ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

COVID-19 and COVID vaccination in patients with hematological malignancies

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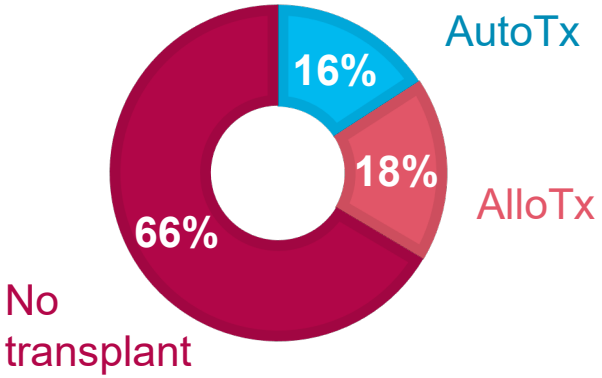
Bristol Myers Squibb™

466-BE-2100027 – 10/21

COVID-19 in hematological malignancies

Spanish experience

Retrospective analysis (N=367)



Symptoms

- Fever
- Fatigue
- Cough
- Diarrhea (22%)

71-82% had abnormal radiological findings

Transplant patients

- COVID-related mortality: **17%** (auto) and **18%** (allo)
- Median time from transplant: 790 days (auto) & 441 days (allo)
- Median age: 61 yrs (auto) & 48 yrs (allo)

No-transplant patients

- **31%** COVID-related mortality
- 11% active smoker
- 21% cardiomyopathy
- 48% AHT

Older (median age 71 years), more comorbidities

Risk factors for COVID-related mortality

Multivariate analysis:

- CRP > 20 (x 3.3)
- Uncontrolled hematological malignancy (x 2.9)
- ANC < 500/mm³ (x 2.8)
- ECOG 3-4 (x 2.6)
- Age > 70 yrs (x 2.1)

Piñana JL, et al. *Exp Hematol Oncol.* 2020;9:21.

COVID-19 in MM patients

Czech experience

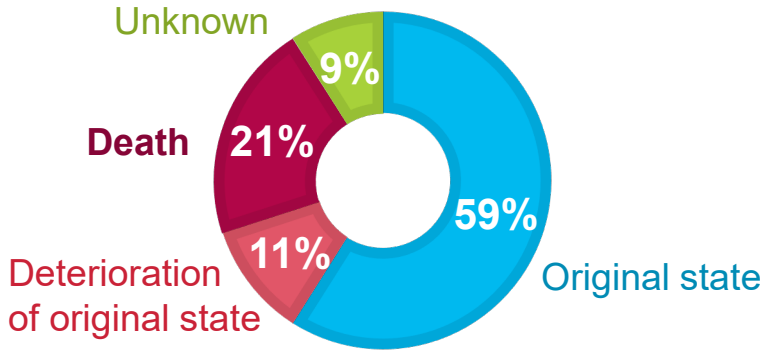
MM patients with COVID-19 (N=371)

