May 24, 2024

Intuitive Surgical
Emily Hovick
Senior Regulatory Affairs Specialist
1266 Kifer Road
Sunnyvale, California 94086

Re: K240723
Trade/Device Name: da Vinci Xi Surgical System (IS4000); da Vinci X Surgical System (IS4200)
Regulation Number: 21 CFR 876.1500
Regulation Name: Endoscope and accessories
Regulatory Class: Class II
Product Code: NAY
Dated: March 15, 2024
Received: March 18, 2024

Dear Emily Hovick:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Mark Trumbore -S

Digitally signed by Mark Trumbore -S
Date: 2024.05.24 09:50:55 -04'00'

Mark Trumbore, Ph.D.
Assistant Director
DHT4A: Division of General Surgery Devices
OHT4: Office of Surgical and Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

Device Name

da Vinci Xi Surgical System (IS4000);
da Vinci X Surgical System (IS4200)

Indications for Use *(Describe)*

The Intuitive Surgical Endoscopic Instrument Control System (da Vinci Surgical System, Models: IS4000 and IS4200) is intended to assist in the accurate control of Intuitive Surgical Endoscopic Instruments including rigid endoscopes, blunt and sharp endoscopic dissectors, scissors, scalpels, forceps/pick-ups, needle holders, endoscopic retractors, electrocautery and accessories for endoscopic manipulation of tissue, including grasping, cutting, blunt and sharp dissection, approximation, ligation, electrocautery, suturing, and delivery and placement of microwave and cryogenic ablation probes and accessories, during urologic surgical procedures, general laparoscopic surgical procedures, gynecologic laparoscopic surgical procedures, general thoracoscopic surgical procedures and thoracoscopically-assisted cardiotomy procedures. The system can also be employed with adjunctive mediastinotomy to perform coronary anastomosis during cardiac revascularization. The system is indicated for adult and pediatric use. It is intended to be used by trained physicians in an operating room environment in accordance with the representative, specific procedures set forth in the Professional Instructions for Use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary (21 CFR § 807.92)

I. Submitter Information

510(k) Owner:	Intuitive Surgical, Inc. 1266 Kifer Road Sunnyvale, CA 94086
Contact Person:	Emily Hovick Senior Regulatory Affairs Specialist Phone: 314-359-8534 Email: Emily.hovick@intusurg.com
Date Summary Prepared:	March 15, 2024

II. Subject Device

Trade Name:	da Vinci Xi Surgical System da Vinci X Surgical System
Common Name:	System, surgical, computer-controlled instrument
Classification:	Class II
Regulation:	21 CFR § 876.1500, Endoscope and Accessories
Product Code:	NAY

III. Predicate Device Information

Predicate Devices:	da Vinci Xi Surgical System, K131861 da Vinci X Surgical System, K171294

IV. Device Description

This premarket notification is for a labeling modification only, to revise the Precaution for Representative Uses statement so that it does not apply to radical prostatectomy performed using the subject devices. This labeling change is supported by real-world evidence (RWE). There are no changes to the technological characteristics or the indications for use of the cleared da Vinci Xi or X Surgical Systems (Models IS4000 and IS4200) proposed in this submission. The da Vinci Xi and X Surgical Systems, Models IS4000 and IS4200, are software-controlled, electro-mechanical systems designed for surgeons to perform minimally invasive surgery. The Model IS4000 and Model IS4200 Surgical Systems consist of a Surgeon Console, a Patient Side Cart (PSC), and a Vision Side Cart (VSC) and are used with an Endoscope, EndoWrist Instruments, and Accessories.

