RESPONSE TO FDA ON INFORMATION REQUEST #43RECEIVED ON JANUARY 07, 2022

The Sponsor acknowledges INFORMATION REQUEST #43dated 07 JANUARY 2022 in (**BOLD**)

**Product:** COVID-19 Vaccine, mRNA (SPIKEVAX)

**Subject:** Clinical IR – Safety Data For P301

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing.

**ITEM 1:**

**In Part A of Study P301, for adverse events of herpes zoster within 28 days after any vaccination, in the mRNA-1273 group and placebo group, please provide the following details in a Word table:**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Investigational Product** | **Age/Sex** | **Onset after Dose 1 or 2** | **Day of Onset after most recent vaccination** | **Resolution status** | **Grade/SAE** | **Possible Risk Factors** | **Relateda** |
| **mRNA-1273** |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Placebo** |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

**a Classification of events as SAEs and relatedness determined by study investigators**

**Sponsor Response:**

Please find below two tables addressing the request above. One for mRNA-1273 and one for placebo.

| Clinical Study mRNA-1273-P301 Part AAdverse Events of Herpes Zoster mRNA-1273 Treatment Group Within 28 Days After Any Vaccination |
| --- |
| Sex | Age | MedDRA Preferred Term | Onset After Dose 1 or 2 | Day of Onset After Most Recent Vaccination | Resolution Status | Grade | Serious Event (Y=yes, N=No) | Other Risk Factors | Causality |
| M | 73 | Herpes zoster | 1 | 25 | RECOVERED/RESOLVED | MODERATE | N | Medical history: prostate cancer, radiotherapy to prostate, squamous cell cancer. Concomitant medications: Nasonex (mometasone furoate) and Budesonide (corticosteroids)/chronic sinusitis | NOT RELATED |
| F | 68 | Herpes zoster | 1 | 26 | RECOVERED/RESOLVED | MILD | N | None | NOT RELATED |
| F | 87 | Herpes zoster | 2 | 22 | RECOVERED/RESOLVED | MILD | N | None | NOT RELATED |
| F | 49 | Herpes zoster | 2 | 12 | NOT RECOVERED/NOT RESOLVED | MILD | N | Medical history: Herpes simplex.  | NOT RELATED |
| M | 62 | Herpes zoster | 1 | 19 | RECOVERED/RESOLVED | MILD | N | None | NOT RELATED |
| F | 66 | Herpes zoster | 1 | 19 | RECOVERED/RESOLVED | MODERATE | N | Medical history: thyroid papillary thyroid cancer in 2014; bilateral breast ductal carcinoma in situ in 2014. AE of urinary tract infection (UTI) 16 Sep 2020 (21 days post dose 1) with Herpes zoster onset 2 days prior to onset of UTI. | NOT RELATED |
| F | 67 | Herpes zoster | 1 | 4 | RECOVERED/RESOLVED | MODERATE | N | Medical history: Hepatitis C since 2014; cancer surgery, squamous cell removal off chest 2014.  | NOT RELATED |
| F | 64 | Herpes zoster | 1 | 22 | RECOVERED/RESOLVED | MILD | N | Medical history: Type 1 diabetes mellitus.  | NOT RELATED |
| M | 38 | Herpes zoster | 1 | 18 | RECOVERED/RESOLVED | MODERATE | N | None | NOT RELATED |
| F | 56 | Herpes zoster | 1 | 8 | RECOVERED/RESOLVED | MODERATE | N | Medical history: Herpes simplex | NOT RELATED |
| M | 54 | Herpes zoster | 2 | 14 | RECOVERING/RESOLVING | MODERATE | N | Concomitant medications: Influenza vaccine 27 days prior to Herpes zoster onset | NOT RELATED |
| M | 60 | Herpes zoster | 2 | 16 | RECOVERED/RESOLVED | MODERATE | N | None | NOT RELATED |
| M | 61 | Herpes zoster | 1 | 9 | RECOVERED/RESOLVED | SEVERE | N | None | NOT RELATED |
| M | 55 | Herpes zoster | 1 | 22 | RECOVERED/RESOLVED | MILD | N | Medical history: Herpes zoster Oct 2017 - Nov 2017 | NOT RELATED |
| F | 62 | Herpes zoster | 1 | 7 | RECOVERED/RESOLVED | MODERATE | N | Medical history: Herpes zoster 7 days post dose 1, recovered; colorectal cancer/pelvic cancer diagnosed 22 days post dose 2 | NOT RELATED |
| M | 70 | Herpes zoster | 1 | 14 | RECOVERED/RESOLVED | MILD | N | None  | NOT RELATED |
| F | 62 | Herpes zoster | 1 | 21 | RECOVERED/RESOLVED | MODERATE | N | Concomitant medication: fluticasone propionate(seasonal allergies) | NOT RELATED |
| F | 70 | Herpes zoster | 1 | 5 | RECOVERED/RESOLVED WITH SEQUELAE | MODERATE | N | Medical history: malignant melanoma Nov 2017.  | RELATED |
| F | 77 | Herpes zoster | 1 | 7 | RECOVERED/RESOLVED | MILD | N | None | RELATED |
| F | 56 | Herpes zoster | 1 | 7 | RECOVERED/RESOLVED | MODERATE | N | None | NOT RELATED |
| F | 59 | Herpes zoster | 1 | 14 | RECOVERED/RESOLVED | MILD | N | None | NOT RELATED |
| F | 64 | Herpes zoster | 1 | 11 | RECOVERED/RESOLVED | MILD | N | Herpes zoster ongoing at start of study, AE of worsening Shingles 11 days post dose 1; Concomitant medication: fluticasone propionate, salmeterol xinafoate/Advair corticosteroids (asthma/COPD), fluticasone/corticosteroids (seasonal allergies) | NOT RELATED |

