

Impact of ⁸⁹Zr-girentuximab PET/CT versus conventional imaging on clinical decision making in patients with indeterminate renal masses (ZIRCON-X)

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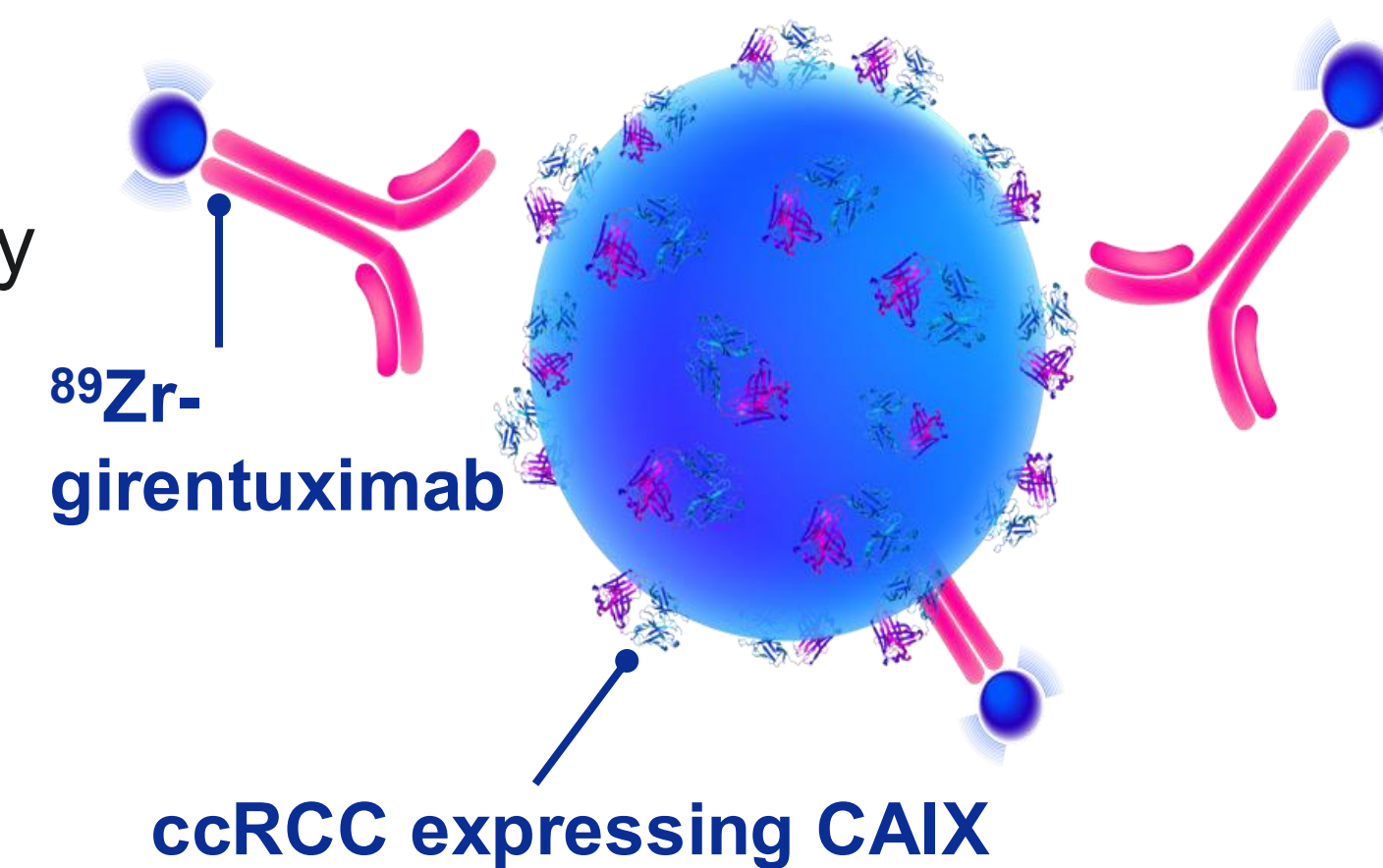
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Background: Unmet need for accurate ccRCC detection

