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HYBRID EDITION

INNOVAZIONE E RICERCA PER LA PRATICA CLINICA

XVI Workshop Nazionale

TERAPIA E PREVENZIONE DELL'INFEZIONE DA HIV E MICRORGANISMI EMERGENTI

VACCINI IN HIV: DA MONKEYPOX A HERPES ZOSTER

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SOD Malattie Infettive e Tropicali

TIPI DI VACCINI: componente attiva

TIPO DI VACCINO		ESEMPIO
Vivo attenuato		
	Virale	Morbillo, Parotite, Rosolia, varicella, febbre gialla, Varicella,HZ, polio orale, rotavirus, influenza nasale, Vaiolo
	Batterico	BCG, Tifo orale
Inattivato		
	Virus interi	Polio, Influenza, HAV, Rabbia, Encefalite giapponese
	Batteri interi	Pertosse, colera
Frazioni	Tossoide	Difterite, tetano
	Subunità (proteine)	influenza, pertosse acellulare, papilloma virus
	Polisaccaridico	Pneumococco, meningococco,
	Coniugato	Hib, Pneumococco, Meningococco
	Ricombinante	HBV, menigocco B, HZ
m-RNA/Vettore Virale		COVID-19

CONTROINDICAZIONI E PRECAUZIONI

- **Controindicazione:** una condizione nel ricevente che aumenta il rischio di una grave reazione avversa.
- **Precauzione:** una condizione nel ricevente che può aumentare **il rischio di una grave reazione avversa o che può compromettere la capacità del vaccino** di produrre l'immunità ed esige, pertanto, una valutazione rischio/beneficio

La vaccinazione può essere raccomandata in presenza di una precauzione, quando il beneficio derivante dalla somministrazione del vaccino supera il rischio di una reazione avversa o di una incompleta risposta

Controindicazione: reazione allergica severa (anafilassi) ad un componente del vaccino o ad una precedente dose dello stesso vaccino

Precauzioni: malattia moderata o severa con o senza febbre; allergia al lattice (qualora presente nel dispositivo)

E NELLE PERSONE CHE VIVONO CON HIV?

VACCINAZIONE IN PERSONE CON HIV: poche regole ma buone

Le raccomandazioni relative alle vaccinazioni nelle persone che vivono con infezione da HIV non si discostano in generale da quelle riservate ad altre categorie di pazienti. Tuttavia:

- la risposta vaccinale che potrebbe essere alterata e dunque rivelarsi meno protettiva rispetto a quanto accade nell'ospite normoergico,
- Stimolazione del sistema immunitario potrebbe favorire la replicazione di HIV. Utilizzo di vaccini vivi
- Controindicazione in CD4+ < 200 cellule/µL

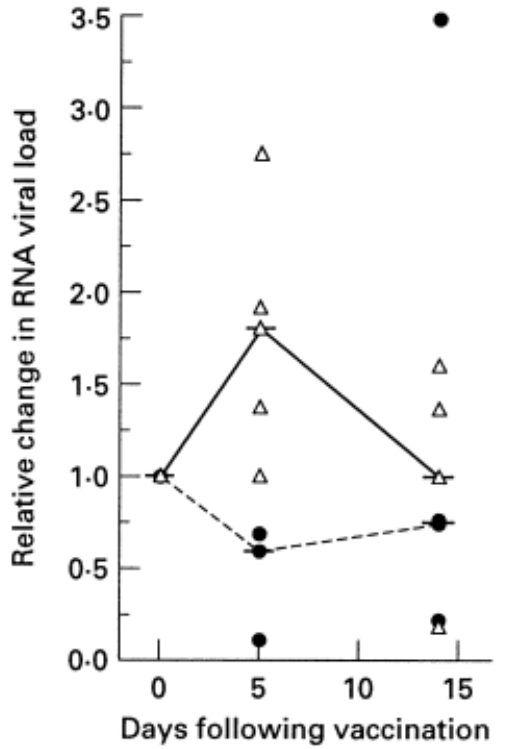

Fig. 1. Post-immunization data showing changes in viral load following influenza vaccination in individuals with viral load higher than 2×10^5 (●) and lower than 2×10^5 (△) HIV RNA copies/ml. The dotted and full lines connect the median values of the two groups, respectively.

Røsok B et al 1999

VACCINAZIONE IN PERSONE CON HIV

- Vaccinate according to national guidelines for healthy population, preferably after having achieved suppressed viraemia and immune reconstitution (CD4 count > 200 cells/µL)
- Consider repeating vaccinations performed at CD4 count < 200 cells/µL (< 14%) or unsuppressed viraemia once adequate immune reconstitution is achieved (HIV-VL undetectable and CD4 count > 200 cells/µL)
- As vaccine responses may be significantly lower in persons with HIV (i.e. lower seroconversion rates, faster titer decline), do not use rapid schedules (e.g. rabies, tick-borne encephalitis, HAV/HBV) and consider antibody titres to assess their effectiveness if vaccinated at CD4 count < 200 cells/µL or unsuppressed viremia (e.g. rabies, tick-borne encephalitis, HAV, meningococci). Be attentive to observe boosters and all post-exposure measures (particularly after potential rabies exposure)
- Avoid polysaccharide vaccination
- For background data, see http://www.bhiva.org/vaccination-guidelines.aspx

- For attenuated live vaccines(i)
  (in addition to restrictions for general population):
  - ***Varicella, measles, mumps, rubella, yellow fever**
    Contraindicated if CD4 count < 200 cells/µL (14%) and/or AIDS. Impaired protection after vaccination with unsuppressed viraemia. Administer immunoglobulins if exposed and not yet vaccinated
  - **Oral live typhoid**
    Preferred if CD4 count > 200 cells/µL (> 14%). Contraindicated if CD4 count < 200 cells/µL (14%): then give inactivated parenteral polysaccharide vaccine

INDICAZIONI ALLE VACCINAZIONI NELLE PLHIV

Vaccino	Immunodeficienza congenita[1],condizioni associate a immunodepressione[2-3] (es.trapianto d'organo o terapia antineoplastica, compresa la terapia sistemica corticosteroidea ad alte dosi), perdita di fluidi cerebrospinali	Infezione da HIV		Diabete (con complicanze o non controllato), malattie polmonari croniche, alcolismo cronico	Asplenia anatomica o funzionale, candidati alla splenectomia, deficienza terminale del complemento	Malattie epatiche croniche gravi	Insufficienza renale cronica, riceventi fattori della coagulazione concentrati	Operatori sanitari
		Conta dei linfociti T CD4+						
		< 200/µL	>= 200/µL					
dTpa	1 DOSE BOOSTER OGNI 10 ANNI							
MPR	CONTROINDICATO[1]	2 DOSI (0, 4-8 SETTIMANE)						
Varicella	CONTROINDICATO[1]	2 DOSI (0, 4-8 SETTIMANE)						
Influenza	1 DOSE ANNUALE							
Pneumococcico	2 DOSI (INIZIALE PCV+PPV23 A NON MENO DI 8 SETT.)							
Epatite B	3 DOSI (0,1,6 MESI)							
Epatite A	2 DOSI (0, 6-12 MESI)							
Meningococco coniugato ACWY135	2 dosi a distanza di almeno 8 settimane una dall'altra (vedi note specifiche per i soggetti ad alto rischio)							
Meningococco B	2 DOSI (vedi note specifiche per i soggetti ad alto rischio) - per gli intervalli tra le dosi in base all'età, vedi quanto riportato nella scheda tecnica							
HPV		2/3 a seconda dell'età						
Hib	1 DOSE							
Herpes Zoster	vedere paragrafo specifico n. 2.3.13							

Per tutte le persone in questa categoria con requisiti di età e che mancano di evidenza di immunità

(es.perdita di documenti di vaccinazione o non evidenza di precedente infezione)

Raccomandato se altri fattori di rischio sono presenti (es. su base medica, stili di vita o altre indicazioni)

Controindicato

Delibera Regionale 19-12-2022

HERPES ZOSTER: alcuni numeri

- Dopo la risoluzione clinica dell'infezione primaria, il VZV rimane quiescente nei gangli sensitivi delle radici dorsali del midollo spinale e/o dei nervi cranici, dove dà luogo all'infezione latente che, in seguito alla riattivazione del virus, determina un'eruzione cutanea dolorosa monolaterale, generalmente limitata al dermatomero innervato dal ganglio nervoso interessato.

- Si tratta di una condizione particolarmente comune: esami di screening **rivelano la presenza di anticorpi VZV nel 95%** circa della popolazione.

- Si calcola che **l'incidenza media di Herpes Zoster in Italia sia pari a 6,46/1000 abitanti**. I più colpiti sono gli anziani: 2/3 dei casi si manifestano in persone oltre i 50 anni di età, dato importante alla luce dell'aumento dell'aspettativa di vita. In un mondo che invecchia, **si stima che circa 1/4 - 1/3 dei soggetti nella fascia d'età > 50 anni svilupperà l'Herpes Zoster**.

- L'incidenza d HZ nelle persone che vivono con HIV stabilmente in ART è stimata **intono 9.3. per 1000 anni-persona**. Rimane comunque dalle 3 alle 5 volte più alta della popolazione generale.

HZ QUANTI VACCINI ESISTONO?

ZLV (Zoster Live vaccine)

- ZVL è indicato per la prevenzione dell'herpes zoster ("zoster" o fuoco di S. Antonio) e della nevralgia post-erpetica (post-herpes neuralgia, PHN) associata all'herpes zoster
- Virus della varicella-zoster1 , ceppo Oka/Merck, (vivo, attenuato)
- È indicato per l'immunizzazione di soggetti di età pari o superiore a 50 anni.
- Tale immunizzazione. in grado di ridurre di circa il 65% i casi di nevralgia post-erpetica e del 50% tutti i casi clinici di zoster.
- Approvato FDA/EMA 2006
- 1 dose

RZV (Recombinant Zoster Vaccine)

- RZV è indicato per la prevenzione dell'herpes zoster (HZ) e della nevralgia post-erpetica (postherpetic neuralgia, PHN),
- Glicoproteina E (gE) prodotta con tecnologia DNA ricombinante
- È indicato adulti di età pari o superiore a 50 anni e in per adulti di età pari o superiore a 18 anni ad aumentato rischio di HZ.
- EFFICACIA per HZ risultata di circa il 97% in soggetti di 50 anni d'età e del 91% nei soggetti con più di 70 anni. Per quanto riguarda la nevralgia post erpetica (PHN) si va da un 70% di efficacia nelle persone con più di 80 anni al 100% nei cinquantenni
- Approvato FDA/EMA nel 2017
- 2 dosi a distanza di 2 mesi (possibile schedula abbreviata)

Sia ZLV che RZV possono essere somministrati contemporaneamente agli altri vaccini previsti per la stessa età, in sedi anatomiche diverse, in particolare antinfluenzale, vaccini antipneumococcici, anti difterite tetano pertosse.

STUDI IN HIV: ZLV

Table 2. Primary Safety Endpoints and Vaccine Adverse Events

Endpoint/Adverse Event	ZOSTAVAX (n = 295) Estimate, % (95% CI)	Placebo (n = 97) Estimate, % (95% CI)	*P* Value[a]
Primary safety endpoints[b]	n = 15 5.1 (2.9–8.2)	n = 2 2.1 (.3–7.3)	.261
Injection site reactions	n = 124 42.0 (36.3–47.9)	n = 12 12.4 (6.6–20.6)	<.001
Rashes (generalized, varicella-like, or HZ-like)	n = 15 5.1 (2.9–8.2)	n = 4 4.1 (1.1–10.2)	1.00
Fever >38.3°C	n = 12 4.1 (2.1–7.0)	n = 6 6.2 (2.3–13.0)	.405

Table 3. Characteristics and Timing of Primary Safety Endpoints

Primary Safety Endpoint[a]	ZOSTAVAX			Placebo		
	Event	Week	$CD4^+$ Stratum	Event	Week	$CD4^+$ Stratum
SAE[a]	Cutaneous VZV[b]	1	High	Avascular hip necrosis	8	Low
	Pneumonia	6	Low	Malaise, pneumonia	12	Low
	Drug-induced delirium	6	High			
	Complex migraine	6	High			
	Bulimia	8	Low			
	Depression	8	Low			
	UTI	8	High			
	Cellulitis	9	Low			
Grade ≥3 non-SAE[a]	Fever	0	High			
	Acute pain	2	Low			
	Hypertension	4	Low			
	Fever	5	Low			
	Headache	9	High			
	Anorexia	12	Low			
	Fever	12	High			

Abbreviations: SAE, serious adverse event; UTI, urinary tract infection; VZV, varicella-zoster virus.

