^{89}Zr-DFO-girentuximab for PET/CT imaging of clear cell renal cell carcinoma: Results from phase 3 ZIRCON study

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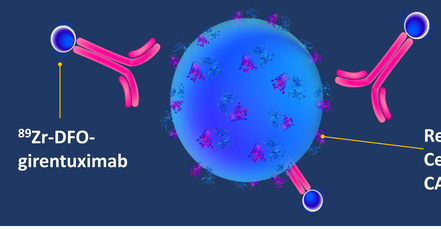
Background

- Clear cell renal cell carcinoma (ccRCC) is ~75% of RCC and causes ~90% of deaths[1,2]
- Up to 30% of resected small renal masses are found to be benign[3]
- Conventional tools (eg, CT, MRI, biopsy) have major limitations
- Unmet medical need: non-invasive diagnosis and characterization of ccRCC
- ZIRCON – phase 3, open label, multicenter trial evaluating performance of ^{89}Zr-DFO-girentuximab PET/CT for detection of ccRCC

Methods

- Enrolled patients with a single indeterminate renal mass ≤7 cm (cT1) on CT or MRI suspicious for ccRCC, scheduled for partial or radical nephrectomy within 90 days after ^{89}Zr-girentuximab administration
- Abdominal PET/CT imagining 5 ± 2 days after administration
- Blinded central image review with histopathology results as standard of truth

^{89}Zr-DFO-girentuximab, an **antibody-based PET imaging agent** that **targets CAIX,** has the potential to help **risk stratify patients** and **guide management** (e.g., selection for surgical vs. conservative management)



Results

Table 1. Performance of ^{89}Zr-DFO-girentuximab PET/CT (N=284)

	Reader 1	Reader 2	Reader 3	Mean % (SD)
Sensitivity, %	84.13	85.19	87.30	**85.5** (1.62)
Lowest bounds, Wilson 95% CI	*78.24*	*79.42*	*81.80*	
Specificity, %	88.42	88.42	84.21	**87.0** (2.43)
Lowest bounds, Wilson 95% CI	*80.45*	*80.45*	*75.57*	
Positive predictive value**, %	93.53	93.60	91.67	**93** (1.10)
Negative predictive value**, %	73.68	75.00	76.92	**75.2** (1.63)
Accuracy**, %	85.56	86.27	86.27	**86.0** (0.41)

* 95% CI had to be > 0.7 for sensitivity and > 0.68 for specificity, for ≥ 2 independent readers to declare the study positive
** Secondary objectives
Abbreviations: CI, confidence interval; SD, standard deviation.

Disclosures: Sponsored by Telix Pharmaceuticals. ^{89}Zr-DFO-girentuximab is not currently approved in any jurisdiction. Clinical Trial.gov Identifier: NCT03849118. Acknowledgements: Thank you to participating sites and patients.

1. Abu Haeyeh et al. *Bioengineering (Basel).* 2022;9:423.
2. Metin et al. *Medicina (Kaunas).* 2022;58:221.
3. Oei et al. *Imaging Med.* 2011;3:207-18.

Results (cont)

Table 2. Performance for lesions ≤2 cm (n=20)

	Reader 1	Reader 2	Reader 3	Mean % (SD)
Sensitivity, %	100.0	100.0	90.0	**96.7 (5.77)**
Lowest bounds, Wilson 95% CI	*72.25*	*72.25*	*59.58*	
Specificity, %	100.0	100.0	90.0	**96.7 (5.77)**
Lowest bounds, Wilson 95% CI	*72.25*	*72.25*	*59.58*	
Positive predictive value, %	100.0	100.0	90.0	**96.7 (5.77)**
Negative predictive value, %	100.0	100.0	90.0	**96.7 (5.77)**
Accuracy, %	100.0	100.0	90.0	**96.7 (5.77)**

Table 3. Mean CAIX H-scores by reader (n=179)

	n	CAIX H-Score Mean ± SD	CAIX H-Score Median	P-value (Wilcoxon)
Reader 1				
ccRCC PET+	152	214 ± 95	242	**0.032**
ccRCC PET-	27	129 ±137	55	
Reader 2				
ccRCC PET+	154	214 ± 96	249	**0.004**
ccRCC PET-	25	122 ± 131	55	
Reader 3				
ccRCC PET+	157	215 ± 96	250	**<0.001**
ccRCC PET-	22	102 ± 127	8	

Note: The H-Score was assessed by immunostaining and was calculated:
H-Score = (0 x [% cat. 0]) + (1 x [% cat. 1]) + (2 x [% cat. 2]) + (3 x [% cat. 3])

Future Directions for Research:

Ongoing work evaluates ^{89}Zr-DFO-girentuximab for **staging in ccRCC and imaging other solid tumors** (true hypoxia)