March 2020 – May 2021

Hospitalization

45% were hospitalized (median of 11 days)
→ 30% ICU

Final state after COVID-19



Associated with mortality

Older age
Prior transplant
Prior anti-CD38

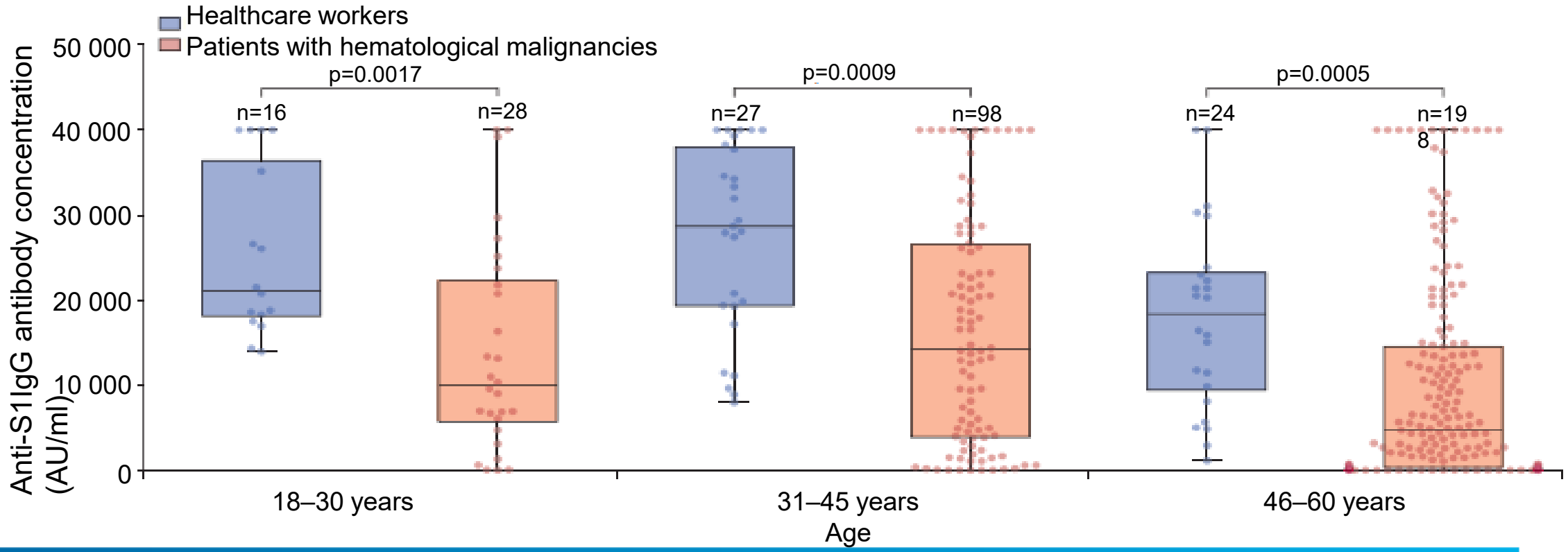
Radocha J, et al. Oral presentation at the 18th International Myeloma Workshop, September 8–11 2021, Vienna, Austria.

COVID mRNA vaccine in hemato malignancies

Lithuanian experience

857 patients included

- 2 vaccinations with BNT162b2 COVID mRNA vaccine
- Anti-SARS-CoV-2-S1 IgG antibodies quantified with Abbott Architect assay

