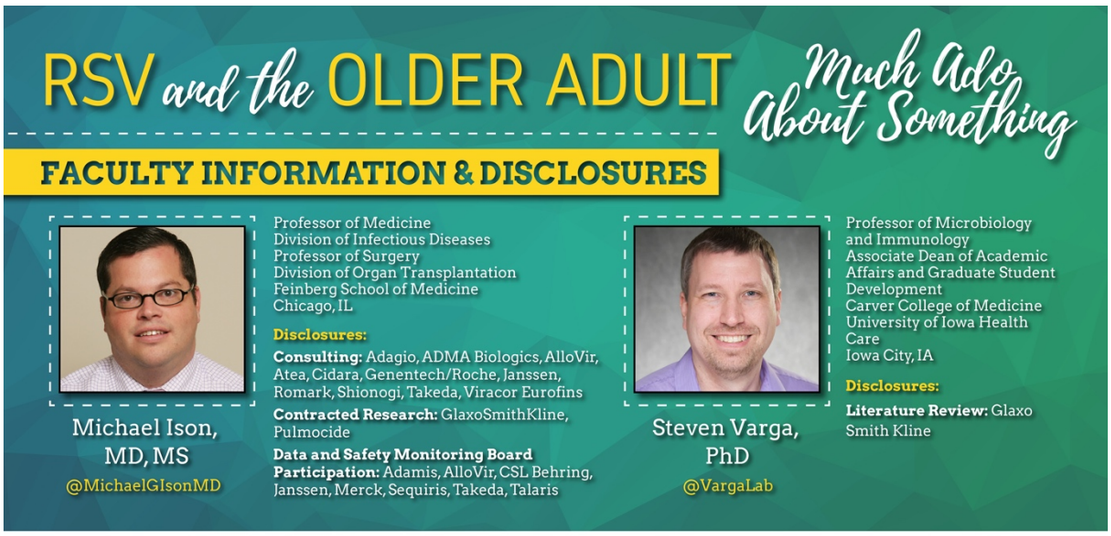
RSV *and the* Older Adult

Much Ado About Something

RSV Tweetorial #4

Tweets	References
1/ #RSV vaccines #MedTweetorial🧵#2 🏹Adenovirus Type 26 Viral Vectors💉 🔎Older adults 🔥Data from #idweek2022 #rsv2022 ✍️Me & @VargaLab @BonumCE #IDTwitter #MedTwitter #CME ℹ️👉bit.ly/3UoESDs Supported by an edu grant from @JanssenUS 🟢What's your specialty?👇 ☐ ID MD/DO ☐ IM, PCP, FP MD/DO ☐ Fellow, Resident, Trainee ☐ APP, RN, PharmD, Other	CME Info 🔗 bit.ly/3UoE SDs
2/ #MedTwitter #IDTwitter #IDMedEd #respiratorysyncitialvirus ✅ Answer the polls 📃 Read the #MedTweetorial 🏆Claim FREE #CME👉 bit.ly/3UoESDs 📸 Faculty disclosures & important info👇	



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3/ 🧩#RespiratorySyncytialVirus in older adults
❗Not just for #Pediatrics

🗓️ Causes >177k hospitalizations 🏥 of adults annually
🚨Need better prophylactic strategies, including vaccines 💉

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Ref #
1
12

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🔎#RSV #Vaccine pipeline
🔬Many vaccines💉 for older adults in development🔬

