Suboptimal immune response to SARS-CoV-2 mRNA vaccination in myeloma is associated with anti-CD38 and BCMA-targeted treatment

Oliver Van Oekelen
Parekh Lab, Icahn School of Medicine at Mount Sinai

International Myeloma Workshop 2021, Vienna

Icahn School of Medicine at Mount Sinai

Disclosure

I have no financial disclosure or conflicts of interest with the presented material in this presentation.

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Study design and cohort

MARS study (Myeloma Antibody Response Study): opened early after vaccine approval

- Collaboration with Personalized Virology Initiative and SERONET

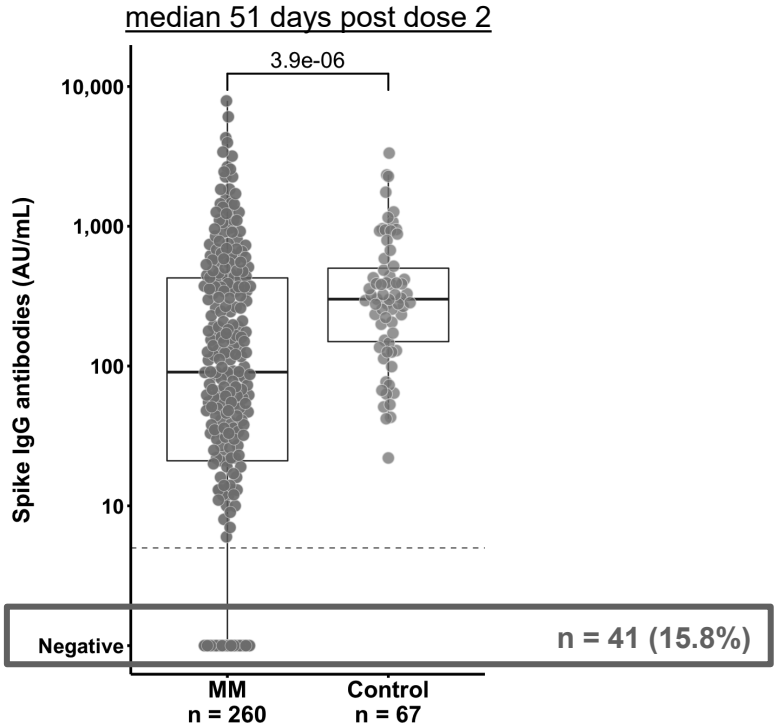
- **Goal: characterize humoral and cellular immune response to SARS-CoV-2 in MM patients**
  - 225 patients enrolled (09/2021)
  - Longitudinal collection of blood/saliva
  - Detailed clinical annotation
  - High-dimensional immune phenotyping

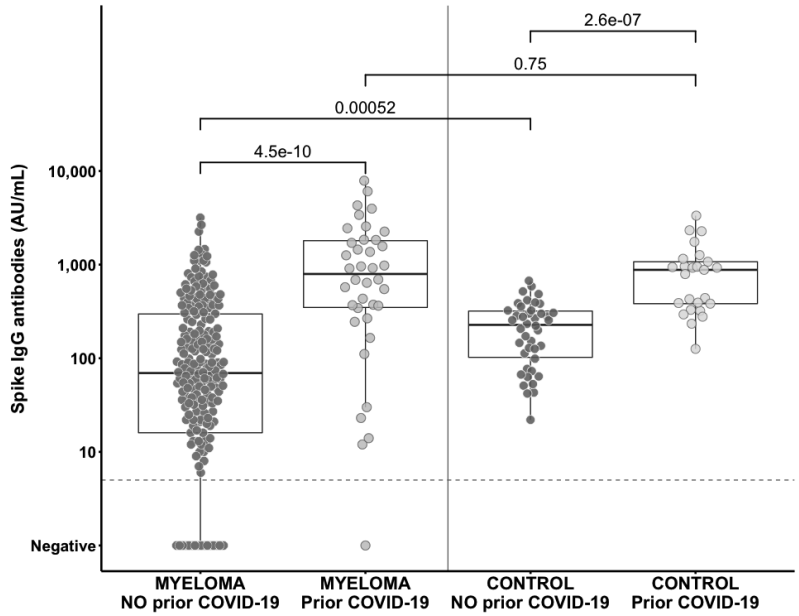
- Retrospective data collected on MM patients treated at MSH for which anti-spike IgG available

