

Janssen Vaccines & Prevention B.V. *

Pharmacokinetics Tabulated Summary

MODULE 2.6.5

VAC31518 JNJ-78436735

Prophylactic COVID-19 Vaccine

* Janssen Vaccines & Prevention B.V. is a Janssen pharmaceutical company of Johnson & Johnson and is hereafter referred to as the sponsor.

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2.6.5.1 Pharmacokinetics: Overview

Test Article: Ad26.COV2.S							Test Article: Ad26.COV2.S
Type of Study	Test System	Route	Number of Injections	Test Article: Dose Level (Dose Volume)	GLP	Test Facility	Location in CTD/Study No.
Biodistribution Study with Ad26 vectored vaccine	NZW Rabbits	IM	Single Injection	Ad26 (b) (4) 5×10 ¹⁰ vp (0.5 mL)	Yes	(b) (4)	(b) (4)
Biodistribution Study with Ad26 vectored vaccine	NZW Rabbits	IM	Single Injection	Ad26 (b) (4) ± (b) (4) (b) (4) 1×10 ¹¹ vp ± 150 µg (0.5 mL or 1 mL of mixture)	Yes	(b) (4)	(b) (4)

GLP = Good Laboratory Practice; IM = intramuscular; NZW = New Zealand White; SC = subcutaneous; TCID₅₀ = 50% tissue culture infective dose; vp = virus particles

2.6.5.5A Pharmacokinetics: Tissue/Organ Distribution**Test Article:** Ad26 (b) (4)

Report Title:	Ad26 (b) (4) 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits		
Study No.	(b) (4)		
Species:	New Zealand White rabbits (HsdOkd)		
No. of animals:	Total of 10 animals (5/sex) analyzed per timepoint per group (3/sex/timepoint in Group 1)		
Test Article - Dose	Group 1	Placebo ^(a)	0 vp (0.5 mL)
	Group 2	Ad26 (b) (4) ^{b)}	5x10 ¹⁰ vp in 0.5 mL
Route of Administration:	Intramuscular (IM) injection		
Sampling timepoint:	Days 11, 61, 91		
Tissues assessed by q-PCR:	Blood, gonads, liver, thymus, heart, lung, kidney, spleen, mesenteric lymph node, iliac lymph node, bone marrow, brain, skin at injection site, muscle at injection site		
Assay Characteristics:	Limit of detection, LOD = 10 copies/μg DNA; Lower limit of quantitation, LLOQ = 50 copies/μg DNA		
Tissue^(c)	Group 2 (Ad26 (b) (4) IM)		
	Copies/μg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Muscle at injection site			
Day 11	61 to 11,981	7/10	1/10
Day 61	-	0/10	2/10
Day 91	120	1/10	1/10
Skin at injection site			
Day 11	-	0/10	1/10
Day 61	-	0/10	0/10
Day 91	-	0/10	0/10
Iliac lymph nodes			
Day 11	119 to 8676	10/10	0/10
Day 61	84 to 1400	4/10	1/10
Day 91	50 to 1807	2/10	0/10
Spleen			
Day 11	50 to 116	4/10	5/10
Day 61	-	0/10	0/10
Day 91	-	0/10	0/10
^(a) Ad26 (b) (4) placebo:	(b) (4)		
^(b) Ad26 (b) (4) drug product: 1x10 ¹⁰ vp/mL Ad26 (b) (4) formulated in	(b) (4)		

- ^(c) Samples collected from Group 1 had Ad26 (b) (4) vector DNA results below the LOD of the assay for all tissues and fluids at all timepoints. For Group 2 animals, only tissues with vector DNA levels above LOD are listed. All other tissues collected had vector DNA results below the LOD of the assay at all time points.
- Levels for all animals were below LLOQ at this time point

IM = intramuscular(ly); LLOQ = lower limit of quantitation; LOD = limit of detection; q-PCR = quantitative polymerase chain reaction; vp = virus particles

2.6.5.5B Pharmacokinetics: Biodistribution: Ad26 (b) (4)

Test Article: Ad26 (b) (4)