V. Indications for Use

The Intuitive Surgical Endoscopic Instrument Control System (da Vinci Surgical System, Models: IS4000 and IS4200) is intended to assist in the accurate control of Intuitive Surgical Endoscopic Instruments including rigid endoscopes, blunt and sharp endoscopic dissectors, scissors, scalpels, forceps/pick-ups, needle holders, endoscopic retractors, electrocautery and accessories for endoscopic manipulation of tissue, including grasping, cutting, blunt and sharp dissection, approximation, ligation, electrocautery, suturing, and delivery and placement of microwave and cryogenic ablation probes and accessories, during urologic surgical procedures, general laparoscopic surgical procedures, gynecologic laparoscopic surgical procedures, general thoracoscopic surgical procedures and thoracoscopically-assisted cardiotomy procedures. The system can also be employed with adjunctive mediastinotomy to perform coronary anastomosis during cardiac revascularization. The system is indicated for adult and pediatric use. It is intended to be used by trained physicians in an operating room environment in accordance with the representative, specific procedures set forth in the Professional Instructions for Use.

Precaution for Representative Uses

The demonstration of safety and effectiveness for the representative specific procedures did not include evaluation of outcomes related to the treatment of cancer (overall survival, disease-free survival, local recurrence), except for radical prostatectomy which was evaluated for overall survival, or treatment of the patient's underlying disease/condition. Device usage in all surgical procedures should be guided by the clinical judgment of an adequately trained surgeon.

VI. Technological Characteristics

This premarket notification is for a change to the labeling only. There are no changes to the technological characteristics of the cleared da Vinci Xi or X Surgical Systems (Models IS4000 and IS4200) proposed in this submission. The da Vinci Xi and X Surgical Systems, Models IS4000 and IS4200, are software-controlled, electro-mechanical systems designed for surgeons to perform minimally invasive surgery. The Model IS4000 and Model IS4200 Surgical Systems consist of a Surgeon Console, a Patient Side Cart (PSC), and a Vision Side Cart (VSC) and are used with an Endoscope, EndoWrist Instruments, and Accessories.

VII. Performance Data

There are no changes to the technological characteristic of the subject device in this premarket notification. Therefore, no bench or preclinical data were required.

Clinical Data Summary

Table 1: Study Summary

Title	Use of Real-World Data to Demonstrate That Overall Survival Following Robotic-Assisted Radical Prostatectomy is Non-Inferior to Non-Robotic Assisted Radical Prostatectomy
Study Objective	**Primary objective**: Evaluate non-inferiority of robotic-assisted surgical device (RASD) radical prostatectomy (RP) as compared with non-RASD RP with respect to the difference in probability of 5-year overall survival (OS) among male patients at least 35 years of age with treatment-naive prostate cancer. **Secondary objectives**: Evaluate non-inferiority of RASD RP as compared with non-RASD RP with respect to the difference in 6-year, 7-year, 8-year, 9-year, and 10-year probability of OS among male patients at least 35 years of age with treatment-naive prostate cancer.
Study Design	A retrospective cohort study using secondary administrative healthcare claims data to evaluate OS following RP performed via RASD as compared to non-RASD open surgical approaches among patients with treatment-naive prostate cancer in the United States.
Study Population	Male patients at least 35 years of age with treatment-naive prostate cancer undergoing a RASD versus non-RASD RP procedure.
Number of Patients / Time Period	**Primary analyses**: N = 24,350 patients with an RP procedure between July 2007 and December 2014, restricting the last procedure date to occur 5 years prior to the start of COVID-19. **Sensitivity analyses**: N = 45,215 patients with an RP procedure between July 2007 and December 2020, utilizing all available data.
Data Source	Optum Clinformatics Data Mart (CDM) de-identified administrative healthcare claims data
Study Endpoints	**Primary endpoint**: The difference in the probability of OS at 5 years after the RP procedure (i.e., the difference in the percent of patients who do not have a death event), comparing RASD RP to non-RASD RP. **Secondary endpoints**: The difference in the probability of OS at 6, 7, 8, 9, and 10 years after the RP procedure, comparing RASD RP to non-RASD RP.
Statistical Methods	Propensity score (PS) method with stratification was applied on the outcome-free design. The overall survival rate was estimated based on Average Treatment Effect among the Treated population.