Leveraging CAIX targeting: ⁸⁹Zr-girentuximab PET for detection & characterization of ccRCC

- Induced by hypoxia or by mutation of the Von Hippel-Lindau tumor suppressor gene⁶⁻⁹
- Expressed in >95% of ccRCC¹⁰⁻¹², not by normal kidney tissue¹²
- Girentuximab: monoclonal antibody targeting CAIX



ZIRCON, Ph 3 multinational study¹³

- Co-primary endpoints met: ⁸⁹Zr-girentuximab PET sensitivity 85.5%, specificity 87.0%, favorable safety profile
- Methods overview
- Pts w/ an IDRM ≤7 cm (cT1) in diameter on CT or MRI suspicious for ccRCC
- Scheduled for surgery, histopathology as standard of truth
- Received single IV dose (37 MBq) ⁸⁹Zr-girentuximab, PET 5±2 days later

Can ⁸⁹Zr-girentuximab PET imaging **impact clinical decision-making** for patients with renal cT1 masses?

ZIRCON-X study overview:

Non-interventional, prospective, post-hoc study assessing imaging data collected during ZIRCON study

Primary Objective

Assess if ⁸⁹Zr-girentuximab PET has an impact on clinical decision-making vs SOC conventional contrast-enhanced diagnostic imaging in patients presenting with an IRM, as determined by survey of expert multidisciplinary teams (MDTs)

Primary Endpoints

- Proportion of patients with changes in management plan driven by ⁸⁹Zr-girentuximab PET scan findings vs conventional (SOC) imaging as determined by MDTs reviewing ZIRCON imaging data
- Hypothetical changes in clinical management based on ⁸⁹Zr-girentuximab PET findings vs SOC imaging
- Hypothetical changes in clinical management (**major or minor**) based on ⁸⁹Zr-girentuximab PET findings vs SOC imaging

Methods

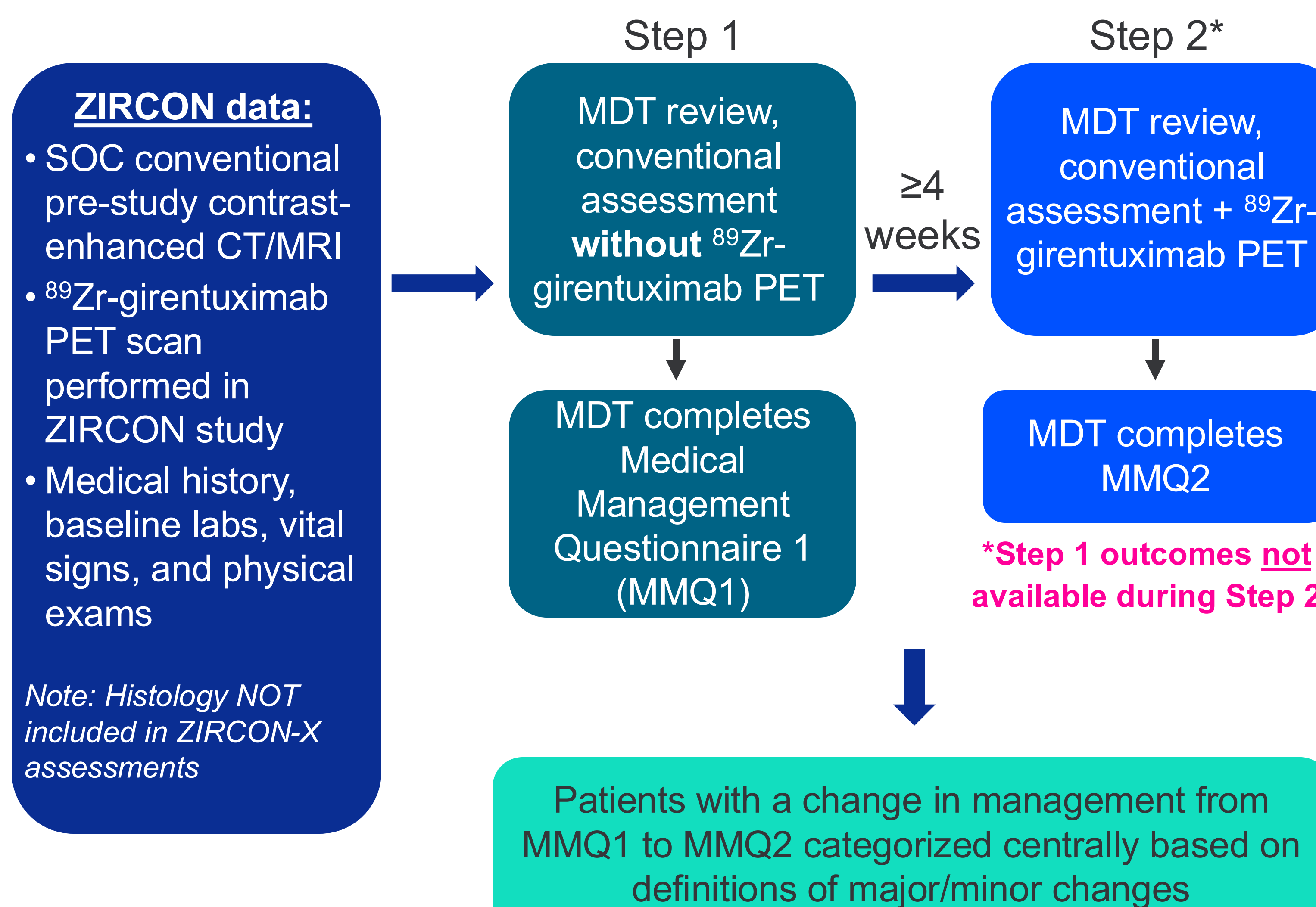
Multidisciplinary Teams (MDTs)

