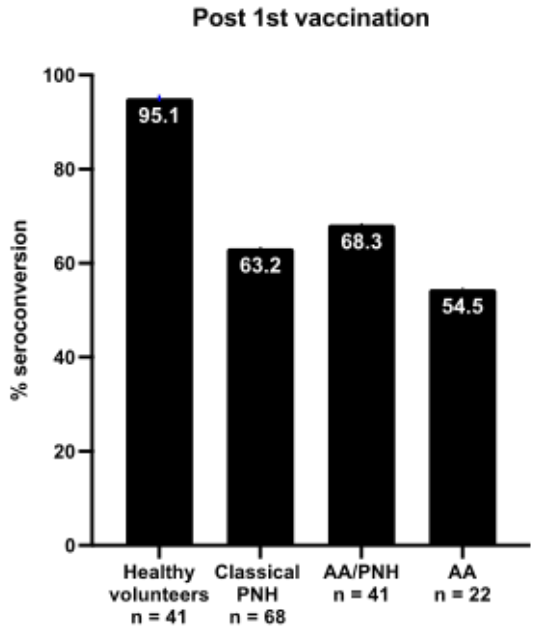

Post 2nd vaccination
% seroconversion
100
80
60
40
20
0
97.6
98.6
100.0
100.0
Healthy volunteers n = 42
Classical PNH n = 71
AA/PNH n = 47
AA n = 38

SARS-CoV-2 spike-specific IgA/G/M antibody responses to vaccination in patients with PNH and AA versus healthy volunteers

