

Mfr Report #	(b) (6)
UF/Importer Report #	
FDA Use Only	

A. PATIENT INFORMATION			
1. Patient Identifier US3432023	2. Age at Time of Event: 83 Years or Date of Birth: (b) (6)/1937	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight ____ lbs or ____ kgs
In confidence			
B. ADVERSE EVENT OR PRODUCT PROBLEM			
1. <input checked="" type="checkbox"/> Adverse Event and/or <input type="checkbox"/> Product Problem (e.g., defects/malfunctions)			
2. Outcomes Attributed to Adverse Event (Check all that apply)			
<input type="checkbox"/> Death: _____ (mm/dd/yyyy)			
<input type="checkbox"/> Life-threatening			
<input checked="" type="checkbox"/> Hospitalization - initial or prolonged			
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)			
<input type="checkbox"/> Disability or Permanent Damage			
<input type="checkbox"/> Congenital Anomaly/Birth Defect			
<input type="checkbox"/> Other Serious (Important Medical Events)			
3. Date of Event (mm/dd/yyyy) 08/20/2020		4. Date of This Report (mm/dd/yyyy) 11/22/2020	
5. Describe Event or Problem Event Verbatim [LOWER LEVEL TERM] (Related symptoms if any separated by commas) POSSIBLE POLYMYALGIA RHEUMATICA [Polymyalgia rheumatica]			
Case Description: This 83-year-old, White, male subject (US3432023) was participating in A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older (mRNA-1273-P301), and experienced possible polymyalgia rheumatica.			
The subject's medical history, as provided by the investigator, included unspecified hypothyroidism, hyperlipidemia, coronary heart disease, aortic stenosis status post transcatheter aortic valve replacement, premature continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates #1 09/09/2020 Antinuclear antibody (continued) #2 08/21/2020 Blood chloride (continued) #3 08/20/2020 Blood creatinine (continued) #4 08/21/2020 Blood creatinine (continued) #5 08/21/2020 Blood glucose 125 OTHER High #6 08/20/2020 Blood magnesium 2.0 OTHER continued in additional info section...			
7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) Race: White #1 --/--/1960 to Ongoing Historical Drug, (Continued) #2 --/--/1980 to Ongoing Current Condition, (Continued) #3 --/--/1980 to Ongoing Current Condition, (Continued) continued in additional info section...			

C. SUSPECT PRODUCT(S)			
1. Name (Give labeled strength & mfr/labeler)			
#1. mRNA-1273 vs Placebo (Code not broken)			
#2.			
2. Dose, Frequency & Route Used		3. Therapy Dates (if unknown, give duration) from/to (or best estimate)	
#1. Blinded, Information withheld.		#1. 08/05/2020 to 08/05/2020	
#2.		#2.	
4. Diagnosis for Use (Indication)		5. Event Abated After Use Stopped or Dose Reduced?	
#1. COVID-19 (Continued)		#1. <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
#2.		#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
6. Lot #		7. Exp. Date	
#1. Blinded		#1. Blinded	
#2.		#2.	
9. NDC# or Unique ID			
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
1) ASPIRIN /00002701/ (ASPIRIN /00002701/) --/--/2011 continued in additional info section...			
G. ALL MANUFACTURERS			
1. Contact Office (and Manufacturing Site for Devices)		2. Phone Number	
Name ModernaTX, Inc. David Martin MD.		617-335-1804	
Address 200 Technology Square Cambridge, MA 02139 United States of America		3. Report Source (Check all that apply)	
Email Address		<input type="checkbox"/> Foreign	
		<input checked="" type="checkbox"/> Study	
		<input type="checkbox"/> Literature	
		<input type="checkbox"/> Consumer	
		<input checked="" type="checkbox"/> Health Professional	
		<input type="checkbox"/> User Facility	
		<input type="checkbox"/> Company Representative	
		<input type="checkbox"/> Distributor	
		<input type="checkbox"/> Other: _____	
4. Date Received by Manufacturer (mm/dd/yyyy) 11/06/2020		5. (A)NDA # _____ IND # _____ BLA # _____ PMA/ 510(k) # _____ Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
6. If IND, Give Protocol # mRNA-1273-P301			
7. Type of Report (Check all that apply)			
<input type="checkbox"/> 5-day <input type="checkbox"/> 30-day			
<input type="checkbox"/> 7-day <input type="checkbox"/> Periodic			
<input type="checkbox"/> 10-day <input type="checkbox"/> Initial			
<input type="checkbox"/> 15-day <input checked="" type="checkbox"/> Follow-up #5			
9. Manufacturer Report Number (b) (6)		8. Adverse Event Term(s) Polymyalgia rheumatica	
E. INITIAL REPORTER			
1. Name and Address Dr. Lindsey Baden Brigham and Womens Hospital Boston, Massachusetts UNITED STATES			
Phone # (b) (6)		Email Address (b) (6) @bwh.harvard.edu	
2. Health Professional?		3. Occupation	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		Physician	
		4. Initial Reporter Also Sent Report to FDA	
		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Unk	