- Comprised of ≥3 board-certified physicians:
 - ≥1 nuclear medicine physician
 - 2 urologists
- 4 MDTs at 4 separate, independent institutions that had participated in ZIRCON study

ZIRCON data:

- SOC conventional pre-study contrast-enhanced CT/MRI
- ⁸⁹Zr-girentuximab PET scan performed in ZIRCON study
- Medical history, baseline labs, vital signs, and physical exams

Note: Histology NOT included in ZIRCON-X assessments



Categories of MAJOR Changes

- Change from planned nephrectomy/locoregional ablation/systemic treatment to active surveillance
- Change from total nephrectomy to partial nephrectomy
- Change from planned nephrectomy/locoregional ablation to systemic treatment
- Change from active surveillance to nephrectomy/locoregional ablation/systemic therapy
- Change from planned nephrectomy to locoregional ablation (vice versa)
- Any other change in planned surgery

*All other changes were considered **MINOR** changes

Results

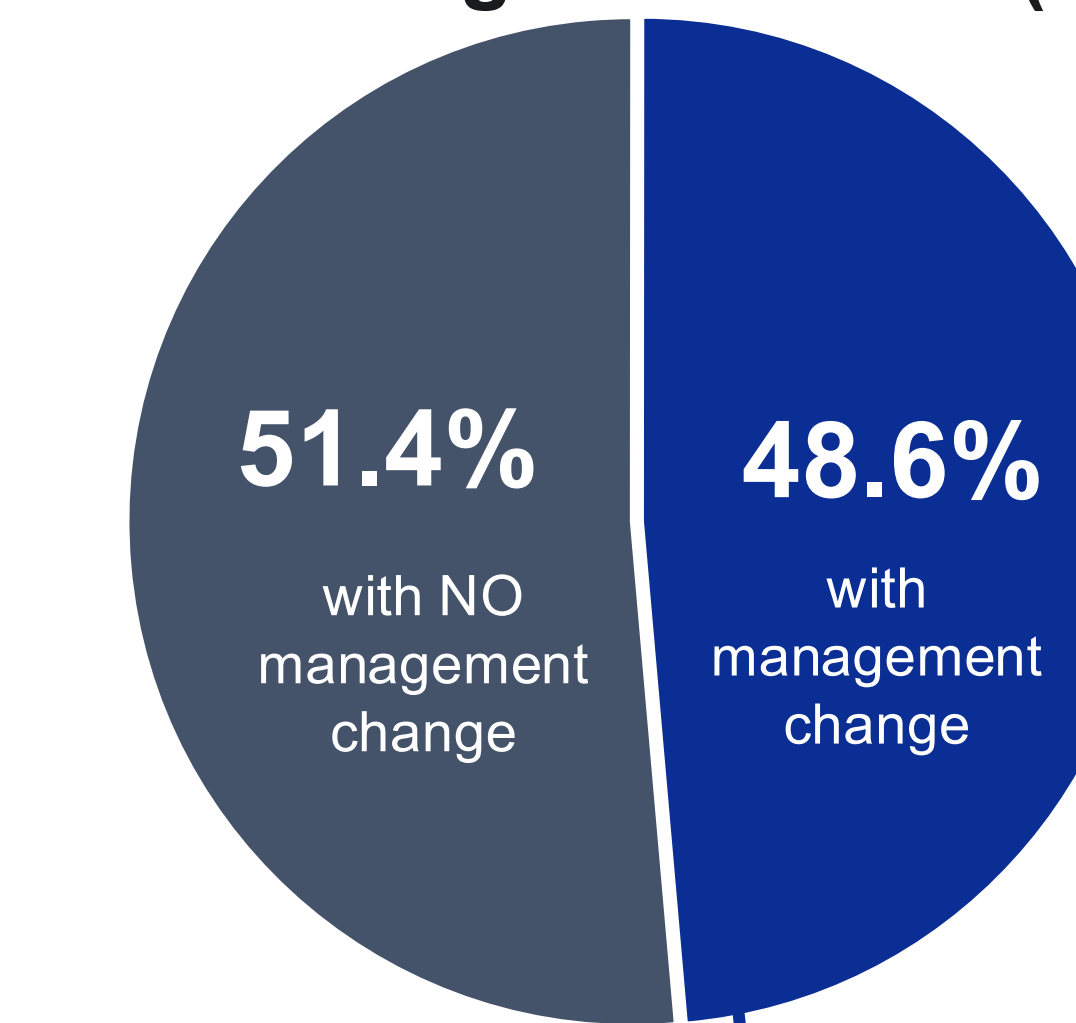
Patient Demographics (N=294)

