**Appendix A**

State-of-the-Science of Human Papillomavirus Vaccination in Women with Human Immunodeficiency Virus: Summary of a Scientific Workshop.

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**Literature review**

Aim: To obtain summary estimates of vaccine efficacy, immunogenicity, and other endpoints (excluding safety) of HPV vaccination in people with HIV (PWH) to inform HPV vaccination in women and girls with HIV.

**Search strategy**

Clinical trials were identified using “HPV vaccine” AND “HIV” in the US National Library of Medicine database of privately and publicly funded clinical studies conducted around the world (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform (<https://trialsearch.who.int/>). The search was limited to trials that were completed, terminated, or suspended. We excluded studies focusing only on men (NCT00513526, NCT02503111, NCT02087384, NCT01923116, NCT01209325).

We also hand-searched PubMed to identify trial results using the registered trial ID or the protocol number and allowed multiple entrances for the same study. We identified 22 studies. We excluded 7 studies: HIV-negative only (NCT01489527), therapeutic vaccination in treated HIV disease (NCT03606213), no HPV vaccine/prevalence/behavioral study (NCT01311752, NCT01788852, NCT04401670, NCT00840905), and no results available (NCT00798265).

We included 16 unique studies (23 published reports). We also checked our review against the recent systematic review and meta-analysis by Staadegaard et al. (Staadegaard et al., 2022). We included 3 reports (Firnhaber et al., 2021; Kojic et al., 2014; Palefsky et al., 2014) not incorporated in Staadegaard’s review.

**Supplementary Table 1. Summary results of published efficacy, immunogenicity, and other endpoints from completed HPV vaccine trials among HIV-infected subjects (trials in men only were excluded)**