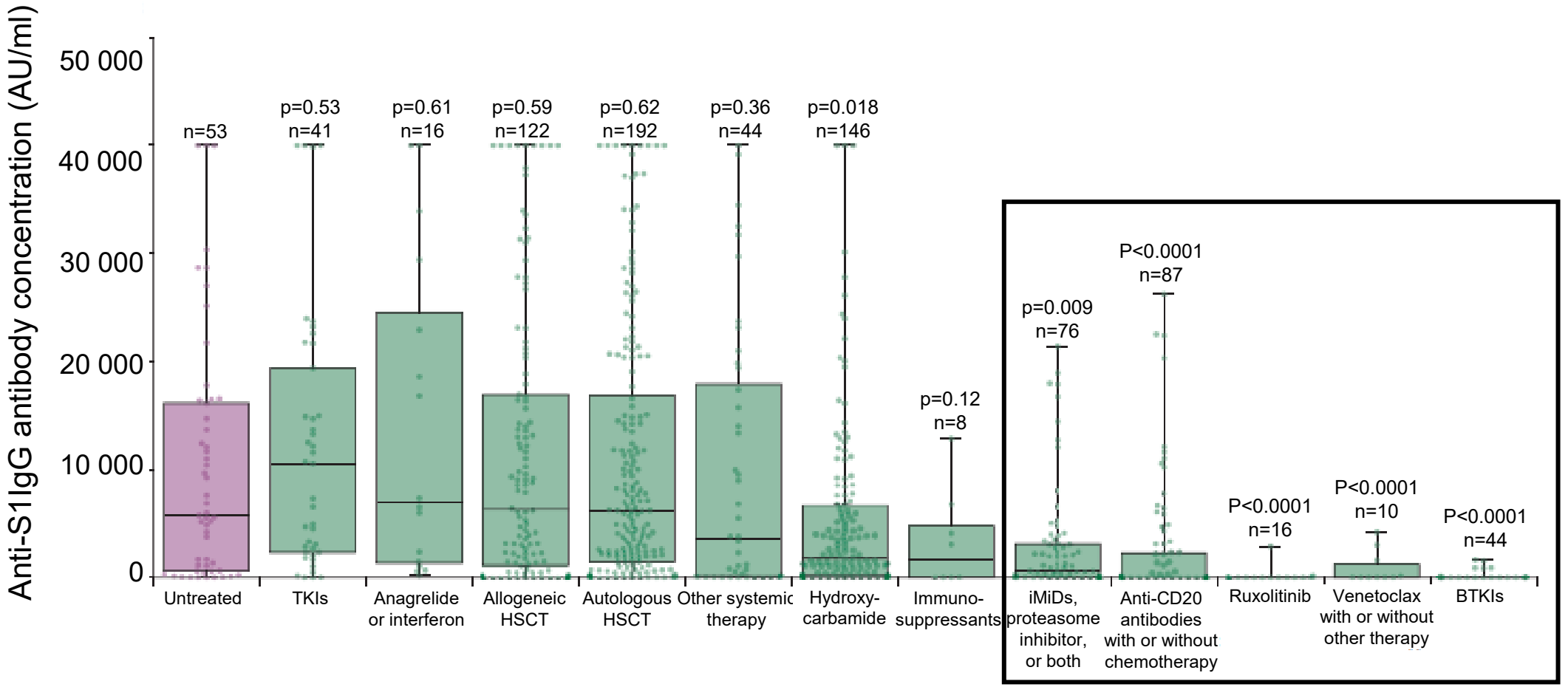


Maneikis K, et al. *Lancet Haematol.* 2021;8(8):e583-e592.

BNT162b2 COVID mRNA vaccine in hemato malignancies

Very low/absent responses in patients treated with:

- Anti-CD20



Responses if >12 months after stop of treatment

Maneikis K, et al. *Lancet Haematol.* 2021;8(8):e583-e592.

COVID-19 vaccine response trial in MM and MW

Massachusetts General Hospital and Dana-Farber Cancer Insititute experience

Prospective clinical trial

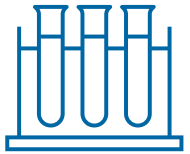
3 types of vaccines:

- BNT162b2 (Pfizer)
- mRNA-1273 (Moderna)
- JNJ-78436735 (Johnson&Johnson)

Measuring immune response

Samples 1 month after first and second vaccination (if done)

SARS-CoV-2 spike protein antibody detection



Elecsys assay titers **>250 U/mL** are associated with **clinical protection**

Patient population	Any Ab response	Median Ab response	Ab titers > 250	Better responses (expected in 50–65% of cases)
89 Patients with MM	**91%** Patients with MM	**178 U/mL** Patients with MM	**58%** Patients with MM	MM: First line CR/VGPR
45 Patients with (MW)	**46%** Patients with MW	**3 U/mL** Patients with MW	**24%** Patients with MW	MW: Treatment-naive

Branagan A, et al. Oral presentation at the 18th International Myeloma Workshop, September 8–11 2021, Vienna, Austria.

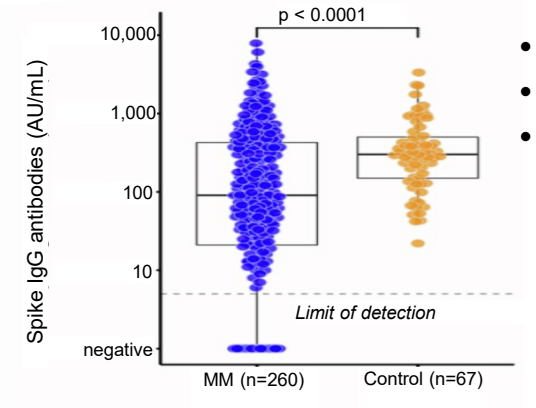
COVID-19 vaccine response evaluation in MM

Mount Sinai experience

Retrospective analysis (N=320)

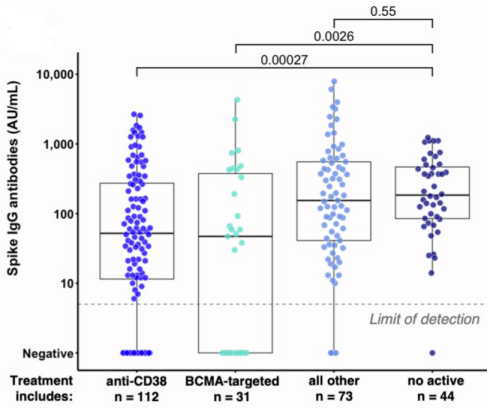
- Patients with MM
- 2 doses of mRNA vaccine
- 70% BNT162b2 (Pfizer)
- 30% mRNA-1273 (Moderna)

Highly variable responses



- Median titer 100 U/mL
- 16% had no response
- Limited durability as compared to healthy controls

Associated with lower and less durable responses



No CR
Lymphopenia
BCMA-targeted treatment
Anti-CD38 antibody treatment

CD4 T cell responses

CD4 T cell responses diminished in anti-spike IgG non-responders (correlation?)

