Immunogenicity and tolerability of HPV vaccine in women aged 15-55: Study findings and way forward

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Conflict of interest 2019

- Honoraria for lecturing from Pfizer, GSK, MSD, Roche, Biogen
- Honoraria as member of advisory boards from Pfizer and GSK
- Honoraria for clinical trials from GSK and Pfizer

Methods

- Study design: long-term (10-year) follow-up study (HPV-014 EXT; NCT00947115) of a phase III, multi-centre, open-label study (HPV-014; NCT00196937)
- Participants: women aged 15–55 years at the time of vaccination who received 3 doses of AS04-HPV-16/18 Vaccine (at months 0, 1, 6) in HPV-014; study sites in Germany and Poland
- Measurements:
  - Serum and cervico-vaginal secretions (CVS) anti-HPV-16/18 antibody responses were assessed by enzyme-linked immunosorbent assay (ELISA)
  - Samples were collected at years 5, 6, 7, 8, 9, 10
  - Safety was assessed throughout the study
- Analyses: participants were stratified by age at vaccination: 15–25, 26–45, 46–55 years

PERSISTENCE OF IMMUNE RESPONSE 10 YEARS AFTER ADMINISTRATION OF THE HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED VACCINE TO WOMEN AGED 15–55 YEARS EUROGIN 2016;
Schwarz TF et al. Cancer Med 6:2723-2731 (2017)

Seropositivity rates in serum at Year 10

In initially seronegative women (Year 10 ATP cohort for immunogenicity)

Age group	≥cut-off* for anti-HPV 16 VLP IgG, n/N (% [95% CI])	≥cut-off† for anti-HPV 18 VLP IgG, n/N (% [95% CI])
15–25 years	123/123 (100 [97.0–100])	126/127 (99.2 [95.7–100])
26–45 years	120/121 (99.2 [95.5–100])	133/142 (93.7 [88.3–97.1])
46–55 years	103/107 (96.3 [90.7–99.0])	109/130 (83.8 [76.4–89.7])

*Assay cut-off 19 EU/mL
†Assay cut-off 18 EU/mL
ATP, according to protocol; CI, confidence interval; VLP, virus-like particle

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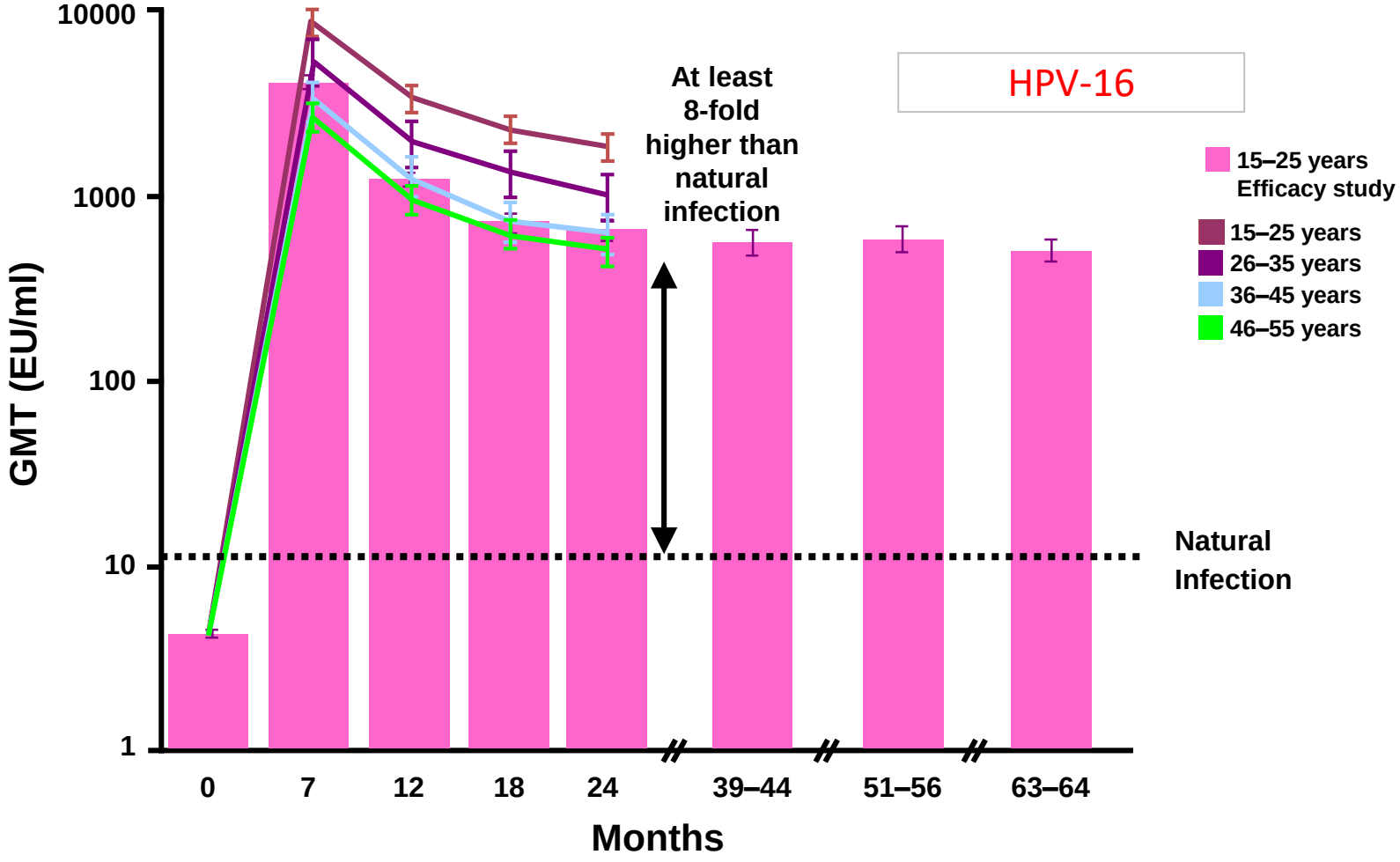
Antibody Levels in 15-55 Year Olds Comparable to those Observed in Efficacy Study HPV-001/007