Post 1st vaccine



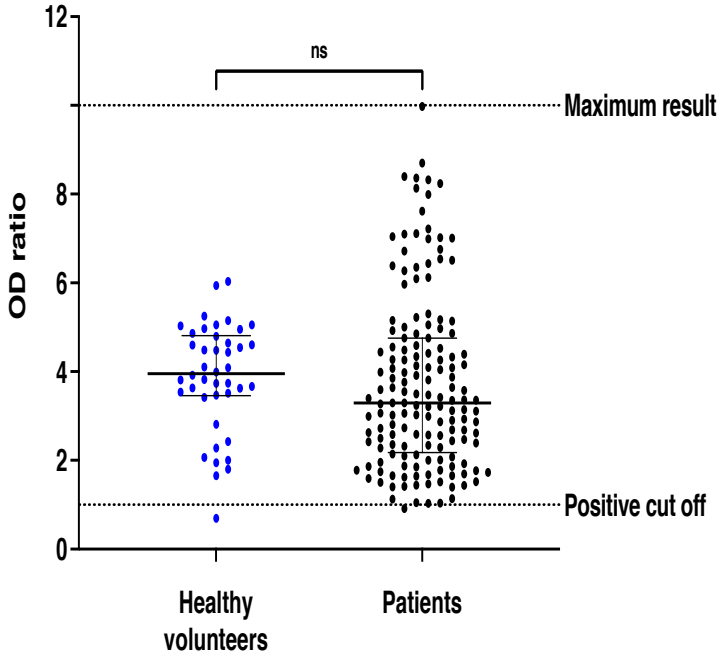


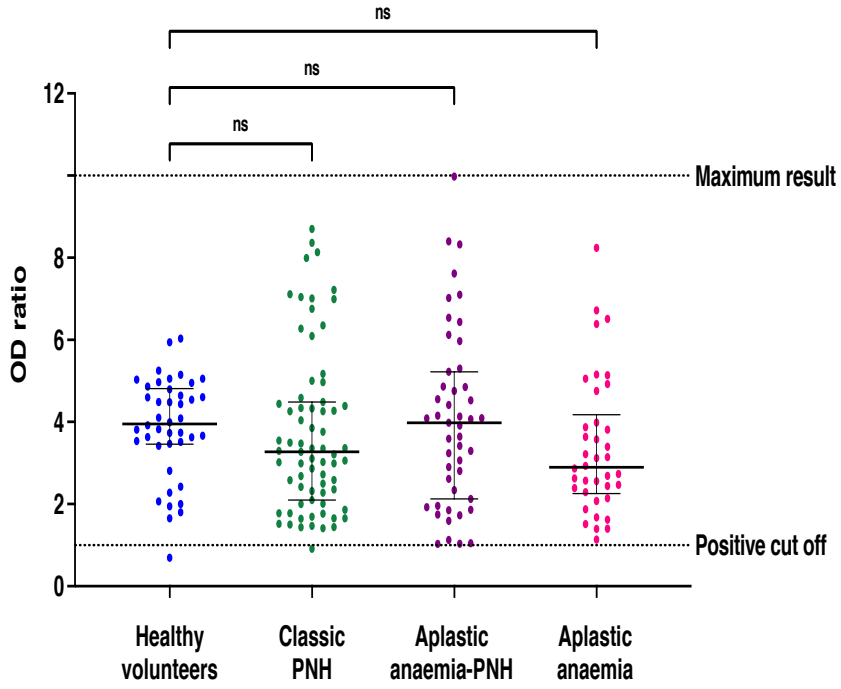


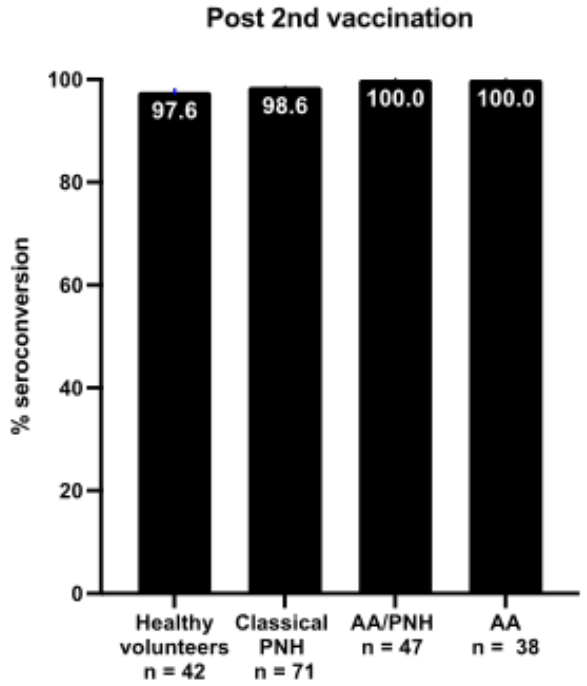
*Data points represent mean of duplicates. Bars show median and IQR. *p<0·05; **p<0·01; ***p<0·001; ****p<0·0001; ns, not significant. Pending publication by Lancet Haematology. A.Pike et al. University of Leeds, 2022*

SARS-CoV-2 spike-specific IgA/G/M antibody responses to vaccination in patients with PNH and AA versus healthy volunteers