[a]International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use–defined SAEs and Division of AIDS grade 3 and 4 non-SAE-associated signs or symptoms occurring during the 6 weeks following each vaccination.

[b]Cutaneous VZV event was originally reported as possible disseminated VZV, later updated to the adverse event term "vaccine-related rash," deemed probably related to study therapy.

- Studio clinico randomizzato, in doppio cieco, ZLV è stato somministrato ad adulti affetti da HIV con conta delle cellule T CD4+ ≥ 200 cellule/mL sottoposti ad appropriata terapia antiretrovirale. E' stato usato un regime a due dosi. Le risposte immuno specifiche contro il virus della varicella zoster a seguito delle Dosi 1 e 2 sono risultate essere simili
- La sicurezza e l'efficacia di ZLV non sono state stabilite negli adulti affetti da HIV con o senza evidenza di immunosoppressione tuttavia, è stato completato uno studio di fase II di sicurezza e immunogenicità in adulti affetti da HIV
- Gli eventi avversi sono stati monitorati fino al Giorno 42 dopo la vaccinazione e gli eventi avversi gravi sono stati monitorati nel corso dell'intero periodo dello studio (ossia fino al Giorno 180). Tra i 295 soggetti che hanno ricevuto ZOSTAVAX, è stato riportato un caso grave di rash maculo-papulare correlato al vaccino

CID 2018:67 (1 December) • Benson et al

STUDI IN HIV:RZV

Safety and Immunogenicity of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in HIV-Infected Adults: A Phase 1/2a Randomized, Placebo-Controlled Study

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Background. Human immunodeficiency virus (HIV)–infected individuals are at increased risk of herpes zoster (HZ), even in the antiretroviral therapy (ART) era. Because concerns exist about the use of live-attenuated vaccines in immunocompromised individuals, a subunit vaccine may be an appropriate alternative.

Methods. This phase 1/2, randomized, placebo-controlled study evaluated the immunogenicity and safety of an investigational HZ subunit vaccine (HZ/su). Three cohorts of HIV-infected adults aged ≥18 years were enrolled: 94 ART recipients with a $CD4^+$ T-cell count of ≥200 cells/mm^3, 14 ART recipients with a $CD4^+$ T-cell count of 50–199 cells/mm^3, and 15 ART-naive adults with a $CD4^+$ T-cell count of ≥500 cells/mm^3. Subjects received 3 doses of HZ/su (50 μg varicella-zoster virus glycoprotein E [gE] combined with $AS01_B$ adjuvant) or 3 doses of saline at months 0, 2, and 6.

Results. One month after dose 3, serum anti-gE antibody concentrations and frequencies of gE-specific $CD4^+$ T cells were higher following HZ/su vaccination than after receipt of saline ($P < .0001$). Median cell-mediated immune responses peaked after dose 2. Humoral and cell-mediated immune responses persisted until the end of the study (month 18). No vaccination-related serious adverse events were reported. No sustained impact on HIV load or $CD4^+$ T-cell count was noted following vaccinations.

Conclusions. HZ/su was immunogenic and had a clinically acceptable safety profile in HIV-infected adults.

Clinical Trials Registration. NCT01165203.

Keywords. herpes zoster; zoster vaccine; HIV infection; varicella-zoster virus; immunodeficiency; glycoprotein E.

Table 2. Incidence of Solicited Local and General Symptoms Reported During the 7-Day Postvaccination Period Overall by Subject

	HZ/su (n = 73)		Saline (n = 48)	
Symptoms	No. (%)	95% CI, %	No. (%)	95% CI, %
Local				
Pain				
Any	72 (98.6)	92.6–100	6 (12.5)	4.7–25.2
Grade 3[a]	12 (16.4)	8.8–27	0 (0)	0–7.4
Redness				
Any	28 (38.4)	27.2–50.5	0 (0)	0–7.4
Grade 3[b]	4 (5.5)	1.5–13.4	0 (0)	0–7.4
Swelling				
Any	20 (27.4)	17.6–39.1	0 (0)	0–7.4
Grade 3[b]	1 (1.4)	0–7.4	0 (0)	0–7.4
General				
Fatigue				
Any	55 (75.3)	63.9–84.7	14 (29.2)	17–44.1
Grade 3[a]	12 (16.4)	8.8–27	4 (8.3)	2.3–20
Vaccine related	41 (56.2)	44.1–67.8	8 (16.7)	7.5–30.2
Gastrointestinal				
Any	28 (38.4)	27.2–50.5	11 (22.9)	12–37.3
Grade 3[a]	2 (2.7)	.3–9.5	1 (2.1)	.1–11.1
Vaccine related	16 (21.9)	13.1–33.1	7 (14.6)	6.1–27.8
Headache				
Any	47 (64.4)	52.3–75.3	15 (31.3)	18.7–46.3
Grade 3[a]	6 (8.2)	3.1–17	2 (4.2)	.5–14.3
Vaccine related	34 (46.6)	34.8–58.6	8 (16.7)	7.5–30.2
Myalgia				
Any	54 (74)	62.4–83.5	9 (18.8)	8.9–32.6
Grade 3[a]	10 (13.7)	6.8–23.8	1 (2.1)	.1–11.1
Vaccine related	44 (60.3)	48.1–71.5	8 (16.7)	7.5–30.2
Shivering				
Any	37 (50.7)	38.7–62.6	5 (10.4)	3.5–22.7
Grade 3[a]	11 (15.1)	7.8–25.4	0 (0)	0–7.4
Vaccine related	29 (39.7)	28.5–51.9	5 (10.4)	3.5–22.7
Fever				
Any[c]	22 (30.1)	19.9–42	3 (6.3)	1.3–17.2
Grade 3[d]	0 (0)	0–4.9	0 (0)	0–7.4
Vaccine related	17 (23.3)	14.2–34.6	2 (4.2)	.5–14.3

Abbreviations: CI, confidence interval; HZ/su, herpes zoster subunit vaccine candidate.

[a] Defined as preventing normal everyday activities.

[b] Defined as a diameter of >100 mm.

[c] Defined as an oral/axillary temperature of ≥37.5°C.

[d] Defined as an oral/axillary temperature of >39°C.

Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis

Zoster-039

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Summary

Background The adjuvanted recombinant zoster vaccine (Shingrix) can prevent herpes zoster in older adults and autologous haemopoietic stem cell transplant recipients. We evaluated the safety and immunogenicity of this vaccine in adults with haematological malignancies receiving immunosuppressive cancer treatments.

Methods In this phase 3, randomised, observer-blind, placebo-controlled study, done at 77 centres worldwide, we randomly assigned (1:1) patients with haematological malignancies aged 18 years and older to receive two doses of the adjuvanted recombinant zoster vaccine or placebo 1–2 months apart during or after immunosuppressive cancer treatments, and stratified participants according to their underlying diseases. The co-primary objectives of the study were the evaluation of safety and reactogenicity of the adjuvanted recombinant zoster vaccine compared with placebo from the first vaccination up to 30 days after last vaccination in all participants; evaluation of the proportion of participants with a vaccine response in terms of anti-glycoprotein E humoral immune response to the adjuvanted recombinant zoster vaccine at month 2 in all participants, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia; and evaluation of the anti-glycoprotein E humoral immune responses to the vaccine compared with placebo at month 2 in all participants, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia. We assessed immunogenicity in the per-protocol cohort for immunogenicity and safety in the total vaccinated cohort. The study is registered with ClinicalTrials.gov, number NCT01767467, and with the EU Clinical Trials Register, number 2012-003438-18.

Findings Between March 1, 2013, and Sept 10, 2015, we randomly assigned 286 participants to adjuvanted recombinant zoster vaccine and 283 to placebo. 283 in the vaccine group and 279 in the placebo group were vaccinated. At month 2, 119 (80·4%, 95% CI 73·1–86·5) of 148 participants had a humoral vaccine response to adjuvanted recombinant zoster vaccine, compared with one (0·8%, 0·0–4·2) of 130 participants in the placebo group, and the adjusted geometric mean anti-glycoprotein E antibody concentration was 23132·9 mIU/mL (95% CI 16642·8–32153·9) in the vaccine group and 777·6 mIU/mL (702·8–860·3) in the placebo group (adjusted geometric mean ratio 29·75, 21·09–41·96; p<0·0001) in all patients, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia. Humoral and cell-mediated immune responses persisted above baseline until month 13 in all strata and, as expected, vaccine was more reactogenic than placebo (within 7 days after vaccination pain was reported by 221 [79·5%] of 278 vaccine group participants and 45 [16·4%] of 274 placebo group participants; fatigue was reported by 162 [58·3%] of 278 vaccine group participants and 102 [37·2%] of 274 placebo group participants). Incidences of unsolicited or serious adverse events, potential immune-mediated diseases, disease-related events, and fatal serious adverse events were similar between the groups.

Interpretation The immunocompromised adult population with haematological malignancies is at high risk for herpes zoster. The adjuvanted recombinant zoster vaccine, which is currently licensed in certain countries for adults aged 50 years and older, is likely to benefit this population.

Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation

A Randomized Clinical Trial

Zoster-002

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IMPORTANCE Herpes zoster, a frequent complication following autologous hematopoietic stem cell transplantation (HSCT), is associated with significant morbidity. A nonlive adjuvanted recombinant zoster vaccine has been developed to prevent posttransplantation zoster.

OBJECTIVE To assess the efficacy and adverse event profile of the recombinant zoster vaccine in immunocompromised autologous HSCT recipients.

DESIGN, SETTING, AND PARTICIPANTS Phase 3, randomized, observer-blinded study conducted in 167 centers in 28 countries between July 13, 2012, and February 1, 2017, among 1846 patients aged 18 years or older who had undergone recent autologous HSCT.

INTERVENTIONS Participants were randomized to receive 2 doses of either recombinant zoster vaccine (n = 922) or placebo (n = 924) administered into the deltoid muscle; the first dose was given 50 to 70 days after transplantation and the second dose 1 to 2 months thereafter.

MAIN OUTCOMES AND MEASURES The primary end point was occurrence of confirmed herpes zoster cases.

RESULTS Among 1846 autologous HSCT recipients (mean age, 55 years; 688 [37%] women) who received 1 vaccine or placebo dose, 1735 (94%) received a second dose and 1366 (74%) completed the study. During the 21-month median follow-up, at least 1 herpes zoster episode was confirmed in 49 vaccine and 135 placebo recipients (incidence, 30 and 94 per 1000 person-years, respectively), an incidence rate ratio (IRR) of 0.32 (95% CI, 0.22-0.44; $P < .001$), equivalent to 68.2% vaccine efficacy. Of 8 secondary end points, 3 showed significant reductions in incidence of postherpetic neuralgia (vaccine, n=1; placebo, n=9; IRR, 0.1; 95% CI, 0.00-0.78; $P = .02$) and of other prespecified herpes zoster–related complications (vaccine, n=3; placebo, n=13; IRR, 0.22; 95% CI, 0.04-0.81; $P = .02$) and in duration of severe worst herpes zoster–associated pain (vaccine, 892.0 days; placebo, 6275.0 days; hazard ratio, 0.62; 95% CI, 0.42-0.89; $P = .01$). Five secondary objectives were descriptive. Injection site reactions were recorded in 86% of vaccine and 10% of placebo recipients, of which pain was the most common, occurring in 84% of vaccine recipients (grade 3: 11%). Unsolicited and serious adverse events, potentially immune-mediated diseases, and underlying disease relapses were similar between groups at all time points.