Table 2: Baseline characteristics of patients with treatment-naive prostate cancer undergoing radical prostatectomy procedure between 7/1/2007 and 12/31/2014, by surgical approach, before and after PS stratification. Note: subgroup analyses were not performed for any endpoint.

	Before PS Stratification			After PS stratification (weighted N, by strata)		
	RASD RP N = 18,949	Non-RASD RP N = 5,401	ASD	RASD RP Weighted N = 3,850.31	Non-RASD RP Weighted N = 1,019.69	ASD
Demographics [Day 0]						
Age in years at index			0.020			0.040
mean (SD)	60.94 (7.29)	61.06 (7.27)		61.12 (3.28)	61.12 (3.29)	
median [IQR]	61.00 [56.00, 66.00]	61.00 [56.00, 66.00]		61.22 [56.00, 66.22]	61.22 [55.81, 66.42]	
Age categories, years						
35 - 44	235 (1.24%)	68 (1.26%)	0.000	47.6 (1.24%)	12.9 (1.23%)	0.060
45 - 54	3,522 (18.59%)	996 (18.44%)	0.000	716.3 (18.59%)	187.7 (18.06%)	0.030
55 - 64	8,799 (46.44%)	2,497 (46.23%)	0.000	1,786.3 (46.43%)	472.4 (46.97%)	0.040
65 - 74	6,000 (31.66%)	1,734 (32.11%)	0.010	1,220.2 (31.67%)	325.7 (31.37%)	0.030
≥75	393 (2.07%)	106 (1.96%)	0.010	79.9 (2.08%)	21.0 (2.37%)	0.040
Race/Ethnicity; n (%)						
Asian	386 (2.04%)	94 (1.74%)	0.020	80.3 (2.04%)	18.5 (2.01%)	0.030
Black	1,787 (9.43%)	597 (11.05%)	0.050	352.5 (9.43%)	109.4 (9.78%)	0.030
Hispanic	1,061 (5.60%)	338 (6.26%)	0.030	211.1 (5.6%)	61.8 (5.42%)	0.040
White	14,713 (77.65%)	4,057 (75.12%)	0.060	3,007.3 (77.64%)	771.8 (77.51%)	0.020
Unknown	1,002 (5.29%)	315 (5.83%)	0.020	199.1 (5.29%)	58.3 (5.28%)	0.010
Region; n (%)						
Midwest	1,676 (8.84%)	413 (7.65%)	0.040	348.0 (8.85%)	81.2 (9.11%)	0.050
Northeast	5,026 (26.52%)	1,495 (27.68%)	0.030	1,015.6 (26.52%)	278.9 (26.41%)	0.030
South	8,349 (44.06%)	2,248 (41.62%)	0.050	1,711.5 (44.06%)	430.2 (43.89%)	0.030
West	3,898 (20.57%)	1,245 (23.05%)	0.060	775.2 (20.57%)	229.4 (20.59%)	0.030
Insurance type; n (%)						
Commercial	14,052 (74.16%)	4,111 (76.12%)	0.050	2,838.4 (74.16%)	771.0 (74.41%)	0.030
Medicare	4,897 (25.84%)	1,290 (23.88%)	0.050	1,011.9 (25.84%)	248.7 (25.59%)	0.030
Year of RP procedure; n (%)						
2007	998 (5.27%)	715 (13.24%)	0.280	157.8 (5.27%)	112.4 (5.98%)	0.020
2008	2,343 (12.36%)	1,150 (21.29%)	0.240	401.4 (12.37%)	192.0 (11.96%)	0.040
2009	2,702 (14.26%)	955 (17.68%)	0.090	517.0 (14.26%)	177.4 (14.34%)	0.030
2010	2,584 (13.64%)	805 (14.90%)	0.040	509.3 (13.64%)	155.2 (13.83%)	0.030
2011	2,968 (15.66%)	672 (12.44%)	0.090	624.8 (15.66%)	139.1 (15.80%)	0.020
2012	2,506 (13.22%)	431 (7.98%)	0.170	550.5 (13.23%)	93.6 (13.52%)	0.050
