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Immunogenicity of 2 compared with 3 doses of the quadrivalent HPV vaccine up to 10 years post-vaccination: *Phase III post-licensure randomized trial*

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Aims

- Evaluate if 2-dose Q-HPV is non-inferior to 3-dose

- Report 120 month anti-HPV antibody in:
  - 2-dose (2D) girls 9-13 years
  - 3-dose (3D) girls 9-13 years
  - 3-dose (3D) women 16-26 years

Background

- BCGOV01: Randomized phase III trial
  - 2 doses *vs.* 3 doses of the Q-HPV vaccine
    - 2 dose girls 9-13 years (0, 6 months)
    - 3 dose girls 9-13 years (0, 2, 6 months)
    - 3 dose women 16-26 years (0, 2, 6 months)

- Assessed at 7, 18, 24, 36, 60, 120 months after last dose

Methods

- Randomized phase III, postlicensure, age-stratified, non-inferiority immunogenicity trial
- Participants recruited in 2007-2008
- Contacted at 120 months
- Serum antibodies to HPV-6, 11, 16 and 18
  - Merck Competitive Luminex ImmunoAssay (cLIA)
  - Total IgG LIA (Luminex Immunoassay)

Analysis

- Seropositivity and GMTs for 4 genotypes compared between groups
- Non-inferiority: lower bound of 95% CI of GMT ratio >0.5
- Trends in antibody concentration compared using a linear mixed effects model on natural log-transformed values from assays

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Immunogenicity of 2 Doses of HPV Vaccine in Younger Adolescents vs 3 Doses in Young Women

A Randomized Clinical Trial

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Importance Global use of human papillomavirus (HPV) vaccines to prevent cervical cancer is impeded by cost. A 2-dose schedule for girls may be possible.

Objective To determine whether mean antibody levels to HPV-16 and HPV-18 among girls receiving 2 doses was noninferior to women receiving 3 doses.

Design, Setting, and Patients Randomized, phase 3, postlicensure, multicenter, age-stratified, noninferiority immunogenicity study of 830 Canadian females from August 2007 through February 2011. Follow-up blood samples were provided by 675 participants (81%).

Intervention Girls (9-13 years) were randomized 1:1 to receive 3 doses of quadrivalent HPV vaccine at 0, 2, and 6 months (n=261) or 2 doses at 0 and 6 months (n=259). Young women (16-26 years) received 3 doses at 0, 2, and 6 months (n=310). Antibody levels were measured at 0, 7, 18, 24, and 36 months.

Main Outcomes and Measures Primary outcome was noninferiority (95% CI, lower bound >0.5) of geometric mean titer (GMT) ratios for HPV-16 and HPV-18 for girls (2 doses) compared with young women (3 doses) 1 month after last dose. Secondary outcomes were noninferiority of GMT ratios of girls receiving 2 vs 3 doses of vaccine; and durability of noninferiority to 36 months.

Results The GMT ratios were noninferior for girls (2 doses) to women (3 doses): 2.07 (95% CI, 1.62-2.65) for HPV-16 and 1.76 (95% CI, 1.41-2.19) for HPV-18. Girls (3 doses) had GMT responses 1 month after last vaccination for HPV-16 of 7736 milli-

Results: 60 months

- N=101 girls
  - 50 girls from 2 dose group
  - 51 girls from 3-dose group
- Seropositivity >95% for all genotypes except HPV-18
- No differences in seropositivity for 2- *vs.* 3-dose girls (p >0.05)
- No significant differences in GMTs using IgG or cLIA between 2- and 3-dose recipients, except HPV-18 cLIA (p=0.04)
- No significant differences between assays

Results: 120 months

- N=114
- Compared to the 830 women originally assessed for eligibility, 3D girls who participated at 120 months were slightly younger at the first visit compared to those loss-to-follow-up (mean age 11.3 yrs *vs.* 11.9 yrs)
- 3D women who participated at 120 months were less likely to be sexually active (48.7% versus 68.1%) but had younger age at sexual debut (mean age 16.6 yrs *vs.* 16.7 yrs)