🎯Protein-based
🎯Nucleic acid
🎯Live attenuated/chimeric
🎯Recombinant vectors

👇Diving into adenovirus (Ad26) viral vector🔰

Ref #
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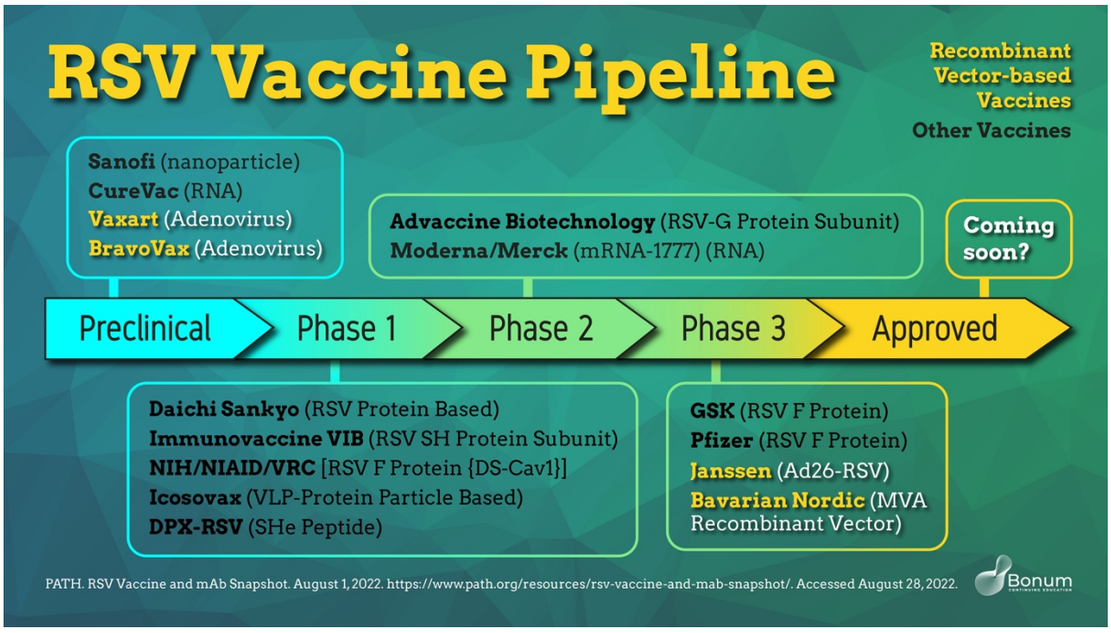

5/ 🌅 Let's look Ad26 viral vector💉 candidates on the horizon👇

🔬Clin trials show Ad26 viral vectors induce robust humoral & cellular immune responses for #RSV, even w/o an adjuvant 💥

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6/ Ad26-based 💉 #vaccines are:
⚡= now available
OR
🚩= in clinical trials for these viruses:

⚡#Ebola 😷
🚩#HIV
🚩#Malaria 🦟
🚩#Filovirus
🚩#Zika 🦟
🚩#HPV
⚡#SARS-COV-2 🦠
🚩#RSV

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Ref #

4

7/#RSV

📢Here's how viral vector vaccines (VVV) work:
1️⃣ VVV + cell membrane fuse
2️⃣🧬code released
3️⃣📝read, target protein made
4️⃣🚚to cell surface; discovered by immune system

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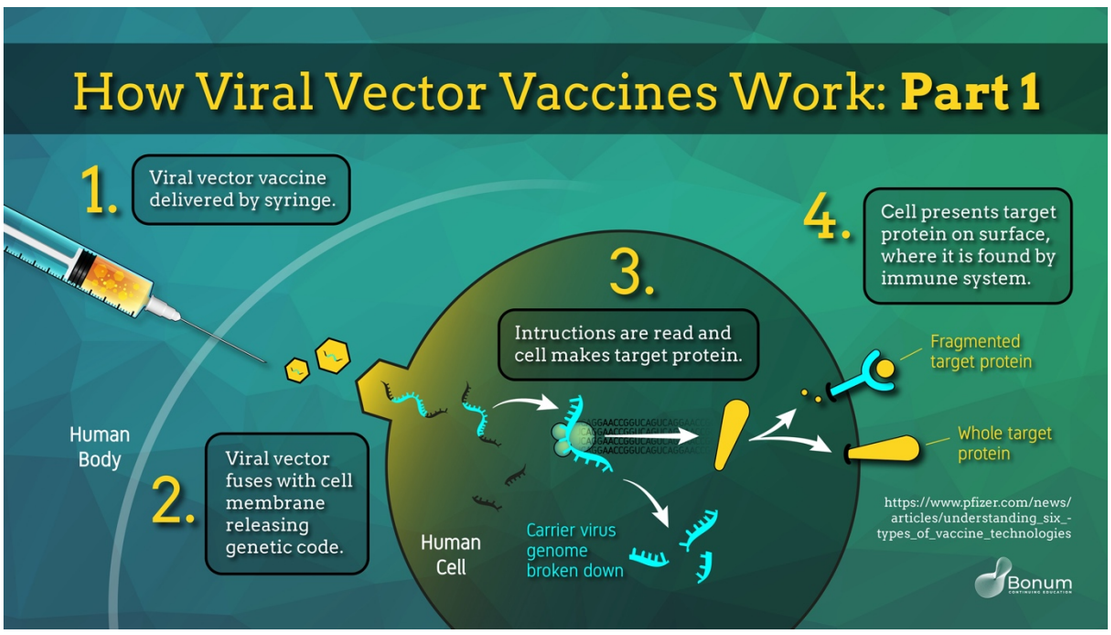
Ref #