Median age	62 years (range 27-87)
Male	71.4%
White	92.2%

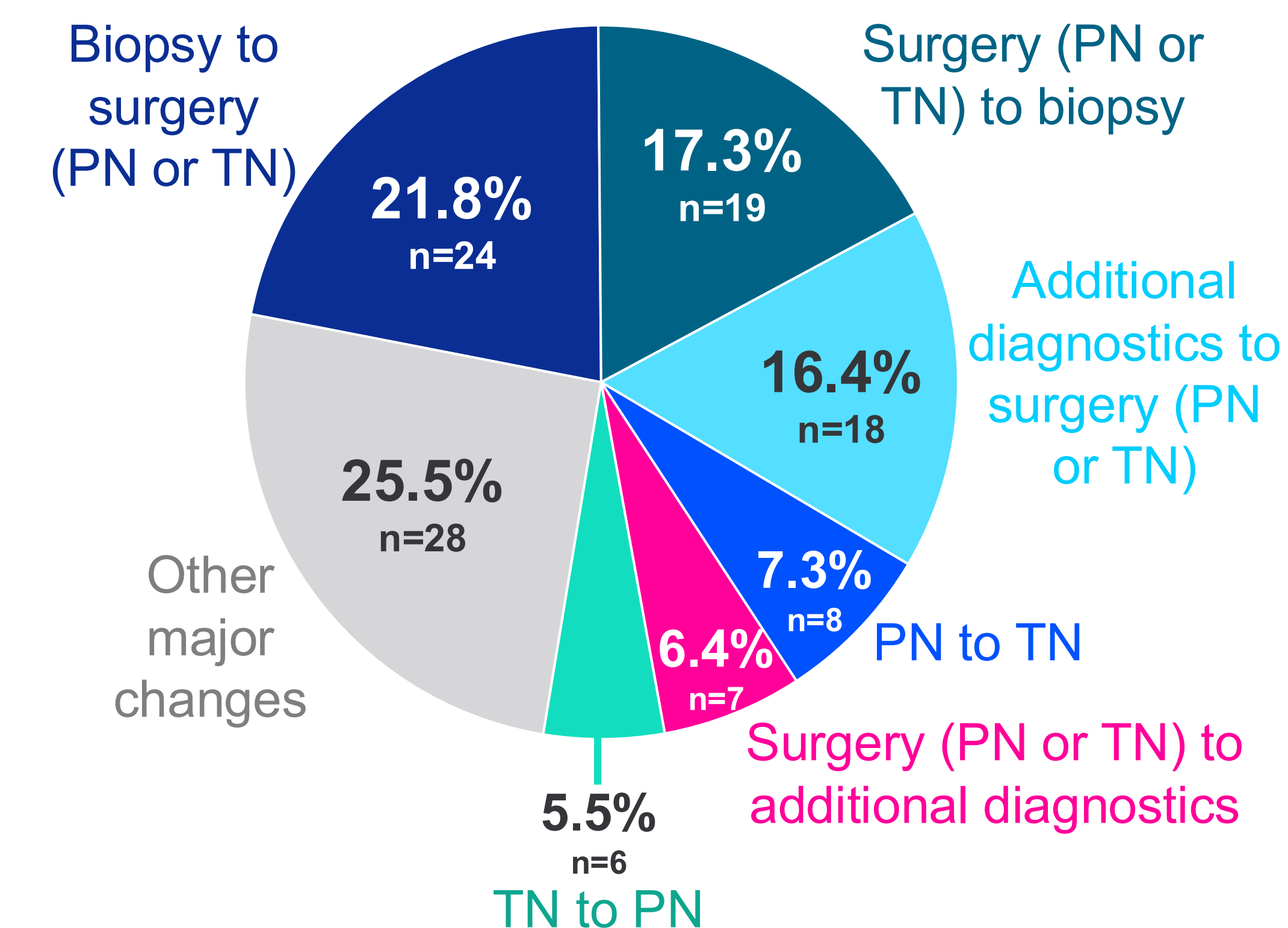
Note

Retrospective data (collected as part of ZIRCON study) was used for this posthoc