ATP analysis
Seronegative prior to vaccination

Assay cut-off: 8 EU/ml

Harper DM *et al. Lancet* 2006; Paavonen J *et al. Lancet* 2007; Schwarz TF. ASCO 2006; Gall S. AACR 2007

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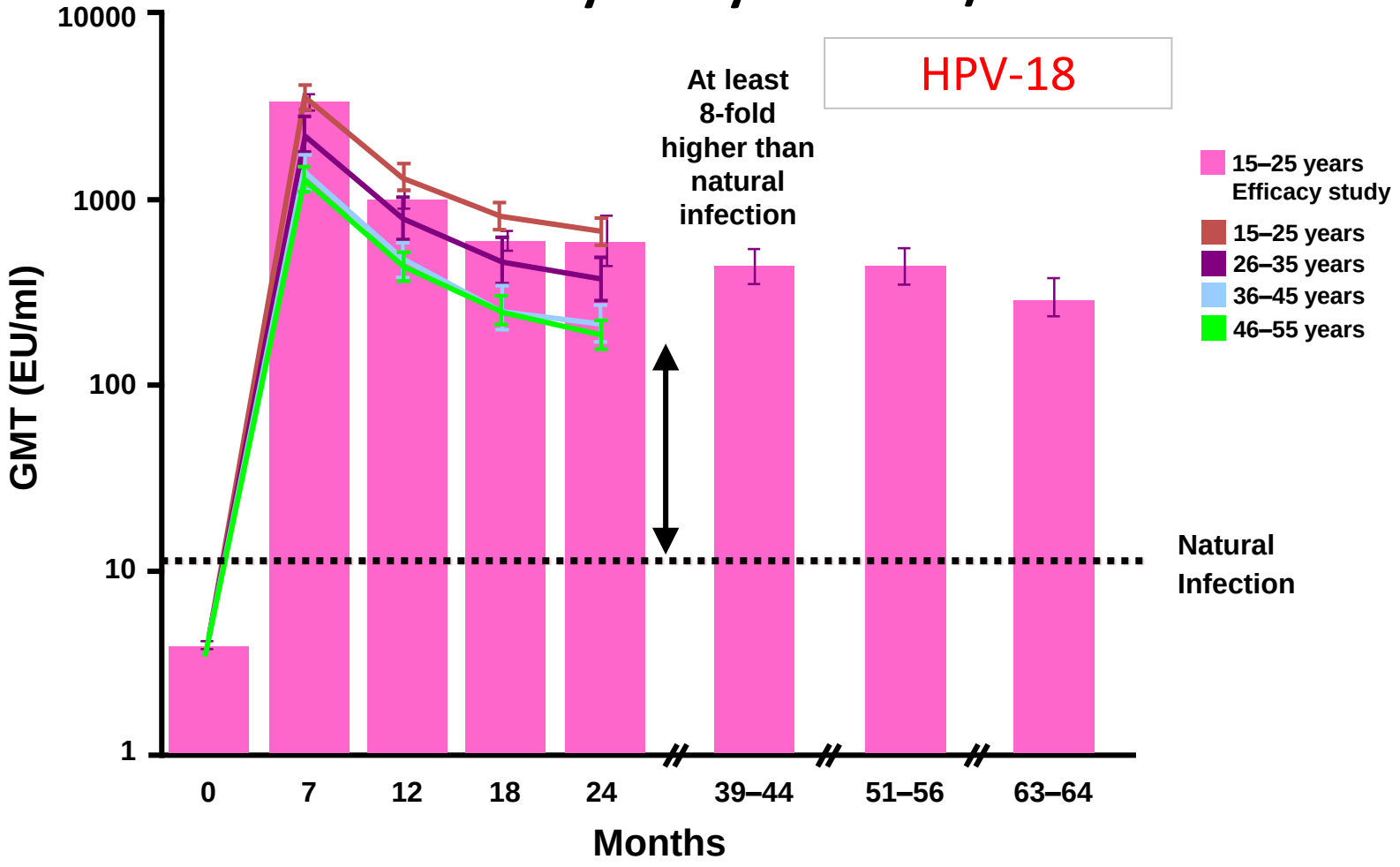


