

## Supplementary results

### Cumulative LGAIN occurrence at FU18

Cumulative LGAIN occurrence at 18 months (ITT worst-case scenario) was 75.0% (21 of 28) for qHPV versus 66.7% (18 of 27) for placebo ( $p=0.50$ ; ARR= -8.3 percentage points (95%CI -32.3–15.6); RR=1.13 (95%CI 0.80–1.58); Table 2). The ITT best-case scenario analysis yielded opposite outcomes, although also non-significant.

### Cumulative anogenital condylomata occurrence at FU18

Cumulative anogenital condylomata occurrence at 18 months (ITT worst-case scenario) was 55.3% (21 of 39) for qHPV versus 44.2% (19 of 44) for placebo ( $p=0.32$ ; ARR= -11.1 percentage points (95%CI -32.8–10.6); RR=1.25 (95%CI 0.80–1.94); Table 2). The ITT best-case scenario analysis yielded comparable outcomes.

### Cross-reactivity for non-vaccine HPV types

Some cross-reactivity was observed for non-vaccine types HPV31, 33, 45, 52, 58. Only for HPV31 and 45 a significant ( $p<0.009$  and  $p<0.022$ , respectively) increase in antibody concentrations was seen in the qHPV group (Supplementary figure 1; Supplementary table 5). In this group, after three vaccinations seropositivity for type HPV31 increased from 48% to 78% and for HPV45 from 52% to 88% (Supplementary table 6).