11



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8/ #RSV

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📣Here's how immunity is created:
🚩 Immune helper 🦠 trigger response
🚩Army of 🅱️-cells make Ab vs 🎯target
🚩Ab tag 🦠cells w/protein for 💥destruction
🚩Infected 🦠cells recognized & destroyed

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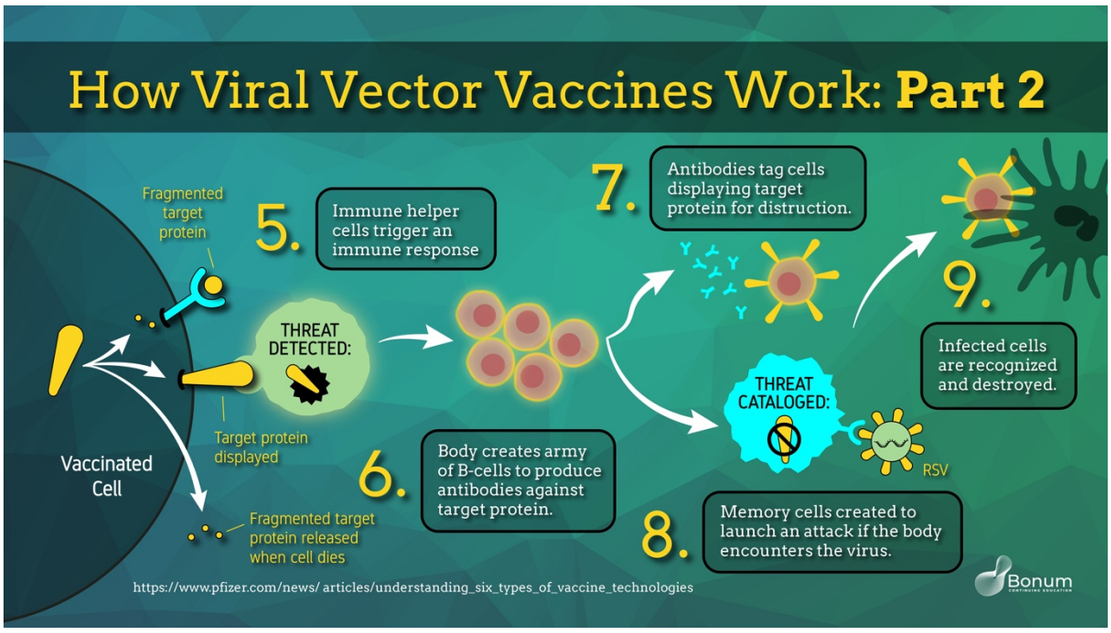

9/ Adenoviral vectors for viral antigen transfer benefits:

Ref # 13

📍Lrg size
📍Well characterized genome
📍Easy to manipulate
📍Safe
📍Uses systemic or resp mucosal routes
📍Induces strong, sustained innate & adaptive immune response
+++

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10/ #BonumCE #IdMedEd #IDTwitter #MedTwitter #RSV #vaccine

Ref #

🟢 Human AdVs (HAdV) are favorable vectors 🪰 for _____.