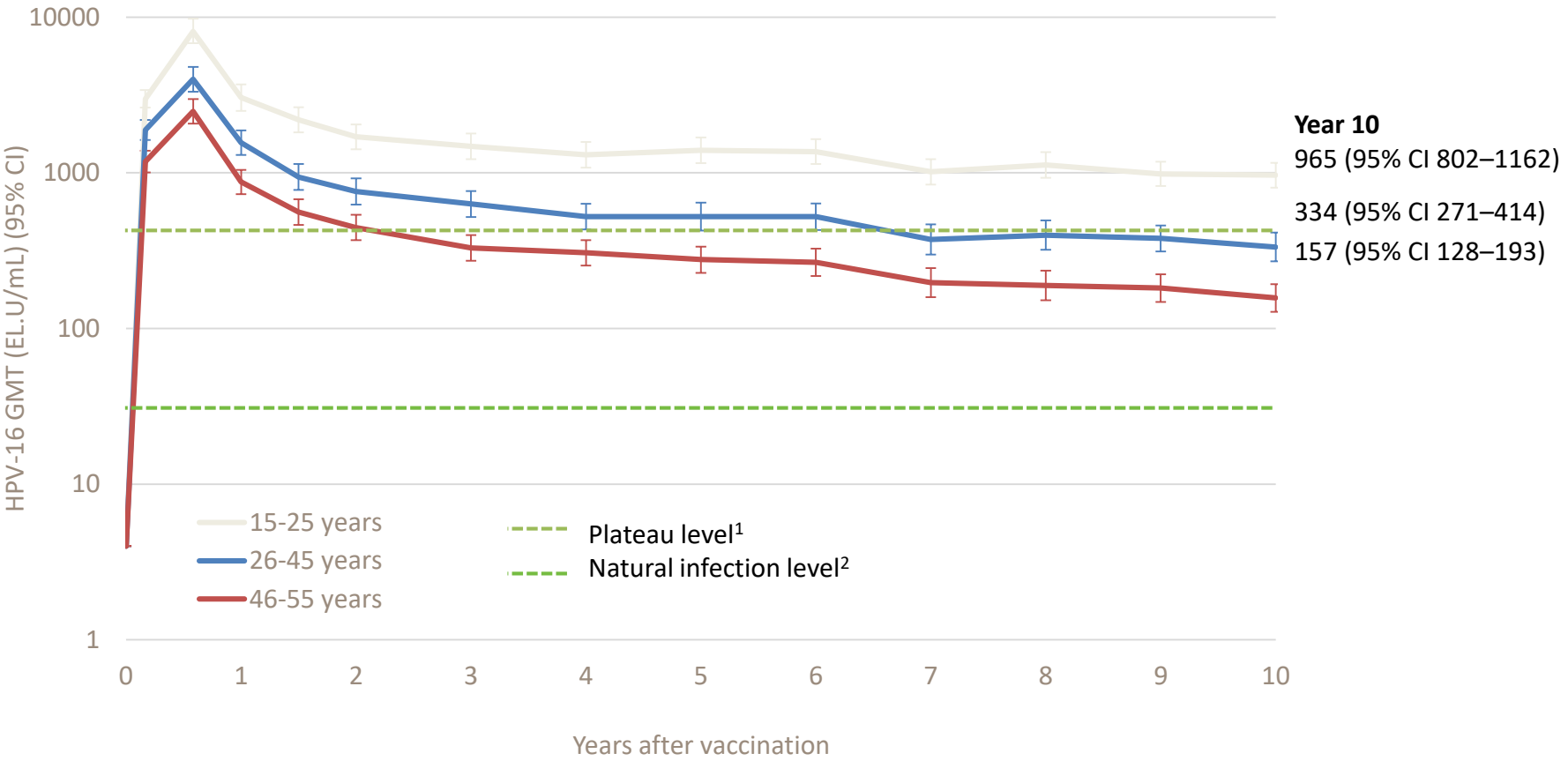
ATP analysis
Seronegative prior to vaccination

Assay cut-off: 7 EU/ml

Harper DM *et al*. *Lancet* 2006; Paavonen J *et al. Lancet* 2007; Schwarz TF. ASCO 2006; Gall S. AACR 2007

Anti-HPV-16 VLP IgG GMTs in serum

In initially seronegative women (Year 10 ATP cohort for immunogenicity)