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| **Location****Clinical Trial No.****(Reference)** | **Description** | **Vaccine product and no. doses****(schedule)** | **Population and age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Efficacy endpoint** |
| **South Africa** NCT01928225(Firnhaber et al., 2021) | Phase II randomized, blinded, placebo-controlled trial of pre-treatment HPV vaccination on outcomes to LEEP treatment of cervical HSIL in HIV-infected women (QHPV-RTC) | 4vHPV3 doses(0, 2, 6M) | WWH39.2 (median)(34.9-45.5) | 174 | 6 | Recurrence of cervical HSIL (histology or cytology) | Risk ratio (95% CI)1.2 (0.87; 1.6) |
|  |  | Recurrence of histologic HSIL (CIN2 or CIN3) | 1.04 (0.67; 1.6) |
|  |  |  | Recurrence of CIN3 | 0.82 (0.36; 1.9) |
| **United States, Puerto Rico, Brazil**NCT01461096(Wilkin et al., 2018) | Phase III, double-blind, randomized, placebo, controlled trial to evaluate the effectiveness of the 4vHPV vaccine at reducing the incidence of 4M persistent anal/oral HPV infections in HIV-infected MSM and HIV-infected women. Ended early due to futility.(ACTG A5298) | 4vHPV3 doses(0, 2, 6M) | PWH≥27 years[30% of men & 50% of women with biopsy-confirmed anal HSIL] | 575(82% men; 18% women)286 vs. 283276 vs. 277 | 48 | Persistent anal infectionmITTPer protocol analysis | VE (95% CI):21% (−61%; 61%)31% (−82%; 74%) |
|  | 288 vs. 286278 vs. 280 |  | Persistent oral infectionmITT-persistent infection onlyPer protocol analysis | 88% (2%; 98%)66% (–70%; 96%) |
|  |  | 288 vs. 286 |  | Improvement of anal HSIL (biopsy outcomes)Full ITT | 0% (–44%; 31%) |
|  |  |  | 231 vs. 229199 vs. 198130 vs. 132 | 122639 | Abnormal anal cytologyAbnormal anal cytologyAbnormal anal cytology | 0% (–19%; 16%)9% (–10%; 25%)17% (–6%; 35%) |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **Kenya** NCT04711265(Mugo et al., 2018) | Single arm trial to assess sustained immunogenicity of the 4vHPV vaccine among HIV-infected girls and boys. (MISP 38406) | 4vHPV3 doses(0, 2, 6M) | HIV infected boys and girls9-14 | 179 | 7 | cLIA(mMU/mL) | HPV16 | 2322 (1912; 2820) | 98.3 |
|  |  | HPV18 | 364 (289; 458) | 93.3 |
| 178 | 12 |  | HPV16 | 657 (529; 817) | 97.8 |
|  |  | HPV18 | 89 (71; 112) | 72.5 |
| NCT01998178,NCT01446718(Mugo et al., 2021)[(MISP)IISP 51802] | HIV+ vs. HIV- (historical control) |  |  | 176  | 24 |  | HPV16 | 243 (183; 322)944 (804; 1108) | 96 |
|  |  |  |  | HPV18 | 39 (29; 52)138 (115; 165) | 82 |
| HIV+ vs. HIV- (historical control) |  |  | 174 | 36 |  | HPV16 | 170 (126; 230)642 (562; 733) | 93 |
|  |  |  |  |  | HPV18 | 29 (21; 39)87 (75; 101) | 78 |
|  | HIV+ |  |  | 164 | 48 |  | HPV16 | 137 (100; 187) | 90 |
|  |  |  |  |  |  | HPV18 | 23 (17; 31) | 77 |
| **Belgium**NCT03525210, NCT03482739(Boey et al., 2021) | Phase III, single-center, open-label study on safety, tolerability and immunogenicity of 9vHPV vaccine among HIV-infected persons (CD4-count ≥200 cells/uL and viral loads below the detection limit) and SOT patients. (Protocol V503-044-IC, EUCTR2017-004322-15-BE) | 9vHPV3 doses(0, 1, 6M) | Men & women 18-4518-55 | 271HIV (n=100) SOT (n=171) | 7 | cLIA(mMU/mL) |  | PPI population |  |
|  |
|  | HIVAll SOT | 63149 |  |  | HPV16 | 2589 (2096; 3197)170 (123; 234) | 100 (94.3; 100) 69.1 (61.0; 76.4) |
|  | HIVAll SOT | 67143 |  |  | HPV18 | 613 (497; 757)84 (72; 98) | 100 (94.6; 100) 51.7 (43.2; 60.2) |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **Brazil, Estonia, India, Thailand** NCT01031069(Folschweiller et al., 2020) | Phase IV, randomized, blind, controlled, multicentric study to compare the safety and immunogenicity of the 2vHPV and 4vHPV vaccines in HIV+ women. (Protocol 2013-003429-28, CTRI/2009/091/ 001039) | 2vHPV 3 doses (0, 1.5, 6M)vs.4vHPV3 doses(0, 1.5, 6M) | Women 15-25 | WWH (ATP)80 vs. 83 | 7 | PBNA | HPV16HPV18 | Non-inferiorityAdjusted GMT ratio:2.95 (1.92; 4.52)7.83 (4.84; 12.66) |  |