| Clinical Study mRNA-1273-P301 Part AAdverse Events of Herpes Zoster Placebo Treatment Group Within 28 Days After Any Vaccination |
| --- |
| Sex | Age | MedDRA Preferred Term | Onset After Dose 1 or 2 | Day of Onset After Most Recent Vaccination | Resolution Status | Grade | Serious Event (Y=yes, N=No) | Other Risk Factors | Causality |
| F | 49 | Herpes zoster | 1 | 4 | RECOVERED/RESOLVED | MILD | N | None | NOT RELATED |
| M | 75 | Herpes zoster | 2 | 1 | RECOVERED/RESOLVED | MILD | N | Medical history: Herpes zoster, Post herpetic neuralgia. Concomitant medication: FLUTICASONE PROPIONATE; Recent AE of diarrhea 23 days prior to Herpes zoster onset | NOT RELATED |
| F | 48 | Herpes zoster | 2 | 19 | RECOVERED/RESOLVED | MODERATE | N | None  | NOT RELATED |
| M | 58 | Herpes zoster | 1 | 17 | RECOVERED/RESOLVED | MILD | N | Medical history: Diabetes mellitus.  | NOT RELATED |
| F | 63 | Herpes zoster | 2 | 22 | RECOVERING/RESOLVING | MILD | N | None | NOT RELATED |
| F | 71 | Herpes zoster | 1 | 8 | RECOVERED/RESOLVED | MODERATE | N | Medical history: Type 2 diabetes mellitus.  | NOT RELATED |
| F | 31 | Herpes zoster | 1 | 10 | NOT RECOVERED/NOT RESOLVED | MODERATE | N | None | NOT RELATED |
| M | 18 | Herpes zoster | 1 | 7 | RECOVERING/RESOLVING | MILD | N | None | NOT RELATED |
| F | 53 | Herpes zoster | 2 | 19 | RECOVERED/RESOLVED | MODERATE | N | None | NOT RELATED |
| F | 40 | Herpes zoster | 2 | 27 | RECOVERED/RESOLVED | MODERATE | N | Concomitant medication: FLUTICASONE PROPIONATE | NOT RELATED |
| M | 65 | Herpes zoster | 1 | 4 | RECOVERED/RESOLVED | MODERATE | N | Recent AE of diarrhea 1 day prior to Herpes zoster | NOT RELATED |
| M | 30 | Herpes zoster | 2 | 21 | RECOVERED/RESOLVED | MODERATE | N | Concomitant medication BECLOMETASONE (asthma), TRIAMCINOLONE (seasonal allergies). Receiving EMTRICITABINE;TENOFOVI for HIV PrEP since 2016, influenza vaccine given same day as Herpes zoster onset. | NOT RELATED |
| M | 62 | Herpes zoster | 2 | 11 | RECOVERED/RESOLVED | MODERATE | N | Recent AE of diverticulitis 19 days prior to Herpes zoster onset.  | NOT RELATED |
| F | 59 | Herpes zoster | 1 | 28 | RECOVERED/RESOLVED | MODERATE | N | None | NOT RELATED |
| M | 67 | Herpes zoster | 1 | 28 | RECOVERED/RESOLVED | MODERATE |  | Recent AE of right chest incision infection with onset 19 days prior to Herpes zoster; Medical history: Type 2 diabetes mellitus, prostate cancer | NOT RELATED |