Post 2nd vaccine







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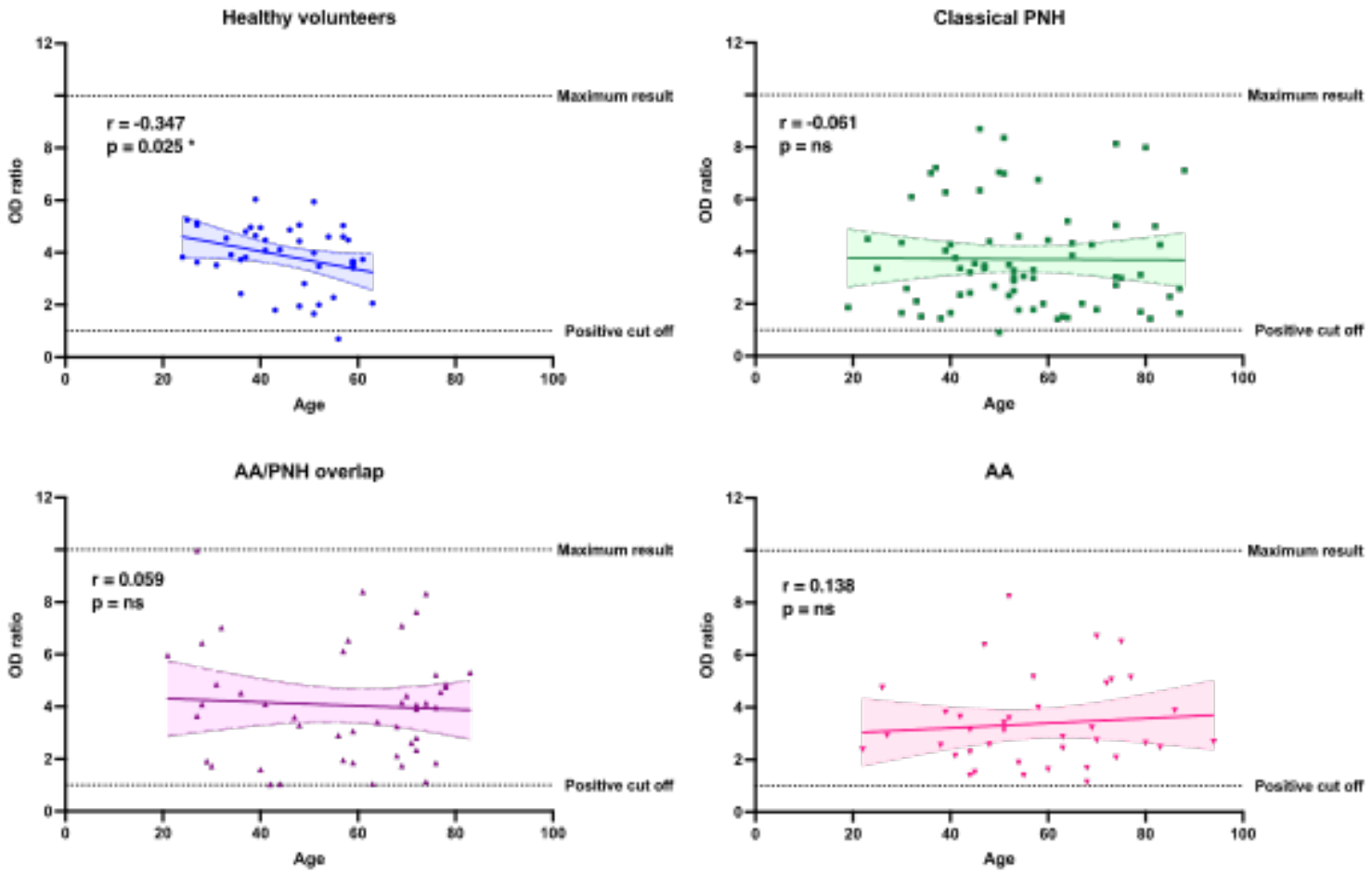
