Single dose HPV vaccine trials in India

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South Asia Regional Meeting

HPV Prevention and Control Landscape and the way forward.

13th , 14th and 15th - Dec 2022– New Delhi, India.

Outline

- Genesis of single dose trials in India
- How serendipity led to new knowledge and strategy
- Present situation

Randomised Trial of 2 versus 3 doses of HPV vaccination in India – India IARC Trial

World Health Organization (WHO)
International Agency for Research on Cancer (IARC)
Lyon, France

In collaboration with

AIIMS-New Delhi

TMH-Mumbai

NDMCH-Barshi

JCDC-Pune

CFCHC-Ambillikai

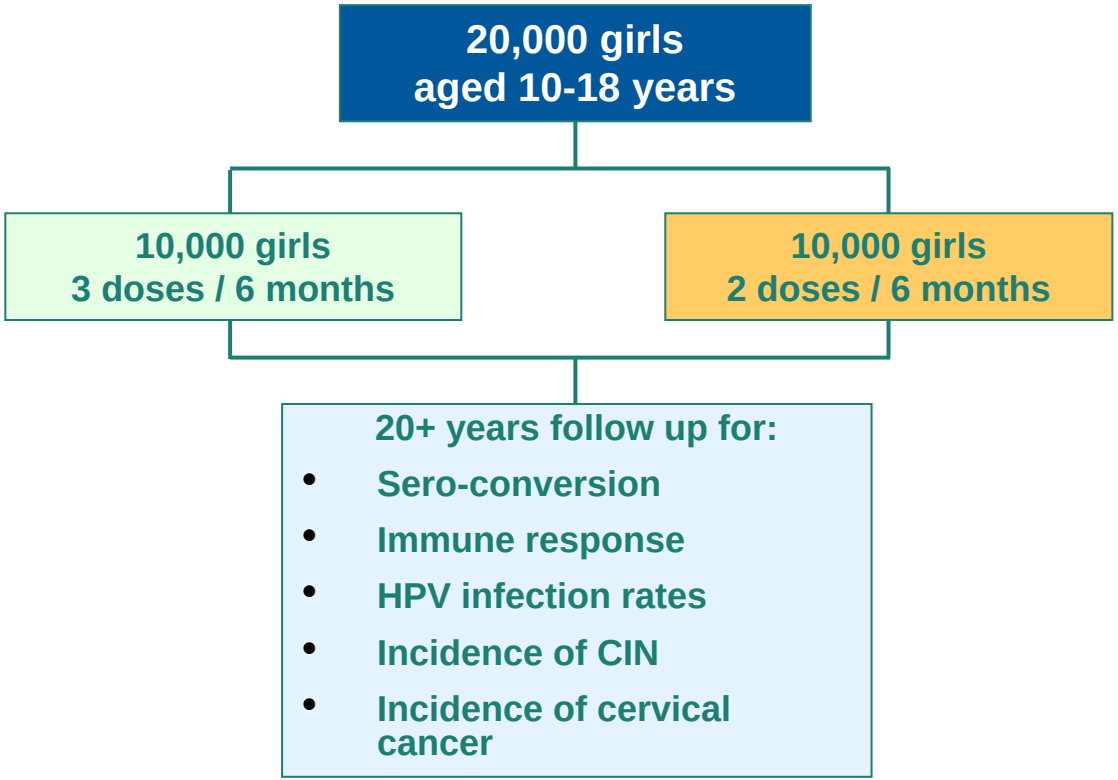
GCRI-Ahmedabad

MNJ Institute of Oncology and RCC, Hyderabad

Cancer Foundation of India (CFI), Kolkata

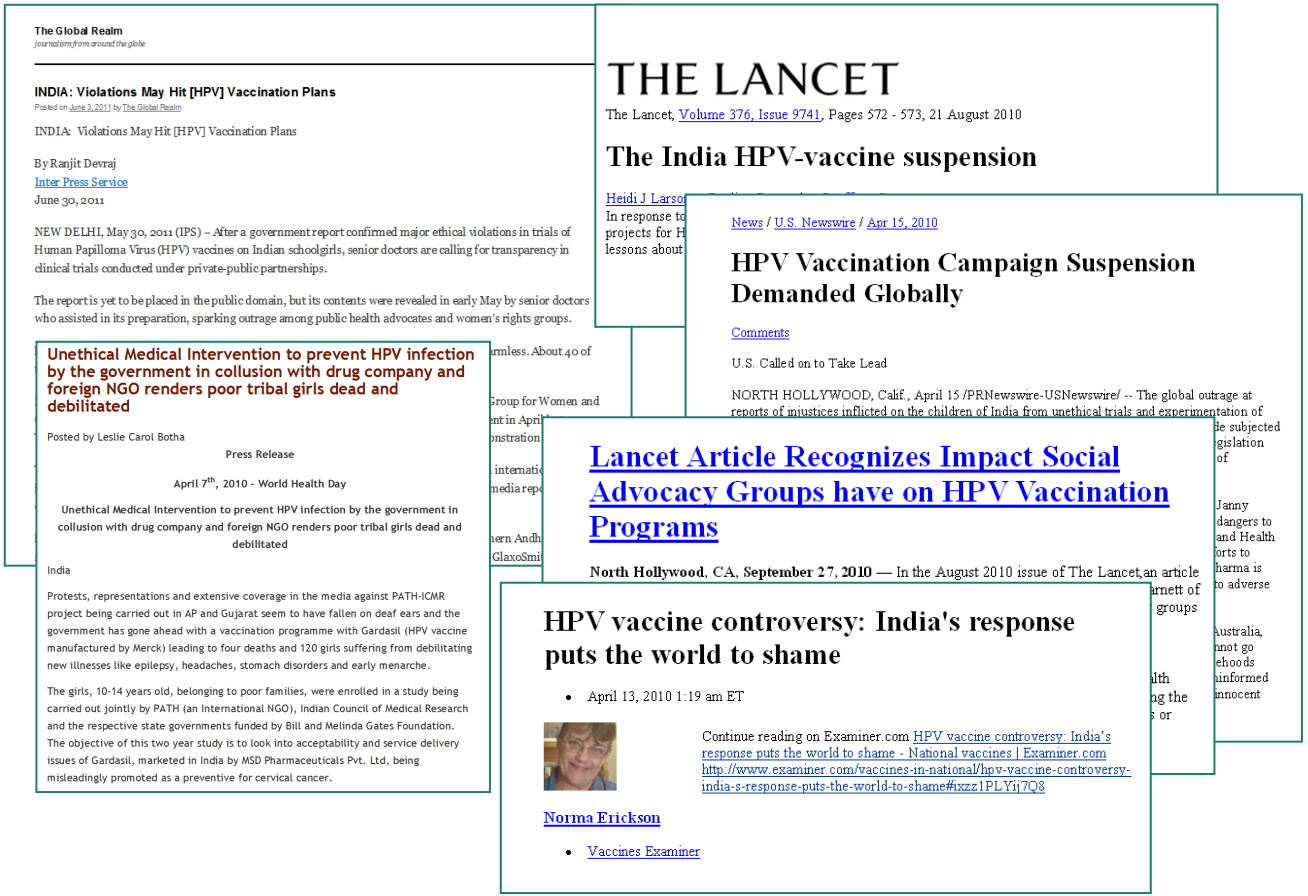
Supported by the Bill & Melinda Gates Foundation

Randomised Trial of 2 versus 3 doses of HPV vaccination in India – India IARC Trial



Randomised Trial of 2 versus 3 doses of HPV vaccination in India

April 2010 - Turn of Events



The Global Realm
journalism from around the globe

INDIA: Violations May Hit [HPV] Vaccination Plans

Posted on June 3, 2011 by The Global Realm

INDIA: Violations May Hit [HPV] Vaccination Plans

By Ranjit Devraj
Inter Press Service
June 30, 2011

NEW DELHI, May 30, 2011 (IPS) – After a government report confirmed major ethical violations in trials of Human Papilloma Virus (HPV) vaccines on Indian schoolgirls, senior doctors are calling for transparency in clinical trials conducted under private-public partnerships.

The report is yet to be placed in the public domain, but its contents were revealed in early May by senior doctors who assisted in its preparation, sparking outrage among public health advocates and women's rights groups.

Unethical Medical Intervention to prevent HPV infection by the government in collusion with drug company and foreign NGO renders poor tribal girls dead and debilitated

Posted by Leslie Carol Botha

Press Release

April 7th, 2010 - World Health Day

Unethical Medical Intervention to prevent HPV infection by the government in collusion with drug company and foreign NGO renders poor tribal girls dead and debilitated

India

Protests, representations and extensive coverage in the media against PATH-ICMR project being carried out in AP and Gujarat seem to have fallen on deaf ears and the government has gone ahead with a vaccination programme with Gardasil (HPV vaccine manufactured by Merck) leading to four deaths and 120 girls suffering from debilitating new illnesses like epilepsy, headaches, stomach disorders and early menarche.