|  | 2vHPV vs. 4vHPV |  | WWH (TVC)109 vs. 110 | 7 | PBNA | HPV16HPV18 | Superiority analysisAdjusted GMT ratio2.74 (1.83; 4.11)7.44 (4.79; 11.54) |  |
|  |  | 2vHPV vs. 4vHPV |  | Women w/o HIV (TVC)105 vs. 102 |  |  | HPV16HPV18 | 3.05 (1.84; 5.06)5.38 (3.20; 9.06) |  |
|  | WWH (2vHPV) vs. women w/o HIV (4vHPV) |  |  | ATP80 vs. 80 | 7 | PBNA | HPV16HPV18 | Superiority analysisAdjusted GMT ratio0.83 (0.57; 1.20)1.77 (1.20; 2.61) |  |
|  | CD4 T-cell response median frequency in initially seronegative WWH | 2vHPV vs. 4vHPV |  | 14 vs. 10 | 12 |  | HPV16 | Median (IQR)2155.0 (1225.0; 4614.0)1715.0 (1106.0; 2511.0) |  |
|  |  |  |  | 11 vs. 13 |  |  | HPV18 | 1715.0 (1070.0; 4063.0)987.0 (346.0; 1932.0) |  |
|  | Memory B-cell response in initially seronegative WWH | 2vHPV vs. 4vHPV |  | 18 vs. 8 | 12 |  | HPV16 | Median (IQR)256.5 (45.0; 1003.0)180.0 (64.5; 476.0) |  |
|  |  |  |  | 16 vs. 10 | 12 |  | HPV18 | 103.0 (1.0; 705.5)37.5 (1.0; 102.0) |  |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **United States, Puerto Rico**(Levin et al., 2010) | Randomized, double-blinded, placebo-controlled trial of the safety and immunogenicity of the 4vHPV vaccine in HIV-infected children. (IMPAACT P1047, NCT00339040) | 4vHPV3-dosesvs. placebo | HIV infected children7-11 | All 4vHPV (n=96)vs placebo (n=30)  | 7 | cLIA(mMU/mL) | HPV16HPV18 | 5231 (4108; 6660)931 (656; 1321) | 4vHPV vs placebo100 vs 497 vs 0 |
| CD4% nadir < 15 and CD4% ≥ 15 at screening |  |  | 4vHPV (n=31) |  |  | HPV16HPV18 | 5984 (3617; 9900)1078 (506; 2300) | 100 vs. 090 vs. 0 |
| CD4% nadir ≥ 15 and CD4%15 – 24 at screening |  |  | 4vHPV (n=32) |  |  | HPV16HPV18 | 5129 (3224; 8161)984 (544; 1779) | 100 vs. 10100 vs. 0 |
| CD4% nadir ≥ 25 and CD4% ≥ 25 at screening |  |  | 4vHPV (n=33) |  |  | HPV16HPV18 | 4700 (3394; 6508)759 (455; 1268) | 100 vs. 0100 vs. 0 |
| HIV+HIV – (historical controls)  |  | 9-12 | 65560 |  |  | HPV16 | 4987 (3685; 6751)6444 (5840; 7110) |  |
| HIV+HIV – (historical controls) |  | 9-12 | 65565  |  |  | HPV18 | 845 (547; 1306)1558 (1416; 1716) |  |
| **United States, Puerto Rico**(Weinberg et al., 2012) | HPV type-specific antibodies 18M after 3-dose or 4-dose series of 4vHPV vaccine in HIV-infected children. Mucosal and CMI responses to vaccine genotypes and cross-reactive responses to HPV31 (IMPAACT P1047). | 4vHPV4 dose(0, 2, 6, 24M) vs. 3 doses (0, 2, 6M –initial placebo group) | HIV infected children7-11 | 1264 doses (n=96)3 doses (n=30) | 1 after 3rd dose | cLIA(mMU/mL) | HPV16HPV18 |  | 100 vs. 100 97 vs. 100  |
| 18after 3rd dose |  | HPV16HPV18 | Declines from 2.2-fold to 6.3-fold for all genotypes | 99 76 |
|  | 0.25 after 4th dose |  | HPV16HPV18 | Geometric mean fold-rise610 | 10096 |
| NCT01206556(Levin et al., 2017) | Duration of HPV type-specific antibody after 4vHPV vaccine in HIV-1 infected children previously enrolled in IMPAACT P1047. (IMPAACT P1085) | 4vHPV4 doses (0, 2, 6, 24M) vs. 3 doses (0, 2, 6M –initial placebo group) | HIV infected Children7-11 | 974 doses (n=58)3 doses (n=14) | 48-60 | cLIA(mMU/mL) | HPV16 | 1206 (780; 1863)310 (83; 1160) | 9886 |
|  |  |  |  | HPV18 | 108 (64; 183)42 (15; 117) | 7464 |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **India**NCT00667563(Palefsky et al., 2021) | Phase I, single-arm, open-label pilot study of the safety and immunogenicity of 4vHPV vaccine among HIV-positive women. CTRI/2009/091/ 000298, AMC 054) | 4vHPV3 doses (0, 2, 6M) | WWH19-44 | 150 | 7 | cLIA(mMU/mL) | HPV16HPV18 |  | ATP99 90 |