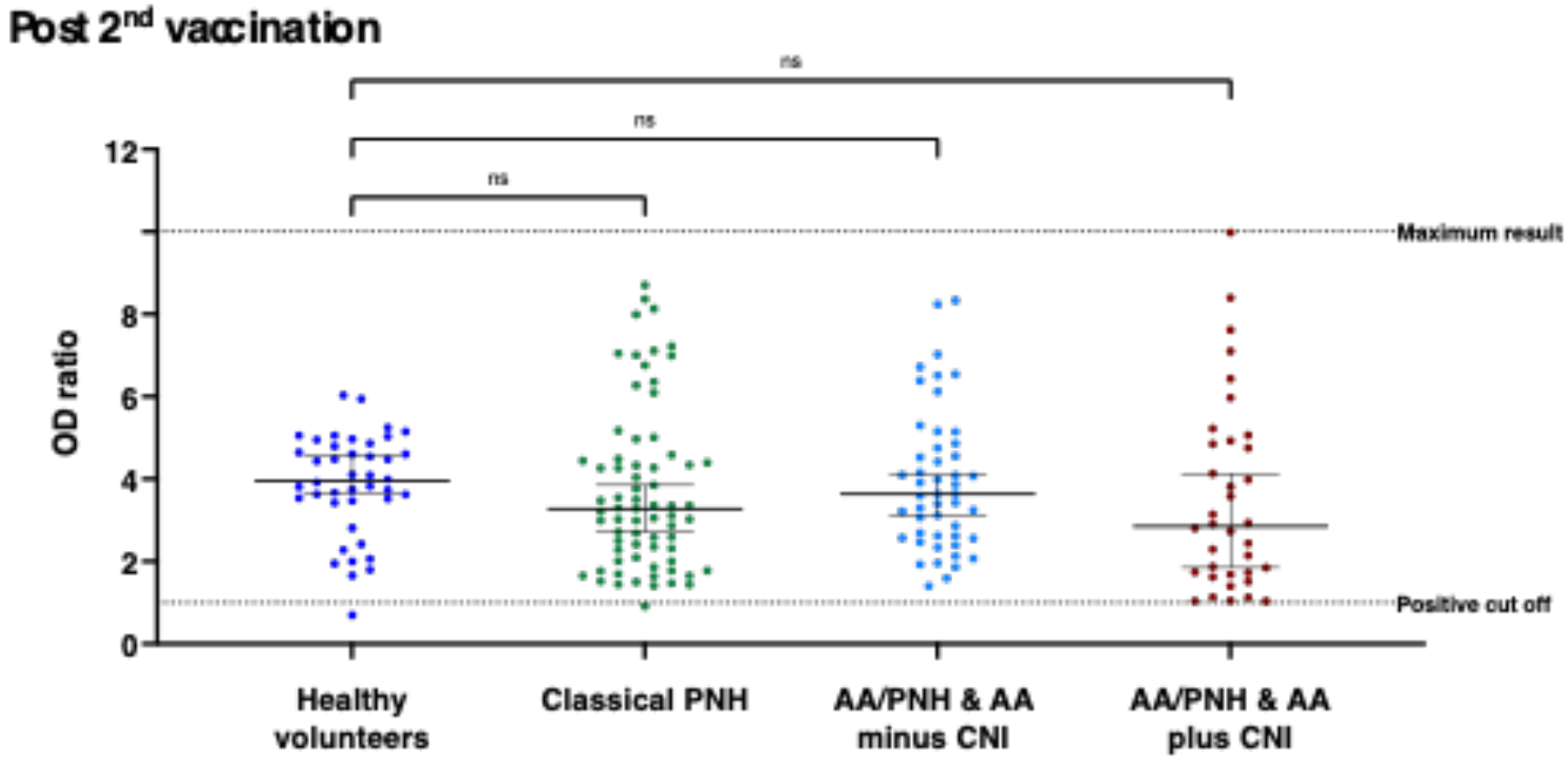
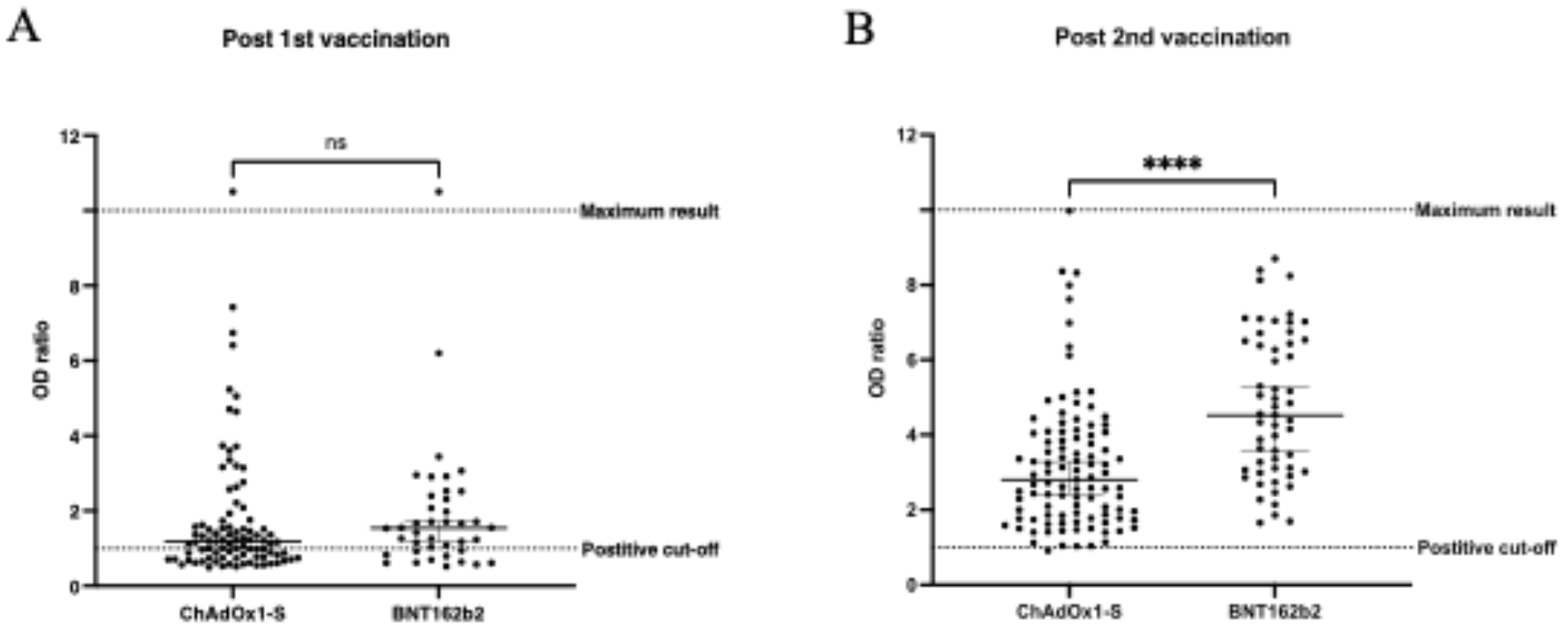
Impact of age