analysis. Management changes are thus hypothetical.

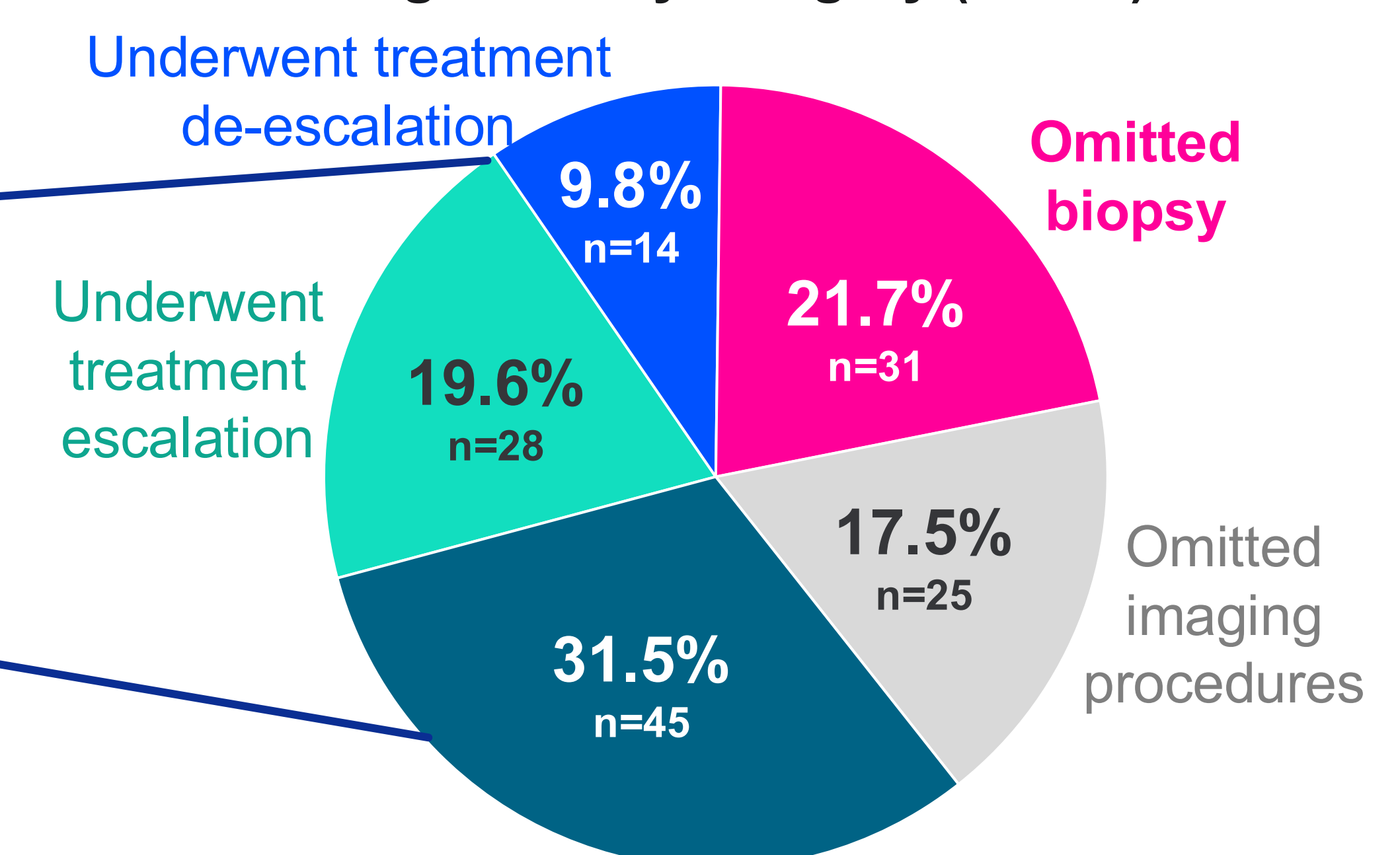
Percent of patients with and without management change with addition of ⁸⁹Zr-girentuximab (N=294)