1. Naud PS, et al. Hum Vaccin Immunother 2014;10:2147-62
2. Paavonen J et al. Lancet 2007;369:2161-70

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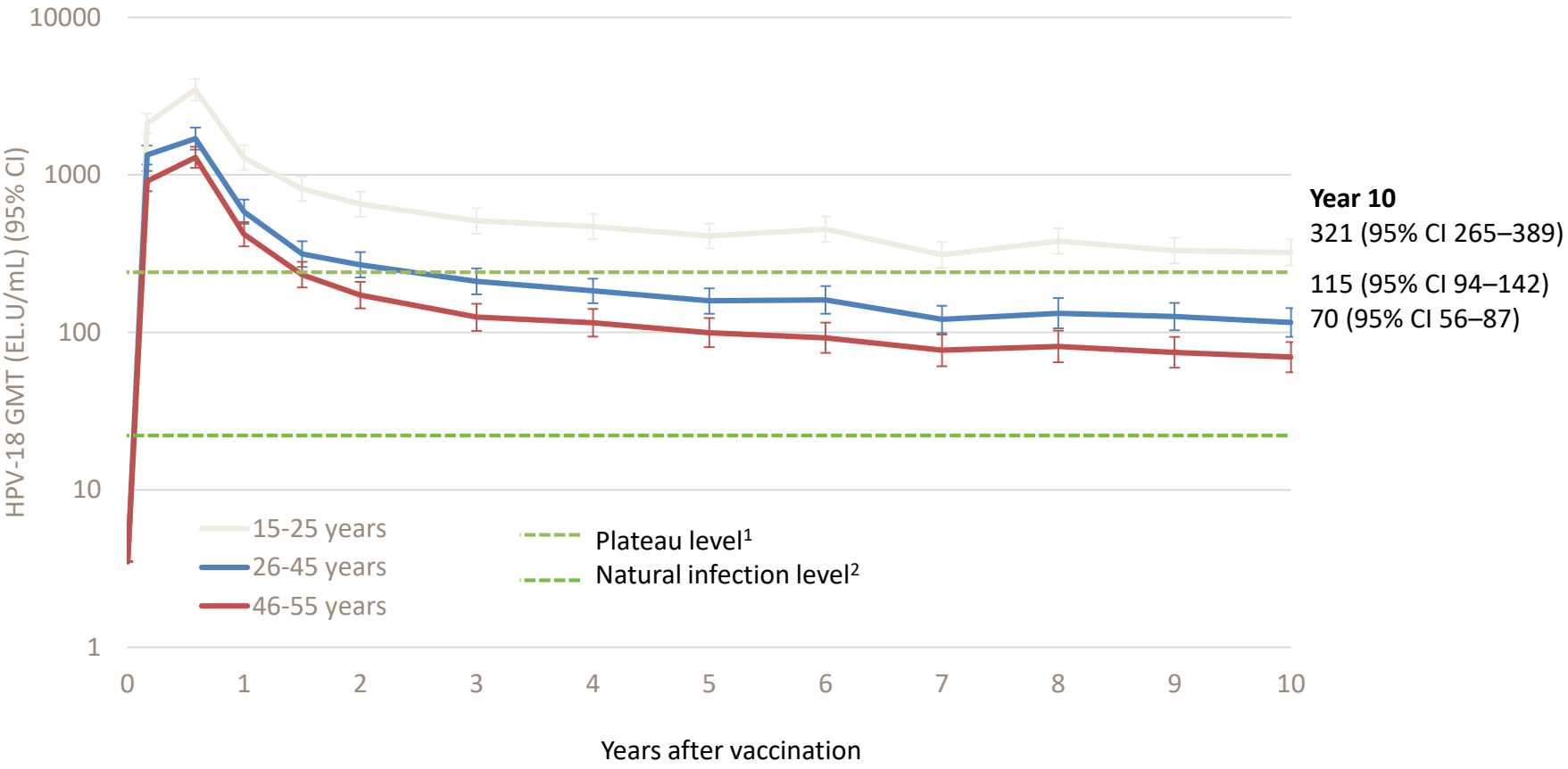
Anti-HPV-18 VLP IgG GMTs in serum

In initially seronegative women (Year 10 ATP cohort for immunogenicity)



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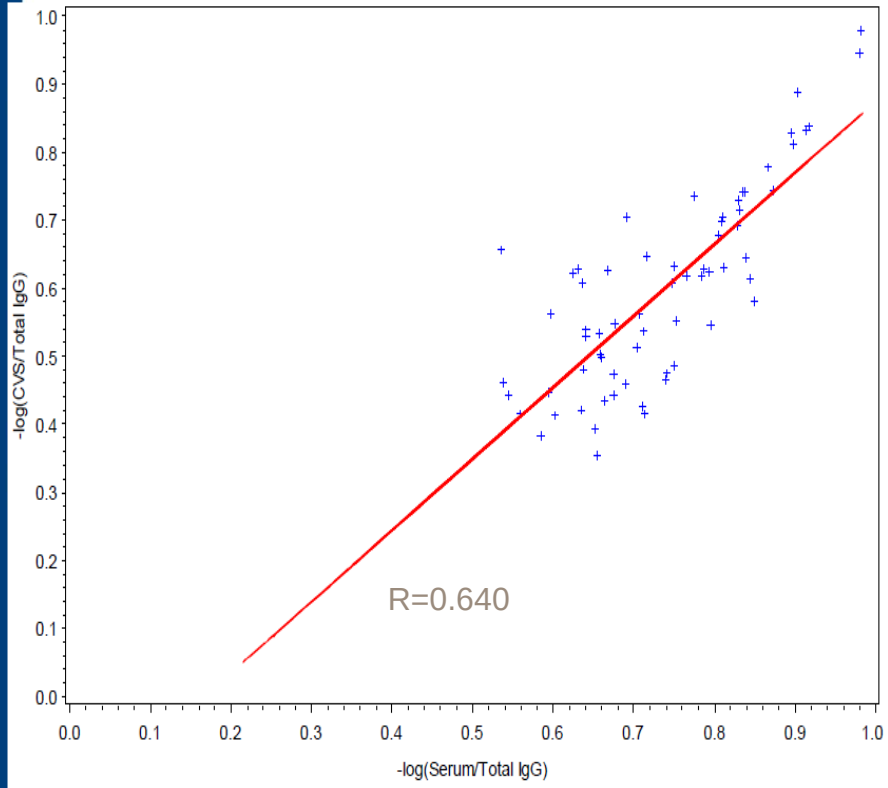
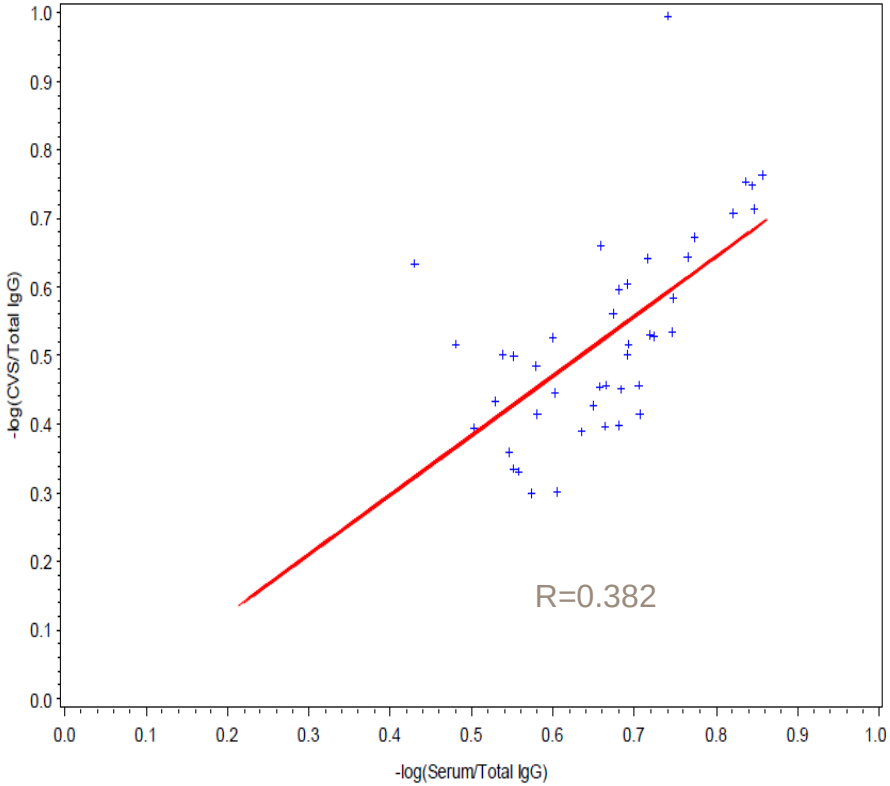
Correlations between serum and CVS anti-HPV-16/18 antibodies*