CONCLUSIONS AND RELEVANCE Among adults who had undergone autologous HSCT, a 2-dose course of recombinant zoster vaccine compared with placebo significantly reduced the incidence of herpes zoster over a median follow-up of 21 months.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT01610414

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Supplemental content

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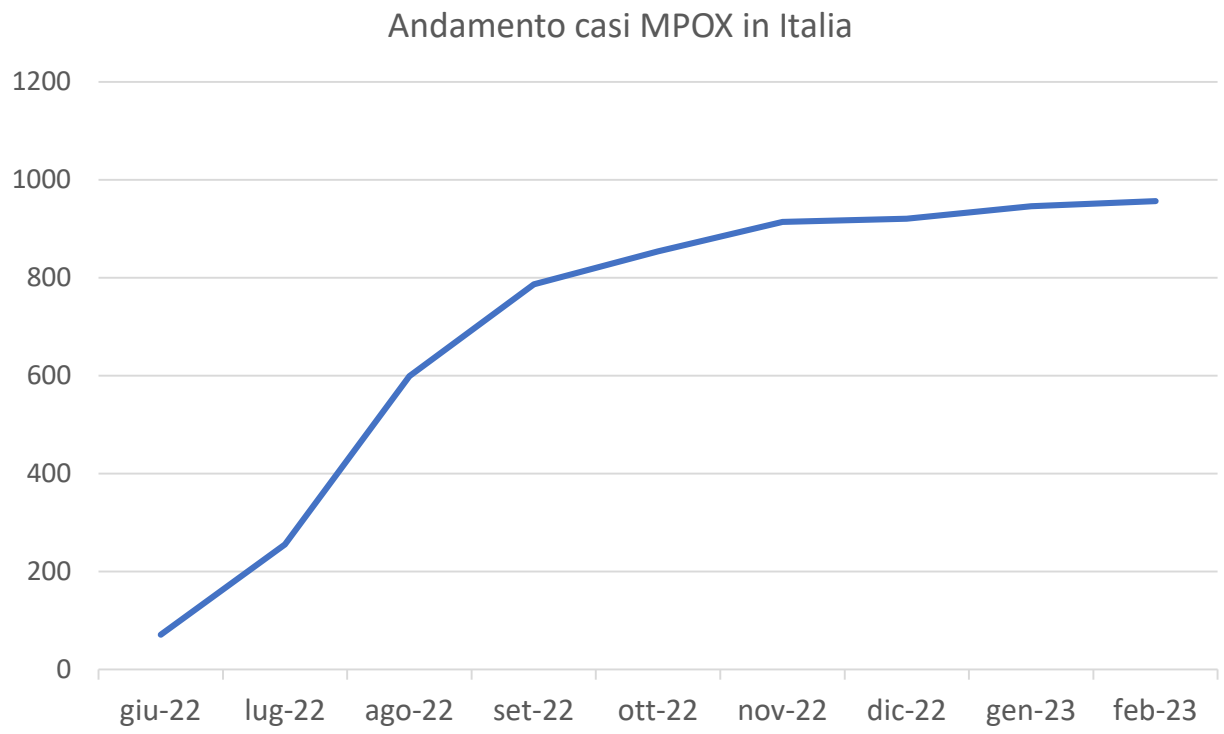
DELIBERA REGIONALE 19-12-2022: per fare ordine

SOGGETTI DI ETÀ SUPERIORE AI 65 ANNI	Una dose di vaccino a virus vivo attenuato ZLV
SOGGETTI TRA I 18 E I 49 ANNI: cardiopatie croniche (esclusa l'ipertensione isolata), diabete mellito, malattie polmonari croniche, candidati a terapia immunosoppressiva, malattie reumatologiche o immunologiche in attesa o in corso di terapia immunosoppressiva, patologie oncologiche e oncoematologiche, trattamento dialitico, **positività al virus dell'immunodeficienza umana acquisita (HIV),** attesa di trapianto di organo solido, trapiantati di organo solido e trapiantati con cellule staminali emopoietiche; zoster recidivante.	2 dosi di vaccino glicoproteico ricombinante RZV a distanza di 2 mesi
SOGGETTI DI ETÀ SUPERIORE AI 50 ANNI se affetti da diabete mellito tipo 2 senza complicanze, in terapia al massimo con un solo farmaco antidiabetico orale, cardiopatie croniche in buon compenso, scompenso cardiaco classe NYHA I e II, BPCO se VEMS > 50% con sintomi lievi.	Una dose di vaccino a virus vivo attenuato ZLV
SOGGETTI DI ETÀ PARI O SUPERIORE AI 50 ANNI: con alta fragilità per diabete mellito trattato con terapia insulinica o con almeno due farmaci ipoglicemizzanti o diabete con complicanze, cardiopatie croniche con scompenso cardiaco in classe avanzata – NYHA III-IV, post shock cardiogeno, portatori di dispositivi medici cardiaci impiantati attivi,broncopneumopatie croniche ostruttive, asma, fibrosi polmonare idiopatica, soggetti in ossigenoterapia, candidati a terapia immunosoppressiva, malattie reumatologiche in attesa o in corso di terapia immunosoppressiva, patologie oncologiche e oncoematologiche, trattamento dialitico, **positività al virus dell'immunodeficienza umana acquisita (HIV)**, attesa di trapianto di organo solido, trapiantati di organo solido e trapiantati con cellule staminali emopoietiche), zoster recidivante.	2 dosi di vaccino glicoproteico ricombinante RZV a distanza di 2 mesi

MPOX: alcuni numeri



Bollettino di VENERDÌ 10 FEBBRAIO 2023

DATI NAZIONALI	
Casi confermati	957
Incremento rispetto all'ultima rilevazione	0
Casi collegati a viaggi all'estero	252
Età mediana in anni (range)	37 (14-71)
Genere	943 M; 14 F

DATI REGIONALI		
Regioni	**Casi confermati**	**Incremento rispetto all'ultima rilevazione**
Abruzzo	5	0
Basilicata	0	0
Calabria	0	0
Campania	47	0
Emilia - Romagna	89	0
Friuli - Venezia Giulia	14	0
Lazio	161	0
Liguria	28	2
Lombardia	410	0
Marche	8	0
Molise	0	0
Piemonte	34	0
Puglia	21	0
Sardegna	6	0
Sicilia	16	0
Toscana	47	0
PA. Bolzano	1	0
PA. Trento	4	0
Umbria	0	0
Valle d'Aosta	0	0
Veneto	66	0

VACCINI DISPONIBILI PER VAIOLO (e poi MPOX)

	Pre-exposure indications	Post-exposure indications*	Administration	Common side-effects	Serious adverse events	Contraindications
Replication-competent vaccinia virus, second-generation (ACAM2000)	Research laboratory personnel working with orthopoxviruses; clinical laboratory personnel doing diagnostic testing for orthopoxviruses; designated response team members; health care-personnel who administer ACAM2000 or care for patients infected with orthopoxviruses; and not recommended for the general population as of June, 2022	Unprotected direct contact with an active orthopoxvirus lesion or fluid or a contaminated item; being within 2 m of an individual with an active orthopoxvirus case for 3 h or more	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, fatigue, and bacterial infection at the administration site	Myopericarditis and pericarditis, encephalitis, progressive vaccinia, erythema multiforme major, eczema, vaccinatum, generalised vaccinia, post-vaccinial encephalitis or encephalomyelitis, blindness due to autoinoculation, and fetal death in pregnant women	Atopic dermatitis†, active exfoliative skin conditions†, immunosuppression†, pregnancy†, age <1 year†, breastfeeding, serious vaccine component allergy, underlying heart disease, and ≥3 major cardiac risk factors
Attenuated, minimally replication-competent vaccinia virus, third-generation (LC16m18, available in Japan)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis; not recommended for the general population as of June, 2022	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women if modified vaccinia virus Ankara-Bavarian Nordic not available; licensed in Japan for use in children	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, and fatigue	None noted in clinical trials	Serious vaccine component allergy
Replication-deficient modified vaccinia Ankara, third-generation (JYNNEOS)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women	Two subcutaneous doses, 28 days apart	Injection site reactions, myalgia, headache, fatigue, nausea, and chills	None	Serious vaccine component allergy

*Post-exposure vaccination is ideally provided within 4 days of exposure to prevent infection; however, vaccination within 4–14 days of exposure can reduce disease severity if infection were to occur. †Including household contacts with the condition.

Table 1: **Indications, administration, side-effects, and contraindications for smallpox and monkeypox vaccination**[32-37]

Although the United States has a large supply of ACAM2000, this vaccine has more side effects and contraindications than JYNNEOS. Therefore, JYNNEOS should be used for people who are at high risk for severe disease caused by infection with mpox virus including, but not limited to, people with human immunodeficiency virus (HIV) infection or other immunocompromising conditions. At this time, the safety of JYNNEOS in pregnant people and children has not been studied. Therefore, the risks and benefits should be weighed in the decision to vaccinate.

CDC

IMMUNITY AGAINST SMALLPOX & MPOX

- Increase in monkeypox incidence linked to the cessation of smallpox vaccination is due to an increasingly immunologically naive population
- High degree of sequence similarity between orthopoxviruses (+++ shared immune epitopes)
- Cross-reactivity / cross immunity between orthopoxviruses
- The effectiveness of Jynneos for the prevention of monkeypox disease is inferred from the antibody responses in the smallpox clinical study participants and from studies in non-human primates that showed protection of animals vaccinated with Jynneos who were exposed to the monkeypox virus. (Earl et al., 2008; Keckler et al., 2011; Stittelaar et al., 2005).
- T-cell responses recognise epitopes within a wide diversity of viral proteins
- Current available vaccine have ben developed as smallpox vaccines (against variola virus)

Poland GA, et al. *Lancet Infect Dis*. 2022

SUPPORTO CROSS-PROTEZIONE: dati studi

- Surveillance data from Zaire 1980–84: monkeypox attack rates are higher in individuals without previous smallpox vaccination than in those with previous vaccination (estimated protective efficacy of 85%)

- USA outbreak (2003): 10 of 23 (43.5%) unvaccinated cases experienced moderate to severe monkeypox illness compared to 1 of 6 (16.6%) vaccinated cases

- Field evaluation of effectiveness of IMVAMUNE® in health care workers in RD Congo *ongoing* (clinical trial started in 2017)

Fine PE, et al *Int J Epidemiol* 1988
Karem KL, et al *Clin Vaccine Immunol*. 2007
Petersen BW, et al *Antiviral Res*. 2019

Cortesia Prof. L. Zammarchi

AUTORIZZAZIONE VACCINO MVA-BN IN ITALIA

Il 4 Agosto 2022 il Ministero della Salute ha approvato l'utilizzo del vaccino vivo attenuato, non replicativo MVA-BN (Jynneos®).

- personale di laboratorio con possibile esposizione diretta a orthopoxvirus.
- persone gay, transgender, bisessuali e altri uomini che hanno rapporti sessuali con uomini (MSM), che rientrano nei seguenti criteri di rischio:

• storia recente (ultimi 3 mesi) con più partner sessuali;
• partecipazione a eventi di sesso di gruppo;
• partecipazione a incontri sessuali in locali/club/cruising/saune;
• recente infezione sessualmente trasmessa (almeno un episodio nell'ultimo anno);
• abitudine alla pratica di associare gli atti sessuali al consumo di droghe chimiche (Chemsex).

STRATEGIA VACCINALE: non solo prima dell'esposizione

Post-Exposure Prophylaxis (PEP)
Vaccination **after known or presumed exposure** to mpox virus. Eligible populations include:

- People who are known contacts to someone with mpox and who are identified by public health authorities, for example via case investigation, contact tracing, or risk exposure assessment; or
- People who are aware that a recent sex partner within the past 14 days was diagnosed with mpox; or
- Gay, bisexual, or other men who have sex with men, and transgender or nonbinary people (including adolescents who fall into any of the aforementioned categories), who have had any of the following within the past 14 days: sex with multiple partners (or group sex); sex at a commercial sex venue; or sex in association with an event, venue, or defined geographic area where mpox transmission is occurring.