- ☐ Effector proteins
- ☐ Gene transfer
- ☐ Genomic opsonization
- ☐ Serum activation

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11/ HAdV = double-stranded🧬viruses

Ref # 7 8

♦️Cause mild GI,😔respiratory, or 👁️infections
♦️Used as vectors for gene transfer and vaccinations➡️deletion of their replication genes (E1 +/or E3) & replacement w/ an antigen of interest

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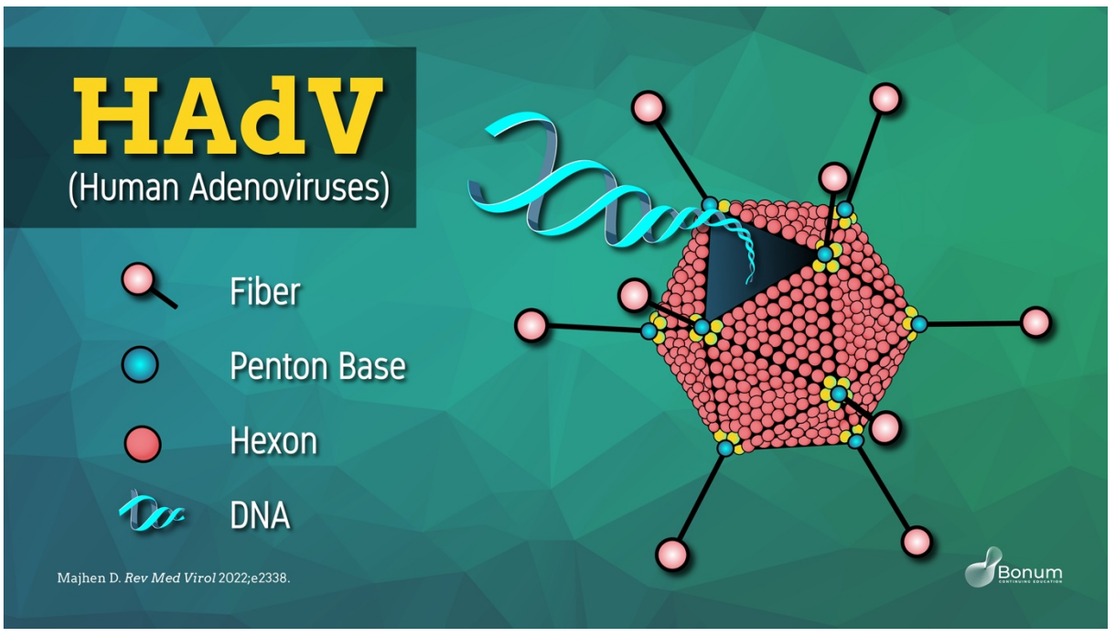

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🟢 HAdV26 is an optimal vaccine vector because of its:

- ☐ ⬇️ seroprevalence in ppl
- ☐ Oncogenecity
- ☐ Nuclear glycoproteins
- ☐ ❌ liposomes needed

13/ Human Adenovirus type 26 (Ad26) excellent candidate as a 🚚delivery vector for💉s:

Ref # 4 7

✔️🔽seroprevalence in various 👫 compared to other adeno🦠 types
✔️Immunogenic
✔️Grows in high titers
✔️Used vs 🫁 pathogens w poorly understood biology
✔️Used repeatedly
✔️Stable
#RSV

14/ Compared to Ad5, the other most studied adenovirus, Ad26=

Ref # 4 7

💎Accrues in the endosome to a greater extent
💎Differentially activates innate immune pathways in 🙈mammals
💎Once released, 🚐 transported to the cell nucleus & activates host immune system