HPV-16



HPV-18



Standardised for total IgG (Year 10 TVC)

*No statistical testing was performed

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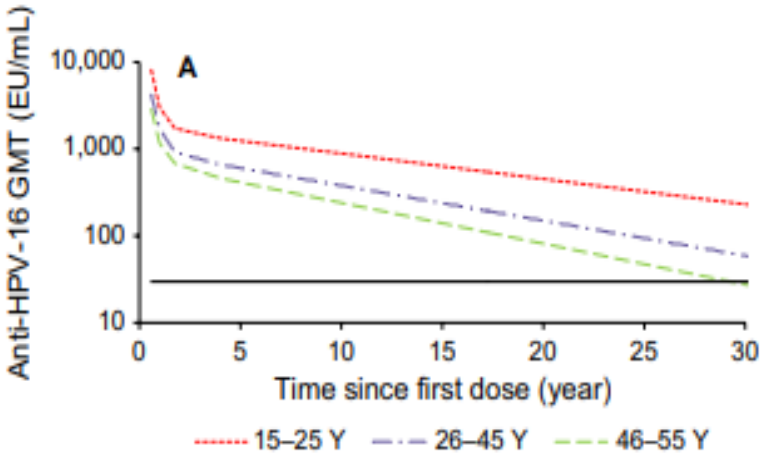
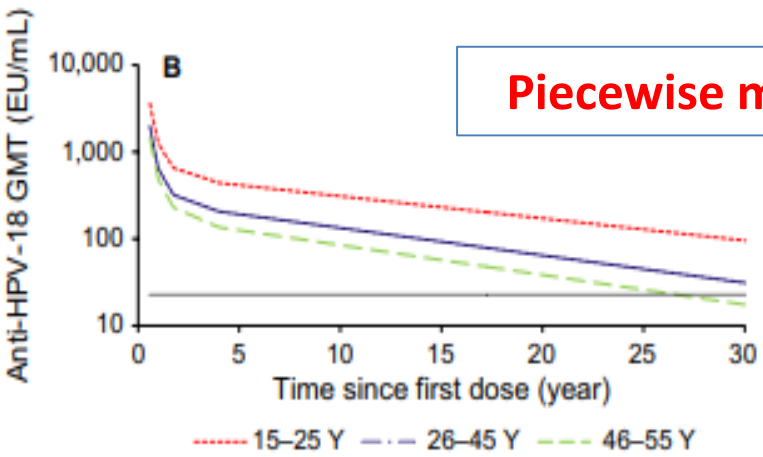
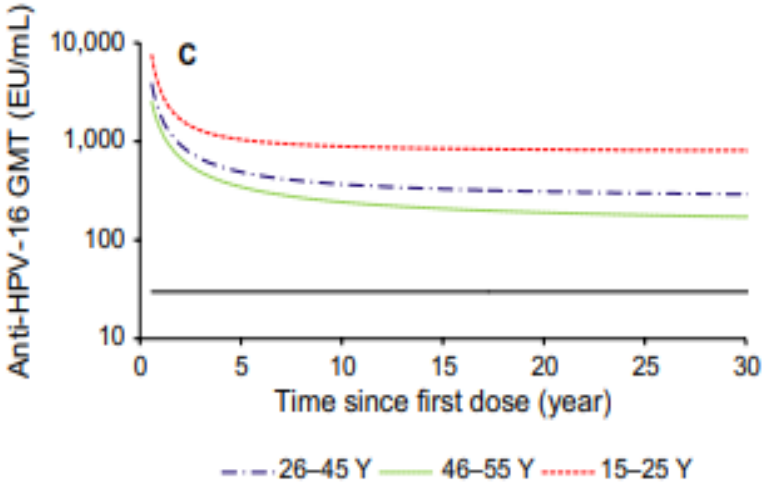
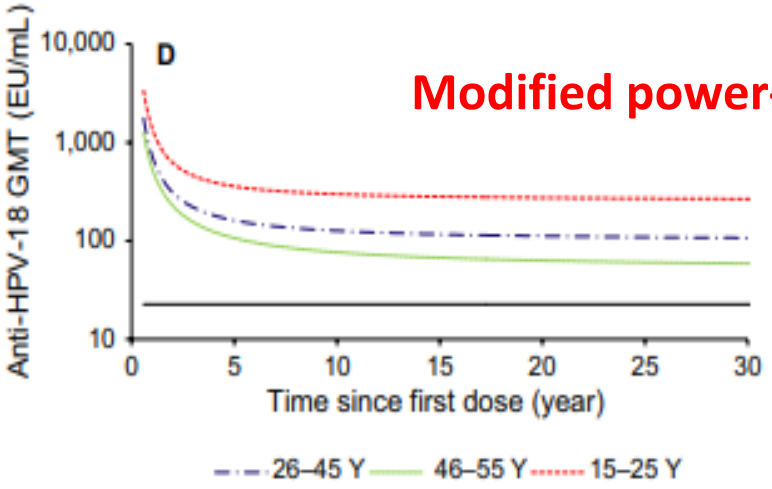
Prediction of antibody responses