- The efficacy of these therapies for mpox PEP is unknown
- Early use of vaccination (within 4 days from exposure) could prevent mpox, later use (5 days or more after exposure) may decrease the severity of mpox if infection does occur.
- In a person who is severely immunocompromised with a known high-risk exposure (who is at risk for severe mpox), the benefits of vaccination more than 14 days after exposure may still outweigh risks.

E NELLE PERSONE CHE VIVONO CON HIV?

MPOX in HIV una relazione pericolosa

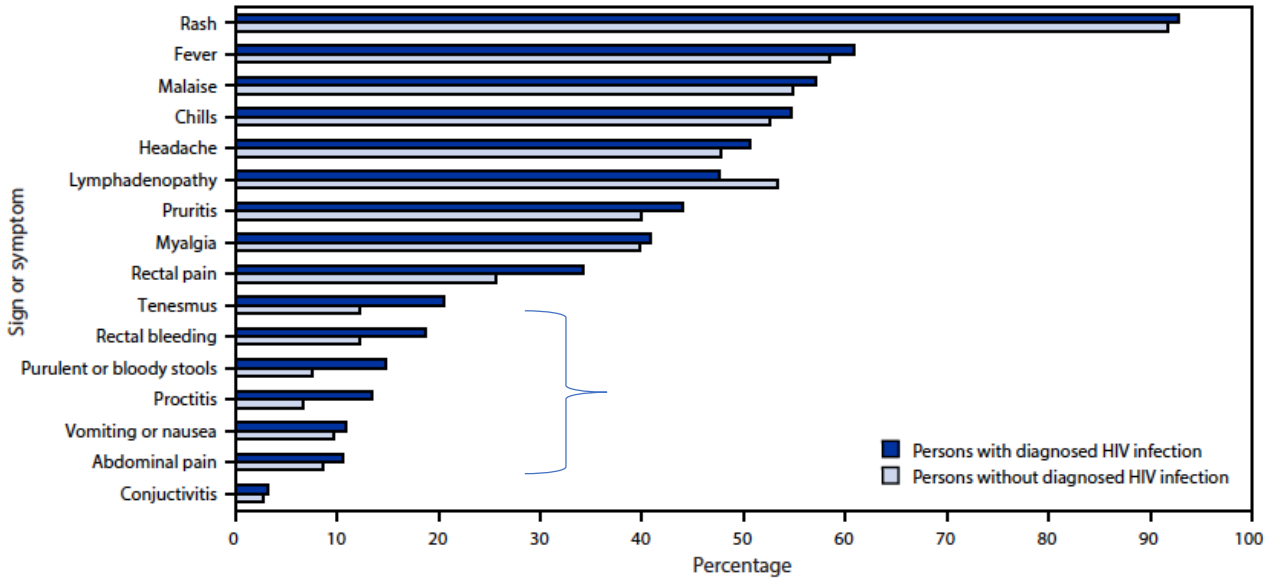
TABLE 2. Monkeypox hospitalization, sexually transmitted infections, and HIV prevention and care characteristics, by HIV infection status* — eight U.S. jurisdictions,† May 17–July 22, 2022

Characteristic	No. (%) of persons with monkeypox§	No. (%) of persons without diagnosed HIV infection§	No. (%) of persons with diagnosed HIV infection§
Total	**1,969**	**1,214**	**755**
Hospitalization during monkeypox illness			
Hospitalized for monkeypox¶	68 (5)	26 (3)	42 (8)
Duration of hospitalization, median, days (range)**	3 (0–10)	3 (0–10)	2 (0–7)
History of STIs			
Reportable STI diagnosis during preceding yr	816 (41)	453 (37)	363 (48)
Gonorrhea	546 (28)	307 (25)	239 (32)
Chlamydia	489 (25)	278 (23)	211 (28)
Syphilis	165 (8)	69 (6)	96 (13)
STI diagnosis since May 1, 2022	297 (15)	166 (14)	131 (17)
No. of STIs diagnosed during preceding yr			
1	396 (20)	220 (18)	176 (23)
2	222 (11)	117 (10)	105 (14)
≥3	198 (10)	116 (10)	82 (11)
HIV prevention and care characteristic			
Received HIV care in preceding yr††	NA	NA	713 (94)
Suppressed HIV viral load§§	NA	NA	618 (82)
Recent CD4 count cells/μL, median (IQR)¶¶	NA	NA	639 (452–831)
CD4 count <350 cells/μL	NA	NA	91 (12)
CD4 count <200 cells/μL	NA	NA	25 (3)
Yrs since HIV diagnosis, median (IQR)	NA	NA	10 (6–15)
HIV diagnosis since May 1, 2022	NA	NA	19 (3)
Current HIV PrEP use***	NA	115 (67)	NA

MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 36
September 9, 2022

HIV and Sexually Transmitted Infections Among Persons with Monkeypox — Eight U.S. Jurisdictions, May 17–July 22, 2022

FIGURE. Signs and symptoms of monkeypox,*,† by HIV infection status§ — eight U.S. jurisdictions,¶ May 17–July 22, 2022



- Tra le 1969 persone con MPOX, 38% era una PLHIV e 41% aveva una precedente STI
- Dati limitati suggeriscono che persone con più bassi CD4 possano andare incontro a quadri clinici più severi e più frequenti ospedalizzazioni

Curran et al MMWR Morb Mortal Wkly Rep. 2022

MPOX in HIV una relazione pericolosa

TABLE 1. Characteristics of hospitalized patients with severe manifestations of monkeypox* for whom CDC provided clinical consultation (N = 57) — United States, August 10–October 10, 2022

Characteristic	No. (%)
Median age, yrs (range)	34 (20–61)
Sex	
Male	54 (94.7)
Race and ethnicity	
Black or African American, non-Hispanic	39 (68.4)
White, non-Hispanic	8 (14.0)
Hispanic or Latino	8 (14.0)
Asian, non-Hispanic	1 (1.8)
Multiple races, non-Hispanic	1 (1.8)
Experiencing homelessness†	13 (22.8)
Any immunocompromising condition§	51 (89.5)
HIV infection	47 (82.5)
History of solid organ transplantation	3 (5.3)
Hematologic malignancy (current chemotherapy)	2 (3.5)
Pregnant	3 (5.3)
Clinical manifestation¶	
Dermatologic	57 (100.0)
Mucosal**	39 (68.4)
Pulmonary	12 (21.1)
Ocular	12 (21.1)
Deep tissue (muscle or bone)	5 (8.8)
Neurologic	4 (7.0)
Monkeypox-directed therapy††	
Tecovirimat (oral)	53 (93.0)
Tecovirimat (intravenous)	37 (64.9)
VIGIV	29 (50.9)
Cidofovir††	13 (22.8)
Received ICU-level care	17 (29.8)
STI coinfection§§	16 (28.1)

FIGURE. Disseminated lesions on the back and hands of a patient* with severe monkeypox — United States, August 10–October 10, 2022

Photos/Alexandra Dretler
* Patient has consented to the publication of these photographs.

TABLE 2. Laboratory and treatment characteristics of hospitalized patients with HIV infection and severe monkeypox* for whom CDC provided clinical consultation (N = 47) — United States, August 10–October 10, 2022

Characteristic (no. with information available)	No. (%)
HIV CD4, cells/mm^3 (43)	
<50	31 (72.1)
50–200	9 (20.9)
>200	3 (7.0)
HIV Treatment (47)	
On ART at the time of monkeypox diagnosis	4 (8.5)

Abbreviation: ART = antiretroviral therapy.
* Severe manifestations of monkeypox include, but are not limited to, the clinical findings listed at https://emergency.cdc.gov/han/2022/han00475.asp.

- This report summarizes findings from CDC clinical consultations provided for 57 patients aged ≥18 years who were hospitalized with severe manifestations of monkeypox¶ during August 10–October 10
- Twelve patients died, and monkeypox was a cause of death or contributing factor in five patients to date, with several other deaths still under investigation.

Miller et al MMWR Morb Mortal Wkly Rep. 2022

MPOX in HIV una relazione pericolosa

Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report

Adesola Yinka-Ogunleye, Olusola Aruna, Mahmood Dalhat, Dimie Ogoina, Andrea McCollum, Yahyah Disu, Ibrahim Mamadu, Afolabi Akinpelu, Adama Ahmad, Joel Burga, Adolphe Ndoreraho, Edouard Nkunzimana, Lamin Manneh, Amina Mohammed, Olawunmi Adeoye, Daniel Tom-Aba, Bernard Silenou, Oladipupo Ipadeola, Muhammad Saleh, Ayodele Adeyemo, Ifeoma Nwadiutor, Neni Aworabhi, Patience Uke, Doris John, Paul Wakama, Mary Reynolds, Matthew R Mauldin, Jeffrey Doty, Kimberly Wilkins, Joy Musa, Asheena Khalakdina, Adebayo Adedeji, Nwando Mba, Olubunmi Ojo, Gerard Krause, Chikwe Ihekweazu*, for the CDC Monkeypox Outbreak Team†*

Summary

Background In September, 2017, human monkeypox re-emerged in Nigeria, 39 years after the last reported case. We aimed to describe the clinical and epidemiological features of the 2017–18 human monkeypox outbreak in Nigeria.

Methods We reviewed the epidemiological and clinical characteristics of cases of human monkeypox that occurred between Sept 22, 2017, and Sept 16, 2018. Data were collected with a standardised case investigation form, with a case definition of human monkeypox that was based on previously established guidelines. Diagnosis was confirmed by viral identification with real-time PCR and by detection of positive anti-orthopoxvirus IgM antibodies. Whole-genome sequencing was done for seven cases. Haplotype analysis results, genetic distance data, and epidemiological data were used to infer a likely series of events for potential human-to-human transmission of the west African clade of monkeypox virus.

Findings 122 confirmed or probable cases of human monkeypox were recorded in 17 states, including seven deaths (case fatality rate 6%). People infected with monkeypox virus were aged between 2 days and 50 years (median 29 years [IQR 14]), and 84 (69%) were male. All 122 patients had vesiculopustular rash, and fever, pruritus, headache, and lymphadenopathy were also common. The rash affected all parts of the body, with the face being most affected. The distribution of cases and contacts suggested both primary zoonotic and secondary human-to-human transmission. Two cases of health-care-associated infection were recorded. Genomic analysis suggested multiple introductions of the virus and a single introduction along with human-to-human transmission in a prison facility.

Interpretation This study describes the largest documented human outbreak of the west African clade of the monkeypox virus. Our results suggest endemicity of monkeypox virus in Nigeria, with some evidence of human-to-human transmission. Further studies are necessary to explore animal reservoirs and risk factors for transmission of the virus in Nigeria.

Nigeria, which is the largest known outbreak of the west African clade of monkeypox virus to date. Genomic analysis of seven samples from Rivers state, combined with contact information, suggested that there have been multiple introductions into the human population, with some evidence of human-to-human transmission. Seven people with monkeypox virus infection died, four of whom had HIV infection. By contrast with previous outbreaks, which mostly affected children and rural dwellers, cases were mostly young adults and people living in urban or peri-urban areas.

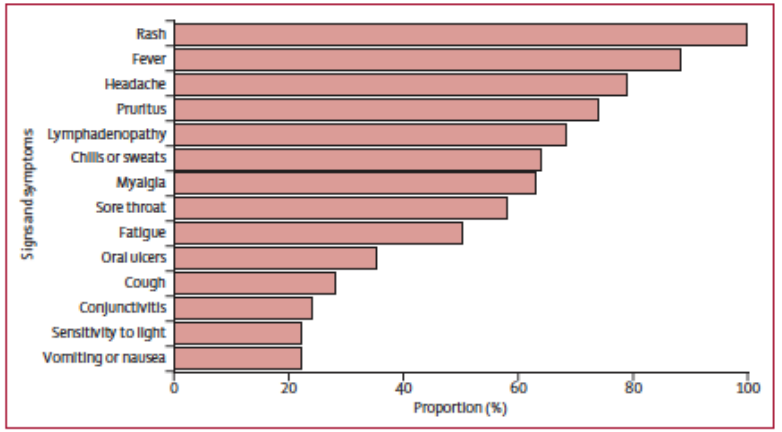


Figure 4: **Frequency of signs and symptoms in people with confirmed monkeypox virus infection in Nigeria, 2017–18**
Percentages were calculated individually for each symptom on the basis of the number of patients with available data.

