Additional 9-valent HPV vaccination

Considerations for guidance

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Additional 9-valent HPV vaccine (9vHPV) Summary

- One randomized trial evaluated 9vHPV vs placebo among prior 3-dose 4vHPV recipients
  - After dose 3 of 9vHPV, positivity to all 5 additional types was >98%
- In a cross study comparison
  - GMTs for 5 addition types after 3 doses of 9vHPV were lower in prior 4vHPV recipients than in HPV vaccine naïve females
  - Clinical significance of the lower titers not known because no immune correlate of protection
- No safety concerns apparent
  - In cross study comparison, higher rates of injection site reactions compared with 9vHPV in HPV vaccine naïve females

Additional 9vHPV vaccination Summary

- Benefit of protection against the 5 additional types would be mainly for females
  - For prevention of cervical cancers and precancers
- Cost per QALY gained >$100,000 for additional 3 doses among females 13 to 18 years
  - Higher cost per QALY for females over age 18 years
  - Higher cost per QALY for males at any age
- In contrast, models have estimated that routine 9-valent HPV vaccination for females and males in the U.S. is cost-saving
  - Compared with routine quadrivalent HPV vaccination

QALY, quality-adjusted life year

Additional 9vHPV vaccination Work Group considerations

- Work Group felt the highest priority was raising 9vHPV coverage for the routine vaccination series
- Programmatic issues considered
- Health economic considerations varied in the Work Group
- Routine cervical cancer screening continues to be recommended for women age 21 through 65 years, same for vaccinated and unvaccinated women

Additional 9vHPV vaccination Work Group considerations

- Work Group members not in favor of routine additional 9vHPV vaccination of persons who previously completed a 3-dose HPV vaccination series
- Guidance and information needed:
  - Persons who started the series with another vaccine product
  - Persons who completed a 3-dose HPV vaccination series
  - Clarify what data are and are not available

Questions about additional 9vHPV vaccination have been common

- Some providers/patients may be interested in protection against the 5 additional types
- Some may be seeking information about guidance
- Providers recall PCV7/PCV13 transition
  - Differences between PCV7/PCV13 transition and HPV vaccine transition

PCV, pneumococcal conjugate vaccine

Comparison of transitions

4vHPV to 9vHPV

- No indication in label for additional 9vHPV doses
- Trial evaluated 3 doses of 9vHPV after 3 doses of 4vHPV
- Additional 3-dose vaccination >$100,000/QALY
- Slow transition to 9vHPV vaccine

PCV7 to PCV13

- Indication in label for supplemental PCV13 dose; specific interval guidance
- Trial evaluated 1 dose of PCV13 after 3 doses of PCV7, 2 after 2 doses, and 3 after 1 dose
- Supplemental dose ~$20,000/QALY
- Rapid transition to PCV13

PCV, pneumococcal conjugate vaccine
QALY, quality-adjusted life year

Plans for communication of guidance

- No additional Policy Note in MMWR
- Information to be posted on CDC website
  - Link from ACIP website recommendation page
  - Announcement in MMWR with link to online information

Examples of guidance for providers

- 9vHPV vaccination for persons who started the series with another HPV vaccine product
- 9vHPV vaccination for persons who completed an HPV vaccination series
- 9vHPV vaccination – information available

Examples of guidance for providers:
Vaccination for persons who started the series with another vaccine product

If a series was started with quadrivalent HPV vaccine or bivalent HPV vaccine, can it be completed with 9-valent HPV vaccine?

- Yes, ACIP recommendations state that 9-valent HPV vaccine may be used to continue or complete a series started with a different HPV vaccine product.

Are additional 9-valent HPV vaccine doses recommended after a series started with quadrivalent or bivalent HPV vaccine and completed with 9-valent HPV vaccine?

- There is no ACIP recommendation for additional 9-valent HPV vaccine doses for persons who started the series with quadrivalent or bivalent HPV vaccine and completed the 3-dose series with 9-valent HPV vaccine.