- **Cohort presented here:**
  - 320 MM patients in total, of 23 SMM patients
  - 260 (81%) with available anti-spike IgG >10 days after second dose of mRNA vaccine
  - 70.3% BNT162b2 (Pfizer) vaccine
  - T cell data in subset of 45 MM patients

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Variable anti-spike IgG in myeloma patients following 2 doses of mRNA vaccine

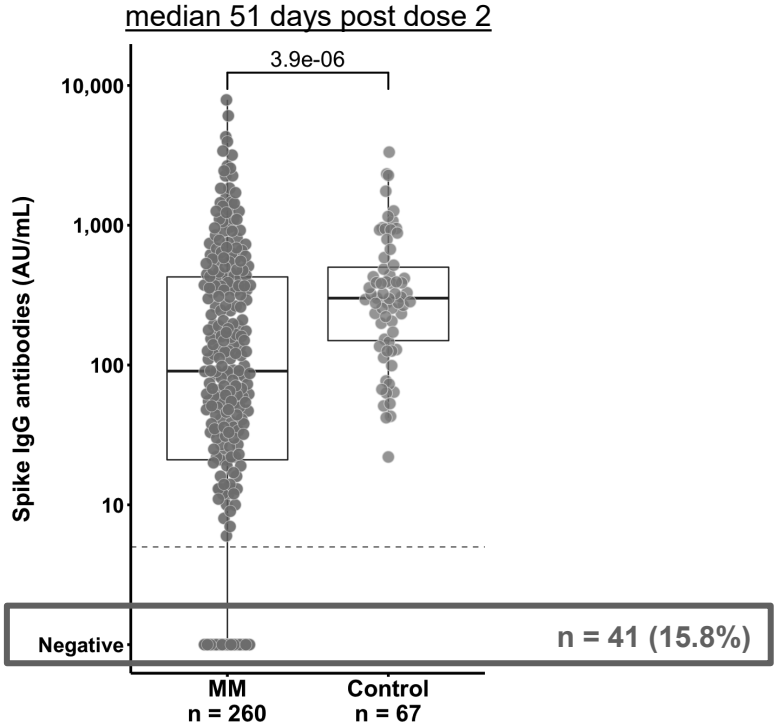




Van Oekelen O et al. Cancer Cell 2021;39(8):1028-1030.

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Variable anti-spike IgG in myeloma patients following 2 doses of mRNA vaccine

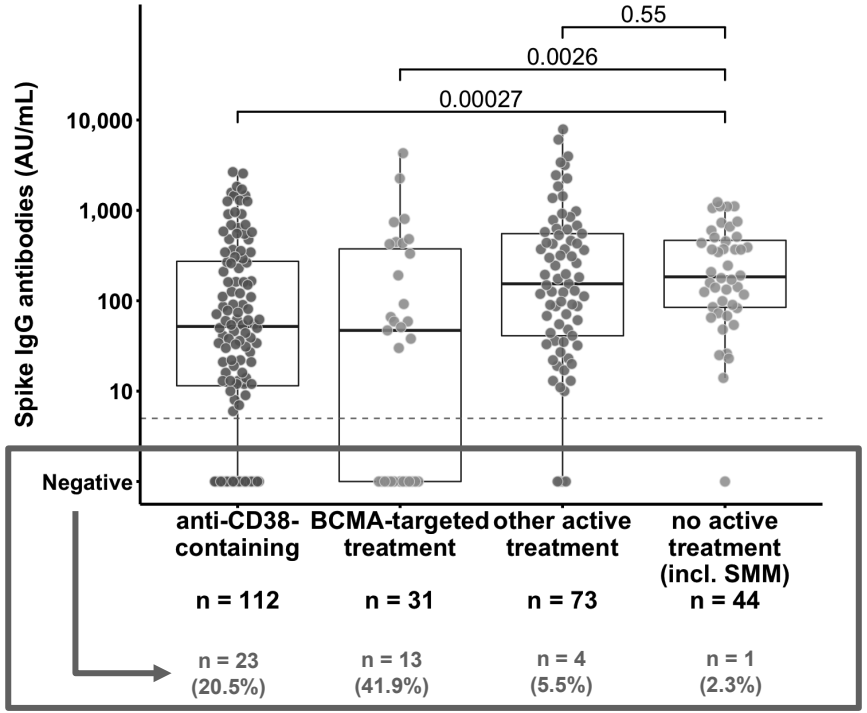


1. **Who are the non-responders?**
   - Can we predict who will not respond?
   - Clinical/disease-related associations?
2. **Does response persist?**
   - Vaccine vs COVID-19 infection?
   - Effect of treatment?
3. **Does it matter?**
   - Do these patients develop infections?
   - Are they protected via cellular immunity?
4. **How do we treat non-responders?**
   - Counseling?
   - Myeloma treatment modification?
   - Boosters and passive immunization?