Most common MAJOR changes in clinical management with addition of ⁸⁹Zr-girentuximab (n=110 of 143 patients)



Percent of patients with any change to management by category (n=143)



Other changes that could not be categorized in this manner

Conclusions

- Nearly half of patients would have had a change to their intended management plan with addition of ⁸⁹Zr-girentuximab PET to diagnostic workup
- Over one-third of all patients (three-quarters of patients with any change) would have had a **major** change in management, based on defined categories
- Approximately 30% of patients had a treatment escalation or de-escalation
- Over 20% of patients could have **potentially avoided biopsy**
- ⁸⁹Zr-girentuximab PET may provide clarity on **spatial localization** of ccRCC within the kidney

References: 1. Patel HD, et al. *J Urol*. 2016;195(5):1340-1347. 2. Sanchez A, et al. *J Clin Oncol*. 2018;36(36):3591-3600. 3. Branger N, et al. *World J Urol*. 2023;41(2):483-489. 4. Macklin PS, et al. *Eur Urol*. 2019;75(5):861-867. 5. Kim JH, et al. *JAMA Surg*. 2019;154(3):225-231. 6. Aldera AP, et al. *J Clin Pathol*. 2021;74(6):350-354. 7. Becker HM. *Br J Cancer*. 2020;122(2):157-167. 8. Wykoff CC, et al. *Cancer Res* 2000;60(24):7075-7083. 9. Maxwell PH, et al. *Nature* 1999;399(6733):271-275. 10. Courcier J, et al. *Int J Mol Sci* 2020;21(19):7146. 11. Bui MHT, et al. *Clin Cancer Res* 2003;9(2):802-811. 12. Stillebroer AB, et al. *Eur Urol* 2010;58(1):75-83. 13. Shuch B, et al. *Lancet Oncol*. 2024;25(10):1277-1287.

Abbreviations: CAIX, carbonic anhydrase IX; ccRCC, clear-cell renal cell carcinoma; CT, computed tomography; IRM, indeterminate renal mass; MDT, multidisciplinary teams; MMQ, medical management questionnaire; MRI, magnetic resonance imaging; PET, positron emission tomography; PN, partial nephrectomy; SOC, standard of care; TN, total nephrectomy

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