Piecewise model



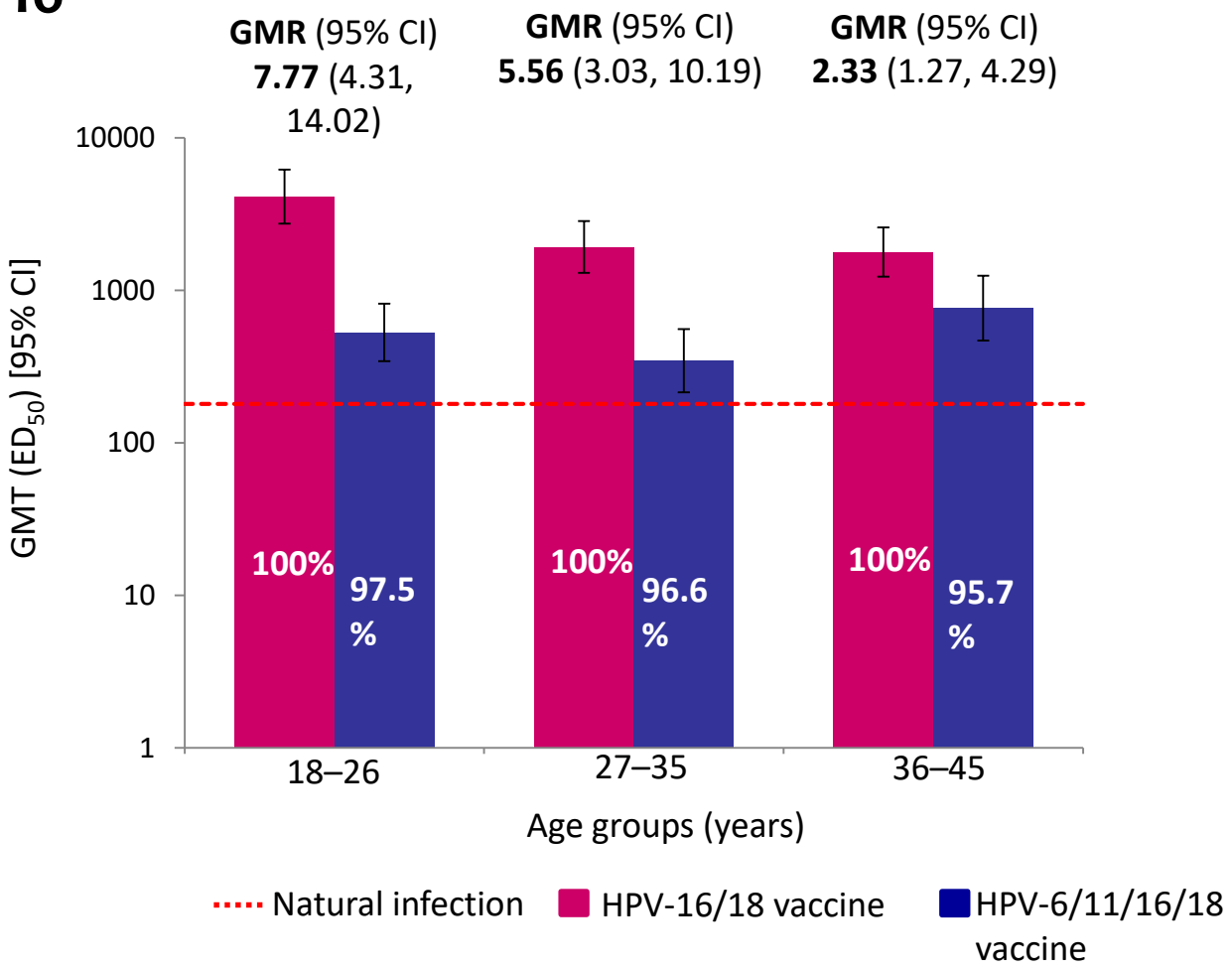


Modified power-law

Schwarz TF et al. Cancer Med 6:2723-2731 (2017)