2013	2,546 (13.44%)	376 (6.96%)	0.220	569.5 (13.44%)	83.4 (13.33%)	0.020
2014	2,302 (12.15%)	297 (5.50%)	0.240	520.2 (12.15%)	66.5 (11.25%)	0.040
Comorbidities and clinical characteristics [Day -180, Day 0]						
Evidence of smoking or smoking cessation; n (%)	4,646 (24.52%)	1,287 (23.83%)	0.020	948.1 (24.52%)	245.9 (24.98%)	0.030
Alcohol related disorders; n (%)	31 (0.16%)	7 (0.13%)	0.010	6.5 (0.16%)	1.4 (0.17%)	0.020
Obesity; n (%)	1,940 (10.24%)	504 (9.33%)	0.030	401.4 (10.24%)	97.3 (10.28%)	0.020
Cancers other than prostate cancer; n (%)	1,575 (8.31%)	577 (10.68%)	0.080	306.1 (8.31%)	104.0 (8.82%)	0.030
Benign prostatic hyperplasia; n (%)	637 (3.36%)	187 (3.46%)	0.010	129.3 (3.36%)	35.1 (3.22%)	0.040
Lower urinary tract conditions; n (%)	7,206 (38.03%)	2,248 (41.62%)	0.070	1,441.4 (38.03%)	417.2 (39.03%)	0.040
Hypertension; n (%)	11,671 (61.59%)	3,412 (63.17%)	0.030	2,361.3 (61.59%)	641.3 (62.13%)	0.020
Diabetes mellitus; n (%)	3,168 (16.72%)	932 (17.26%)	0.010	640.5 (16.72%)	175.6 (17.24%)	0.030
Kidney disease; n (%)	1,468 (7.75%)	465 (8.61%)	0.030	293.8 (7.75%)	85.6 (7.77%)	0.030
Gagne Comorbidity Index			0.120			0.030
mean (SD)	1.21 (1.45)	1.39 (1.64)		1.23 (0.63)	1.23 (0.64)	
median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]		1.00 [0.00, 1.55]	1.00 [0.00, 1.77]	
Frailty score			0.110			0.040
mean (SD)	0.10 (0.03)	0.10 (0.03)		0.10 (0.01)	0.10 (0.01)	
median [IQR]	0.10 [0.08, 0.12]	0.10 [0.08, 0.12]		0.10 [0.08, 0.12]	0.10 [0.08, 0.12]	
Medications and treatments [Day -180, Day -1]						
Pelvic or abdominal surgery; n (%)	17,736 (93.60%)	5,118 (94.76%)	0.050	3,595.5 (93.6%)	964.7 (93.97%)	0.030
Transurethral prostate surgery; n (%)	70 (0.37%)	41 (0.76%)	0.050	12.6 (0.37%)	6.7 (0.4%)	0.030
Urethral or bladder neck surgery; n (%)	2,805 (14.80%)	819 (15.16%)	0.010	567.3 (14.8%)	153.9 (15.01%)	0.020
Treatment for other cancers:						
Radiotherapy; n (%)	13 (0.07%)	7 (0.13%)	0.020	2.2 (0.07%)	1.2 (0.08%)	0.020
Chemotherapy; n (%)	8 (0.04%)	5 (0.09%)	0.020	1.4 (0.04%)	0.8 (0.05%)	0.000
Immunotherapy; n (%)	0 (0.00%)	0 (0.00%)	0.000	0.0 (0%)	0.0 (0%)	0.000
Hormonal therapy; n (%)	11 (0.06%)	3 (0.06%)	0.000	2.3 (0.06%)	0.6 (0.05%)	0.030
Anticoagulants; n (%)	462 (2.44%)	86 (1.59%)	0.060	100.3 (2.44%)	17.7 (2.32%)	0.020
Antiplatelets (including aspirin); n (%)	650 (3.43%)	167 (3.09%)	0.020	134.3 (3.43%)	32.5 (3.5%)	0.020
NSAIDs; n (%)	2,679 (14.14%)	745 (13.79%)	0.010	546.5 (14.14%)	141.3 (14.11%)	0.020
Laboratory results [Day -180, Day -1]						