|  |  |  | 12 |  | HPV16HPV18 |  | 99 71 |
| (Palefsky et al., 2014) | Seronegative and DNA-negative at baseline |  |  |  |  |  |  |  |  |
|  | CD4 nadir ≤ 350 on HAART |  |  |  | 713 |  | HPV16 | 2271771  |  |
|  | CD4 nadir >350, CD4 350-500, not on HAART |  |  |  | 713 |  |  | 2205484  |  |
|  | CD4 nadir >350, CD4 >500, not on HAART |  |  |  | 713 |  |  | 3045730 |  |
|  | CD4 nadir ≤ 350 on HAART |  |  |  | 713 |  | HPV18 | 18333 |  |
|  | CD4 nadir >350, CD4 350-500, not on HAART |  |  |  | 713 |  |  | 19835 |  |
|  | CD4 nadir >350, CD4 >500, not on HAART |  |  |  | 713 |  |  | 27038 |  |
| **Canada**ISRCTN33674451(Money et al., 2016) | Open-label, multicenter, single-arm study evaluating immunogenicity and safety of 4vHPV vaccine among women and girls with HIV. | 4vHPV3 doses(0, 2, 6M) | WWH 15-66 | 310 | 7 |  | HPV16HPV18 |  | PP98.193.6 |
|  | 24 |  | HPV16HPV18 |  | 97.767.0 |
|  | Suppressed vs. unsuppressed viral load |  |  | PP84 vs. 28 111 vs. 34 |  | cLIA(mMU/mL) | HPV16HPV18 | GMT ratio1.74 (1.17; 2.59)3.05 (1.94; 4.80) |  |
|  | HIV- (historical control) vs. HIV+ |  | 15–26 | 2573 vs. 18 | 7 |  | HPV16 | 2294 (2185; 2408)3473 (2168; 5566) |  |
|  |  |  |  | 2800 vs. 19 |  |  | HPV18 | 462 (444; 480)334 (189; 591) |  |
|  |  |  |  | 2381 vs. 12 | 24 |  | HPV16 | 460 (441; 481)319 (167; 610) |  |
|  |  |  |  | 2603 vs. 14 |  |  | HPV18 | 52 (49; 55)16 (9; 27) |  |
| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **Canada**ISRCTN33674451(Brophy et al., 2018) | Sub-study of open-label, multicenter Canadian study evaluating the immunogenicity and safety of 4vHPV vaccine among girls with HIV. | 4vHPV3 doses(0, 2, 6M) | Girls with HIV9-13 | 35 | 7 | cLIA(mMU/mL) | HPV16HPV18 |  | 100100 |
|  | 24 |  | HPV16HPV18 |  | 10072.0 |
|  | HIV+ vs. HIV- (historical control) |  |  | 32 vs. 251 | 7 | cLIA(mMU/mL) | HPV16 | Age adjusted GMT ratio0.52 (0.33; 0.82) |  |
|  | HIV+ vs. HIV- (historical control) |  |  | 31 vs. 252 |  |  | HPV18 | 0.31 (0.20; 0.49) |  |
|  | HIV+ vs. HIV- (historical control) |  |  | 26 vs. 186  | 24 | cLIA(mMU/mL) | HPV16 | 0.36 (0.24; 0.55) | 100 vs. 100 |
|  | HIV+ vs. HIV- (historical control) |  |  | 25 vs. 187 |  |  | HPV18 | 0.22 (0.12; 0.40) | 72.0 vs. 93.6 |
| **Canada**ISRCTN33674451(Moscicki et al., 2019) | Cohort study to compare antibody titers against 4vHPV types and rate of abnormal cytology betweenperinatally HIV-infected (PHIV) and perinatally HIV-exposed, uninfected (PHEU) youth part of the Adolescent Master Protocol for Participants 18 Years of Age and Older (AMP Up; NCT02119702). | 4vHPV recipients (1, 2, or 3 doses)  | Children 7-16 | Vaccinated population: 278 PHIV vs. 115 PHEU [1-dose : 154 vs 91 ; 2-doses: 34 vs 13; 3-doses: 90 vs 11] | Median 35 (IQR: Q1, Q3 22, 49) | cLIA(mMU/mL) | HPV16HPV18 |  | 90% vs. 99% 62% vs. 87% |
|  | PHIV Youth  | 1 dose (ref.)2 doses≥3 doses |  |   |  |  | HPV16 | Antibody titers change1.55 (−1.30; 3.15)−1.06 (−2.01; 1.79) |  |
|  |  | 1-dose (ref.)2-doses≥3 doses |  |  |  |  | HPV18 | 1.52 (−1.21; 2.80)−1.24 (−2.16; 1.41) |  |
|  | CD4% ≥ 25% at first vaccinedose | At least one vaccine dose |  |  |  |  | HPV16HPV18 | 1.85 (1.04; 3.29)1.43 (−1.16; 2.35) |  |
|  | HIV RNA (copies/mL) <400 (ref.)400 to <1000≥1000 | At least one vaccine dose |  |  |  |  | HPV16 | −3.70 (−8.55; −1.60)−4.09 (−7.12; −2.34) |  |
|  | 400 to <1000≥1000 |  |  |  |  |  | HPV18 | −2.23 (−4.61; −1.07)−2.91 (−4.72; −1.80) |  |