The girls, 10-14 years old, belonging to poor families, were enrolled in a study being carried out jointly by PATH (an International NGO), Indian Council of Medical Research and the respective state governments funded by Bill and Melinda Gates Foundation. The objective of this two year study is to look into acceptability and service delivery issues of Gardasil, marketed in India by MSD Pharmaceuticals Pvt. Ltd, being misleadingly promoted as a preventive for cervical cancer.

THE LANCET

The Lancet, Volume 376, Issue 9741, Pages 572 - 573, 21 August 2010

The India HPV-vaccine suspension

Heidi J Larson

In response to
projects for H
lessons about

News / U.S. Newswire / Apr 15, 2010

HPV Vaccination Campaign Suspension Demanded Globally

Comments

U.S. Called on to Take Lead

NORTH HOLLYWOOD, Calif., April 15 /PRNewswire-USNewswire/ -- The global outrage at reports of injustices inflicted on the children of India from unethical trials and experimentation of

Lancet Article Recognizes Impact Social Advocacy Groups have on HPV Vaccination Programs

North Hollywood, CA, September 27, 2010 — In the August 2010 issue of The Lancet, an article

HPV vaccine controversy: India's response puts the world to shame

- April 13, 2010 1:19 am ET

Continue reading on Examiner.com HPV vaccine controversy: India's response puts the world to shame - National vaccines | Examiner.com
http://www.examiner.com/vaccines-in-national/hpv-vaccine-controversy-india-s-response-puts-the-world-to-shame#ixzz1PLYi7Q8