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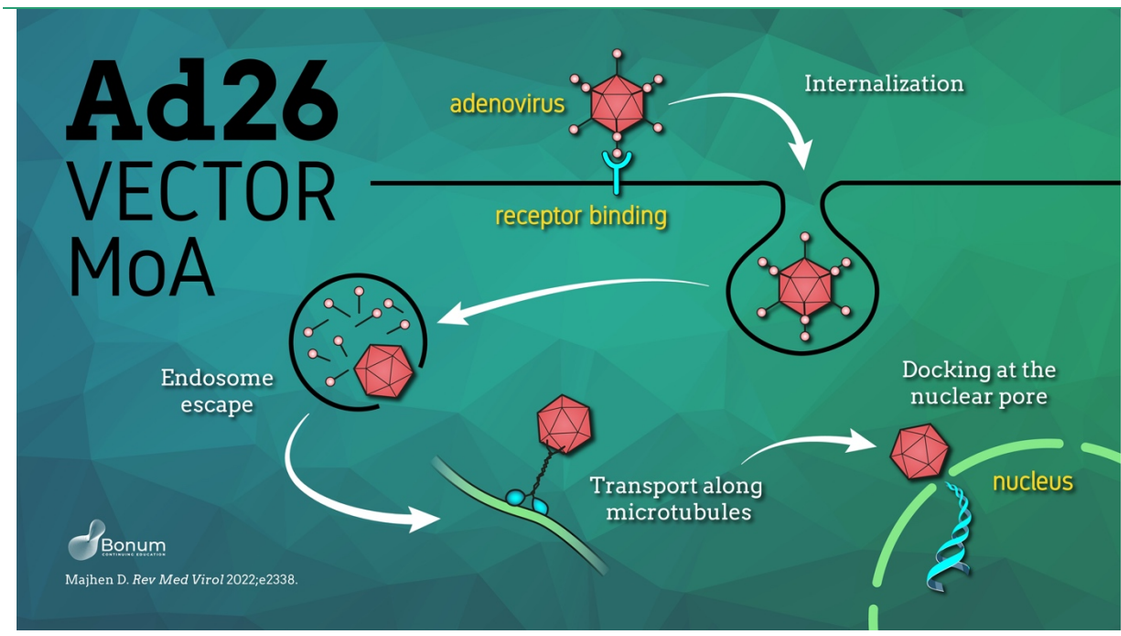

🔸 Immunogenicity of Ad26💉
1️⃣dose Ad26-based vaccines stimulate💪humoral immune response
💎Includes both neutralizing & non-neutralizing antibody activity
💎Responses by CD8+ T cells & CD4+ T cells to clear #RSV-infected🦠 cells

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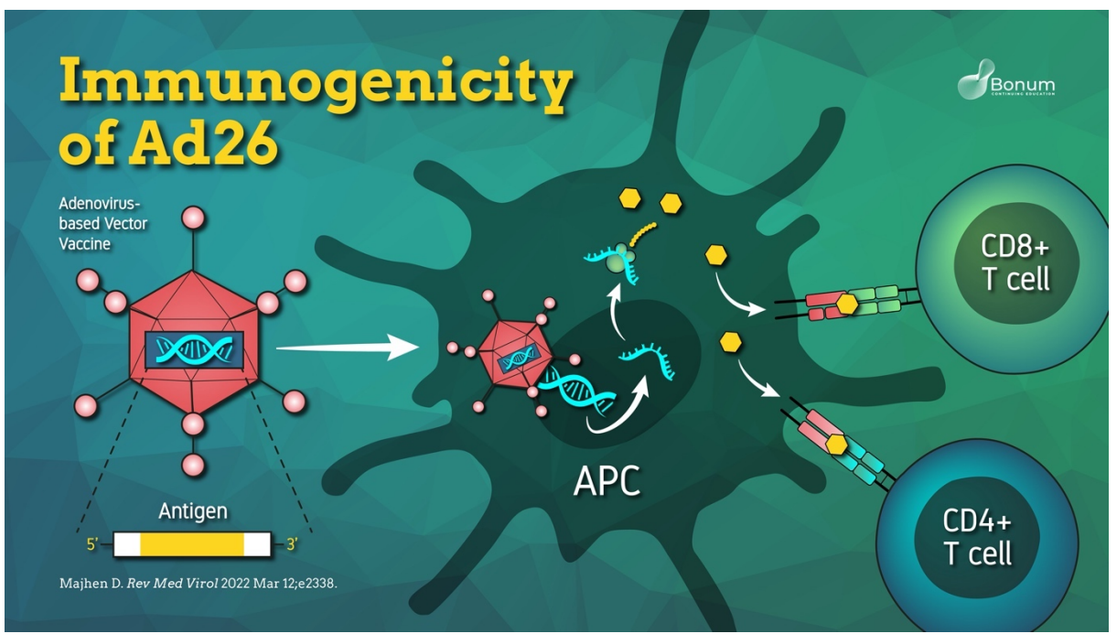

