Humoral and cellular immune response against SARS-CoV-2 variants following heterologous and homologous Vaccination

Reinhold Förster and Georg Behrens
for the Hannover CoCo-Study group
Analysis scheme

Homologous/heterologous vaccine

- **ChAd** prime
  - Day 0
  - n=88

- **Plasma**
  - 30d (12-44) after prime
  - n=127

- **Plasma**
  - 68d (45-91) after prime
  - n=127

- **Plasma/PBMC**
  - 73d (45-85) after prime
  - n=32
  - ChAd boost

- **Plasma/PBMC**
  - 16d (13-22) after boost

- **BNT** boost
  - 74d (62-84) after prime
  - n=55

- n=15 (27%) male
  - n=40 (73%) female
  - Mean age 39y (22-61y)

- n=12 (38%) male
  - n=20 (62%) female
  - Mean age 41y (21-64y)
Parameters determined

- Anti-S1 IgG (Euroimmune; QuantiVac)
- Anti-S- IgA
- Surrogate virus neutralization test (sVNT)
- S-specific B cells
- S-specific CD4 T cells
- S-specific CD8 T cells
- IGRA
No drop in ISW S-specific B cells

preliminary results
Strong drop in S1 antibodies 6 month after boost in BNT/BNT vaccinees

Median: 27.8 162.6 60.5 44.9 626.7 236.4

1 RU = 3.2 BAU

preliminary results
Strong drop in S1 antibodies 6 month after boost in BNT/BNT vaccinees

Median: 27.8 162.6 60.5 44.9 626.7 236.4 112.0 648.1 248.9

85% compared to 2 wks

1 RU = 3.2 BAU

preliminary results
Surrogate virus neutralization test

Hammerschmidt, re-submitted
Bosnjak et al, Cell. Mol Immunol; 2020
Correlation of sVNT with pVNT

A correlation analysis was performed for each of the four classes: Alpha, Beta, Gamma, and Delta. The graphs show the relationship between % inhibition and log(pVNT50) for each class.

- **Alpha**: $R^2 = 0.6213$, p < 0.0001
- **Beta**: $R^2 = 0.5016$, p = 0.0002
- **Gamma**: $R^2 = 0.6907$, p < 0.0001
- **Delta**: $R^2 = 0.8820$, Outlier

De Barros-Martins et al.; Nat. Med.; 2021
Drop in neutralizing antibodies 4 month after boost

preliminary results
Strong drop in neutralizing antibodies 6 month after boost in BNT/BNT vaccinees

preliminary results
Frequencies of Spike-specific CD4+ T cells

preliminary results
Reduced frequencies of Spike-specific CD8+ T cells

preliminary results
Interferon gamma release assay

![Graph showing IFN-g mU/ml levels over time for different groups: ChAd, ChAd 2 wks, ChAd 4 mths, ChAd - 2 wks, ChAd - 4 mths, ChAd BNT 2 wks, ChAd BNT 4 mths. Preliminary results.](image)
Summary

- Heterologous immunization with ChAd followed by BNT or MOD induces Spike –specific CD4 and CD8 T cell responses as well as high titers of neutralizing antibodies.

- 4 month after booster immunization a drop in T cell responses is observed with all immunization protocols.

- ChAd/ChAd vaccinees have lowest Spike-specific T cell counts as well as lowest titers of all vaccination protocols

- Mod/Mod induces highest titers of Delta neutralizing antibodies

- After six month Delta neutralizing antibodies dropped in BNT/BNT vaccinees by approx 85%
Acknowledgement

Inst. Immunologie, MHH
Joana Barros-Martins
Swantje I. Hammerschmidt
Ivan Odak
Christiane Ritter
Michaela Friedrichsen
Christian Schultze-Florey
Inga Ravens
Stefanie Willenzon
Anja Bubke
Jasmin Ristenpart
Anika Janssen
Günter Bernhardt
Berislav Bošnjak

Klinik für Rheumatologie und Immunology, MHH
Anne Cossmann
Metodi V. Stankov
Gema Morillas Ramos
Alexandra Dopfer-Jablonka
Annika Heidemann
Georg M. N. Behrens

Inst. für Biochemie
Uni Lübeck
George Ssebyatika
Thomas Krey

Inst. für Virologie
Uni Ulm
Jan Münch

Inst. für Immunologie
Uni Magdeburg
Christoph Thurm
Annegret Reinhold
Dirk Reinhold,
Burkhart Schraven²

Deutsches Primaten Zentrum, Göttingen
Markus Hoffmann
Stefan Pöhlmann