Third dose mRNA vaccine

Anecdotally effective in heavily treated MM patient

Van Oekelen O, et al. Oral presentation at the 18th International Myeloma Workshop, September 8–11 2021, Vienna, Austria.
Van Oekelen O, et al. *Cancer Cell.* 2021;39(8):1028-1030.

COVID-19 vaccine response evaluation in MM patients

US experience[1]

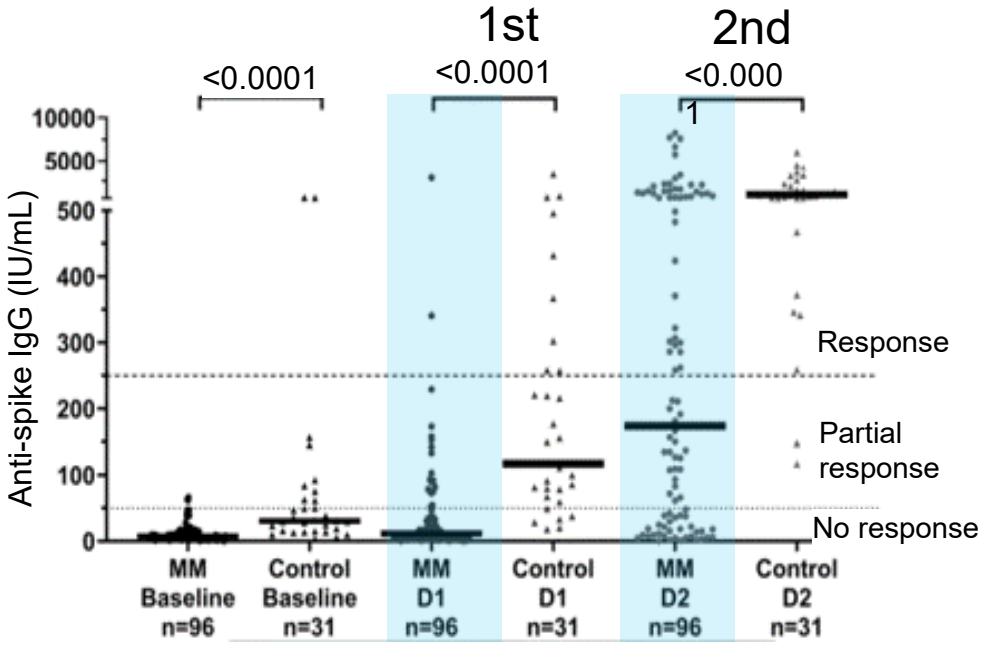
Observational trial (N=103)

- Patients with MM
  - BNT162b2 (Pfizer)
  - mRNA-1273 (Moderna)

Responders after 2 injections

- 33% <50 IU/mL
- 22% 50-250 IU/mL
- **45% >250 IU/mL**

Anti-SARS-CoV-2 spike IgG levels



Associated with inferior responses

- Older age (> 68 yrs)
- Low lymphocyte counts
  - Cfr Hamburg study (IMW Vienna 2021): < 30 circulating CD19+ cells[2]
- Reduced levels of uninvolved immunoglobulins
  - UCLH study (IMW Vienna 2021): IgM < 400 mg/L[3]
- Steroid use
- More advanced disease state
- No CR

Inferior responses in multivariate analysis:

Low uninvolved IgM
Vaccination with Pfizer (27%) vs Moderna (63%) vaccine

1. Stampfer SD, et al. *Leukemia.* July 29, 2021; online ahead of print. doi: 10.1038/s41375-021-01354-7. 2. Ghandili S, et al. Oral presentation at the 18th International Myeloma Workshop, September 8–11 2021, Vienna, Austria. 3. Chan WY, et al. Oral presentation at the 18th International Myeloma Workshop, September 8–11 2021, Vienna, Austria.

