

Ontwikkeling van SARS-CoV2 vaccins

5.1.2e

klinisch beoordelaar

Disclaimer

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The views and opinions expressed in this talk are my own and do not necessarily reflect the position of the Medicines Evaluation Board or any other regulatory body.

Overzicht



- **CBG-MEB**
- **Overzicht vaccin ontwikkeling**
- **Stand van zaken SARS-CoV2 vaccins**
- **De immune response SARS-CoV2, SARS-CoV2 vaccins**
- **Aantonen werkzaamheid en veiligheid**
- **Tenslotte, wanneer wordt een vaccin goed gekeurd**

Wat is het CBG?



Het College ter Beoordeling van Geneesmiddelen (CBG) reguleert als onafhankelijke autoriteit de **kwaliteit, werking** en **veiligheid** van medicijnen. En stimuleert het **juiste gebruik** door de juiste patiënt.

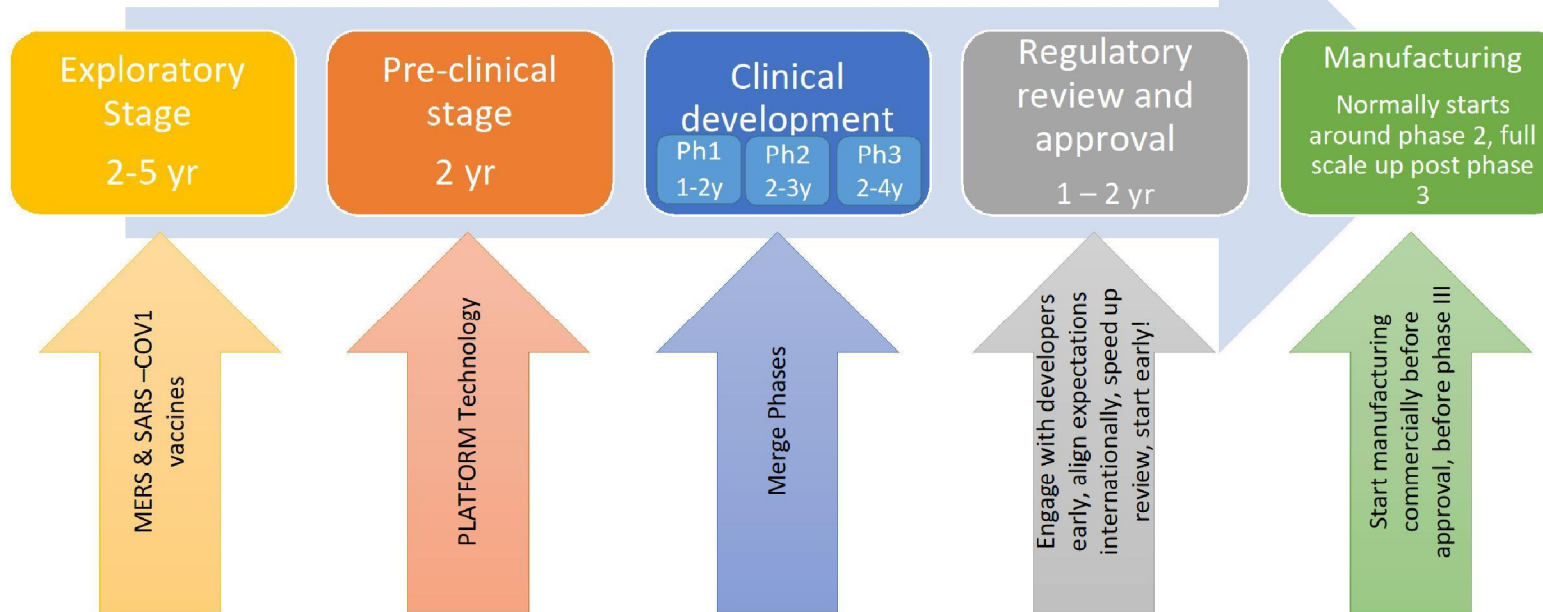
Voordat een medicijn op de markt komt, beoordeelt het CBG of het medicijn aan de wettelijke eisen voldoet.

Zo kijken we vooral naar de balans werkzaamheid & risico's van het vaccin. En of het van goede kwaliteit is.