|  | On 3+ months continuous cART at first vaccine dose | At least one vaccine dose |  |  |  |  | HPV16HPV18 | −1.07 (−1.95; 1.71)1.60 (−1.05; 2.71) |  |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **Denmark**NCT01386164(Toft et al., 2014) | Phase IV, randomized, double-blind trial to compare the immunogenicity and reactogenicity of 2vHPV and 4vHPV in HIV-infected adult men and women. | 2vHPV vs. 4vHPV | HIV+ women ≥18 | 15 vs. 15 | 712 | cLIA(mMU/mL) | HPV16 | GMT ratio2.98 (0.76; 11.6)3.90 (1.05; 14.6) |  |
|  |  |  | 712 |  | HPV18 | 3.93 (1.02; 15.2) 6.02 (1.05; 14.6) |  |
|  | 2vHPV vs. 4vHPV | HIV+ men ≥18 | 30 vs. 31 | 712 | cLIA(mMU/mL) | HPV16 | No difference in GMTs 2vHPV vs 4vHPV |  |
|  |  |  |  | 712 |  | HPV18 | 4.54 (2.15; 9.59)3.55 (1.48; 8.53) |  |
| **United States, Puerto Rico** NCT00710593(Kahn et al., 2013) | Phase II, open-label, multicenter trial to evaluate the immunogenicity and safety of 4vHPV vaccine in HIV-infected young women. | 4vHPV3 doses(0, 2, 6M) | Women 16-23 |  99(69 not ART; 30 ART) |  |  |  | Mean GMT (PP) |  |
|  | non-ART group |  |  | 42 | 7 | cLIA(mMU/mL) | HPV16 | 2393 (1252; 3534) | 96.4 (81.7; 99.9) |
|  | ART group |  |  |  |  |  |  | 5046 (2338; 7755)  | 100 (75.3; 100.0) |
|  | Historical comparison (negative for all 4vHPV types) |  |  | 267 |  |  |  | 3892 (3324; 4558) | 100 (--) |
|  | non-ART group |  |  | 57 |  |  | HPV18 | 463 (247; 679) | 92.3 (79.1; 98.4) |
|  | ART group |  |  |  |  |  |  | 979 (302; 1655) | 100 (79.4; 100.0) |
|  | Historical comparison (negative for all 4vHPV types) |  |  | 267 |  |  |  | 801 (694; 925) | 100 (--) |
| **United States, Puerto Rico, Brazil, South Africa**NCT00604175(Kojic et al., 2014) | Phase II, open-label,single-arm study with stratification by CD4+ cell count to assess the immunogenicity and safety of the 4vHPV vaccine. | 4vHPV3 doses(0, 2, 6M) | Women13-45 | 319675656 | 7 | cLIA(mMU/mL) | HPV16 |  | PP98.5 (92.0; 100)98.2 (90.4; 100)92.9 (82.7; 98.0) |
|  |  | 787161 |  |  | HPV18 |  | 91.0 (82.4; 96.3)84.5 (74.0; 92.0)75.4 (62.7; 85.5) |
|  | CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  | 736364 | 7 | cLIA(mMU/mL) | HPV16 | ITT 1200 (871; 1654)1117 (746; 1672)571 (328; 994) |  |
|  | CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  | 868069 |  |  | HPV18 | 175 (126; 243)171 (115; 255)94 (59; 149) |  |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **Results** |
| **Immunogenicity endpoint** | **Assay** | **HPV type** | **GMT (95% CI)** | **Seroconversion****% (95% CI)** |
| **United States, Puerto Rico, Brazil, South Africa**NCT00604175(Cespedes et al., 2018) | Sustained seropositivity CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  |  | 18 | cLIA(mMU/mL) | HPV16 |  | 95.2 (86.5; 99.0) 87.7 (76.3; 94.9)85.5 (73.3; 93.5) |
| CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  |  |  |  | HPV18 |  | 69.1 (56.7; 79.8)71.7 (58.6; 82.5) 53.2 (38.1; 67.9) |
|  | CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  | 635964 | 18 | cLIA(mMU/mL) | HPV16 | 249 (171; 362)170 (107; 272)98 (62; 156) |  |
|  | CD4 >350 cells/μLCD4 201–350 cells/μLCD4 ≤200 cells/μL |  |  | 757369 |  |  | HPV18 | 42 (30; 60)41 (27; 61)21 (15; 30) |  |
| **South Africa**NCT00586339(Denny et al., 2013) | Phase I/II, partially blind, partially randomized, placebo-controlled trial of 2vHPV vaccine in HIV-positive women.  | 2vHPV3 doses(0, 1, 6M)vs. placebo | Women 18-25 | 150120 HIV+30 HIV- | Mo 7& M12 | ELISA(EU/ml) | HPV16HPV18 |  | 100100 |
|  | HIV+HIV- |  |  | 7 |  | HPV16 | 3558 (2724; 4649)8169 (6341; 10,524) |  |
|  | HIV+HIV- |  |  |  |  |  | HPV18 | 1946 (1451; 2609) 3703 (2503; 5479) |  |
|  | HIV+HIV- |  |  |  | 12 |  | HPV16 | 748 (520; 1076)2794 (2088; 3738) |  |
|  | HIV+HIV- |  |  |  |  |  | HPV18 | 343 (236; 498)1021 (627; 1663) |  |