Van Oekelen O et al. Cancer Cell 2021;39(8):1028-1030.

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Lower anti-spike IgG levels / non-response in myeloma patients on anti-CD38 mAb and BCMA-targeted treatment

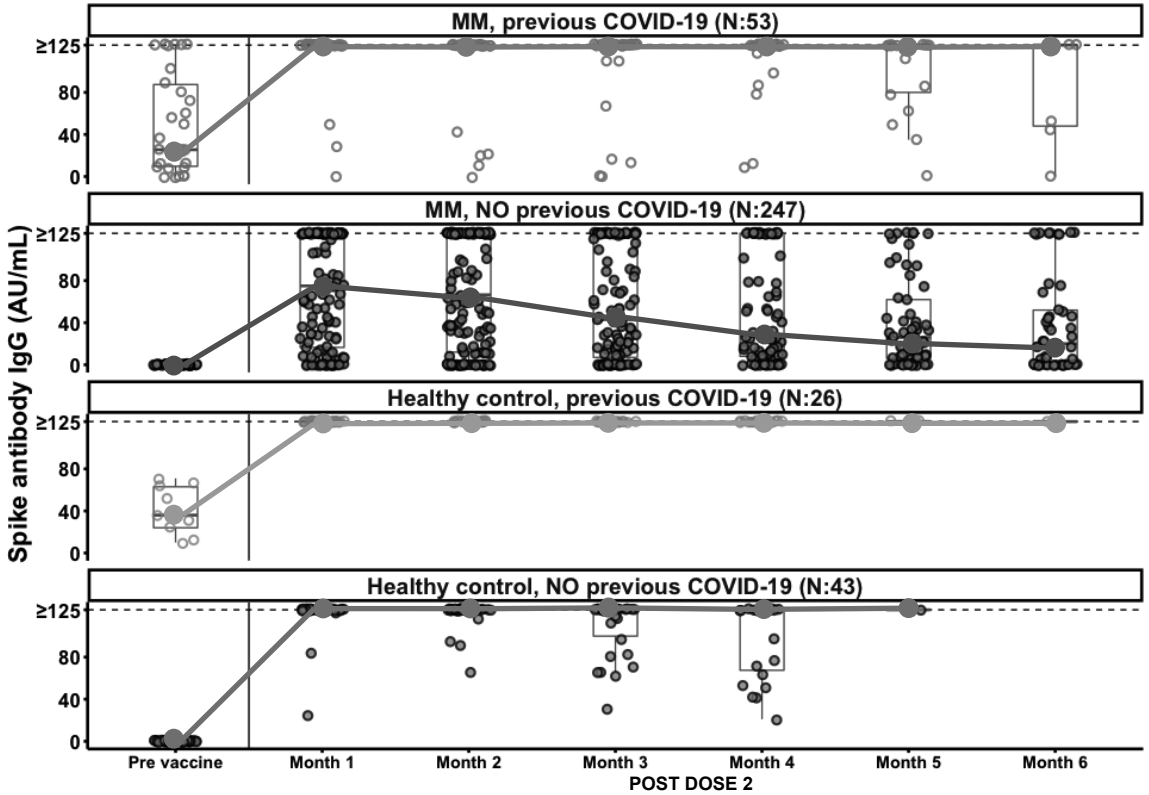


Independent variable	OR	95% C.I.	p value
Age (y)	1.023	[0.980 - 1.070]	0.303
Male gender (0/1)	1.538	[0.693 - 3.568]	0.299
Vaccine type Moderna (0/1)	0.640	[0.243 - 1.553]	0.341
Lines of treatment (n)	1.152	[0.968 - 1.376]	0.109
Time since MM diagnosis (mo)	0.997	[0.986 - 1.006]	0.506
Response status (s)CR (0/1)	0.389	[0.152 - 0.917]	**0.037**
Lymphopenia ≥ Grade 3 (0/1)	2.463	[0.884 - 6.623]	**0.076**
Current regimen contains:			
BCMA-targeted treatment (0/1)	10.269	[2.898 - 40.405]	**<0.001**
anti-CD38 monoclonal antibody (0/1)	4.258	[1.660 - 12.694]	**0.005**

Van Oekelen O et al. Cancer Cell 2021;39(8):1028-1030.