Serum neutralising antibodies (PBNA) at Month 60 (M60 ATP cohort*)

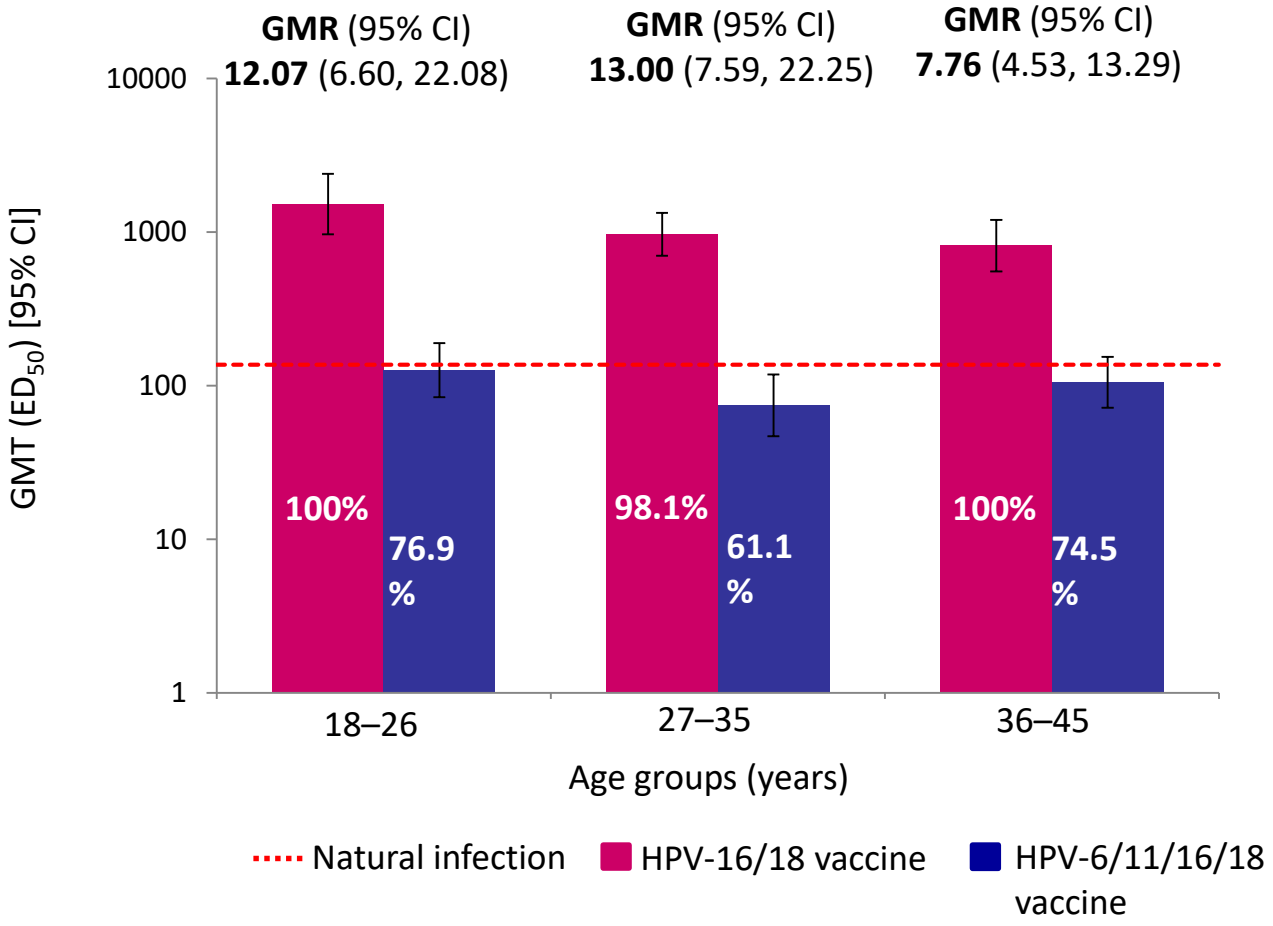
HPV-16



Einstein MH et al. Hum Vaccin Immunother. 2014;10(12):3435-45.