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| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **HPV type** | **Results** |
| **Other endpoints** |
| **Canada**(McClymont et al., 2019) | Cohort study to evaluate vaccine failure of the 4vHPV among participants of an open-label, multicenter, single-arm study evaluating the immunogenicity and safety of the 4vHPV vaccine among women and girls with HIV (ISRCTN33674451) | 4vHPV3 doses(0, 2, 6M) | Women and girls with HIV9-65 | 420Efficacy cohort:n=212/4 casesn=211/4 casesn=177/0 cases | 24 |  | Incident rate per 100 person-yearsPer-protocol efficacy populationBreakthrough persistent infections: 1.0 (0.3; 2.6)Genital warts: 1.0 (0.3; 2.5)CIN2+: 0 (0.0; 1.1) |
|  |  |  | n=268/11 casesn=264/11 casesn=217/0 cases | 24 |  | ITT populationBreakthrough persistent infections: 2.3 (1.1; 4.1)Genital warts: 2.3 (1.2; 4.1)CIN2+: 0 (0.0; 0.9) |
|  | Vaccinated population: WWH vs. HIV- |  |  |  |  |  | Rate ratios of infection and disease Per-protocol efficacy: 11.7 (2.6; 52.1) |
|  | Vaccinated WWH vs. placebo HIV- |  |  |  |  |  | 0.8 (0.2; 2.5) |
|  | Vaccinated population: WWH vs. HIV- |  |  |  |  |  | ITT1.1 (0.6; 2.2) |
|  | Vaccinated WWH vs. placebo HIV- |  |  |  |  |  | 0.8 (0.4; 1.5) |
| **Denmark**(Zurek Munk-Madsen et al., 2018) | Phase IV, randomized, double-blind clinical trial to compare the immunogenicity and reactogenicity of 2vHPV and 4vHPV in HIV-infected adult men and women (NCT01386164) to determine the cellular immunity to HPV vaccines in HIV-infected, ART-treated men and women. |  |  |  |  |  | HPV vaccine-specific CD4/CD154/IL-2 positive T cellsT cells median frequency (IQR) |
| 4vHPV(0, 1.5, 6M) | HIV+ men and women ≥18 | 15 | 0712 | HPV16 L1 | 0.005 (0.000–0.030)0.040 (0.020–0.100)\*\*0.050 (0.020–0.070)\*\* |
| 2vHPV(0, 1.5, 6M) |  |  15 | 0712 |  | 0.010 (0.000–0.020)0.050 (0.010–0.113)\*\*0.030 (0.010–0.050)\*\* |
|  |  | 4vHPV(0, 1.5, 6M) |  | 15 | 0712 | HPV18 L1 | 0.000 (0.000–0.003)0.030 (0.010–0.040)\*\*0.020 (0.010–0.050)\*\* |
|  |  | 2vHPV(0, 1.5, 6M) |  |  15 | 0712 |  | 0.000 (0.000–0.005)0.040 (0.010–0.070)\*\*0.020 (0.000–0.060) |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Location****Clinical trial No.****(Reference)** | **Description** | **Vaccine product****No. Doses****(schedule)** | **Population** **Age (years)** | **Sample size** | **Timing of measure****(months)** | **HPV type** | **Results** |
| **Other endpoints** |
| **United States,** **Puerto Rico**(Weinberg et al., 2018) | Evaluation of additional potential protective mechanisms by investigating the persistence of memory B and T cell responses to 4HPV for 4 to 5 years after the last vaccine dose among HIV-1 infected children previously enrolled in IMPAACT P1047. (IMPAACT P1085; NCT01206556) |   |  |  |  |  | IFN T cell responses [median (Q1-Q3)] |
| 4 doses(0, 2, 6, 24M)  | Children7-11 |  54 | 244248-60 | HPV16 vs. HPV18 | 5 (SFC/105PBMC) (2-17) vs. 3 (2-9)\*\*5 (3-10) vs. 4 (2-8)\*\*4 (1-12) vs. 3 (1-9)\*\* |
|  | 3-doses(0, 2, 6M –initial placebo group) |  |  12 | 244248-60 | HPV16 vs. HPV18 | 5 (4-15) vs. 2 (1-3)\*\*2 (1-8) vs. 2 (1-6)1 (1-2) vs. 2 (0-5)\*\* |
|  |  |  |  |  |  |  | IL2 T cell responses [median (Q1-Q3)] |
|  |  | 4 doses(0, 2, 6, 24M) |  | 54 | 244248-60 | HPV16 vs. HPV18 | 28 (SFC/105PBMC) (8-59) vs. 15 (6-38)\*\*25 (7-50) vs. 13 (5-45)\*\*17 (2-36) vs. 17 (3-33) |
|  |  | 3 doses(0, 2, 6M –initial placebo group) |  |  12 | 244248-60 | HPV16 vs. HPV18 | 16 (8-46) vs. 9 (2-23)\*\*12 (2-48) vs. 19 (1-40)3 (1-13) vs. 2 (0-10)\*\* |