	Before PS Stratification			After PS stratification (weighted N, by strata)		
	RASD RP N = 18,949	**Non-RASD RP** N = 5,401	**ASD**	**RASD RP** Weighted N = 3,850.31	**Non-RASD RP** Weighted N = 1,019.69	**ASD**
Preoperative PSA, ng/mL (last value observed, among those with ≥1 value)			0.120			0.130
mean (SD)	6.74 (6.43)	7.84 (10.79)		7.90 (2.87)	7.90 (5.31)	
median [IQR]	5.24 [4.20, 7.30]	5.42 [4.30, 8.00]		5.49 [4.17, 7.23]	5.49 [4.31, 7.96]	
Among N with non-missing value	4,567	1,020		956.10	199.90	
Preoperative PSA categories, ng/mL; n (%)						
< 10	3,989 (21.05%)	844 (15.63%)	0.140	834.0 (21.05%)	165.9 (18.23%)	0.070
10 - <20	461 (2.43%)	133 (2.46%)	0.000	97.3 (2.43%)	25.7 (2.72%)	0.030
≥20	117 (0.62%)	43 (0.80%)	0.020	24.8 (0.62%)	8.3 (0.85%)	0.040
Missing	14,382 (75.90%)	4,381 (81.11%)	0.130	2,894.2 (75.9%)	819.8 (78.19%)	0.050
Healthcare resource utilization [Day -180, Day -1]						
Days hospitalized, among those with ≥0 hospitalizations			0.010			0.030
mean (SD)	0.27 (2.12)	0.30 (2.82)		0.26 (0.96)	0.26 (0.85)	
median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Number of outpatient visits, among those with ≥0 outpatient visits			0.060			0.040
mean (SD)	12.31 (6.32)	11.95 (6.26)		12.38 (2.88)	12.38 (3.25)	
median [IQR]	11.00 [8.00, 15.00]	11.00 [8.00, 14.00]		11.07 [8.23, 14.88]	11.07 [8.23, 14.68]	

RASD = Robotic-assisted surgical device; RP = radical prostatectomy; SD = standard deviation; IQR = interquartile range; NSAID = non-steroidal anti-inflammatory drugs; ASD = absolute standardized difference

Bracketed date ranges describe the time period over which characteristics were assessed. Day 0 refers to the date of RP procedure, and date ranges with hard brackets are inclusive of start/end dates.

With the exception of age, PSA results, days hospitalized, and number of outpatient visits, which are reported as the mean (SD) and median (IQR) for patients in each surgical approach group, characteristics are described as the total number of patients with evidence of each characteristic during the specified assessment period and the percent of the total number of patients within each treatment group, reported as n (%).

ASDs ≥ 0.1 have been bolded to indicate meaningful differences between groups.

Table 3: Absolute differences in overall survival among patients with a radical prostatectomy procedure between 7/1/2007 and 12/31/2014, comparing patients with RASD RP vs. non-RASD RP, primary and secondary analyses.

