Use of Real-World Evidence to Support Regulatory Clearance of a Labeling Revision for Robotic-Assisted Radical Prostatectomy in the United States

HPR24

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Background & Objective

- Radical prostatectomy (RP) is the most common definitive local therapy for prostate cancer, especially for those with cancer at risk for spread, with most procedures currently performed via minimally invasive robotic-assisted surgical devices (RASD; da Vinci® Surgical Systems)
- At the time of this study, the da Vinci label in the United States (US) included language that the device had been evaluated as a surgical tool but not for outcomes related to the treatment of cancer, including overall survival (OS)

Objective: Use real-world evidence (RWE) to support regulatory clearance for a US labeling revision for RASD for RP by evaluating its non-inferiority relative to non-RASD RP with respect to long-term (up to 10-years) OS.

Methods

Data

- Optum's de-identified Clinformatics® Data Mart Database (CDM) claims data, study period 2007 – 2019
- Linked mortality data sourced from the the Social Security Administration, the Centers for Medicare and Medicaid Services, obituary data, hospitalizations with discharge status "Expired," and claims enrollment coverage discontinuation with a reason of death, the majority of which are available for patients both during and after enrollment
- These data were relevant and reliable to support this US regulatory clearance objective

Study population

- Male patients aged ≥35 years with treatment-naive prostate cancer with an RP procedure code between July 2007 and December 2014
- Compared RASD RP (those with a procedure code indicating robotic assistance) to non-RASD RP (those with a procedure code indicating perineal or retropubic open RP approaches)

Statistical analysis

- OS outcome: the absence of a reported death during follow-up, evaluated for 5- through 10-year follow-up periods (patients were followed until maximum follow-up [e.g., 5 years for 5-year OS] or Dec 2019, the end of the study period)
- Differences in probability of OS: calculated using a Kaplan-Meier approach after propensity score (PS) stratification in quintiles to control for measured confounding
- Non-inferiority testing: margin of 2% with a test size of 2.5% using a hierarchical approach among the same cohort (demonstrating significance for 5-year OS before evaluating 6-year, and so on)
- Analysis software: Aetion® Substantiate software for real-world data analysis and R 4.3

Results

Study sample

- N = 18,949 with RASD RP
- N = 5,401 with non-RASD RP

Unadjusted results

- Unadjusted OS, RASD vs non-RASD:
  - 5-year: 96.13% vs 95.65%
  - 10-year: 89.18% vs. 87.31%
- Crude differences (95% CI) in OS probabilities per 100 patients for RASD vs non-RASD:
  - 5-year: 0.48 (-0.13, 1.09)
  - 10-year: 1.87 (0.75, 2.99)

After PS stratification

- Adjusted differences (95% CI) in OS probabilities per 100 patients for RASD vs non-RASD:
  - 5-year: 0.20 (-0.46, 0.86)
  - 10-year: 0.88 (-0.35, 2.11)

Non-inferiority

- RASD RP was non-inferior to non-RASD RP at 5- through 10-year follow-up ($p < 0.0001$ for all)

Conclusions

In this collaborative demonstration case, **RWE was successful in supporting US regulatory clearance for a labeling revision** for the da Vinci Xi/X® Surgical System to modify a precaution statement that FDA did not evaluate overall survival related to the treatment of prostate cancer.

Previous label precaution language, da Vinci Xi/X® Surgical Systems:

"The demonstration of safety and effectiveness for the representative-specific procedures was based on evaluation of the device as a surgical tool and did not include evaluation of outcomes related to the treatment of cancer (overall survival, disease-free survival, local recurrence) or treatment of the patient's underlying disease or condition."

Revised label precaution language, da Vinci Xi/X® Surgical Systems:

"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."

Disclosures

As part of its commitments outlined in the 2023 Medical Device User Fee Amendments (MDUFA V), the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) provides User Fee funds to the National Evaluation System for health Technology Coordinating Center (NESTcc) in the Medical Device Innovation Consortium (MDIC) to: i) support the development of RWD resources to facilitate appropriate access for research studies; ii) convene experts to develop best practices and, advance innovative methodology approaches with respect to RWE development and analysis. Funding for this work was made possible by FDA of HHS from industry user fees administered through a financial assistance award (FAIN# U01FD006292) to the MDIC. Aetion has received funding for this work as a sub-contractor for NESTcc. The contents are those of the author(s) and/or presenter(s) and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government. LRG, PG, AB, DL, and EMG are employees of Aetion, Inc and hold stock options. USK and JAW are employees of Intuitive Surgical, Inc., the manufacturer of the Da Vinci robot, with stock options and equity.

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