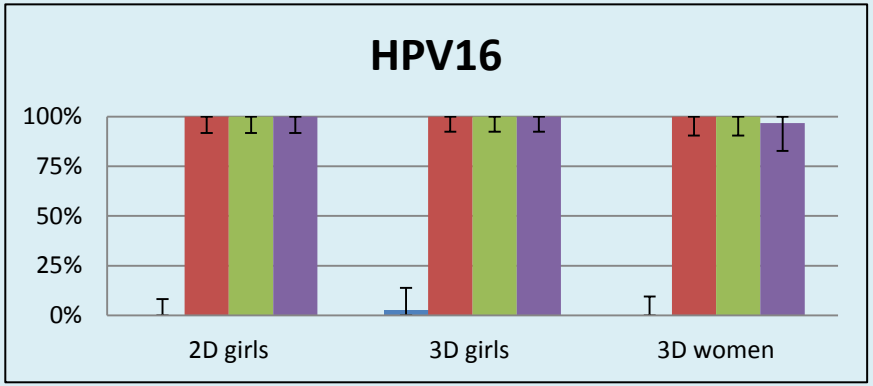
Results: 120 months

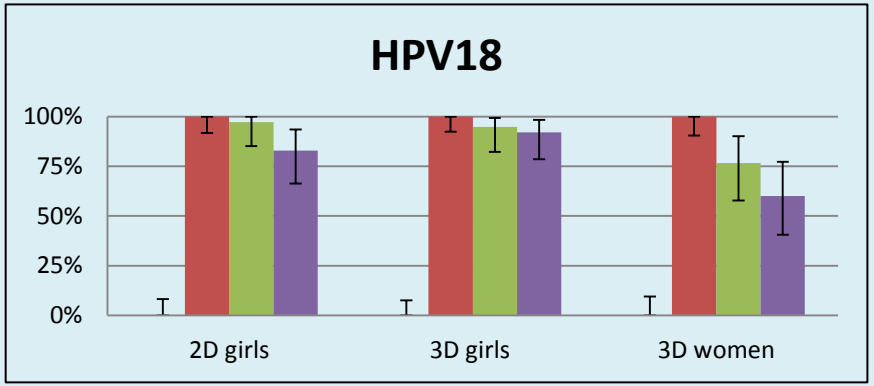
- We included participants who contributed at all visits on day 1; 7, 24 and 120 months post-vaccination: n=103

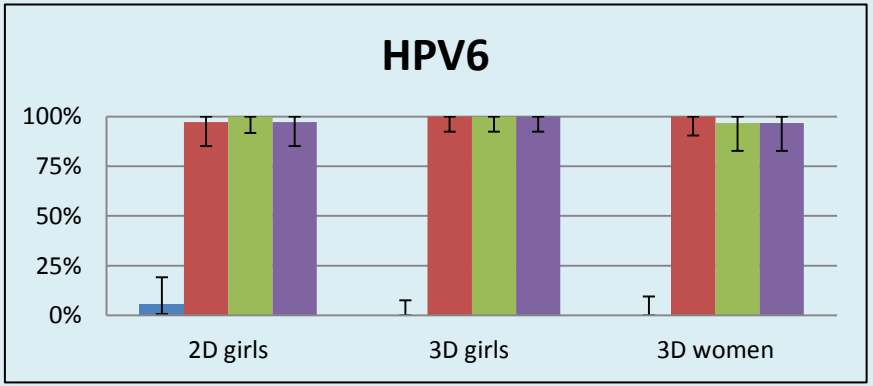
- 2 doses (9-13): 35 participants
- 3 doses (9-13): 38 participants
- 3 doses (16-26): 30 participants