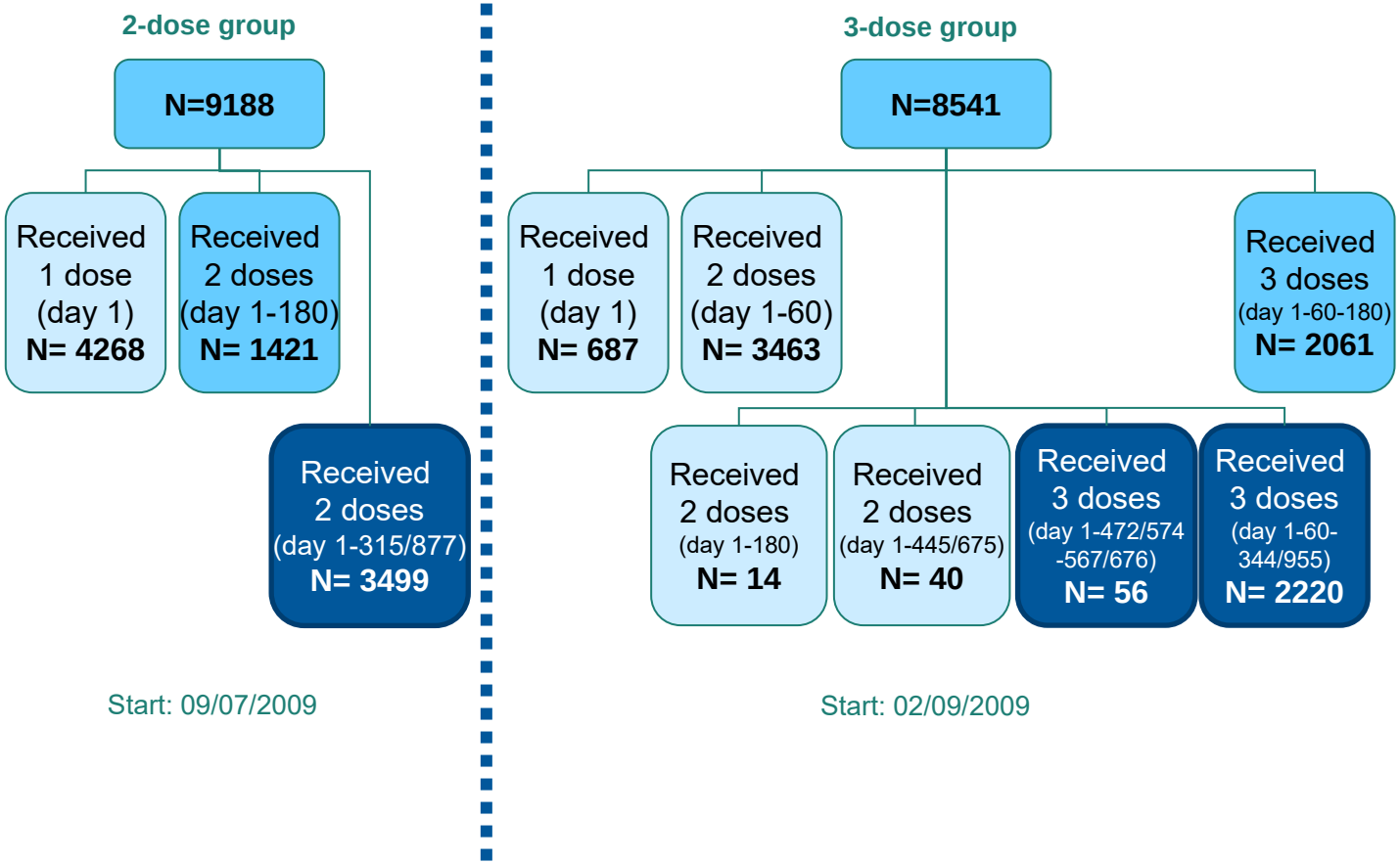
Norma Erickson

- Vaccines Examiner

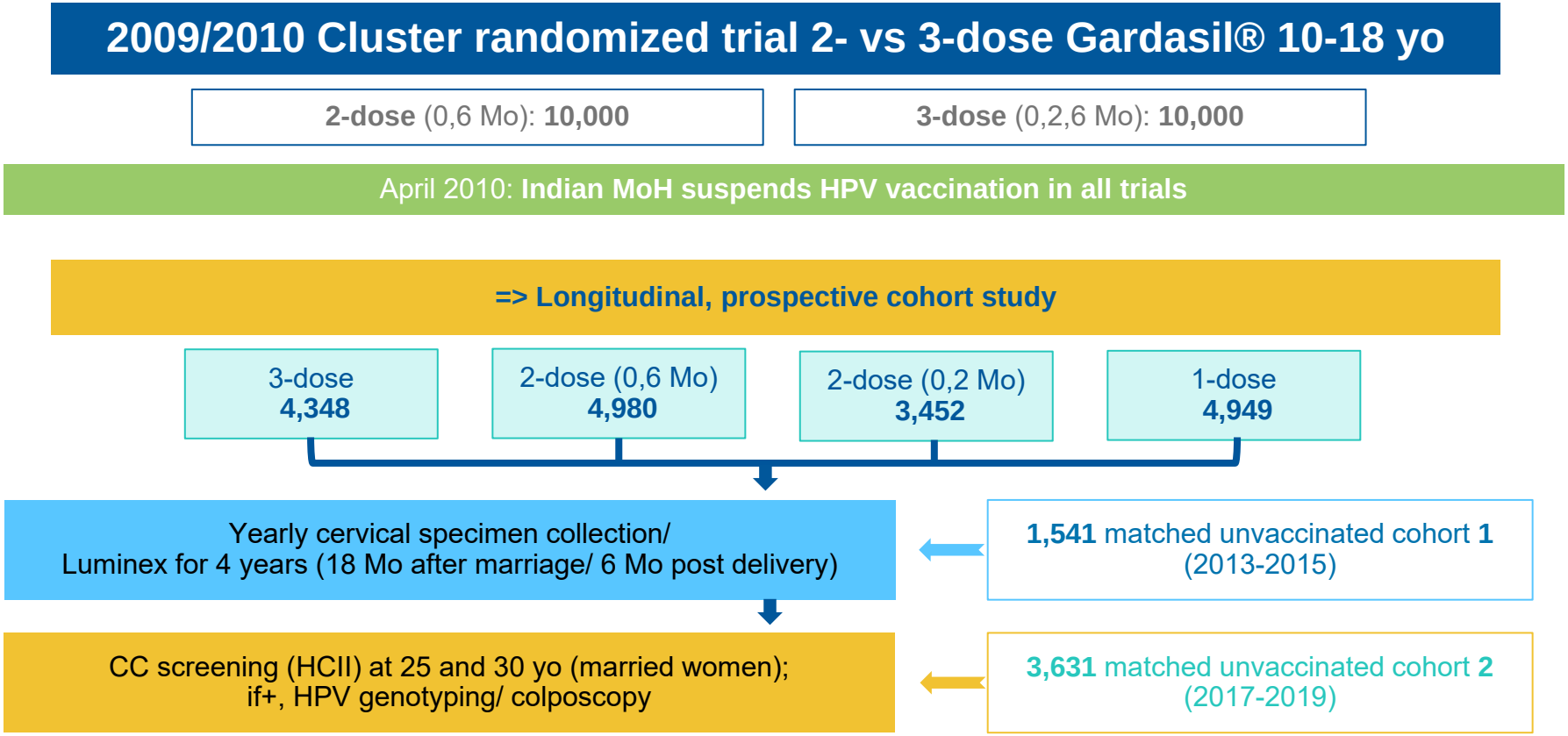
Randomised Trial of 2 versus 3 doses of HPV vaccination in India

