

1. Cardiac Adverse Events of Special Interest

Cardiac adverse events were 6 x more frequent for Jynneos if the subject had never had a small pox vaccine before compared to placebo, and 10 x more frequent for Jynneos if the subject had received a small pox vaccine previously compared to placebo.

- 1.3% (95/7,093) of JYNNEOS recipients (**1 in 77 vaccinated**)
- 0.2% (3/1,206) of placebo recipients who were smallpox vaccine-naïve.
- 2.1% (16/766) of JYNNEOS recipients who were smallpox vaccine-experienced. (**1 in 48 vaccinated**)

2. Serious Adverse Events

36% increase after vaccination if subject had never had a small pox vaccine before, and 109% increase after vaccination if the subject had received a small pox vaccine previously.

- 1.5% of JYNNEOS recipients who were smallpox vaccine-naïve (**1 in 66 vaccinated**)
- 1.1% of placebo recipients. Among the smallpox vaccine-experienced subjects enrolled in studies without a placebo comparator, SAEs were reported for 2.3% of JYNNEOS recipients
- 2.3% of JYNNEOS recipients who were small pox vaccine-experienced (**1 in 44 vaccinated**)

3. Elevated Troponin

152 cases of elevated troponin in 1211 subjects = 12.6 % (1 in 8 vaccinated)

- 28 cases of asymptomatic post-vaccination elevation of troponin-I :
- Study 5, which enrolled 482 HIV-infected subjects and 97 healthy subjects
- Study 6, which enrolled 350 subjects with atopic dermatitis and 282 healthy subjects.
- An additional 127 cases of asymptomatic post-vaccination elevation of troponin-I above the upper limit of normal but not above 2 times the upper limit of normal **were documented in JYNNEOS recipients throughout the clinical development program**, 124 of which occurred in Study 5 and Study 6.

Proportions of subjects with troponin-I elevations were similar between healthy and HIV-infected subjects in Study 5 and between healthy and atopic dermatitis subjects in Study 6. A different troponin assay was used in these two studies compared to the other studies, and these two studies had no placebo controls.