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event

ADDITIONAL INFORMATION**B5. EVENT DESCRIPTION (Continued)**

ventricular complex, chronic low back pain with intermittent flare, congestive heart failure, depression, monoclonal gammopathy of undetermined significance (MGUS), chronic renal failure (mild per clinical database; Stage 3b/4 per medical records), chronic anemia, stroke, pneumococcal pneumonia, hypertension, constipation and allergies to penicillin (serum sickness), sulfa and barbiturates. Concomitant medications included aspirin, clopidogrel bisulfate, bupropion, multivitamin, vitamin D, calcium, bisoprolol, rosuvastatin, atenolol, docusate sodium, fluticasone propionate and levothyroxine sodium. The Investigator confirmed that the subject had not received any vaccinations in the six months prior to study entry.

Additional information concerning the subject's medical history of MGUS was provided in response to queries. The subject was seen by a Hematology/Oncology specialist for evaluation of MGUS several years ago; however, upon evaluation, additional follow-up with the specialist was deemed unnecessary. The subject had been monitored by his primary care provider for any changes and his last Immunofixation, on 17 Apr 2020, showed no monoclonal band.

A few days prior to study drug administration, the subject started to develop mild back pain, which he associated with his ongoing medical history of chronic low back pain.

The subject received a single dose of study drug, 15 days prior to event onset, on 05 Aug 2020. Afterwards, the subject denied any local injection site reaction, but did develop a slight headache, which quickly resolved.

On 07 Aug 2020, the subject returned to the clinic for an unscheduled visit, due to a complaint of mild body aches. He had a negative nasopharyngeal reverse transcriptase polymerase chain reaction SARS-CoV-2 test.

On 20 Aug 2020, the subject presented to the emergency room and was hospitalized due to three-day history of severe myalgias, and generalized weakness. In the days leading up to hospitalization, the subject developed progressive, migratory myalgias of bilateral lumbar/sacroiliac joint, bilateral deltoid, right occiput, and cervical paraspinal muscles which had worsened over two weeks, as well as progressive weakness until, finally, he was unable to get out of bed. The subject reported difficulty abducting bilateral upper extremities due to weakness and pain. In addition, he experienced headache, which was relieved by paracetamol. The subject denied fever or chills. The subject did not experience vertigo, unilateral weakness/numbness or speech changes; thus, stroke was felt unlikely.

Laboratory results included C-reactive protein at 96.9 mg/L (0.0-5.0), erythrocyte sedimentation rate of 56 mm/h (0-15), troponin 30 then 29, creatinine 2.6 (subject's baseline was 1.9-2.1) and magnesium 2.0 (reference ranges not provided). Infectious work-up was negative including unremarkable urinalysis, negative COVID-19 test and negative chest x-ray. Electrocardiogram was unchanged from prior.

The admitting physician, primary investigator and infectious disease consultant originally assessed that the myalgias were unlikely related to mRNA-1273 or placebo, given timing of onset of symptoms and insignificant findings in clinic seven days post study drug dose. Rheumatology was consulted and provided a possible diagnosis of polymyalgia rheumatica; however, had suspicion of vaccine side effect. Their recommendation included a one-time dose of prednisone 15 mg. After the one time-dose was administered, the subject's pain resolved.

On 21 Aug 2020, abnormal laboratory results included: chloride 113 (high), carbon dioxide 15 (low), blood urea nitrogen 37 (high), creatinine 2.03 (high), glucose 125 (high), red blood cell count 2.61 (low), hemoglobin 7.5 (low), hematocrit 22.9 (low), and platelet count 125 (low) (units and reference ranges not provided). Vital signs were temperature 97.9 degrees Fahrenheit, heart rate 59 beats per minute, respiratory rate 18 breaths per minute, blood pressure 153/65 mmHg and oxygen saturation 97% on room air. The subject reported feeling much better; however, still had mild tenderness over right occiput, deltoid and cervical paraspinal areas on exam. His range of motion (ROM) had improved, he was able to fully abduct bilateral shoulders, and ROM of cervical spine was intact. His sensation and strength were equal bilaterally, with no focal deficits. On the same day, he was discharged on a 15-day prednisone taper (starting dose of 20 mg daily) with plans to follow-up on symptoms and labs after taper completed.

On 26 Aug 2020, the subject reported that he felt good during the day, however, upon waking up in the morning, he experienced some pain in his shoulders and neck. The pain went away approximately 2 hours after taking prednisone.

On 04 Sep 2020, the subject completed his prednisone taper; however, the subject experienced recurrence of axial myalgias.