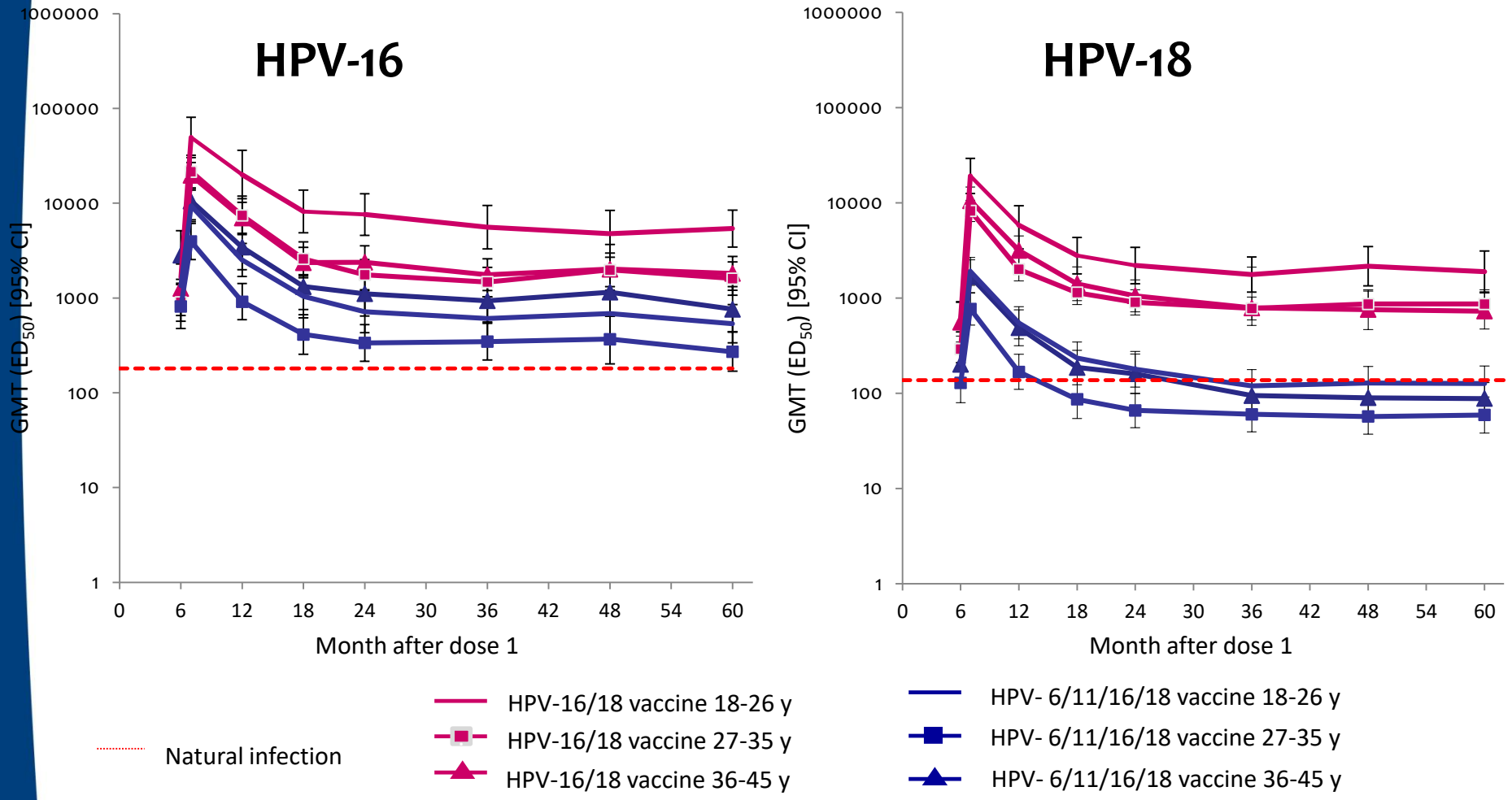
Serum neutralising antibodies (PBNA) at Month 60 (M60 ATP cohort*)

HPV-18



Einstein MH et al. Hum Vaccin Immunother. 2014;10(12):3435-45.

Serum neutralising antibodies (PBNA): kinetic cohorts* (all age groups)



*Kinetic cohort = sub-cohort of the M60 according-to-protocol cohort for immunogenicity that includes seronegative and DNA-negative subjects at baseline with available and valid results for the HPV type analysed at each time point. ED50 = serum dilution giving a 50% reduction of the signal compared with a control. PBNA, pseudovirion-based neutralisation assay. Natural infection = 180.1 ED50 and 137.3 ED50 for HPV-16 and -18 neutralising antibodies, respectively (Einstein *et al.*, *Hum Vacc* 2009; 7:1343-1358).

Einstein MH et al. Hum Vaccin Immunother. 2014;10(12):3435-45.

Safety during the entire 10-year study period

Year 10 TVC

- Fatal adverse events
  - 1 chronic lymphocytic leukaemia (considered not vaccine related)
  - 1 malignant lung neoplasm (considered not vaccine related)
- Serious adverse events considered related to vaccine
  - 1 cervical dysplasia at Year 8 (subject was HPV-16 seropositive and unknown DNA status before vaccination). The subject recovered

TVC, total vaccinated cohort

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Conclusions

Immunogenicity up to 10 years after first vaccination with HPV-16/18 vaccine was sustained in women aged 15–55 years at vaccination[1,2]

- ≥96.3% seropositivity for anti-HPV-16 antibodies
- ≥83.8% seropositivity for anti-HPV-18 antibodies

Antibody GMTs at year 10 were[1,2]

- ≥70 EL.U/mL, with an age at vaccination-dependant decrease in serum antibody levels
- Among those aged 15–25 years, similar to or above the plateau level observed in studies where vaccine efficacy was demonstrated in those aged 15–25 years
- Among the older age groups, similar to or below this plateau level above natural infection levels (as determined in unvaccinated women who had cleared an infection)
- Good correlation between antibodies (IgG) in the serum and in the CVS indicates likely transudation to the cervical epithelium[1,2]

The 10-year safety profile of HPV-16/18 vaccine was acceptable[1,2]

The difference in serum neutralising antibody response to HPV-16 and -18 observed at Month 7 between the two prophylactic HPV vaccines was sustained up to Month 60[3]

1. PERSISTENCE OF IMMUNE RESPONSE 10 YEARS AFTER ADMINISTRATION OF THE HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED VACCINE TO WOMEN AGED 15–55 YEARS EUROGIN 2016; 2. Schwarz TF et al. Cancer Med 6:2723-2731 (2017); 3. Einstein MH et al. Hum Vaccin Immunother. 2014;10(12):3435-45.