Vaccin ontwikkelingen: speeding up development

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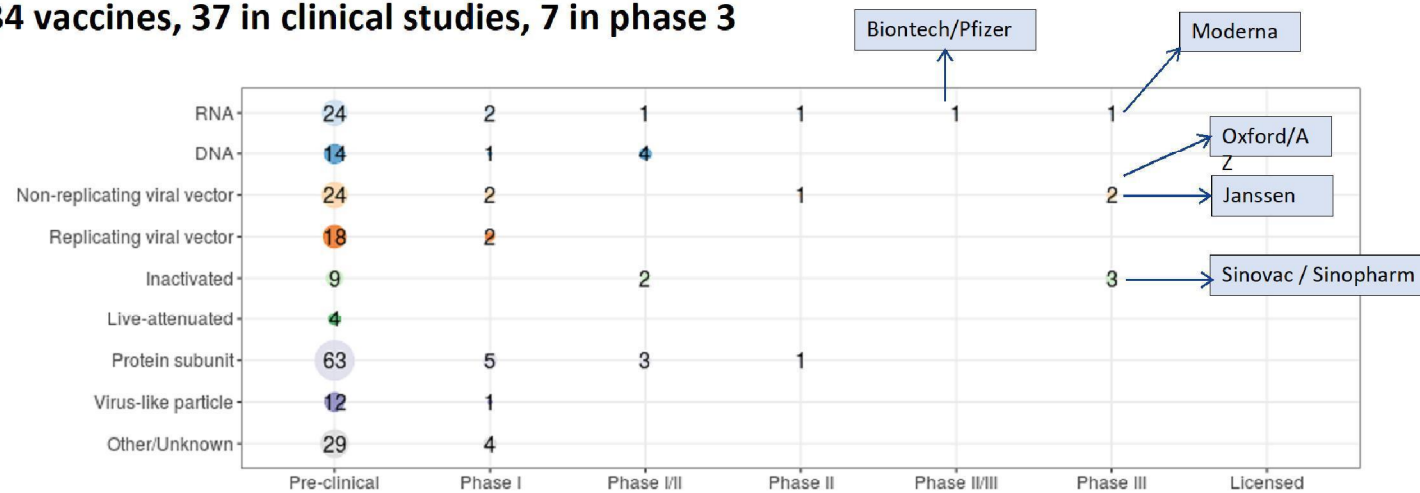
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informed by Lurie et al. <https://www.nejm.org/doi/full/10.1056/NEJMp2005630>

Stand van zaken SARS-CoV2 vaccins

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234 vaccines, 37 in clinical studies, 7 in phase 3



Update 24-08-2020

https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

Response op vaccinatie: waar letten wij op

$\frac{C \ B \ G}{M \ E \ B}$

- **Characterisation immune response:** T-cell, binding & neutralising antibodies
- How this translates into **efficacy**
- Is the dose (also) sufficient for **risk groups – older adults**
- **Safety:** reactogenicity & adverse reactions, safety in risk groups
- **Duration** of immune response, protection (possibly post-licensure?)

Immune response SARS-CoV2

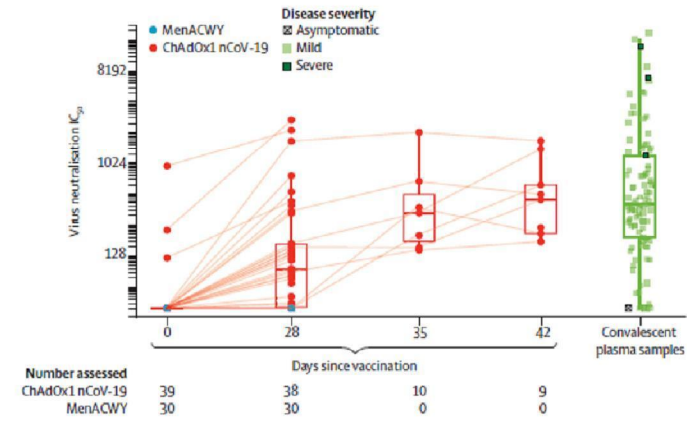
$\frac{C \ B \ G}{M \ E \ B}$

- Generally with vaccines: neutralising antibodies correlate with protection
- **SARS-CoV1, MERS**: short lived antibody response, lasting T-cell response
- Emerging picture **SARS-CoV2**: similar, uncoupled B and T-cell response.
- Interest in the **Th1 vs Th2** balance: indicator for pathological response?

Altmann & Boyton, Sci. Immunol.
10.1126/sciimmunol.abd6160 (2020).