MPOX in HIV con robusto sistema immunitario

- In contrast, reports from European countries, where the majority of persons with HIV are taking antiretroviral therapy (ART) and have high CD4 cell counts, have not described excess hospitalizations among people who are coinfected with HIV and mpox.

The WHO has stated that:

"*people with HIV…who take ART and have a robust immune system have not reported a more severe course of disease*."

CDC; WHO

Serological responses to the MVA-based JYNNEOS monkeypox vaccine in a cohort of participants from the Democratic Republic of Congo

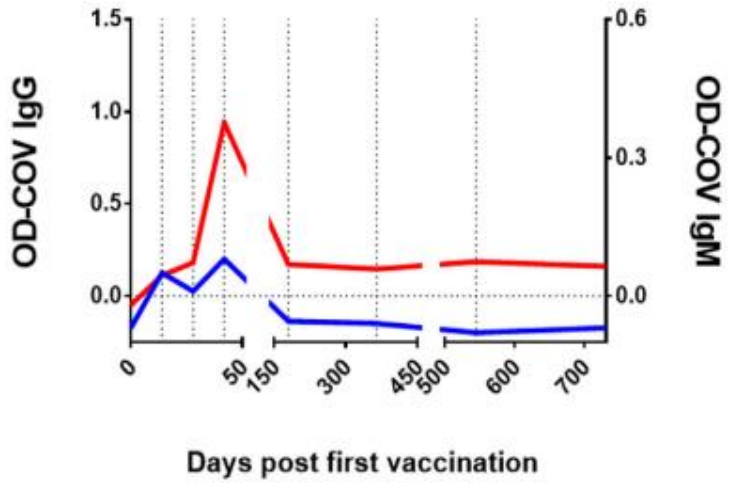
Lalita Priyamvada [a], William C. Carson [a], Eddy Ortega [a], Terese Navarra [a], Stephanie Tran [a], Todd G. Smith [a], Elisabeth Pukuta [b], Elisabeth Muyamuna [b], Joelle Kabamba [c], Beatrice U. Nguete [d], Toutou Likafi [d], Gaston Kokola [d], Robert Shongo Lushima [e], Jean-Jacques Muyembe Tamfum [b], Emile W. Okitolonda [d,1], Didine K. Kaba [d], Benjamin P. Monroe [a], Andrea M. McCollum [a], Brett W. Petersen [a], Panayampalli S. Satheshkumar [a], Michael B. Townsend [a,*]

A B S T R A C T

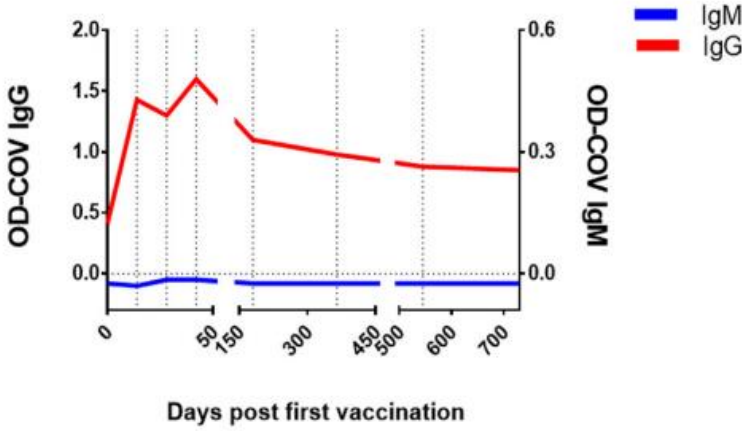
The current worldwide monkepox outbreak has reaffirmed the continued threat monkeypox virus (MPXV) poses to public health. JYNNEOS, a Modified Vaccinia Ankara (MVA)-based live, non-replicating vaccine, was recently approved for monkeypox prevention for adults at high risk of MPXV infection in the United States. Although the safety and immunogenicity of JYNNEOS have been examined previously, the clinical cohorts studied largely derive from regions where MPXV does not typically circulate. In this study, we assess the quality and longevity of serological responses to two doses of JYNNEOS vaccine in a large cohort of healthcare workers from the Democratic Republic of Congo (DRC). We show that JYNNEOS elicits a strong orthopoxvirus (OPXV)-specific antibody response in participants that peaks around day 42, or 2 weeks after the second vaccine dose. Participants with no prior history of smallpox vaccination or exposure have lower baseline antibody levels, but experience a similar fold-rise in antibody titers by day 42 as those with a prior history of vaccination. Both previously naïve and vaccinated participants generate vaccinia virus and MPXV-neutralizing antibody in response to JYNNEOS vaccination. Finally, even though total OPXV-specific IgG titers and neutralizing antibody titers declined from their peak and returned close to baseline levels by the 2-year mark, most participants remain IgG seropositive at the 2-year timepoint. Taken together, our data demonstrates that JYNNEOS vaccination triggers potent OPXV neutralizing antibody responses in a cohort of healthcare workers in DRC, a monkeypox-endemic region. MPXV vaccination with JYNNEOS may help ameliorate the disease and economic burden associated with monkeypox and combat potential outbreaks in areas with active virus circulation.

Published by Elsevier Ltd.

NAIVE

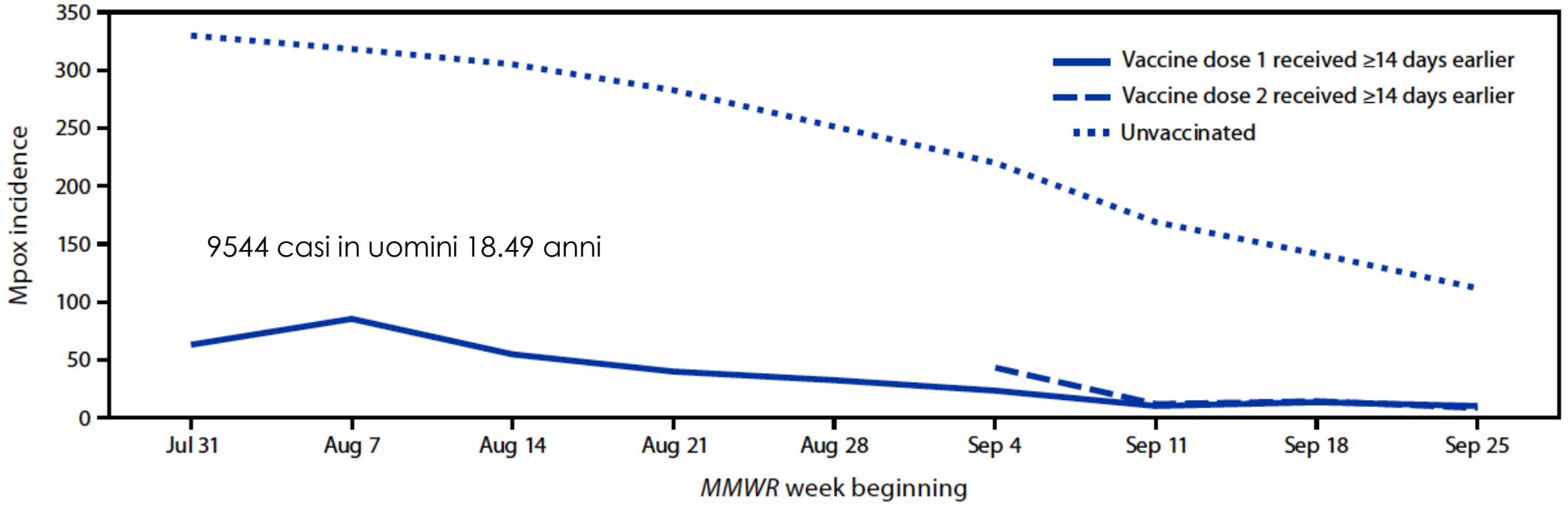


Prior Vaccination



EFFICACIA VACCINAZIONE MPOX: dati real-life

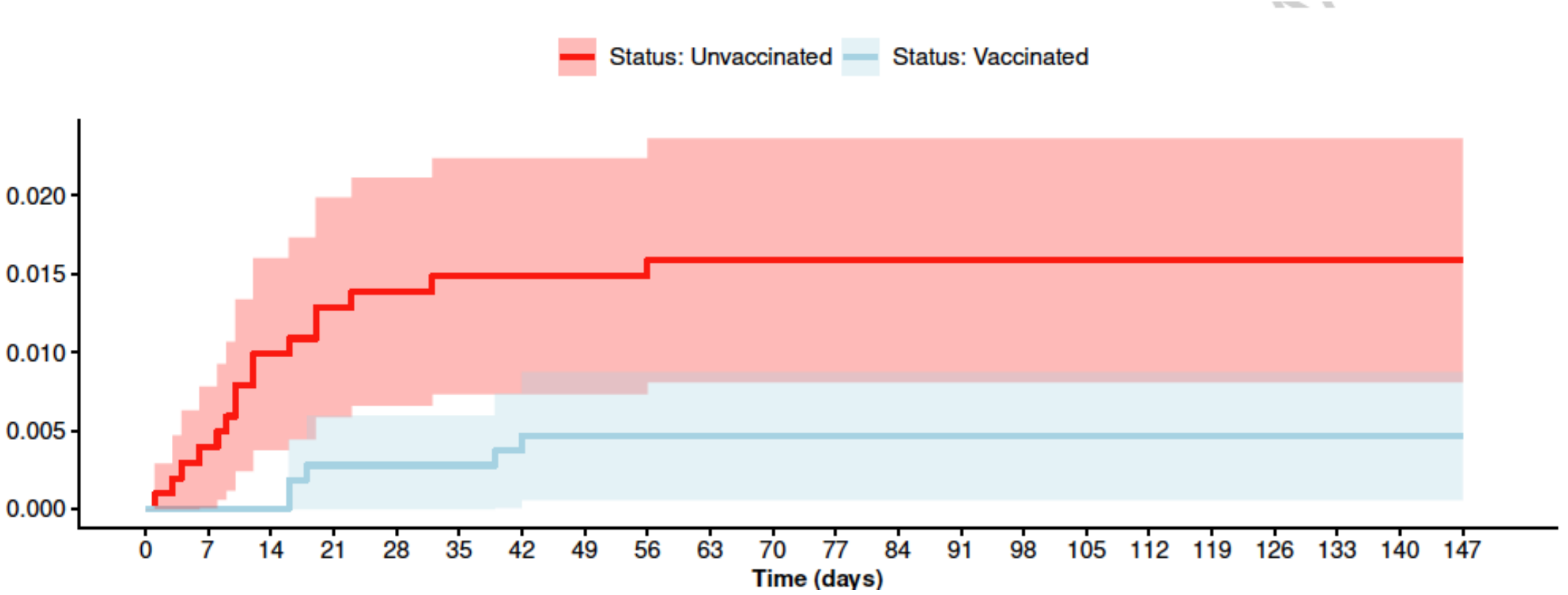
FIGURE. Weekly mpox incidence* among vaccine-eligible† men aged 18–49 years, by vaccination status§ — 43 U.S. jurisdictions,¶, July 31–October 1, 2022**



- Among JYNNEOS vaccine-eligible men aged 18–49 years
- Incidenza nei NON vaccinati 7.4 (95%CI 6.0-9.1) volte maggiore rispetto a chi si è vaccinato con una dose
- Incidenza nei NON vaccinati 9.6 (95%CI 6.9-13.2) volte maggiore rispetto a chi si è vaccinato con due dosi
- Nessuna differenza di distrubuzione tra via sottocutanea o intradermica