Impact of cyclosporin



Impact of type of vaccine



SARS-CoV-2 vaccination responses in PNH and Aplastic Anaemia Study

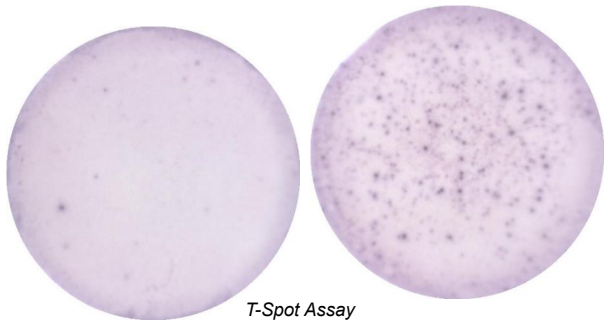
Summary:

- Reduced response to 1 vaccination
- **Factors predictive of lack of response**: patients versus healthy volunteers, female sex, viral vector vaccination
- **Factors not predictive of lack of response**: current CNI immunosuppressant, current complement inhibitor, age, previous reduced response to meningococcal vaccination

- Importance of at least 2 vaccinations in patients with PNH/AA
- Similar side effects to healthy volunteer studies
- No excess adverse events

Ongoing work:

- Quantitative IgG levels
- Post 3rd/4th vaccine analysis
- Viral neutralization (Francis Crick Institute collaboration)
- T cell responses



T-Spot Assay

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Corrado Girmenia

Specialist in Hematology,

Specialist in Microbiology and Virology

UOSD Pronto soccorso e Accettazione Ematologica

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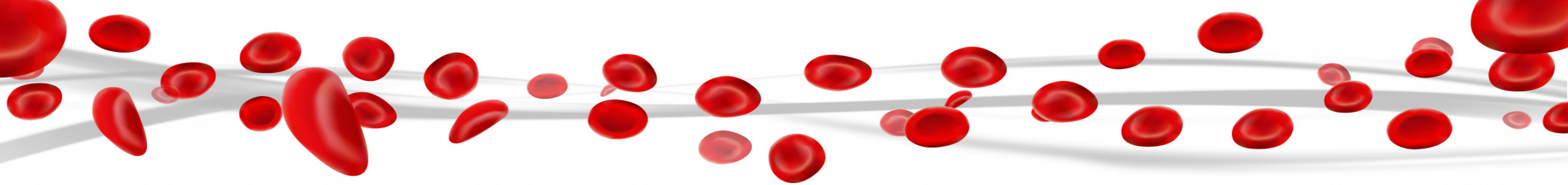
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
MSD					X	X	
Biotest					X	X	
Janssen						X	
Novartis						X	
Abbvie					X		
Amgen					X		
Alexion Pharma					X	X	



Key issues in the management of COVID-19 in PNH and AA patients

- What is the risk for PNH and AA patients of getting COVID-19 and of severe COVID-19 compared to the general population?
- Is SARS CoV-2 vaccination effective in PNH and AA patients?
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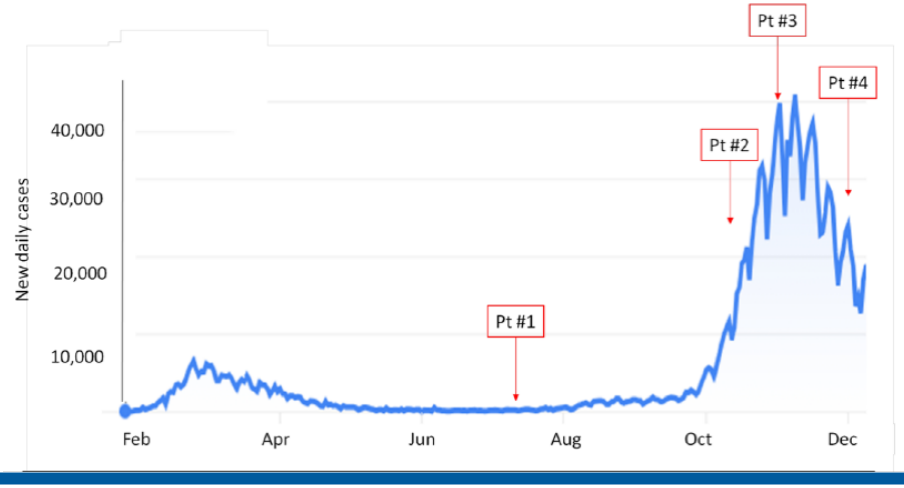
COVID-19 in patients with paroxysmal nocturnal haemoglobinuria: an Italian multicentre survey

Barcellini et al. BJH. 2021 Sep;194(5):854-856.