16/
🛟No significant safety issues identified
🦺Extensive safety/immunogenicity data obtained from diff trials (#HIV, #RSV, #Ebola, #SARS-CoV-2, #Zika) ➡️show Ad26-based vaccines to be well tolerated
🛟Most post-💉 events are mild-to-mod

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17/ Ad26.RSV.preF is a recombinant adeno🦠serotype 26 vector (Ad26) vaccine

Ref # 12

⛓️Encodes for a full-length, stabilized pre-RSV-F protein expressed on the cell surface

🔬In clinical trials to assess 🤺protection against #RSV infection & disease

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18/ #RSV #MedTwitter #IDTwitter #IDMedEd #pulmtwitter #BonumCE

🟢 The overall efficacy of the Ad26.RSV.preF #vaccine for ≥3 sx in the CYPRESS study was:

- ☐ 50%
- ☐ 60%
- ☐ 70%
- ☐ 80%

19/

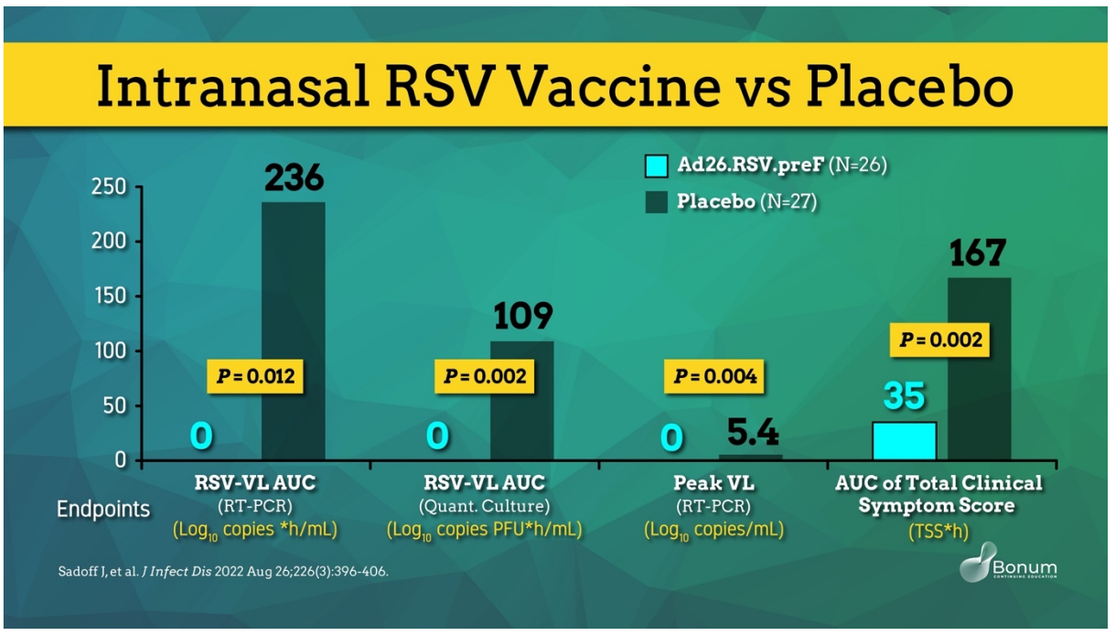
Phase 2a DB RCT intranasal challenge in healthy adults aged 18-50y randomized 1:1 to receive 1x1011 vp Ad26.RSV.preF💉 or PBO, IM