Payne AB, et al *MMWR Morb Mortal Wkly Rep*. 2022

EFFICACIA VACCINAZIONE MPOX: dati real-life



- Valutazione di una dose singola sottocutanea in 2054 soggetti di cui 1037 vaccinati
- 5 infezioni nel gruppo vaccinati | 16 infezioni nel gruppo non vaccinati
- HR 0.14 (95% Confidence Interval (CI) 0.05 – 0.41
- Efficacia di una dose 86% (95%CI 59%-95%)

Sagy, Y. W. et al.. Nature Medicine

SICUREZZA VACCINAZIONE MPOX: dati real-life

- During May 22–October 21, 2022, a total of 987,294 JYNNEOS vaccine doses were administered in the United States
- 66% (652,641) first doses ; 34% (334,568) second doses
- 51% intradermally, 34% subcutaneously, 15% unknown
- 90% male; 1,003 persons aged <18 years
- 1350 reports
- 685 (51%) documented an adverse health event. The reporting rates of adverse health events were similar for intradermal and subcutaneous administration (648 and 627 reports per million doses administered, respectively) (RR = 1.03; 95% CI = 0.87–1.24).
- Fourteen reports (1%) out 1350 reports were classified as serious.
  - **2 deaths** in males aged 37 and 58 years were reported, both within 2 days of vaccination. In one case, **drowning** was the cause of death. The death certificate is pending for the other case.
  - 9 serious because of hospitalization : **myocarditis (2)**, **pericarditis (2)**, appendicitis (1), aseptic meningitis (1), atrial fibrillation (1), idiopathic thrombocytopenic purpura (1), and methemoglobinemia (1).
  - The myocarditis reporting rate was 1.53 cases per million doses within 30 days after receipt of dose 1 and 2.99 after dose 2.
  - **3 anaphylaxis** (3.04; 95% CI = 0.63–8.88 cases per million doses administered)
  - 3 vaccinated permanent damage in their own assessment: injection site discoloration (one), injection site pain (one), and injection site scar (one).

TABLE 3. Reporting rates for adverse events of special interest after JYNNEOS vaccine receipt — Vaccine Adverse Event Reporting System, United States, May 22–October 21, 2022

Adverse event/ Dose	Postvaccination risk interval	No. of reports	No. of doses administered	Reporting rate* (95% CI)
Myocarditis				
After dose 1	30 days	1	652,641	1.53 (0.04–8.54)
After dose 2		1	334,568	2.99 (0.08–16.65)
Anaphylaxis				
After dose 1	24 hours	2	652,641	3.06 (0.37–11.07)
After dose 2		1	334,568	2.99 (0.08–16.65)

* Reports per million doses administered.

Duffy J, et al. *MMWR Morb Mortal Wkly Rep*. 2022

Cortesia Prof. L. Zammarchi

ESPERIENZA AOU CAREGGI: dal 15/09/2022 al 28/11/2022

Table 1. Baseline characteristics of a group of people vaccinated for MPOX from 15/09/2022 to 28/11/2022 at the outpatient clinic of the Infectious and Tropical Diseases unit, Careggi University Hospital, Florence, Italy

	N (183)	%
Gender		
• Man	154	84.1
• Woman	6	3.3
• Transgender woman	23	12.6
Median age in years [IQR]	41	[34-48]
Country of Origin		
• Italy	140	76.5
• Peru	28	15.3
• Brasil	6	3.3
• Other	9	4.9
Self-defining MSM	146	79.8
Self-defining Sex worker	22	12.0
Recruitment site		
• Healthcare workers/laboratory personnel	13	7.1
• Person living with HIV	83	45.4
• Pre-Exposure prophylaxis	25	13.6
• Vaccinated people not in follow-up in the outpatient clinic (external)	62	33.9

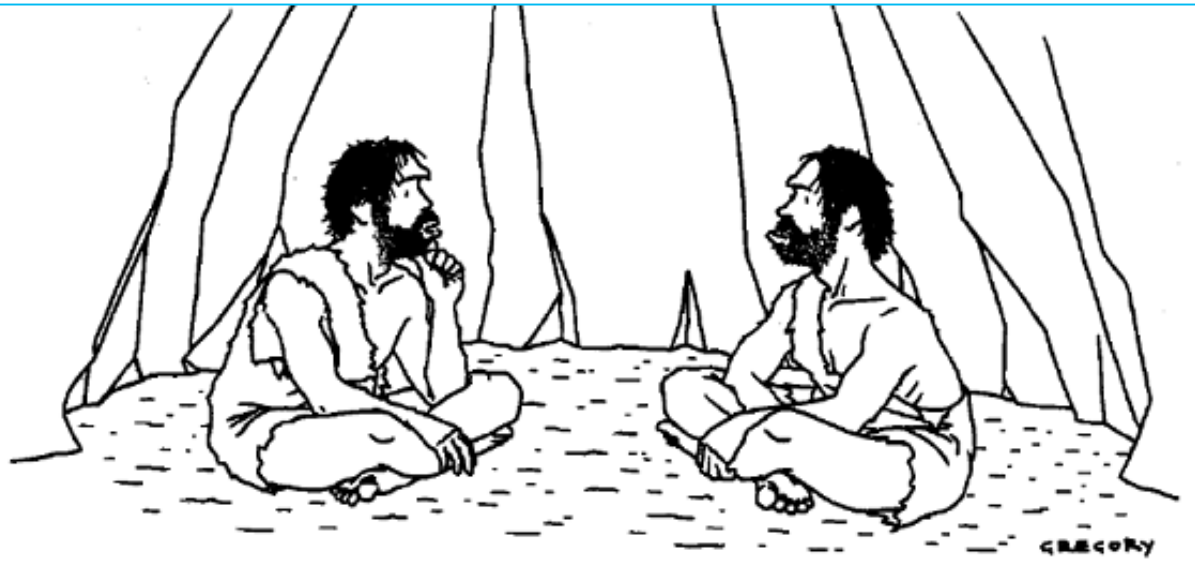
	N (183)	%
HIV screening among vaccinated people not in follow-up at the outpatient clinic		
• Performed and resulted HIV negative	34 out of 62	54.8
• Not performed because last HIV test performed < 1 month before	19 out of 62	30.6
• Patient refusal	9 out of 62	14.5
N° of doses		
• 1 dose completed	34	18.6
• 2 doses completed	100	54.6
• 2 doses to be completed	49	26.8
Adverse reaction after the first dose*		
• Local	27 out of 100	27.0
• Systemic	2 out of 100	2.0
Median days of local skin manifestation [IQR]	7 days	[7-21]
Reported allergies		
• None	146	79.8
• Environmental	26	14.2
• Pharmacological	11	6.0
Cardiovascular diseases	7	3.8
Asthma	8	4.4
Skin disorder	12	6.5
Vaccinations received between 15 to 30 days prior to vaccination for MPOX	11	6.0
• HPV	2	-
• Meningococcal vaccine	1	-
• HAV	2	-
• Chickenpox	1	-
SARS-CoV-2	5	-

*evaluated only in person who got two doses (n=100). Person with only one dose were excluded

CONCLUSIONE

- PLHIV hanno indicazione a effettuare tutte le vaccinazioni consigliate: attenzione ai vaccini vivi in persone con CD4 <200 cell/mL
- L'incidenza di HZ nelle PLHIV rimane comunque dalle 3 alle 5 volte più alta della popolazione generale
- In regione toscana RZV è raccomandato per tutte le PLHIV indipendentemente dall'età con una schedula a due dosi sualla base di dati di efficiacia, sicurezza in popolazione con immunodepressione
- L'interazione tra HIV e MPOX è ancora controversa
- MPOX nelle persone che vivono con HIV in severo stato di immunodepressione è associata un quadro più grave della malattia
- Secondo CDC la vaccinazione per MPOX dovrebbe essere offerta ancora a tutte le popolazioni a Rischio
- I dati sull'efficacia del vaccino per MPOX sono pochi, in particolari nella popolazione HIV
- I vaccini MPOX e RZV sono risultati sicuri ed immunogeni nelle PLHIV

GRAZIE PER L'ATTENZIONE



'Qualcosa proprio non va - la nostra aria è pulita,
la nostra acqua è pura, tutti noi facciamo molto esercizio fisico,
tutto quello che mangiamo è biologico,
eppure nessuno di noi vive più di trent'anni…..'

D. Liotta, 2008

CONCLUSIONE

L'incidenza di HZ nelle PLHIV rimane comunque dalle 3 alle 5 volte più alta della popolazione generale

In regione toscana RZV è raccomandato per tutte le PLHIV indipendentemente dall'età con una schedula a due dosi

MPOX nelle persone che vivono con HIV in severo stato di immunodepressione è associato a

Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects

Sharon E. Frey[a,*], Anna Wald[b], Srilatha Edupuganti[c], Lisa A. Jackson[d], Jack T. Stapleton[e], Hana El Sahly[f], Samer S. El-Kamary[g], Kathryn Edwards[h], Harry Keyserling[i], Patricia Winokur[e], Wendy Keitel[f], Heather Hill[j], Johannes B. Goll[j], Edwin L. Anderson[a], Irene L. Graham[a], Christine Johnston[b], Mark Mulligan[c], Nadine Rouphael[c], Robert Atmar[f], Shital Patel[f], Wilbur Chen[k], Karen Kotloff[k], C. Buddy Creech[h], Paul Chaplin[l], Robert B. Belshe[a]

- JYNNEOS (MVA-BN) è un vaccino indicato per la prevenzione del vaiolo e del vaiolo delle scimmie nei soggetti a partire dai 18 anni di età, ad alto rischio di infezione.
- In caso di vaccinazione primaria (soggetti non vaccinati in precedenza contro il virus del vaiolo o con MVA-BN): due dosi a distanza di almeno quattro settimane (28 giorni) l'una dall'altra.
- Per la vaccinazione di richiamo: una sola dose a chiunque abbia ricevuto in passato almeno una dose di vaccino antivaiolo o di MVA-BN o che abbia concluso il ciclo vaccinale di due dosi di MVA-BN da oltre due anni.
- Il vaccino può essere somministrato per via intradermica (dose da 0,1 mL) o per via sottocutanea (dose da 0,5 mL).
- I vaccini attualmente disponibili contro il virus del vaiolo possono garantire una certa efficacia anche nei confronti della malattia del vaiolo delle scimmie, sebbene i dati a supporto di tale ipotesi al momento siano ancora limitati.