Situation of the different vaccination regimens

All study sites (N=17,729) (as of June 2012)



IARC-India Trial – Study schematic

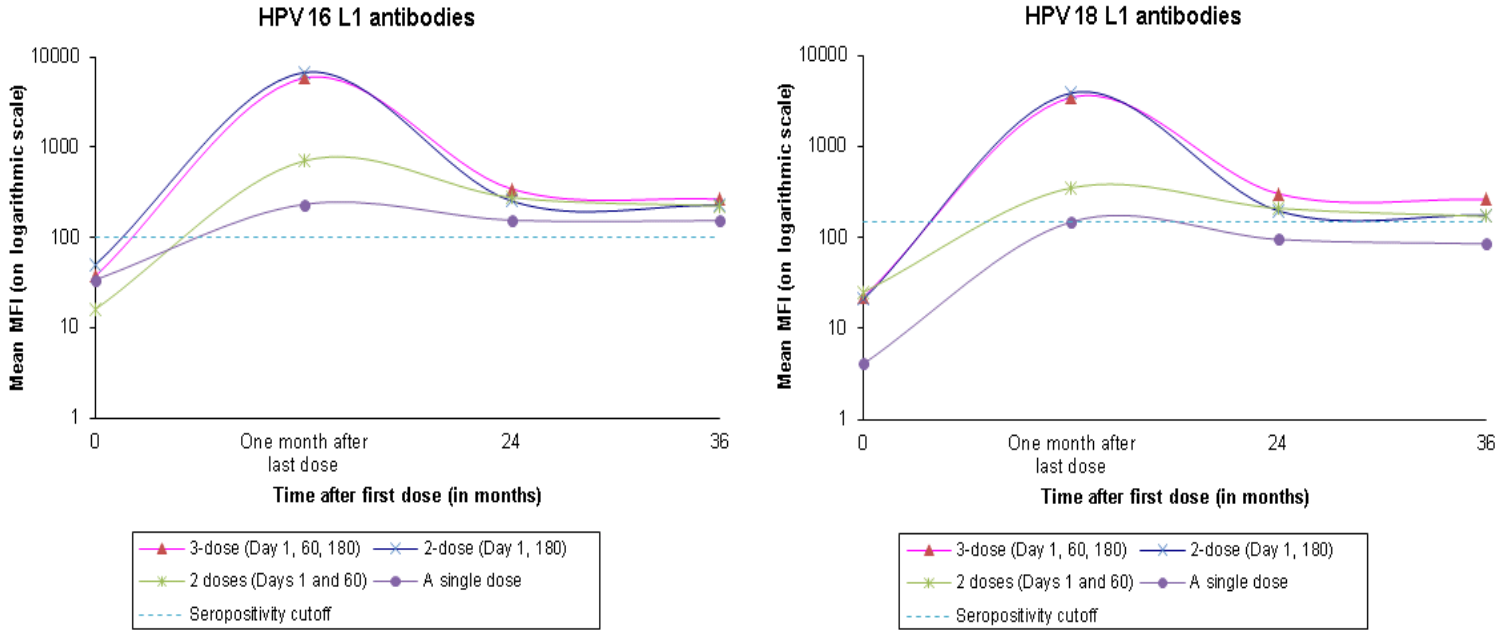


Median duration of follow-up (vaccinated): 9 years (IQR 8.2; 9.6)

CC: Cervical cancer; HCII: hybrid capture II; Mo: month; MoH: Ministry of Health; yo: year of age;

Evaluation of fewer than 3 doses of HPV vaccination in India

Mean MFI values for *HPV 16 and 18 L1* antibodies at different time points among girls who completed vaccination per protocol (vaccination at day 1, 60 and 180 (3-dose group) or day 1 and 180 (2-dose group)), and those who did not have their complete vaccine schedules (vaccination at day 1 and 60 or a single dose)



Sankaranarayanan R, et al. Lancet Oncol. 2016;17(1):67-77 .