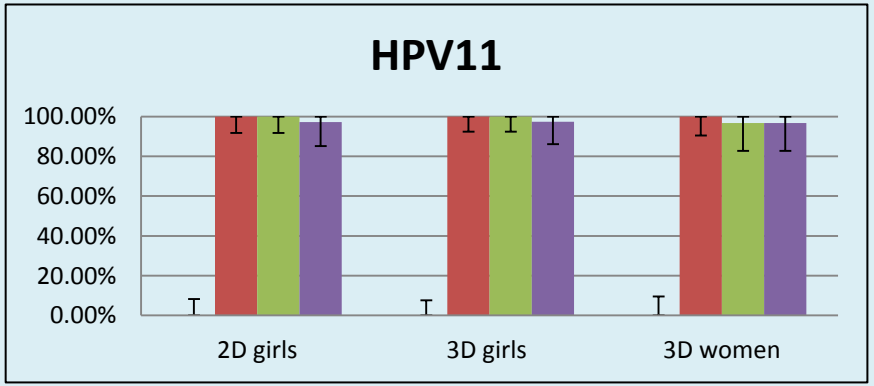
- No difference in 2- *vs.* 3-dose girls at the first study visit with regard to socio-demographics or sexual behavior at both the first or the 120 month visit

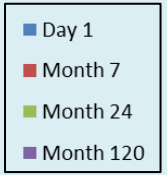
Seropositivity at 120 months



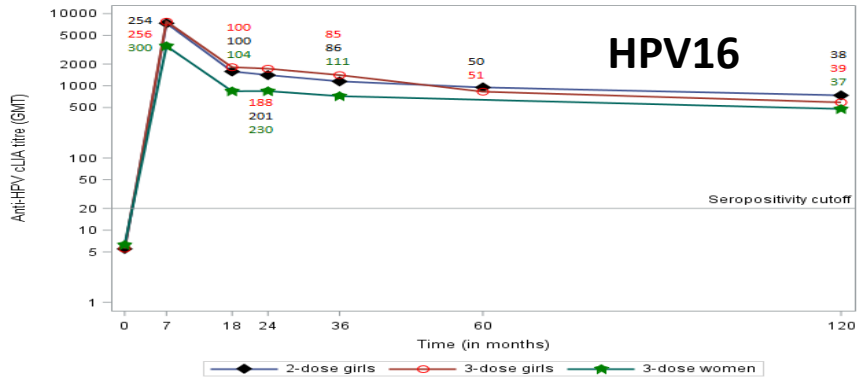


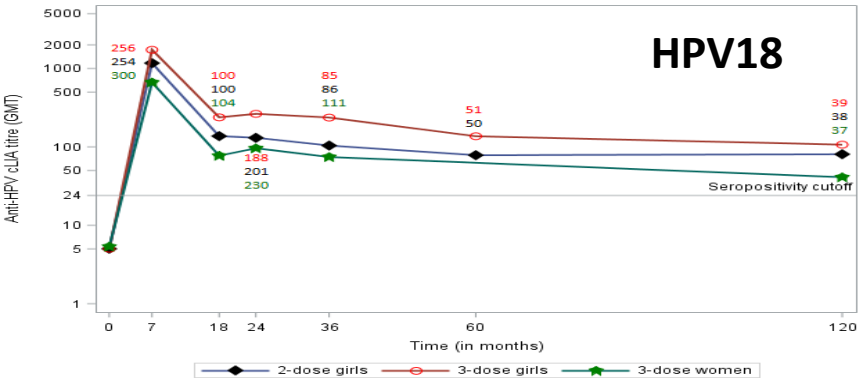