FALSE CONTROINDICAZIONI

- allattamento al seno (bambino o puerpera)
- anamnesi familiare positiva per Sids
- anamnesi positiva per allergia nei familiari
- anamnesi positiva per allergia alla penicillina, alle proteine del latte e ad altre sostanze non contenute nei vaccini
- anamnesi positiva per convulsioni febbrili
- assenza di esame obiettivo in soggetti apparentemente sani
- contatti non vaccinati
- convalescenza dopo malattia
- deficit selettivo IgA (escluso Ty21a) e IgG
- dermatite atopica e seborroica
- diabete tipo 1 e 2
- disturbi della coagulazione
- esposizione recente a malattia infettiva o prevenibile con vaccino
- fibrosi cistica
- gravidanza nei contatti
- immunodepressione nei contatti
- malattia acuta lieve, con o senza febbre
- malattie croniche che non abbiano specifiche controindicazioni
- malattie neurologiche non evolutive o stabilizzate
- malnutrizione
- prematurità
- reazione febbrile dopo precedente dose
- reazioni allergiche non gravi dopo precedente dose
- reazioni locali lievi o moderate (es. edema, dolore, rossore) dopo precedente dose
- sindrome di Down
- terapia antibiotica in corso (escluso Ty21a)
- terapia con antistaminici
- terapia inalante
- terapia desensibilizzante

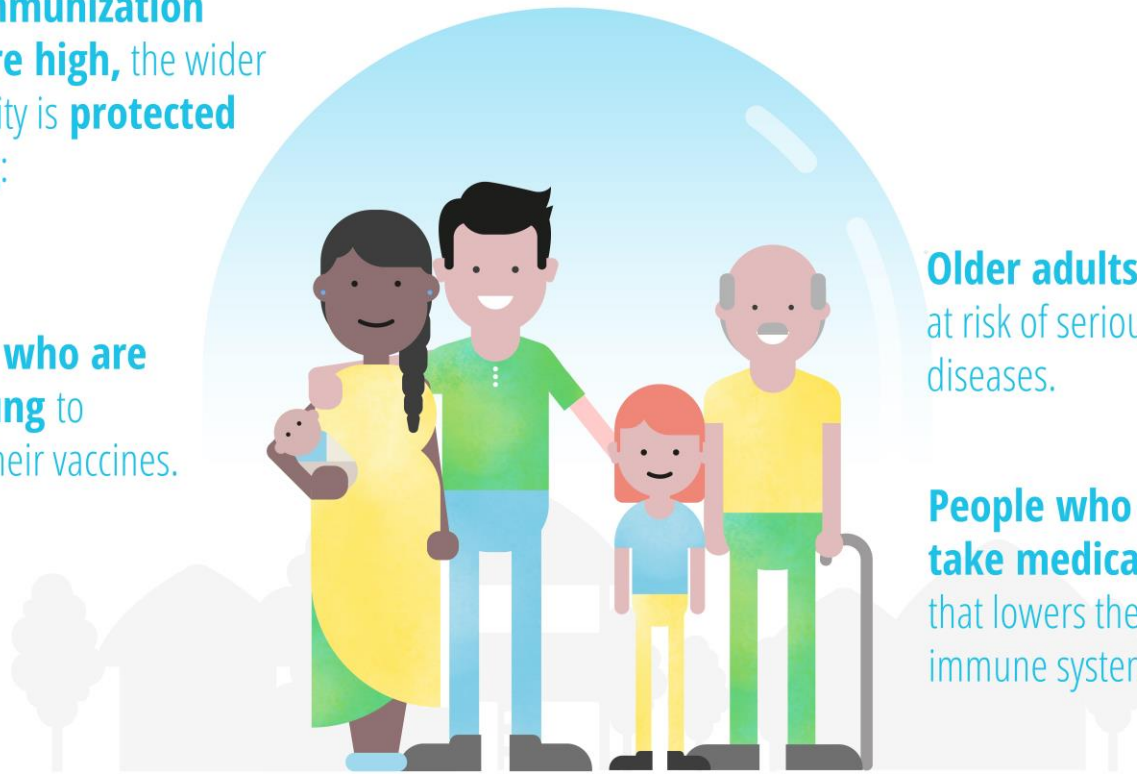
- Il vaccino Jynneos (Bavarian Nordic) è confezionato in flaconcini monodose da 0,5 ml ed è conservato a temperature di -20°C o -80°C.
-
- Jynneos deve essere scongelato prima dell'uso. Una volta scongelato può essere mantenuto a una temperatura compresa tra +2°C e +8°C, al riparo dalla luce, fino a 12 ore.
-
- Il vaccino **non deve essere diluito**.
-
- Prima dell'uso, attendere che il flaconcino abbia raggiunto una temperatura compresa tra +8 °C e +25 °C e scuoterlo leggermente per almeno 30 secondi. La sospensione deve essere ispezionata visivamente per escludere la presenza di particelle o di alterazioni del colore. Prelevare quindi una dose di 0,5 mL con una siringa per preparazioni iniettabili ed eseguire la vaccinazione tramite iniezione sottocutanea, preferibilmente nel braccio.
- JYNNEOS, se mantenute al riparo dalla luce e garantendone la tracciabilità, possono essere conservate in frigorifero a 2 °C – 8 °C per un massimo di 8 settimane dopo scongelamento.

#VACCINESWORK TO PROTECT INDIVIDUALS AND COMMUNITIES

Immunization is our **shield** against **serious diseases**.

When **immunization rates are high,** the wider community is **protected** including:

Infants who are too young to receive their vaccines.



Older adults at risk of serious diseases.

People who take medication that lowers their immune systems.

#VACCINESWORK

Check with your doctor that you are fully vaccinated.

World Health Organization

Si spegne a 105 anni: grazie alla medicina moderna è rimasto attivo ed in buona salute fino alla fine

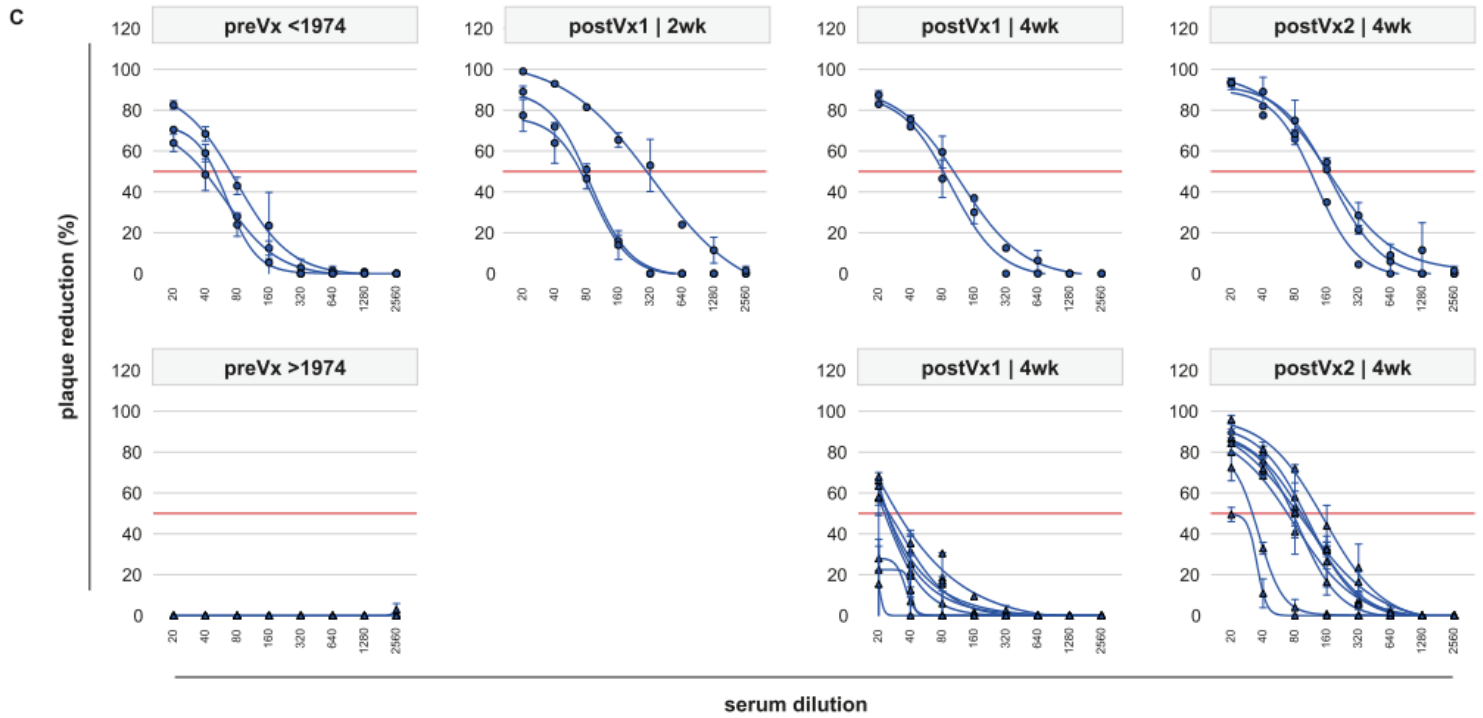
il mattino di Padova

nature medicine

Article

https://doi.org/10.1038/s41591-022-02090-w

Low levels of monkeypox virus-neutralizing antibodies after MVA-BN vaccination in healthy individuals



Extended Data Fig. 4 | See next page for caption.

Zaeck, L.M., et al. *Nat Med* 2022

Morbidity and Mortality Weekly Report

Reduced Risk for Mpox After Receipt of 1 or 2 Doses of JYNNEOS Vaccine Compared with Risk Among Unvaccinated Persons — 43 U.S. Jurisdictions, July 31–October 1, 2022

Amanda B. Payne, PhD[1]; Logan C. Ray, MPH[1]; Matthew M. Cole, MPH[1]; Michelle Canning, MPH[1]; Kennedy Houck, MPH[1]; Hazel J. Shah, MPH[1]; Jennifer L. Farrar, MPH[1]; Nathaniel M. Lewis, PhD[1]; Amy Fothergill, PhD[1,2]; Elizabeth B. White, PhD[1,2]; Leora R. Feldstein, PhD[1]; Lauren E. Roper, MPH[1]; Florence Lee, MPH[1]; Jennifer L. Kriss, PhD[1]; Emily Sims, MPH[1]; Ian H. Spicknall, PhD[1]; Yoshinori Nakazawa, PhD[1]; Adi V. Gundlapalli, MD, PhD[1]; Tom Shimabukuro, MD[1]; Adam L. Cohen, MD[1]; Margaret A. Honein, PhD[1]; Jonathan Mermin, MD[1]; Daniel C. Payne, PhD[1]

REAL LIFE

- 9,544 reported mpox cases among men aged 18–49 years during July 31–October 1, 2022, from 43 U.S. jurisdictions
  - 8,320 (87.2%) unvaccinated persons
  - 1,224 (12.8%) in vaccinated persons
    - 614 (61%) were in persons with illness onset occurred ≤13 days after receipt of dose 1
    - 392 (39%) in persons with illness onset ≥14 days after receipt of dose 1;
    - 48 cases (12.2%) (0.5% of all cases) were among persons with illness onset ≥14 days after receipt of dose 2
- Mpox incidence in unvaccinated at risk subjects:
  - 7.4* (95% CI = 6.0–9.1) times that among persons who received only 1 dose of JYNNEOS vaccine ≥14 days earlier
  - 9.6 (95% CI = 6.9–13.2) times that among persons who received dose 2 ≥14 days earlier
- The observed distribution of subcutaneous and intradermal routes of administration of dose 1 among vaccinated persons with mpox was not different from the expected distribution

Payne AB, et al *MMWR Morb Mortal Wkly Rep*. 2022

* Previous report 14 times

Demographic and Clinical Characteristics of Mpox in Persons Who Had Previously Received 1 Dose of JYNNEOS Vaccine and in Unvaccinated Persons — 29 U.S. Jurisdictions, May 22–September 3, 2022

Jennifer L. Farrar, MPH[1]; Nathaniel M. Lewis, PhD[1]; Kennedy Houck, MPH[1]; Michelle Canning, MPH[1]; Amy Fothergill, PhD[1,2]; Amanda B. Payne, PhD[1]; Adam L. Cohen, MD[1]; Joshua Vance, MPH, MEd[3,4]; Bridget Brassil, MPH[5]; Erin Youngkin, MPH[6]; Bailey Glenn, MS[7,8]; Anil Mangla, PhD[9]; Nikki Kupferman, MS[10]; Katharine Saunders, DNP[2,11]; Cristina Meza, MPH[12]; Dawn Nims, MPH[13]; Susan Soliva, MPH[14]; Brandon Blouse, MPH[15]; Tiffany Henderson, MPH[16]; Emily Banerjee, MPH[17]; Brooklyn White, MPH[18]; Rachael Birn, MPH[8,19]; Anna M. Stadelman, PhD[2,20]; Meaghan Abrego, MPH[21]; Meagan McLafferty, MPH[22]; Michael G. Eberhart, MPH[23]; Michael Pietrowski, MPH[24]; Sandra Miranda De León, MPH[25]; Emma Creegan, MPH[26]; Abdoulaye Diedhiou, MD, PhD[27]; Caleb Wiedeman, MPH[28]; Jade Murray-Thompson, MPH[29]; Elizabeth McCarty, MPH[30]; Jessica Marcinkevage, PhD[31]; Anna Kocharian, MS[32]; Elizabeth A. Torrone, PhD[1]; Logan C. Ray, MPH[1]; Daniel C. Payne, PhD[1]; Mpox Cases in Vaccinated Persons Team