Examples of guidance for providers:
Vaccination for persons who started the series with another vaccine product

If a series was started with quadrivalent HPV vaccine or bivalent HPV vaccine and will be completed with 9-valent HPV vaccine, what are the intervals for the remaining doses in the 3-dose series?

- The current recommended HPV vaccination schedule is for the second dose to be given 2 months after the first dose and the third dose 4 months after the second dose (6 months after the first dose). ACIP does not state maximum intervals between HPV doses.
- Antibody titers have not been found to be diminished after longer than standard intervals between doses. Data from other HPV vaccine studies show equal or higher antibody titers when 2 doses were administered at an interval of 6 months compared with 2 months.
  - An ongoing immunogenicity study is evaluating 2 doses of 9-valent HPV vaccine separated by an interval of 6 or 12 months.

Examples of guidance for providers:
Vaccination for persons who completed an HPV vaccination series

Is additional vaccination with 9-valent HPV vaccine recommended for persons who have completed a 3-dose series of either quadrivalent or bivalent HPV vaccine?

- There is no ACIP recommendation for routine additional 9-valent HPV vaccination of persons who previously completed a quadrivalent or bivalent vaccination series.

Examples of guidance for providers:
Vaccination for persons who completed an HPV vaccination series

If a person desires protection against the 5 additional types prevented by the 9-valent HPV vaccine and has completed a 3-dose series of HPV vaccine, what issues should be considered?

- The benefit of protection against the 5 additional types targeted by 9-valent HPV vaccination is mostly limited to females for prevention of cervical cancers and precancers. This is because only a small percentage of HPV associated cancers in males is due to the 5 additional types in 9-valent HPV vaccine.
- Available data show no serious safety concerns in persons who were vaccinated with 9-valent HPV vaccine after having received quadrivalent HPV vaccine.
- Cervical cancer screening is recommended beginning at age 21 years and continuing through age 65 years for both vaccinated and unvaccinated women.

Examples of guidance for providers: Information available

What data are available on efficacy and immunogenicity of 9-valent HPV vaccination for the 5 additional types, when administered after a complete 3-dose series of another HPV vaccine product?

What data are available on safety of 9-valent HPV vaccination when administered after a complete 3-dose series of another HPV vaccine product?

Examples of guidance for providers: Information available

What data are available on efficacy and immunogenicity of 9-valent HPV vaccination for the 5 additional types, when administered after a complete 3-dose series of another HPV vaccine product?

- In the one immunogenicity trial, 3 doses of 9-valent HPV vaccine vaccination (on a 0,2,6 month schedule) were given to females who had completed a 3-dose quadrivalent HPV vaccine series; the first dose of 9-valent HPV vaccine was administered at least 12 months after completion of the quadrivalent vaccine series.
  - After 3 doses of 9-valent vaccine, over 98% of vaccinees developed antibody to all 5 additional types. Antibody was also measured after the first dose of 9-valent HPV vaccine; most but not all vaccinees developed antibody against all 5 additional types. Antibody was not measured after the second dose.
  - In a cross study comparison, geometric antibody titers for the 5 additional types after 3 doses of 9-valent HPV vaccine were lower, 25-63% of those in persons who received 3 doses of 9-valent HPV vaccine without prior HPV vaccination. The significance of the lower antibody titers is not known because there is no immune correlate of protection.

Examples of guidance for providers: Information available

What data are available on safety of 9-valent HPV vaccination when administered after a complete 3-dose series of another HPV vaccine product?

- In a randomized trial, 9-valent HPV vaccine was compared with placebo in females aged 12-26 years who had previously received 3 doses of quadrivalent HPV vaccine. Among the 608 who received 9-valent HPV vaccine, there was an acceptable safety profile.
- Compared to persons in other studies who were vaccinated with 9-valent HPV vaccine without prior HPV vaccination, those who received 9-valent HPV vaccine after a 3-dose quadrivalent vaccine series had higher rates of injection site swelling and redness.
- Otherwise, the safety profiles of 9-valent vaccine given to HPV vaccine naïve persons and of 9-valent vaccine given to persons who had previously completed a 3-dose series were generally similar.

ACIP Discussion

- Overall approach
- Additional questions or information needed
- Other comments

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