Ref # 12

💪Post challenge results💪

VL, RSV infections & dx severity🔽in Ad26.RSV.preF (n=27) vs PBO (n=26)

⭐primary endpoint met⭐



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20/Pre-F specific sites🎯by neutralizing antibodies

Ref #

12

📍Ad26.RSV.preF💉led to an🔼in pre-F & post-F IgG serum antibody response & RSV A2 neutralizing antibody titers vs PBO
📍Pre-existing Ad26 neutralizing antibodies📏@ BL did not impact💉induced immune responses

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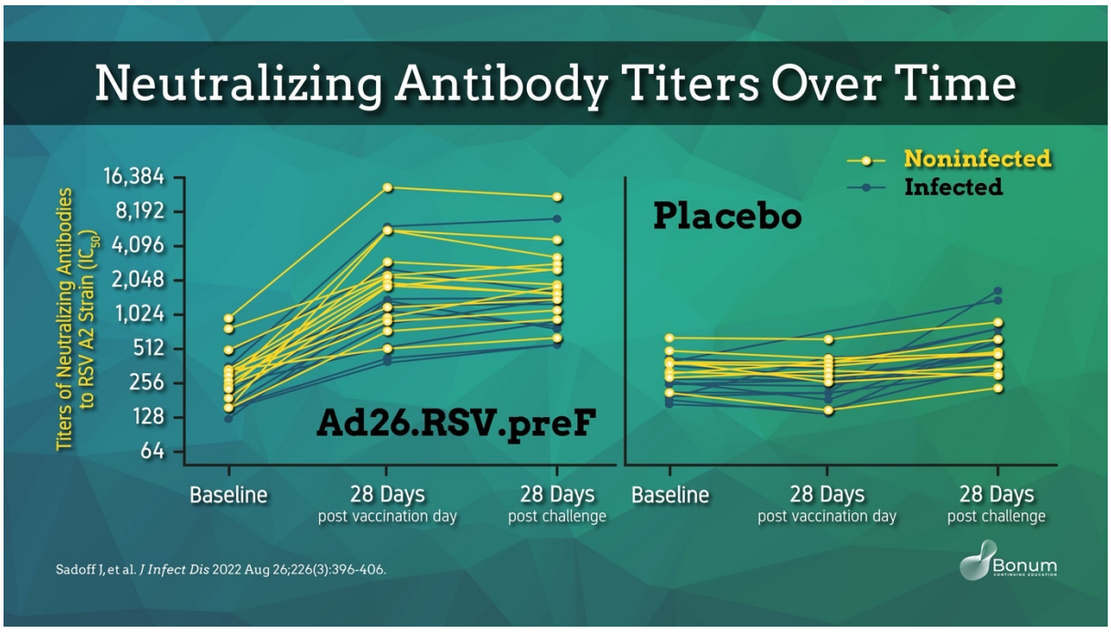

21/
CYPRESS: RCT, DB, PBO-controlled Phase 2b trial Ad26.RSV.preF-based vaccine

Ref #

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🧩5782 Adults ≥65y of age were randomized 1:1 prior to the #RSV season
🧩Sx of ARI collected
🧩LRTI occurrence by 3 case defn
🧩Immunogenicity assessments

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22/CYPRESS Results:

Ref #

5

🚩≥3 sx: 80% (94.2% CI, 52.2-92.9%)
🚩≥2 sx: 75% (50.1-88.5%)
🚩≥2 sx of LRTI or ≥1 sx of LRTI w/ ≥1 systemic sx: 69.8% (43.7-84.7%)
🚩P-value for all: <0.001
🚩GMF🔼in Ab titers 14 d after💉was 13.5 for #RSV nAb and 8.6 for RSV preF-specific binding Ab