REAL LIFE

TABLE 2. Clinical characteristics of mpox patients, by vaccination status* — 29 U.S. jurisdictions,† May 22–September 3, 2022

Characteristic	Mpox patient vaccination status, n/N (%)		
	Vaccinated§ (n = 202)	Unvaccinated¶ (n = 5,326)	Odds ratio (95% CI)
HIV status			
Positive	19/78 (24.4)	1,074/2,585 (41.6)	Not calculated
Negative	46/78 (58.9)	1,153/2,585 (44.5)	
Unknown or missing	137	3,099	
Signs and symptoms			
Abdominal pain	5/190 (2.6)	420/5,069 (8.3)**	0.29 (0.12–0.72)
Chills	23/193 (11.9)	2,015/5,207 (38.7)**	0.21 (0.14–0.33)
Conjunctivitis	2/65 (3.1)	148/2,703 (5.5)	0.57 (0.14–2.36)
Enlarged lymph nodes	62/196 (31.6)	1,841/5,237 (35.2)	0.84 (0.62–1.14)
Fever	55/198 (27.8)	2,451/5,266 (46.5)**	0.44 (0.32–0.60)
Headache	39/195(20.0)	1,908/5,217 (36.6)**	0.43 (0.30–0.61)
Malaise	47/192 (24.5)	2,240/5,204 (43.0)**	0.43 (0.31–0.60)
Myalgia	39/194 (20.1)	1,696/5,212 (32.5)**	0.52 (0.36–0.74)
Proctitis	11/187 (5.9)	360/4,983 (7.2)	0.81 (0.44–1.50)
Pruritis	65/194 (33.5)	1,840/5,193 (35.4)	0.93 (0.68–1.26)
Pus in stool	12/191 (6.3)	558/5,169 (10.8)**	0.55 (0.30–0.99)
Rectal bleeding	17/193 (8.8)	684/5,182 (13.2)	0.63 (0.38–1.04)
Rectal pain	38/194 (19.6)	1,255/5,211 (24.1)	0.77 (0.53–1.10)
Tenesmus	16/190 (8.4)	573/5,164 (11.1)	0.74 (0.44–1.24)
Vomiting or nausea	6/199 (3.0)	494/5,263 (9.4)**	0.31 (0.13–0.69)
Rash			
Presence of rash	195/202 (96.5)	5,173/5,318 (97.3)	0.73 (0.34–1.58)
Rash location			
Arms	20/160 (12.5)	1,860/4,140 (44.9)**	0.18 (0.11–0.28)
Face	26/160 (16.3)	1,386/4,140 (33.5)**	0.39 (0.25–0.59)
Genitals	88/160 (55.0)	1,933/4,140 (46.7)**	1.40 (1.02–1.92)
Head	27/160 (16.9)	1,376/4,140 (33.2)**	0.41 (0.27–0.62)
Legs	19/160 (11.9)	1,628/4,140 (39.3)**	0.21 (0.13–0.34)
Mouth, lips, or oral mucosa	7/160 (4.4)	400/4,140 (9.7)**	0.43 (0.20–0.92)
Neck	5/160 (3.13)	545/4,140 (13.2)**	0.21 (0.09–0.52)
Palms of hands	6/160 (3.8)	806/4,140 (19.5)**	0.16 (0.07–0.37)
Perianal	42/160 (26.3)	1,212/4,140 (29.3)	0.86 (0.60–1.23)
Soles of feet	1/160 (0.6)	445/4,140 (10.8)**	0.05 (0.01–0.37)
Trunk	18/160 (11.3)	1,521/4140 (36.7)**	0.22 (0.13–0.36)
Other locations	68/160 (42.5)	1,574/4,140 (38.0)	1.21 (0.88–1.66)
Number of rash locations reported			
Median (IQR)**	2.0 (1.0–3.0)	3.0 (2.0–5.0)**	<0.001††
Severity			
Hospitalization related to mpox	2/95 (2.1)	237/3,142 (7.5)	0.27 (0.06–1.09)

Farrar JL, et al *MMWR Morb Mortal Wkly Rep.* 2022

Vaccination strategies

1. Pre-exposure vaccination (PPV):

- most efficient vaccination strategy (i.e. increasing the probability of outbreak control per vaccinated individual) even when there is less effective contact tracing
- countries should prioritise PPV among individuals at substantially higher risk of exposure to mpox

2. Post-exposure Preventive Vaccination (PEPV):

- most efficient vaccination strategy in settings with more effective tracing and higher vaccine uptake levels.
- The priority target groups for PEPV are close contacts of cases.
- In the context of limited supply, contacts with a high risk of developing severe disease if infected, such as children, pregnant women, and immunocompromised individuals, should be prioritised for PEPV based on a case by cases risk assessment.

3. Combined (pre- and post-exposure) preventive vaccination

VACCINAZIONE IN ADULTI CON HIV

Vaccino/Tossoide	CD4>200	CD4<200	Dose Booster
dTpa (tetano/difterite/pertosse)	Si	Si	10 anni
Pneumococco	Si	Si	Almeno 5 anni dopo l'ultimo PPSV23
Influenza	Si	Si	Annuale
Epatite A	Si	Si	Non necessario
HBV	(Si)**	Si	Non necessario
• **MPR (Morbillo, Parotite, rosolia),** • **Varicella** • **Febbre gialla**	Si	No	**
Meningococco	Si**	Si	5 anni
HPV (Human papillomavirus)	Si	Si	3 dosi in totale
BCG	No	No	
Zoster	NO	Si	

VACCINAZIONE IN BAMBINI CON HIV

Il PNPV 2017-19 prevede, a partire dall'anno 2017, l'offerta attiva e gratuita per tutti i bambini a 24 mesi e a 5-6 anni della vaccinazione contro la varicella. Questa può essere somministrata separatamente come vaccino monovalente ma è consigliato l'uso del vaccino quadrivalente MPRV.
Il *Committee for Medicinal Products for Human Use* (CHMP) dell'EMA ha effettuato un riesame dell'uso dei vaccini monovalenti e multivalenti antimorbillo, parotite, rosolia e/o varicella (MPRV) durante la gravidanza e in pazienti con deficit del sistema immunitario ed è giunto alla conclusione che la vaccinazione MPRV può essere presa in considerazione in pazienti con deficit meno gravi del sistema immunitario, se i benefici superano i rischi. In particolare nei bambini infetti da HIV, la vaccinazione è controindicata in caso di percentuali di CD4+ età-specifiche inferiori al 25% al di sotto dei 12 mesi, inferiori al 20% tra 12 e 35 mesi o inferiori al 15% tra 36 e 59 mesi.

VACCINI DISPONIBILI PER VAIOLO E MPOX

Trade name	Type of vaccine	Main characteristics	Serius adverse events (per million doses)
Dryvax	First generation smallpox vaccine (retired in 2008 in the US)	Replication competent vaccinia virus	Myopericarditis (519) Generalized vaccinia (241) Eczema vaccinatum (38) Post vaccinial encephalopathy (24) Death (1)
ACAM2000	Second generation smallpox vaccine	Replication competent vaccinia virus	Similar safety profile to Dryvax
LC16m18	Third generation smallpox vaccine	Minimally replication competent vaccinia virus	None noted in clinical trials
• Jynneos - USA • Imvamune - Canada • Imvanex – Europe *	Third generation smallpox vaccine	Replication deficient **Modified Vaccinia Ankara (MVA)**	None , apparently

Although the United States has a large supply of ACAM2000, this vaccine has more side effects and contraindications than JYNNEOS. Therefore, JYNNEOS should be used for people who are at high risk for severe disease caused by infection with mpox virus including, but not limited to, people with human immunodeficiency virus (HIV) infection or other immunocompromising conditions. At this time, the safety of JYNNEOS in pregnant people and children has not been studied. Therefore, the risks and benefits should be weighed in the decision to vaccinate.

CDC

Vignetta satirica
1802 su inoculo del vaccino contro il vaiolo.

Infection	Vaccination rationale	Comment
Influenza Virus	Higher rate of pneumonia. Explicitly recommended in all persons with HIV	Yearly, use 4-valent vaccine if available
Human Papilloma Virus (HPV)	Shared risk with HIV of contracting infection. Higher rate of cervical and anal cancer	Vaccinate with 3 doses between ages 9 and 45 (health insurance coverage differs by country according to age, sex, sexual orientation). Use 9-valent vaccine if available. Persons treated for high grade dysplasia could benefit from a full course vaccination for secondary prevention
Hepatitis B Virus (HBV)	Shared risk with HIV of contracting infection. Untreated HIV accelerates progression of liver disease	Vaccinate if seronegative. Repeat doses until anti-HBs antibodies ≥ 10 IU/L / ≥ 100 IU/L according to national Guidelines. In order to reach ≥ 100 IU/L in non-responders repeat 3 doses if anti-HBs < 10 IU/L, 1 dose if anti-HBs < 100 IU;[ii] consider double dose (40 µg) or use more immunogenic vaccines in particular with low CD4 count and high HIV-VL. No benefit for intradermal application. See page 115
Hepatitis A Virus (HAV)	According to risk profile (travel, close contact with children, MSM, IVDU, active hepatitis B or C infection, chronic liver disease)	Vaccinate if seronegative. Consider checking antibody titres in persons with high risk. Weaker immune response expected with HAV/HBV co-vaccine. See page 115
Neisseria meningitidis	According to risk profile (travel, close contact with children, MSM)	Use conjugated[iii] 4-valent vaccine (for serotypes A, C, W-135, Y; 2 doses 1-2 months apart) if available. Booster every five years if exposure continues. Polysaccharide vaccine no longer recommended. Vaccination against Meningococcus serotype B according to national Guidelines
Streptococcus pneumoniae	Higher rate and severity of invasive disease. Vaccine explicitly recommended for all persons with HIV	One dose of a conjugated vaccine: PCV-13, PCV-15 or PCV-20a for all persons according to availability and national guidelines, also if pre-vaccinated with PPV-23 polysaccharide vaccine. For patients vaccinated with PCV-13 or PCV-15 one dose of PPV-23 at least 2 months after the conjugate vaccine may be considered in some national guidelines for all persons with HIV
Varicella Zoster Virus (VZV)	Higher rate and severity of both chickenpox and zoster	Perform serology if exposure history negative. Vaccinate if seronegative. For contraindications, see*. To prevent shingles, preferably use adjuvant recombinant sub-unit vaccine over live-attenuated vaccine according to national guidelines
Yellow Fever Virus	Mandatory for travel to selected countries (provide exemption letter if no true risk of exposure)	Contraindicated if past or current haematological neoplasia or thymus affection (thymoma, resection/radiation) For other contraindications, see*. Booster q 10 years
Rabies		For persons with CD4 count < 200 cells/µL or unsuppressed viremia consider pre-exposure vaccination with 3 doses (0, 7, 28 days) and titre control 14 days later. In case of exposure: full post-exposure prophylaxis including rabies immunoglobulins (RIG). If pre-exposure rabies vaccination administered when CD4 > 200 cells/µL: Post-exposure prophylaxis as for immunocompetent (one dose day 0 and day 3, without RIG)
Severe Acute Respiratory Syndrome 2 (SARS-CoV-2)	Low CD4 count and non-suppressed HIV-VL may increase the risk of acquiring SARS-CoV-2 infection and/or progressing to severe COVID-19	In a pandemic situation, all persons with HIV should be vaccinated according to the national guidelines irrespective of CD4 count and HIV-VL. Advanced HIV infection (CD4 count < 200 cells/µL) and persons with detectable HIV viremia have poorer humoral immune responses and are candidates for COVID-19 booster doses

i Administer live vaccines simultaneously or with an interval of 4 weeks
ii In case of non-response, ART should contain TDF or TAF
iii Conjugated vaccines are more immunogenic, induce memory cells, respond to boosting and reduce mucosal colonisation