Immune response SARS-CoV2 vaccines

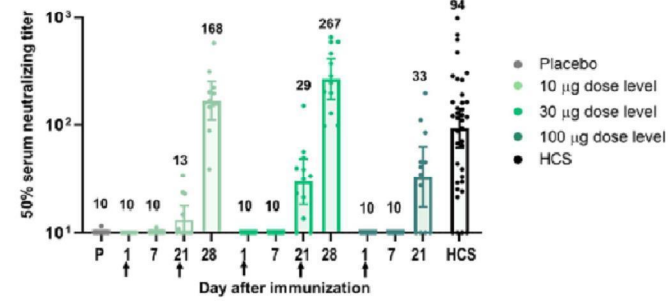
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Pseudoneutralisation titres after prime and boost with ChAOX1 SARS-CoV2 vaccine

[https://doi.org/10.1016/S0140-6736\(20\)31604-4](https://doi.org/10.1016/S0140-6736(20)31604-4)

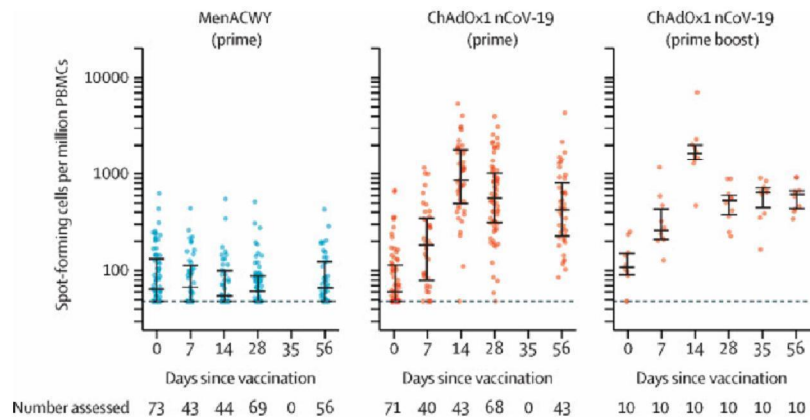
Results from Phase I clinical studies
Example from Biontech mRNA vaccine



medRxiv 2020.06.30.20142570; doi:
<https://doi.org/10.1101/2020.06.30.20142570>

Immune response SARS-CoV2 vaccines

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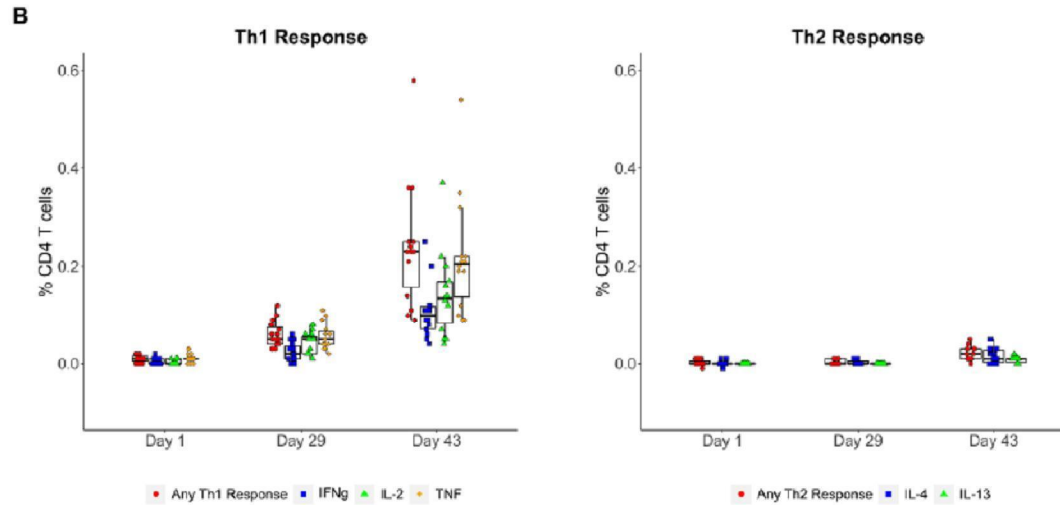


Interferon- γ ELISpot response to peptides spanning the SARS-CoV-2 spike vaccine insert (ChAOX1 SARS-CoV2 vaccine)

[https://doi.org/10.1016/S0140-6736\(20\)31604-4](https://doi.org/10.1016/S0140-6736(20)31604-4)