				Unadjusted			After PS Stratification	
Analysis and treatment group	Total No. of patients in each group	Total No. of patients with a death event	Total No. of patients without a death event	Total No. of patients censored due to end of study period (12/31/2019)^	Probability of OS and 95% CI (risk per 100 patients)	Unadjusted OS difference and 95% CI* (risk difference per 100 patients) RASD vs non-RASD RP	Adjusted OS difference and 95% CI* (risk difference per 100 patients) RASD vs non-RASD RP	Non-inferiority p-value** RASD vs non-RASD RP
Primary analysis: 5-year OS								
RASD RP	18,949	734	18,215	0	96.13 (95.85, 96.40)	0.48 (-0.13, 1.09)	0.20 (-0.46, 0.86)	<0.0001
Non-RASD RP	5,401	235	5,166	0	95.65 (95.11, 96.19)	reference	reference	reference
Secondary analysis: 6-year OS								
RASD RP	18,949	933	18,016	2,188	95.01 (94.69, 95.32)	0.86 (0.16, 1.57)	0.64 (-0.15, 1.42)	<0.0001
Non-RASD RP	5,401	314	5,087	286	94.14 (93.52, 94.77)	reference	reference	reference
Secondary analysis: 7-year OS								
RASD RP	18,949	1,120	17,829	4,586	93.79 (93.44, 94.15)	1.26 (0.47, 2.06)	1.09 (0.14, 2.04)	<0.0001
Non-RASD RP	5,401	393	5,008	643	92.53 (91.82, 93.24)	reference	reference	reference
Secondary analysis: 8-year OS								
RASD RP	18,949	1,309	17,640	6,904	92.33 (91.92, 92.73)	1.34 (0.46, 2.23)	0.61 (-0.41, 1.64)	<0.0001
Non-RASD RP	5,401	463	4,938	1,025	90.98 (90.20, 91.77)	reference	reference	reference
Secondary analysis: 9-year OS								
RASD RP	18,949	1,462	17,487	9,632	90.79 (90.32, 91.26)	1.51 (0.52, 2.49)	0.76 (-0.41, 1.94)	<0.0001
Non-RASD RP	5,401	531	4,870	1,614	89.28 (88.42, 90.16)	reference	reference	reference
Secondary analysis: 10-year OS								
RASD RP	18,949	1,578	17,371	11,961	89.18 (88.64, 89.73)	1.87 (0.75, 2.99)	0.88 (-0.35, 2.11)	<0.0001
Non-RASD RP	5,401	595	4,806	2,322	87.31 (86.34, 88.29)	reference	reference	reference

RASD = Robotic-assisted surgical device; RP = radical prostatectomy; CI = confidence interval; OS = overall survival

Patients are followed from one day after the index date (RP procedure date) until the earliest occurrence of a recorded death, the maximum follow-up period (5 years in the primary analysis; 6, 7, 8, 9, and 10 years, respectively, in each of the secondary analyses), or 12/31/2019 (prior to known increases in mortality starting in 2020 due to the COVID-19 pandemic).

^ Survival probabilities are calculated using a Kaplan-Meier approach to account for censoring.

* 95% CIs are reported to aid interpretation but are distinct from non-inferiority hypothesis testing.

** p-values correspond to hypothesis testing of non-inferiority of RASD RP vs non-RASD RP, where the non-inferiority margin is set to 2.0% and the significance level of the test is set at one-sided 0.025. A hierarchical approach was used to allow testing of each null hypothesis at a significance level of 0.025. No adjustment for multiple testing was conducted, given that null hypotheses were hierarchically ordered and predefined and that the same PS quintiles were used for all primary and secondary endpoints. Specifically, the primary endpoint (5-year OS) was evaluated for statistical significance first, and each subsequent endpoint was evaluated only if the previous was found to be statistically significant. Had any endpoint been found to have $p > 0.025$, no subsequent endpoints would have been evaluated.

VIII. Conclusion

RWE was provided to demonstrate that the retrospective clinical data met all overall survival endpoints. This supports the modification of the Precaution for Representative Uses statement so that it does not apply to RP performed using the subject devices. These data prove the utility of RWE in support of premarket submissions.

The observed all-cause mortality in this study is similar to rates found in a systematic literature review performed by FDA. Based on tipping-point analyses performed by FDA, more than 28% differential bias in all-cause mortality ascertainment between RASD and non-RASD arms of this study would be needed to alter the results of the primary non-inferiority analysis. Additionally, examination of the data did not suggest presence of differential bias in all-cause mortality ascertainment between RASD and non-RASD arms of this study.