On 09 Sep 2020, the subject was seen by rheumatology as an outpatient. Laboratory results included antinuclear antibody <1:40 (normal <1:40) and rheumatoid factor <10 IU/ml (0-15). Prednisone was restarted at 20 mg for two weeks, followed by slow taper.

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During study follow-up visits on 01 Oct 2020 and 13 Oct 2020, the subject was doing well on prednisone regimen prescribed by Rheumatology. He planned to continue follow-up with rheumatology for speed of prednisone taper and overall condition.

Study drug was discontinued in response to the event, as the investigator was concerned that administering the next scheduled study drug dose might interfere with symptom assessment of PMR due to the subject's ongoing prednisone taper.

The event, possible polymyalgia rheumatica, was considered resolving.

The investigator assessed the event, possible polymyalgia rheumatica, as related to study drug. Per the investigator, there may be a possible relationship due to the symptomatology described as polymyalgia and weakness that developed after the study drug was administered. The investigator assessed the event, possible polymyalgia rheumatica, as not related to study procedure.

Follow-up received on 25 Aug 2020, 26 Aug 2020, 27 Aug 2020 included updated event term, causality, testing, treatment, action taken with study drug, course of hospitalization and event details.

Follow-up received on 12 Sep 2020, 16 Sep 2020 and 17 Sep 2020 included updated medical history and concomitant medications. Additionally, the site provided the discharge summary which provided vital signs, labs, and event details.

Follow-up received on 23 Sep 2020 included no new information.

Follow-up received on 13 Oct 2020 and 14 Oct 2020 included updated medical history details, prior CT indication, and subject's response to treatment.

Follow-up received on 21 Oct 2020 included no new information.

Follow-up received on 06 Nov 2020 included vaccination history.

Analysis of Similar Events: On 23-Oct-2020, the safety database was searched for events similar to Polymyalgia rheumatica using the following search criteria: PT: Polymyalgia rheumatica, HLGT: Immune disorders NEC, HLGT: Autoimmune disorders, HLGT: Connective tissue disorders (excl congenital), and SMQ: Arthritis.

As of 23-Oct-2020 under IND 019745 for mRNA-1273 vs Placebo, one IND safety report of similar adverse event has been previously submitted.

This case (b) (6) reporting the event of rheumatoid arthritis was submitted as an IND Safety Report. It concerns a 57-year-old male subject with medical history of hypertension, hypothyroidism, asthma, and environmental allergies, who experienced an unexpected event of rheumatoid arthritis. The event occurred 14 days after the first, and only, dose of study vaccine/placebo. The investigator considered the event related to the study vaccine; however, the subject's medical history of hypertension and hypothyroidism may potentially indicate pre-existing autoimmune disease.

There were five cases that were non-IND Safety Reports reporting the following events: worsening right knee pain (b) (6) left hip arthroplasty (b) (6) left hip osteoarthritis (b) (6) gout exacerbation in right knee (b) (6) and left total shoulder arthroplasty related to osteoarthritis (b) (6)

Based on review of available data, the Sponsor cannot rule out a possible cause and effect relationship between administration of blinded mRNA-1273 SARS-CoV-2 Vaccine/vaccine placebo and the occurrence of polymyalgia rheumatica.

After review of the clinical details and investigator comments pertaining to this adverse event, and based upon experience to date, the Sponsor does not believe that changes to the conduct of this clinical trial are warranted. The Company will continue to monitor these and other serious adverse events reported in association with the administration of blinded mRNA-1273 SARS-CoV-2 Vaccine/vaccine placebo and will communicate any relevant changes to the protocol, Informed Consent Form, Investigator's Brochure, and/or Core Safety Information. submitted.

Case Comment/Sender's Comment:

This case concerns an 83-year-old male subject with multiple comorbidities including chronic kidney disease, hypothyroidism, and chronic low back pain also takes rosuvastatin 40 milligrams once a day. Source documentation provides some indication that back pain and possibly myalgias might have been noted by the subject in the days prior to administration of study drug or placebo. In addition, myalgias have been reported in association with rosuvastatin in approximately 2% of patients treated in clinical trials