Abbreviations: 2vHPV, bivalent HPV vaccine (Cervarix; GlaxoSmithKline); 4vHPV quadrivalent HPV vaccine (Gardasil; Merck & Co.); 9vHPV nonavalent HPV vaccine (GARDASIL 9, Merck & Co.); ART, Antiretroviral therapy; ATP, According to protocol; CI, confidence interval; CIN, cervical intraepithelial neoplasia; cLIA, competitive Luminex immunoassay (milli-Merck Units [mMU]/mL); ELISA, Enzyme-linked immunosorbent assay; GMT, geometric mean antibody titer; HAART, Highly active antiretroviral therapy; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSIL, High-grade squamous intraepithelial lesions; IQR, Interquartile range; ITT, Intention-to-treat; LEEP, Loop electrosurgical excision procedure; M, Month; mITT, modified intention-to-treat (included all participants who received at least 1 study vaccine and all new persistent infections that occurred after the first vaccination); MSM, men who have sex with men; PBNA, Pseudovirion-based neutralization assay; PHEU, perinatally HIV-exposed, uninfected; PHIV, perinatally HIV-infected; PP, Per Protocol; PWH, people with HIV; SOT, Solid-organ transplant (performed at ≥12 months prior to the 1st vaccination, did not have an acute rejection in the 6 months prior to the 1st vaccination); TVC, Total vaccinated cohort; VE, Vaccine efficacy; WWH, women with HIV.

\*\* Statistically significant

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