



Program Pack

HSV (mRNA-1608)

Herpes Simplex Virus Type 2 (HSV-2) infects ~13% of adults globally and is the primary cause of genital herpes

There are an estimated 4 billion people globally infected with HSV, of which 492 million cases are HSV-2¹

Significant unmet medical need

- Globally: ~13% of the population aged 15–49 years has acquired HSV-2²
- US: ~18.6 million people aged 15–49 years living with HSV-2, with ~572,000 new infections/year³

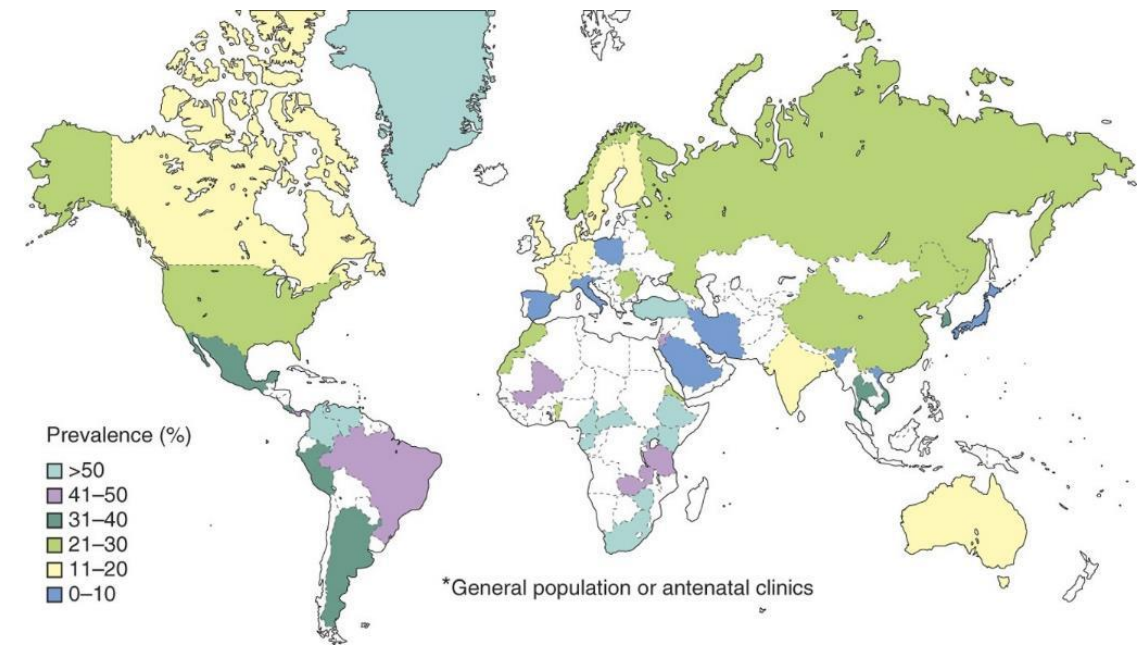
HSV-2 is the leading cause of genital herpes

- Globally: ~178 million cases (95%) of genital herpes attributable to HSV-2⁴

Disease disparities: women, racial and sexual minority populations at highest risk⁵

- Women almost twice as likely to have HSV-2 infection as men
- Seroprevalence highest in non-Hispanic Black persons in the US⁶

Prevalence of HSV-2 infection in women globally



Shiffer & Corey, 2013

1.James et al, 2020: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7265941/>; 2.James et al, 2016: <https://pubmed.ncbi.nlm.nih.gov/32514197/> ; 3.Kreisel et al, 2021: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10245608/>; 4.Looker et al, 2020: <https://gh.bmj.com/content/5/3/e001875> ; 5.Looker et al, 2020: <https://gh.bmj.com/content/5/3/e001875> Spicknall et al, 2021: https://journals.lww.com/stdjournal/fulltext/2021/04000/estimates_of_the_prevalence_and_incidence_of.9.aspx McQuillan et al, 2018 (NCHS Data Brief): <https://www.cdc.gov/nchs/data/databriefs/db304.pdf> ;6.McQuillan et al, 2018 (NCHS Data Brief): <https://www.cdc.gov/nchs/data/databriefs/db304.pdf>

HSV: mRNA-1608 Phase 1/2 trial design of a therapeutic vaccine against HSV-2; fully enrolled

The Phase 1/2 was designed to test safety and immunogenicity and establish a proof-of-concept of clinical benefit of mRNA-1608 in adults 18-55 years of age with recurrent HSV-2 genital herpes



Design

Randomized 1:1:1:1, observer-blind, controlled study



Participants

300 healthy adults 18-55 years of age with a history of HSV-2 infection > 1 year and 3-9 HSV genital recurrences in the prior 12 months

At least 35% participants male in each study arm



Vaccination schedule

1 of 3 dose levels of mRNA-1608 or control (BEXSERO) given at 0 and 2 months



Duration: 6 months

Study participants will be followed up for 12 months after study injection



Site locations

United States

Total N = 300

Randomization = 1:1:1:1

mRNA-1608 (Low dose)

N=75

mRNA-1608 (Medium dose)

N=75

mRNA-1608 (High dose)

N=75

Control (BEXSERO)

N=75

Vaccine against HSV-2 (mRNA-1608)

HSV-2 (Herpes) disease overview

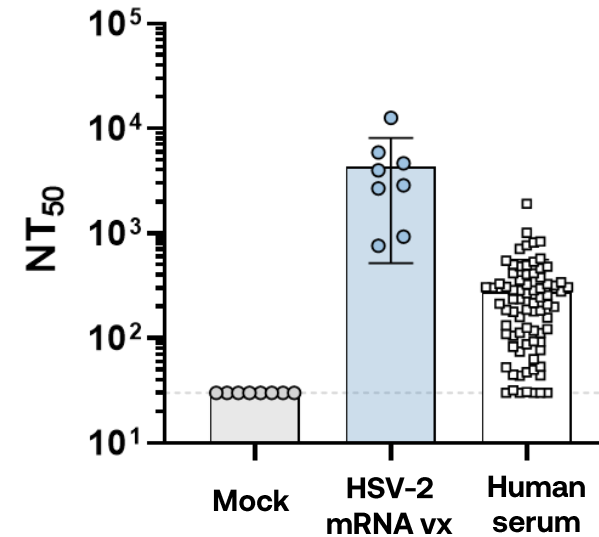
- Herpes simplex virus type 2 (HSV-2) primarily infects the genitals
- HSV-2 establishes **life-long latent infections** within sensory neurons from which it can reactivate
- Significant burden of disease from HSV infections
 - Estimated **18.6 M HSV-2⁺ people** aged 18-49 in the US¹
 - Globally, ~5% of the population in the 18-49 range is HSV-2 seropositive²
- Burden of disease includes a **reduction in quality of life**

(1) Spicknall et al, *Sexually Transmitted Diseases* (2021), <https://doi.org/10.1097/OLQ.0000000000001375>

(2) Looker et al, *BMJ Global Health* (2020), <https://doi.org/10.1136/bmjgh-2019-001875>

HSV-2 Neutralization

mRNA vaccine containing HSV-2 antigens induces strong immune response in preclinical animal studies



Naïve c57/Bl6 mice were immunized twice at 3 weeks interval with either PBS (mock) or HSV-2 mRNA vaccine. Each group contained 8 animals, and neutralizing activity was measured 2 weeks after the second immunization

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