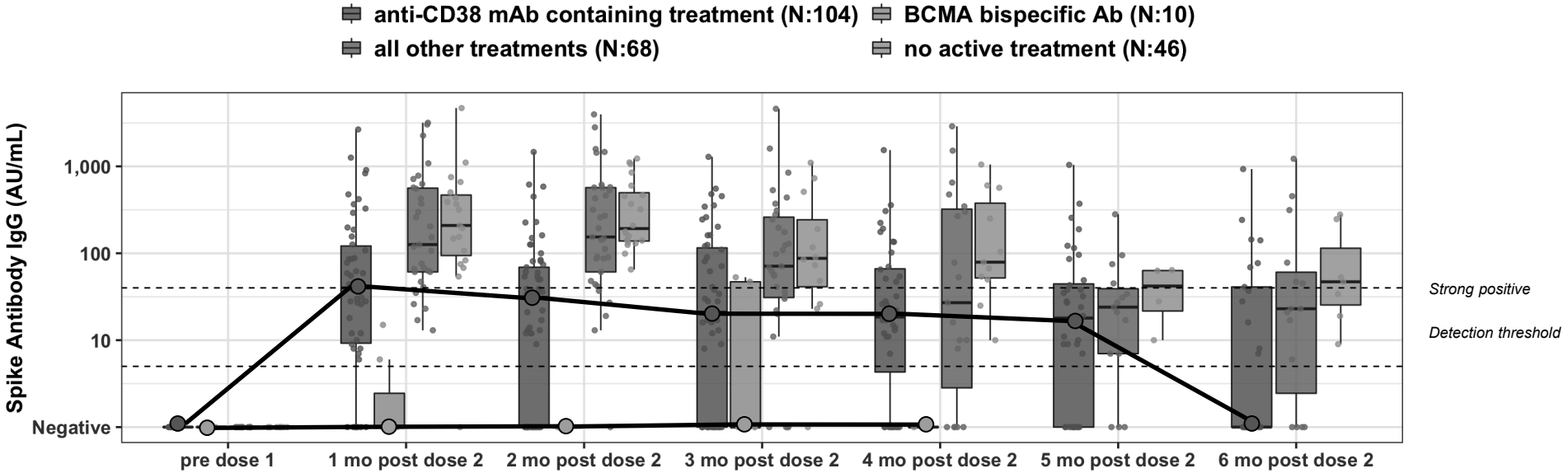
@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Anti-spike IgG persists longer after COVID-19 infection



@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Anti-CD38 mAb and BCMA bispecific impact durability

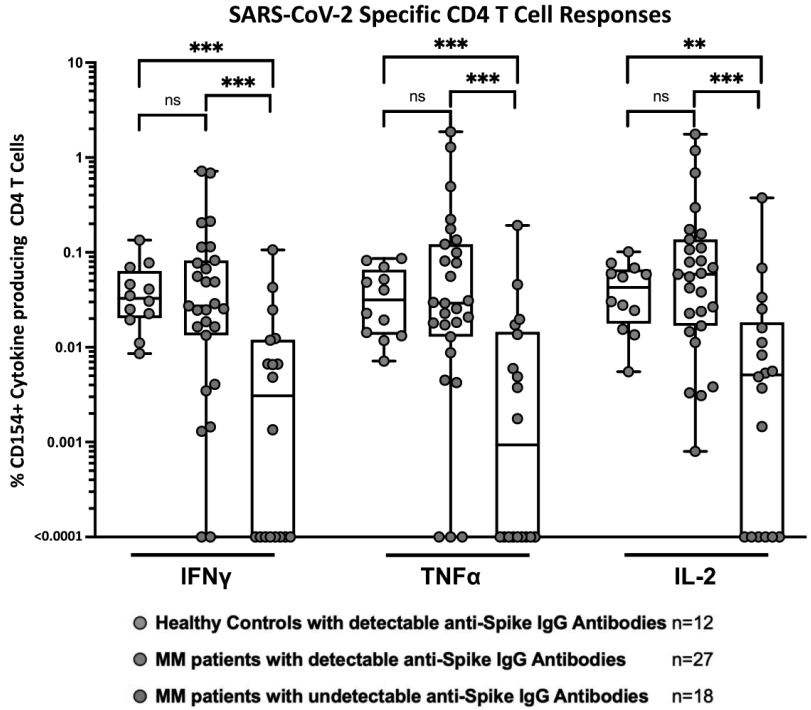


- Patients on treatment with anti-CD38 mAb lose detectable IgG faster than other MM patients
- Patients on BCMA bispecific Ab (N = 10) rarely develop detectable IgG in our cohort
- Clinical significance unclear; collecting more (longitudinal) data