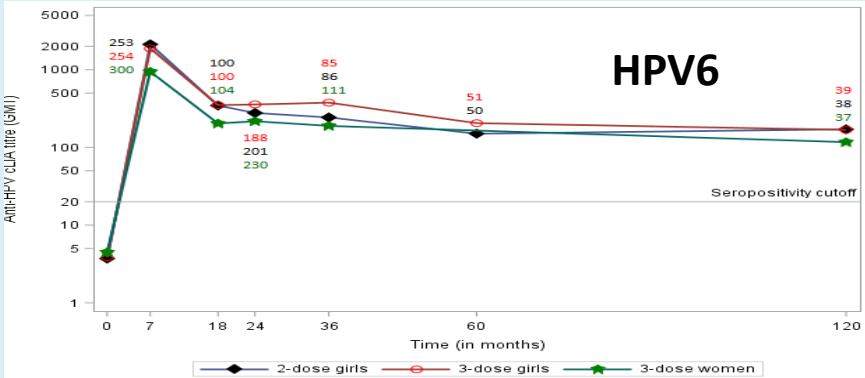


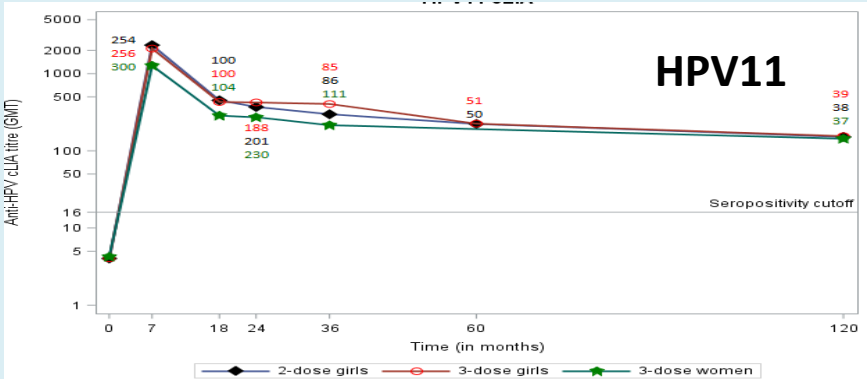


GMT: cLIA

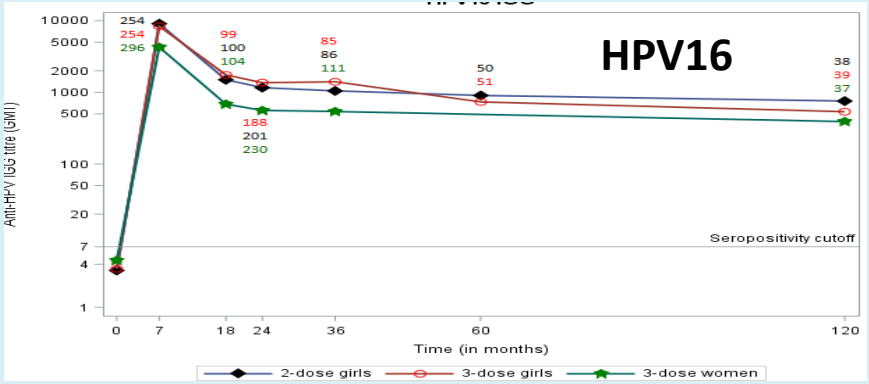

HPV16
Anti-HPV cLIA titre (GMT)
Time (in months)
Seropositivity cutoff
2-dose girls
3-dose girls
3-dose women

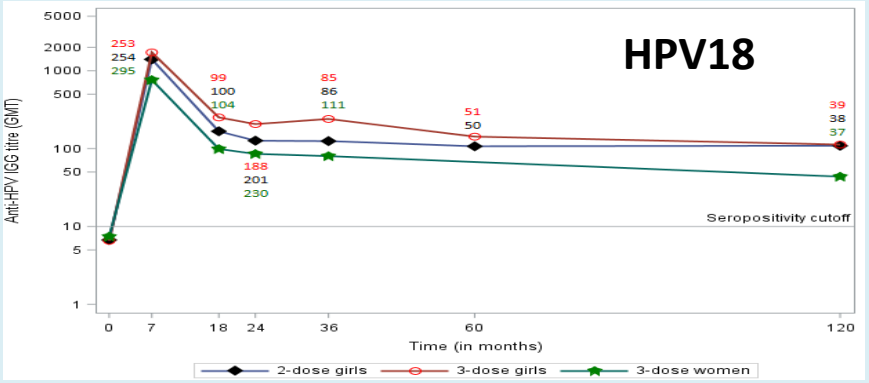

HPV18
Anti-HPV cLIA titre (GMT)
Time (in months)
Seropositivity cutoff
2-dose girls
3-dose girls
3-dose women