Immune response SARS-CoV2 vaccines

C B G
M E B



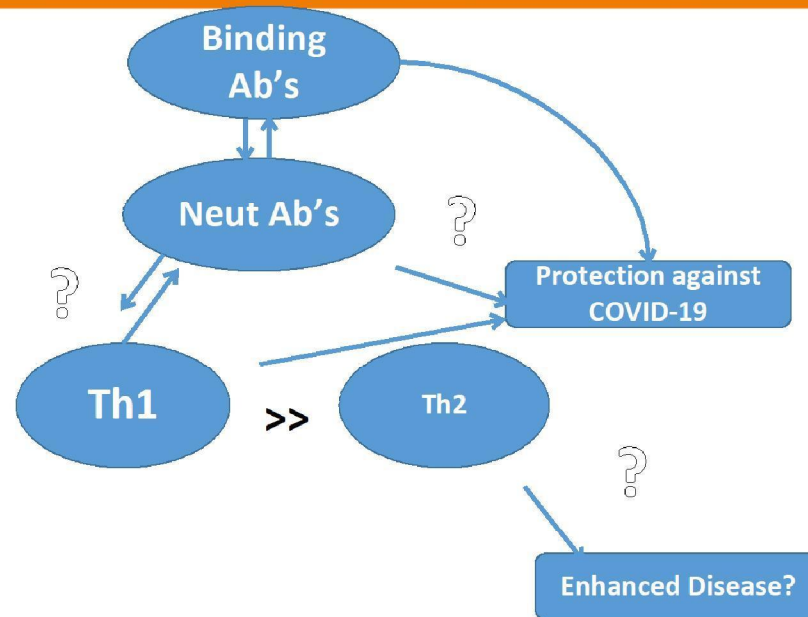
mRNA-1273-specific CD4 T cell responses (S2 peptide pool).
Frequencies of CD4 T cells producing the indicated cytokines from 100mcg (**B**) dose group following stimulation with SARS-CoV-2 S2 peptide pool.

https://www.nejm.org/doi/suppl/10.1056/NEJMoa2022483/suppl_file/nejmoa2022483_appendix.pdf

Immune response SARS-CoV2 vaccines

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- What level of neutralising antibodies signal **protection**?
- What T cell responses are beneficial, protective, and what detrimental?
- How does the T cell response correlate with the neut.ab response for **different constructs**?



Response op vaccinatie: waar letten wij op

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- **Characterisation immune response:** T-cell, binding & neutralising antibodies
- **How this translates into efficacy**
- Is the dose (also) sufficient for **risk groups – older adults**
- **Safety:** reactogenicity & adverse reactions, safety in risk groups, enhanced disease?
- **Duration** of immune response

Aantonen werkzaamheid en veiligheid: voorbeeld

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Voorbeeld van een fase 3 studie

<p>Ad26.COVS-2-S, Jnj</p> <p>(JNJ-78436735)</p> <p>Sponsor: Janssen Vaccines & Prevention B.V., Johnson & Johnson</p>	<p>NCT04505722</p>	<p>US, Brazil, Chile, Columbia, Mexico, Peru, Philippines, South Africa, Ukraine</p>	<p>A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Assess the Efficacy and Safety of Ad26.COVS-2-S for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults Aged 18 Years and Older</p> <p>N=60000 randomised to Ad26.COVS-2-S 1*10¹¹ virus particles (vp) as single dose vaccine on Day 1 or placebo.</p>	<p>Number of Participants with First Occurrence of Molecularly Confirmed Moderate to Severe/Critical Coronavirus Disease (COVID-19) with Seronegative Status [Time Frame: Up to 2.1 years]</p> <p>Moderate defined as one sign and one symptom from a list of signs, such as respiratory rate >90 and symptoms such as shortness of breath or cough or 2 symptoms from a list of symptoms or Severe COVID-19 defined in FDA guidance.</p>	<p>Not yet recruiting; Estimated Primary Completion: March 10, 2023</p>
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https://laegemiddelstyrelsen.dk/da/nyheder/temaer/ny-coronavirus-covid-19/~/_media/3A4B7F16D0924DD8BD157BBE17BFED49.ashx

Tenslotte



In principe kan een MAA afgegeven worden als de B/R positief is!

- Bewijs werkzaamheid: VE met 'voldoende zekerheid' geschat
- Veiligheidsprofiel gekarakteriseerd, en acceptabel
 - Reactogeniciteit
 - Bijwerkingen 1/1.000 – 1/10.000

Maar er zullen onzekerheden zijn:

- Duur bescherming?
- Booster response?
- Subgroepen (ouderen?)
- Zeldzame bijwerkingen

**Iedereen die een medicijn gebruikt
moet daarop kunnen vertrouwen.**

Dit is waar het CBG elke dag aan werkt
in Nederland en in Europa.

wetenschappelijk | in verbinding | waakzaam