A survey on 156 patients with PNH (median age 50 years, range 19–86; 88 females and 68 males) among eight Italian reference centres

Four patients were found to be positive, two asymptomatic and two with mild symptoms (cumulative incidence 2.5%), mostly concomitant to the second wave of infections.



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Out of 237 patients on anti-complement therapy, 4 (1.7%) were diagnosed with SARS CoV 2 infection. All were hospitalized and one requiring ventilation support died after 23 days.

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Out of 23 patients with severe AA and SARS CoV-2 infection only 3 (13%) developed a severe disease and only 1 patient died.

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Giannotta et al, AJH 2022 Mar 23:10.1002/ajh.26545

A systematic survey to evaluate complications and hemolytic flares in 87 PNH patients who received SARS-CoV-2 vaccinations among 8 Italian centers.

13 hemolytic exacerbations were observed in 12 patients (13.8%) three of whom requiring supportive therapy and hospitalization. Anti-spike protein antibodies were available for 18 patients, of whom 16 on anti-complement treatment. Fifteen showed protective titers (median 838 U/mL, range 26;7500 U/mL), whilst 3 had a titer <80 U/mL (1 with an associated bone marrow failure, and 2 on CIs). Anti-complement treatment was not associated with impaired antibody response to vaccine.

International Journal of Hematology (2022) 116:55–59

Hemolysis induced by SARS-CoV-2 mRNA vaccination in patients with paroxysmal nocturnal hemoglobinuria

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Of the 12 patients receiving complement inhibitors, only one had a hemolytic reaction after vaccination, but it did not meet the definition of breakthrough hemolysis. By contrast, hemolytic attacks were observed in two of the five untreated patients with PNH, and one of them required a blood transfusion.

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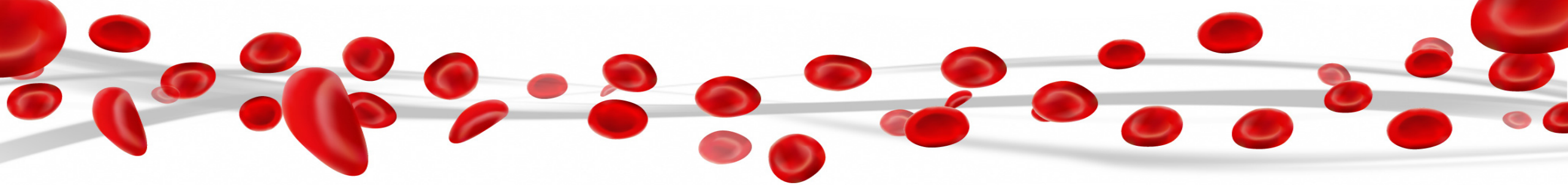

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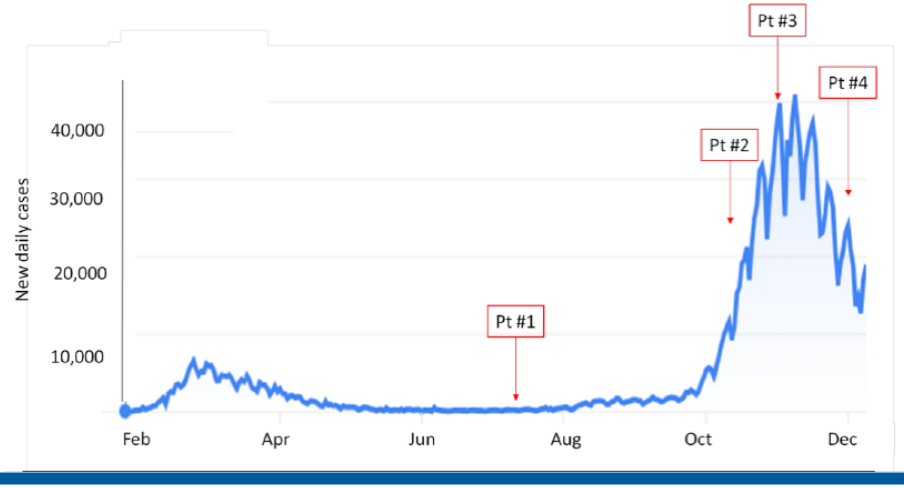

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