India-IARC Trial – Virological efficacy
Persistent HPV 16/18 infections

	Number of women assessed	Number of events	Crude Attack rates (%)	Adjusted VE point estimate	Adjusted VE 95% CI
Unvaccinated	1,260	32	2.54	Referent	
Single dose	2,135	1	0.05	95.4	85.0; 99.9
2-dose (0,6 Mo)	1,452	1	0.07	93.1	77.3; 99.8
3-dose	1,460	1	0.07	93.3	77.5; 99.7

CI: confidence interval; Mo: month; VE: vaccine efficacy

Basu P, ..Bhatla N, et al. Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study [published correction appears in Lancet Oncol. 2022 Jan;23(1):e16]. *Lancet Oncology*. 2021;22(11):1518-1529. doi:10.1016/S1470-2045(21)00453-8.

India-IARC Trial – attack rate non-vaccine HPV types suggesting similar exposure across vaccine groups

	Number of women assessed	Number of events	Attack rates (95% CI)
Single dose	2,135	68	3.2% (2.5; 4.0)
2-dose (0,6 Mo)	1,452	47	3.2% (2.4; 4.3)
3-dose	1,460	49	3.4% (2.5; 4.4)

CI: confidence interval; Mo: month: VE: vaccine efficacy

Non-vaccine targeted HPV infections excluding 31, 33 and 45 in participants with ≥ 2 samples tested

Basu P, ..Bhatla N, et al. Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study [published correction appears in Lancet Oncol. 2022 Jan;23(1):e16]. *Lancet Oncology*. 2021;22(11):1518-1529. doi:10.1016/S1470-2045(21)00453-8.

IARC-India Trial – Efficacy screening populations

	Number of women screened	Number of women positive for HPV 16/18 +	Number of HPV 16/18 associated CIN2+
Unvaccinated	4626	63 (1.4%)	3
Single dose	1511	2 (0.1%)	0
2-dose (0,6 Mo)	1143	4 (0.3%)	0
3-dose	1037	1 (0.1%)	0

CI: confidence interval; Mo: month; VE: vaccine efficacy; yo: year of age

Basu P, ..Bhatla N, et al. Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study [published correction appears in Lancet Oncol. 2022 Jan;23(1):e16]. *Lancet Oncology*. 2021;22(11):1518-1529. doi:10.1016/S1470-2045(21)00453-8.

Results

- **One dose recipients demonstrated a robust and sustained immune response** against HPV 16 and 18, albeit inferior to that of 3- or 2-doses; antibody levels were stable over a 4-year period
- The **frequencies of cumulative incident and persistent HPV 16 and 18 infections** up to 7 years of follow-up were similar and uniformly low in all the vaccinated study groups
- Results indicate that **a single dose of quadrivalent HPV vaccine is immunogenic and provides lasting protection** against HPV 16 and 18 infections similar to the three- and two-dose vaccine schedule
- Significant and long-lasting protective effect of a single dose can be a strong argument to introduce one dose of the HPV vaccine in many low income countries where the current standard of care for cervical cancer prevention is ‘no intervention’.

CERVAVAC™

Quadrivalent (6, 11, 16 & 18) HPV vaccine, first indigenously developed and manufactured vaccine in India (SIIPL), licensed for females and males aged 9-26 years, 2 to 3 doses as applicable

Sterile suspension for intramuscular administration, prepared from highly purified virus-like particles (VLPs) of the recombinant major capsid (L1) structural proteins

>10 years in R & D, animal studies (single dose, repeat dose, reproductive tox), clinical trials (phase I, II/ III); licensed by NRA in July 2022

Jun 2022 - NTAGI recommended the HPV vaccine to be introduced in the National Immunization Schedule for girls aged 9-14 years

DBT– BIRAC announces successful development of indigenous HPV vaccine, New Delhi, Sept 1, 2022