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

T cell responses are diminished in IgG non-responders

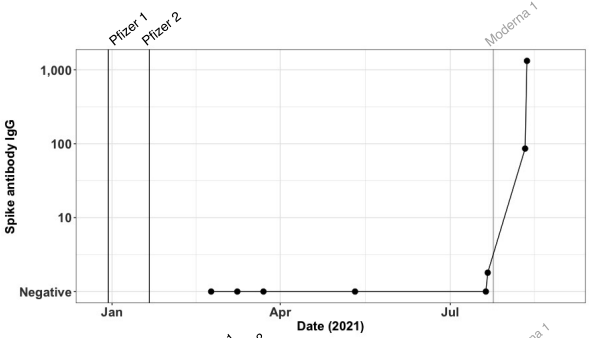
Adolfo Aleman

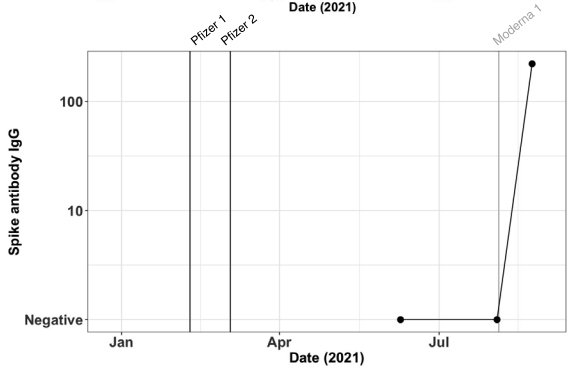


Manuscript Submitted.

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Third dose mRNA vaccine anecdotally effective in myeloma





43-year-old female

- Active treatment: daratumumab + carfilzomib + venetoclax + dexamethasone
- Persistent negative anti-spike IgG levels after 2 doses of BNT162b2 mRNA vaccine

64-year-old male

- SMM, no active treatment
- Negative anti-spike IgG levels after 2 doses of BNT162b2 mRNA vaccine

- Data collection in larger MM cohort currently ongoing:
  - Efficacy?
  - Mixing vaccines vs. same product?
  - Timing?

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Important outstanding questions…

- How can we best **identify** vulnerable patients?
  - Clinical characteristics?
  - Serology?
  - T cell assays?
- How do we properly **counsel** vulnerable patients?
  - Longitudinal serological testing?
  - Continuation of physical distancing and non-pharmacological interventions?
  - Encourage vaccination of social contacts
- How do we **adapt clinical practice**?
  - Adapt anti-myeloma treatment?
  - Timing of vaccination: hold myeloma treatment? Timing post transplantation?
- How do we **boost the immune response** in vulnerable patients?
  - Additional doses of vaccination?
  - Passive immunization strategies?

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Conclusions

- **SARS-CoV-2 anti-spike IgG response** is **suboptimal** and **highly variable** in MM patients after mRNA vaccination
- **Significant fraction (15%) does not develop any detectable anti-spike IgG (non-responders)**

- **Durability** of response is more limited in MM patients compared to healthy controls
- Treatment impacts durability: anti-CD38 mAb, BCMA bispecific, …

- Lack of IgG response associated with **weaker SARS-CoV-2-specific T cell response**

- **Third dose effect** currently being studied, anecdotally effective

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Acknowledgements

- Parekh Lab
  - **Sarita Agte**
  - Katherina Kappes
  - **Adolfo Aleman**
  - **Bhaskar Upadhyaya**
  - Samir Parekh
- Personalized Virology Initiative (PVI) Collaborators
  - Viviana Simon
  - Ania Wajnberg
  - Florian Krammer
  - Carlos Cordon-Cardo
- Human Immune Monitoring Center (HIMC)
  - Miriam Merad
  - Sacha Gnjatic
  - Seunghee Kim-Schulze
- SERONET study group
- Myeloma Center of Excellence
  - Sundar Jagannath
  - Ajai Chari
  - Hearn J. Cho
  - Cesar Rodriguez
  - Shambavi Richard
  - Larysa Sanchez
  - Joshua Richter
  - Adriana Rossi
  - Fellows: Tarek H. Mouhieddine, Bo Wang
  - All nurses and clinical staff

Thank you to all patients!

Icahn School of Medicine at Mount Sinai

@ovanoekelen – oliver.vanoekelen@icahn.mssm.edu

Thank you for your attention.
Happy to answer any questions!