Report Title:	A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period					
Study No.	(b) (4)					
Species:	New Zealand White Rabbit (Hra[NZW]SPF)					
No. of animals:	Total of 10 animals (5/sex) analyzed per timepoint per group (3/sex/timepoint in Group 1)					
Test Article - Dose	Group 1	Reference item ^(a)		0 vp (1 mL)		
	Group 2	Ad26 (b) (4) ^{b)}		1x10 ¹¹ vp in 0.5 mL		
	Group 3	Ad26 (b) (4) + (b) (4) ^{c)}		1x10 ¹¹ vp + 150 µg (b) (4) (1 mL of mixture)		
Route of Administration:	Intramuscular (IM) injection					
Sampling timepoint:	Days 11, 90, 120, and 180					
Tissues assessed by q-PCR:	Blood, ovaries/testes, liver, spleen, kidney, iliac lymph node, heart, lung, brain, skin with subcutis over the injection, bicep femoris muscle at injection site, popliteal lymph node, bone marrow, thymus, mesenteric lymph node					
Assay Characteristics:	Limit of detection, LOD = 7.1 copies/µg DNA					
	Lower limit of quantitation, LLOQ = 28.6 copies/µg DNA					
Tissue^(d)	Group 2 (Ad26 (b) (4) IM)			Group 3 (Ad26 (b) (4) + (b) (4) IM)		
	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Skin at injection site						
Day 11	39.1 to 6304.3	4/10	2/10	88.6 to 272.6	2/10	3/10
Day 90	280.1	1/10	0/10	42.7 to 175.1	2/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Muscle at injection site						
Day 11	-	0/10	1/10	-	0/10	0/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Iliac lymph nodes						
Day 11	63.6 to 387.6	9/10	1/10	108.6 to 347.4	9/10	0/10
Day 90	48.1	1/10	3/10	25.9 to 35.3	2/10	3/10
Day 120	37.9 to 53.4	2/10	1/10	-	0/10	0/10
Day 180	37.6	1/10	2/10	-	0/10	2/10

2.6.5.5B Pharmacokinetics: Biodistribution: Ad26 (b) (4) (Continued)

Report Title: A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period						
Study No. (b) (4)						
Tissue^(d)	Group 2 (Ad26 (b) (4) IM)			Group 3 (Ad26 (b) (4) + (b) (4) IM)		
	Copies/ μ g DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ	Copies/ μ g DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Popliteal lymph nodes						
Day 11	29.0	1/10	1/10	-	0/10	0/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Spleen						
Day 11	37.3 to 118.6	6/10	4/10	26.4 to 75.6	7/10	2/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	1/10	-	0/10	0/10
Day 180	-	0/10	0/10	-	0/10	0/10
Liver						
Day 11	-	0/10	0/10	-	0/10	1/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	NA	NA	NA	NA	NA	NA
Day 180	NA	NA	NA	NA	NA	NA

(a) Reference item: 0.9% Sodium Chloride for Injections, USP

(b) Ad26 (b) (4) 2×10^{11} vp/mL (in (b) (4))

(c) (b) (4) 0.3 mg/mL (in (b) (4))

(d) All tissues collected from euthanasia on Days 11, and 90 from all groups were analyzed for the presence of Ad26 vector DNA using q-PCR. From tissues collected from euthanasia on Days 120, only iliac lymph node, injection site skin, spleen, popliteal lymph node and injection site muscle were analyzed. From tissues collected from euthanasia on Days 180, only spleen and iliac lymph node were analyzed. Samples collected from Group 1 at Day 11 and Day 90 had Ad26 (b) (4) vector DNA results below the LOD of the assay for all tissues at all time points. For Group 2 and Group 3 animals, only tissues with vector DNA levels above LOD are listed. All other tissues collected had vector DNA results below the LOD of the assay at all time points.

- Levels for all animals were below LLOQ at this time point

IM = intramuscular(ly); LLOQ = lower limit of quantitation; LOD = limit of detection; q-PCR = quantitative polymerase chain reaction; NA = not analyzed; vp = virus particles