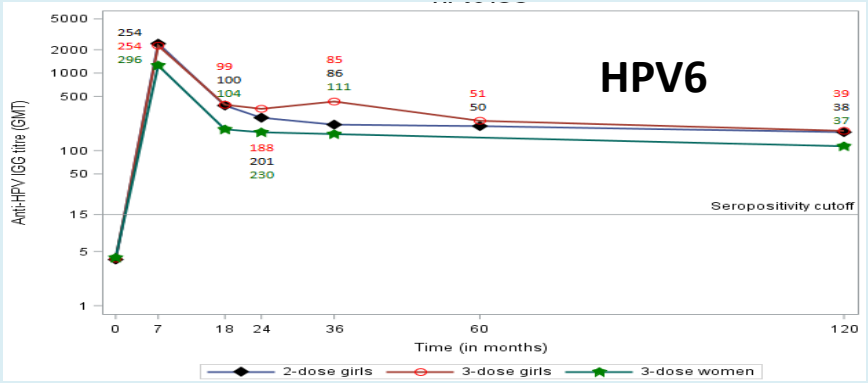

HPV6
Anti-HPV cLIA titre (GMT)
Time (in months)
Seropositivity cutoff
2-dose girls
3-dose girls
3-dose women

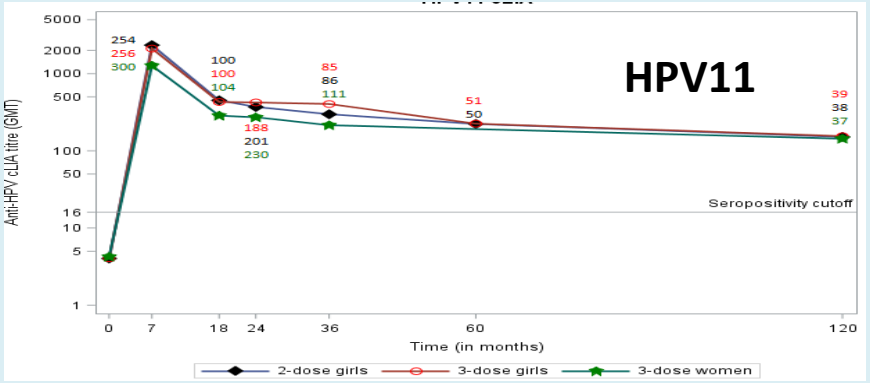

HPV11
Anti-HPV cLIA titre (GMT)
Time (in months)
Seropositivity cutoff
2-dose girls
3-dose girls
3-dose women

GMT: IgG


HPV16
Anti-HPV IGG titre (GMT)
Seropositivity cutoff
Time (in months)
2-dose girls
3-dose girls
3-dose women


HPV18
Anti-HPV IGG titre (GMT)
Seropositivity cutoff
Time (in months)
2-dose girls
3-dose girls
3-dose women


HPV6
Anti-HPV IGG titre (GMT)
Seropositivity cutoff
Time (in months)
2-dose girls
3-dose girls
3-dose women


HPV11
Anti-HPV cLIA titre (GMT)
Seropositivity cutoff
Time (in months)
2-dose girls
3-dose girls
3-dose women

Antibody 24 → 120 months

- Significant ↓ in GMTs for all HPV types in each group
- No sig. difference in ↓ of antibody levels <u>between</u> groups ($p>0.05$)
- Largest difference reduction was found for HPV18 in 3D girls

120 month GMT ratios

- 2D girls remained non-inferior to 3D women

- GMTs for 2D girl vs 3D women
  - HPV16: 1.61 (95%CI 0.91-2.85)
  - HPV18: 2.02 (95%CI 0.99-4.10)

- GMT ratio for 2D girls v 3D girls
  - HPV 16: 1.21 (0.77-1.92)
  - HPV 18: 0.72 (0.38-1.34)

Summary

- Between 24 and 120 months, there was a significant reduction in GMTs for all HPV types, in each of the groups.
- No significant difference in the reduction of antibody levels between the different study groups
- Except for HPV18, 2D in girls were non-inferior to 3D given to girls at 120 months post-vaccination.
- No significant interaction was observed between time and study groups for the development of antibodies
- Ongoing monitoring of effectiveness of 2D in girls continues with QUEST

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