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23/ Ad26.RSV.preF3
Ph3 EVERGREEN Study
DB, RCT, PBO-controlled
📍Obj: Confirm efficacy (overall and LRTD)
📍N=27,500
📍FDA breakthrough designation
📍Follow for 2 #RSV seasons

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24/MVA-BN RSV Multivalent VV w/ surface +internal RSV proteins
5️⃣diff RSV antigens
➡️G (A,B), N, M2, F
🚩Mimics natural rxn to RSV infection +mucosal immune response
🔬In clin trials to assess 🤺protection against #RSV infection & disease

Ref #
14

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25/ #RSV #MedTwitter #IDTwitter #IDMedEd #pulmtwitter #BonumCE

🟢 In the Ph2 intranasal challenge trial, the MVA-BN RSV multivalent VV vaccine reduced moderate RSV symptoms by ___

- ☐ 32%
- ☐ 42%
- ☐ 52%
- ☐ 62%

26/ Efficacy Results: Ph 2 Human Challenge Trial
🚩DB, PBO RCT; randomized 1:1
💎79.3% for preventing mod sx #RSV infection
💎Broad, durable responses (Ab/T-cells) vs RSV
💎No serious AEs
💎Safety consistent w Ph 1/2 results

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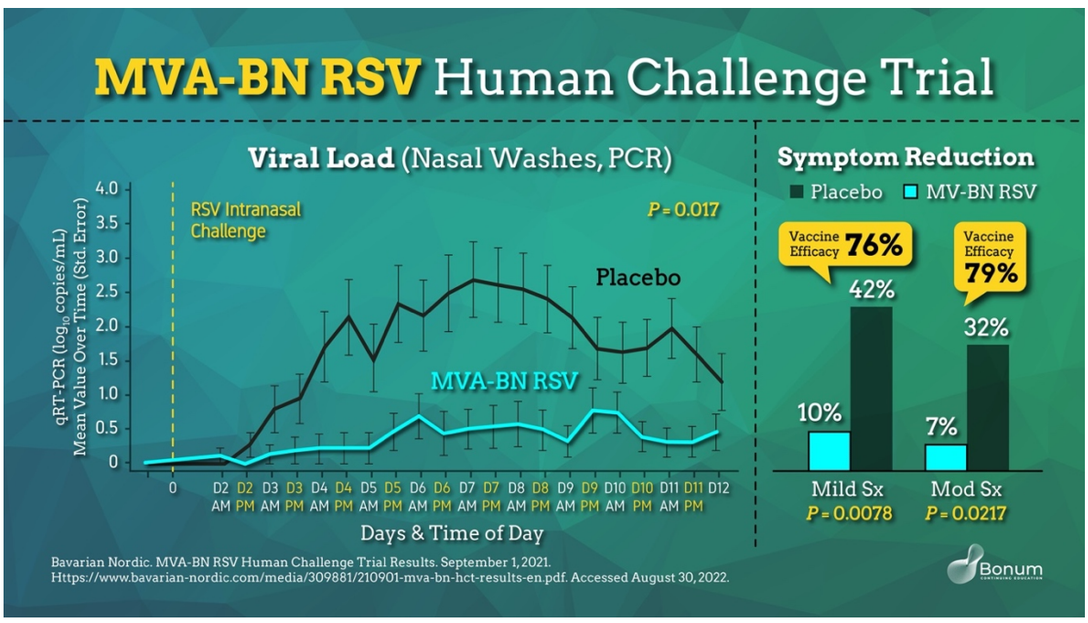

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27/SUMMARY	Ref #
🔑Ad26.RSV.preF-base 💉 well-tolerated & highly effective against RSV-mediated LRTD (even w/o an adjuvant)	2
🔑Stimulated strong, durable humoral & cellular immune RSV-specific response in adults ≥65y after 1️⃣ dose	5
🔑MVA-BN RSV 💉 efficacy of 79.3% in HCT; adv to ph3 trials	

Claim your CME credit by completing the post-survey and evaluation. Link provided👉 🔗 here

Or: bit.ly/3DPXfdH

📚 References 👇

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