COVID-19 vaccine response evaluation in MM patients

Greek experience

Observational trial (N=213)

- Patients with MM
  - BNT162b2 (Pfizer) 2 doses
  - AZD1222 (AstraZeneca) 1 dose

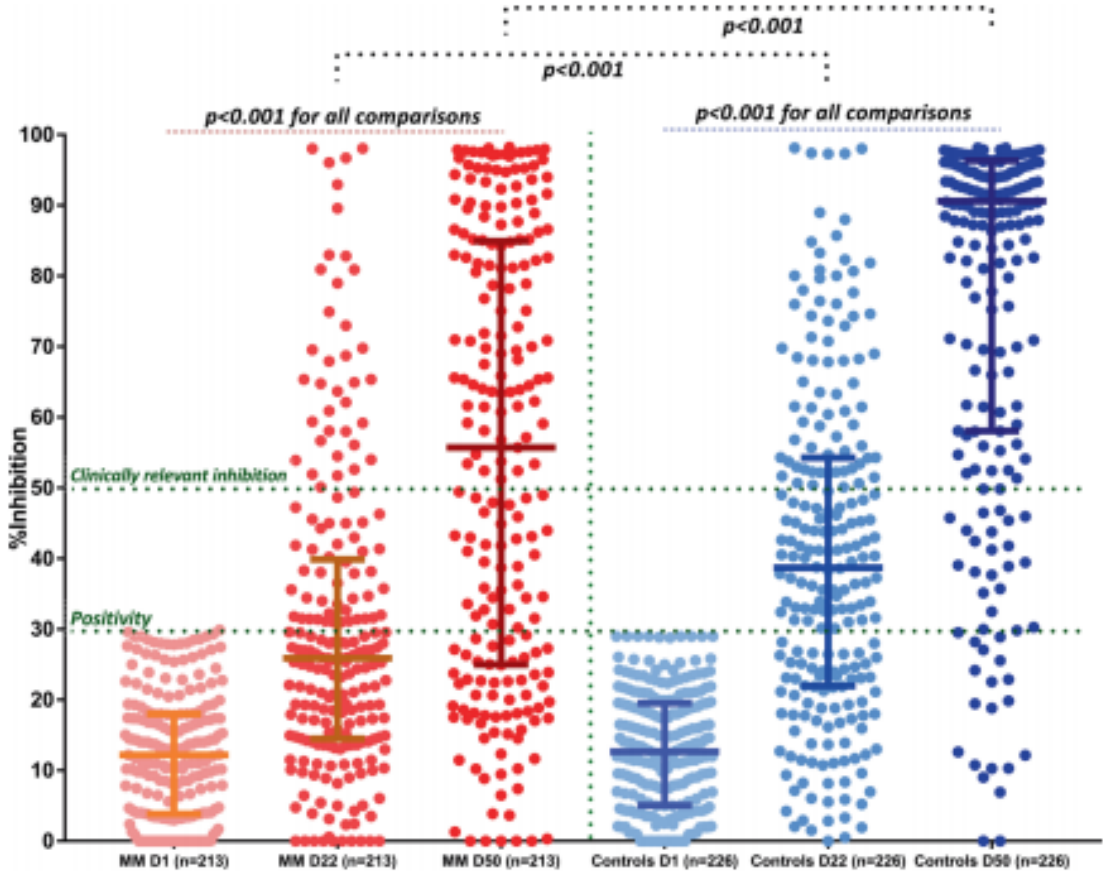
Protective Ab titers

57% Patients with MM

81% Controls

Associated with low responses

- Lymphopenia (<1000/mm³)
- Anti-BCMA therapy
- Anti-CD38 therapy



Terpos E, et al. *Blood Cancer J*. 2021;11(8):138.

Response determinants to COVID vaccination in hemato malignancies

Patient factors

- Age (>70 years)
- Immune paresis
  - Lymphopenia
  - Low polyclonal Ig

Treatment-related factors

- Early vs late post-Tx
- Immunosuppressive therapy
  - Steroids (high-dose)
  - Anti-CD20
  - Anti-BCMA targeting
  - Anti-CD38 targeting
  - Venetoclax
  - BTK inhibitors
  - Ruxolitinib

Disease-related factors

- Type of disease
  - MW < MM < other
- Active disease
  - No CR/VGPR (MM)
  - Active disease (other)
- Late disease
  - > 1st line