

### **Vaccine effectiveness against mortality**

A larger number of individuals at high risk of COVID-19 and higher attack rates would be needed to confirm efficacy of the vaccine against mortality. However, non-COVID vaccines (e.g., influenza) that are efficacious against disease have also been shown to prevent disease-associated death.<sup>11-14</sup> Benefits in preventing death should be evaluated in large observational studies following authorization.

### **Vaccine effectiveness against transmission of SARS-CoV-2**

Data are limited to assess the effect of the vaccine against transmission of SARS-CoV-2 from individuals who are infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 may translate to overall prevention of transmission in populations with high enough vaccine uptake, though it is possible that if efficacy against asymptomatic infection were lower than efficacy against symptomatic infection, asymptomatic cases in combination with reduced mask-wearing and social distancing could result in significant continued transmission. Additional evaluations including data from clinical trials and from vaccine use post-authorization will be needed to assess the effect of the vaccine in preventing virus shedding and transmission, in particular in individuals with asymptomatic infection.

### **8.3. Known Risks**

The vaccine has been shown to elicit increased local and systemic adverse reactions as compared to those in the placebo arm, usually lasting a few days. The most common solicited adverse reactions were injection site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%). Adverse reactions characterized as reactogenicity were generally mild to moderate. The number of subjects reporting hypersensitivity-related adverse events was numerically higher in the vaccine group compared with the placebo group (137 [0.63%] vs. 111 [0.51%]). Severe adverse reactions occurred in 0.0-4.6% of participants, were more frequent after Dose 2 than after Dose 1 and were generally less frequent in older adults (>55 years of age) ( $\leq 2.8\%$ ) as compared to younger participants ( $\leq 4.6\%$ ). Among reported unsolicited adverse events, lymphadenopathy occurred much more frequently in the vaccine group than the placebo group and is plausibly related to vaccination.

Serious adverse events, while uncommon (<1.0%), represented medical events that occur in the general population at similar frequency as observed in the study. Three SAEs in the BNT162b2 group were considered related by the investigator, but not the Sponsor, as related to study vaccination: shoulder injury (n=1), ventricular arrhythmia in a participant with known cardiac conditions (n=1), and lymphadenopathy temporally related following vaccination (n=1). We considered two of the events as possibly related to vaccine: the shoulder injury possibly due to vaccine administration or the vaccine itself and lymphadenopathy. Lymphadenopathy was temporally associated and biologically plausible.

No specific safety concerns were identified in subgroup analyses by age, race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection. Although participants 16 to 17 years of age were enrolled in the phase 3 trial, safety data for this age group is limited. However, available data are consistent with the safety profile in the adult population, and it is biologically reasonable to extrapolate the greater safety experience in adults, in particular younger adults, to the oldest pediatric age group of 16 to 17 years.