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(Section 6 Adverse Reactions), and rosuvastatin contains a warning (Section 5 Warnings and Precautions) noting that the risk of myopathy increases at the highest dose which is 40 milligrams. Per Section 5 rosuvastatin should be prescribed with caution in patients with predisposing factors for myopathy (e.g., age greater than 65 years, inadequately treated hypothyroidism, renal impairment). Potential alternative explanations for this adverse event include incident polymyalgia rheumatica with onset prior to the administration of study drug/placebo or an adverse event associated with a concomitant medication, rosuvastatin. This case is continuing to be followed. Although medical records establishing a definitive diagnosis of polymyalgia rheumatica have not been generated, the subject's symptoms appear to be responsive to prednisone treatment.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09/09/2020	Antinuclear antibody <1:40 [Normal: <1:40]		
2	08/21/2020	Blood chloride High	113 OTHER	
3	08/20/2020	Blood creatinine baseline 1.9-2.1	2.6 OTHER	
4	08/21/2020	Blood creatinine High	2.03 OTHER	
7	08/21/2020	Blood pressure measurement	153/65 mmHg	
8	08/21/2020	Blood urea High	37 OTHER	
9	08/21/2020	Body temperature	97.9 °F	
10	08/--/2020	C-reactive protein	96.9 milligram per litre	5.0 0.0
11	08/21/2020	Carbon dioxide Low	15 OTHER	
12	08/20/2020	Chest X-ray Negative		
13	08/--/2020	Electrocardiogram Unchanged from prior		
14	08/21/2020	Haematocrit Low	22.9 OTHER	
15	08/21/2020	Haemoglobin Low	7.5 OTHER	
16	08/21/2020	Heart rate	59 /min	
17	04/17/2020	Immunology test No monoclonal band		
18	08/21/2020	Oxygen saturation	97 percent	
19	08/21/2020	Platelet count Low	125 OTHER	
20	08/21/2020	Red blood cell count Low	2.61 OTHER	
21	08/--/2020	Red blood cell sedimentation rate	56 OTHER	

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MM/H

22	08/21/2020	Respiratory rate	18 /min
23	09/09/2020	Rheumatoid factor <10	international unit per millilitre 15 0
24	08/07/2020	SARS-CoV-2 test Negative Nasopharyngeal Swab	
25	08/20/2020	SARS-CoV-2 test Negative	
26	08/--/2020	Troponin	30 OTHER
27	08/--/2020	Troponin	29 OTHER
28	08/20/2020	Urine analysis Unremarkable	

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	--/--/1960 Ongoing	Historical Drug PENICILLIN /00042301; Drug Reaction: Serum sickness	
2	--/--/1980 Ongoing	Current Condition Depression	
3	--/--/1980 Ongoing	Current Condition Hyperlipidaemia	
4	--/--/2000 Ongoing	Current Condition Back pain	Chronic; intermittent flare
5	--/--/2005 Ongoing	Current Condition Hypothyroidism	
6	--/--/2010 --/--/2010	Historical Condition Pneumonia pneumococcal	
7	--/--/2010 Ongoing	Current Condition Hypertension	
8	--/--/2010 Ongoing	Current Condition Ventricular extrasystoles	
9	--/--/2011 --/--/2011	Historical Condition Cerebrovascular accident	

10	--/--/2012 Ongoing	Current Condition Hypergammaglobulinaemia benign monoclonal	
11	--/--/2012 Ongoing	Current Condition Anaemia	
12	--/--/2013 Ongoing	Current Condition Chronic kidney disease	Mild per clinical database; Stage 3b/4 per medical records
13	06/--/2019 Ongoing	Current Condition Aortic stenosis	S/P TAVR
14	06/--/2019 Ongoing	Current Condition Cardiac failure congestive	
15	11/--/2019 Ongoing	Current Condition Coronary artery disease	
16	01/--/2020 Ongoing	Current Condition Constipation	
17		Procedure Transcatheter aortic valve implantation	Aortic stenosis S/P
18	Ongoing	Current Condition Drug hypersensitivity	
19	Ongoing	Current Condition Drug hypersensitivity	

C4. DIAGNOSIS FOR USE (Continued)

#1: COVID-19 vaccination (COVID-19 immunisation)

C10. CONCOMITANT MEDICAL PRODUCTS (Continued)

to ongoing

- 2) ASPIRIN /00002701/ (ASPIRIN /00002701/) --/--/2000 to ongoing
- 3) PLAVIX (CLOPIDOGREL BISULFATE) --/--/2011 to ongoing
- 4) ROSUVASTATIN (ROSUVASTATIN) --/--/2018 to ongoing
- 5) ATENOLOL (ATENOLOL) --/--/2010 to ongoing
- 6) COLACE (DOCUSATE SODIUM) 01/--/2020 to ongoing
- 7) FLONASE /00972202/ (FLUTICASONE PROPIONATE) --/--/2010 to ongoing
- 8) BUPROPION (BUPROPION) --/--/1980 to ongoing
- 9) MULTIVITAMIN /07504101/ (VITAMINS NOS) Tablet --/--/2015 to ongoing
- 10) VITAMIN D /07503901/ (VITAMIN D /07503901/) --/--/2015 to ongoing
- 11) CALCIUM (CALCIUM) --/--/2015 to ongoing
- 12) BISOPROLOL (BISOPROLOL) --/--/2016 to 07/--/2020
- 13) LEVOTHYROXIN (LEVOTHYROXINE SODIUM) --/--/2005 to ongoing