TLX250-CDx, multi-center Ph3 Trial for PET/CT Imaging of Clear Cell Kidney Cancer

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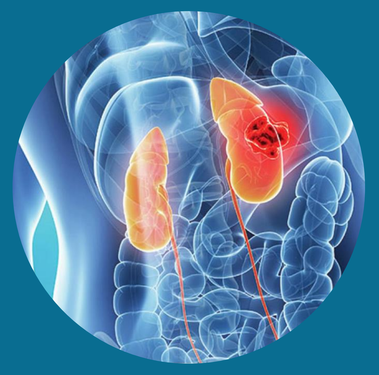
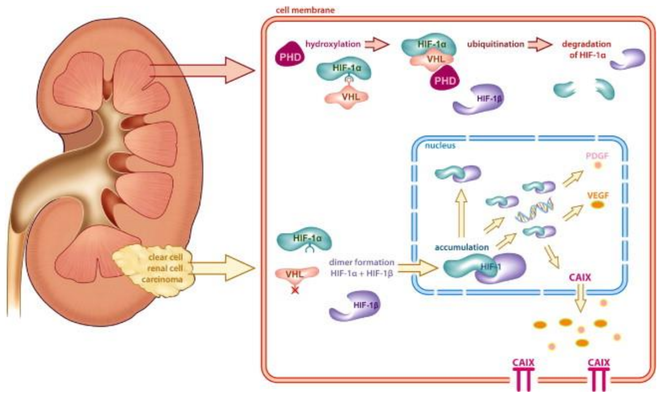


Background

Small renal masses make up the majority of new kidney cancer diagnoses. Overtreatment contributes to significant morbidity/mortality. There are no accurate, non-invasive ways to predict tumor subtype. Clear cell renal cell carcinoma (ccRCC) accounts for ~65% of localized disease and the majority of deaths. Timely and accurate identification of ccRCC may limit biopsies and/or appropriately select patients for treatment. (image adapted[1])



Carbonic Anhydrase IX (CA-IX)

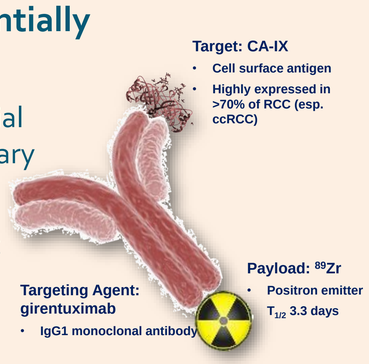
- CA-IX is a transmembrane protein and a tumor-associated carbonic anhydrase isoenzyme
- It is over-expressed in Von Hippel-Lindau syndrome (VHL) mutated clear cell renal cell carcinoma (ccRCC) and hypoxic solid tumors, but is low-expressed in normal kidney and most other normal tissues
- CA-IX shows high expression in carcinomas of the uterine cervix, kidney, oesophagus, lung, breast, colon, brain, and vulva compared to expression in few noncancerous tissue
- VHL loss in ccRCC upregulates CA-IX in 95% of tumors with minimal normal tissue expression.
- Because of the specific overexpression, CA-IX has become a useful target for clear cell RCC tumor imaging and therapy

TLX250-CDx (^{89}Zr-girentuximab)

Monoclonal antibody targeting CA-IX radiolabelled with Zirconium-89 via DFO-TFP chelator as a diagnostic imaging agent.

TLX250-CDx PET can potentially

- ✓ Support minimal invasive treatment options such a partial nephrectomy, avoid unnecessary surgical interventions.
- ✓ Improve staging of metastatic disease by whole body imaging. A high proportion of RCC patients are mis-staged
- ✓ Image to support active surveillance
- ✓ Image for treatment response / therapeutic optimization



Trial Design

ZIRCON (NCT03849118)[2] is an open label, phase 3 study evaluating the performance of (TLX250-CDx) for detecting ccRCC. Sample size N=252 which currently has 90% power to detect a sensitivity of 83% in the cT1a group.

Study Objectives

Primary end-point

Sensitivity and specificity of PET/CT imaging with TLX250-CDx to detect ccRCC in patients with indeterminate renal masses, using histology as standard of truth

Secondary Objectives

- Detect ccRCC in patients with renal masses of ≤ 2 cm;
- Positive predictive value (PPV), negative predictive value (NPV) and accuracy to detect ccRCC.
- A standardized uptake value (SUV) cut-off, suitable to discriminate ccRCC from non-ccRCC
- Intra-reader variability of diagnostic assessment
- Safety and tolerability in patients with indeterminate renal masses

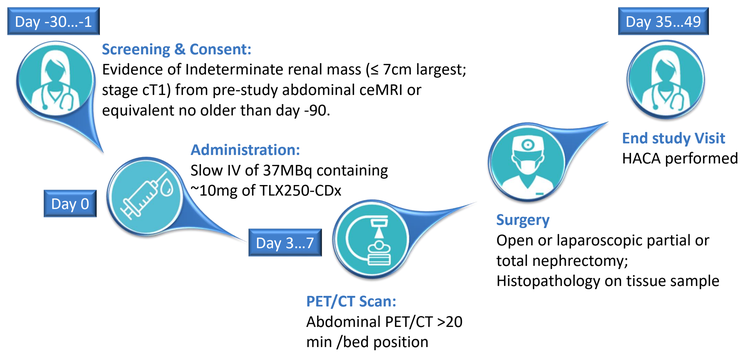
✓ Key Inclusion Criteria

- Imaging evidence of a **single indeterminate renal mass** of ≤ 7 cm in largest diameter (tumor stage cT1), on MRI or equivalent standard of care imaging with contrast agent, not older than 90 days on Day 0, but performed before any screening procedure, suspicious for ccRCC
- **Scheduled for lesion resection** as part of regular diagnostic work-up within 90 days from planned TLX250-CDx administration
- **Sufficient life expectancy** to justify nephrectomy
- Consent to practice double-barrier contraception **until a minimum of 42 days** after IV TLX250-CDx administration

✕ Key Exclusion Criteria

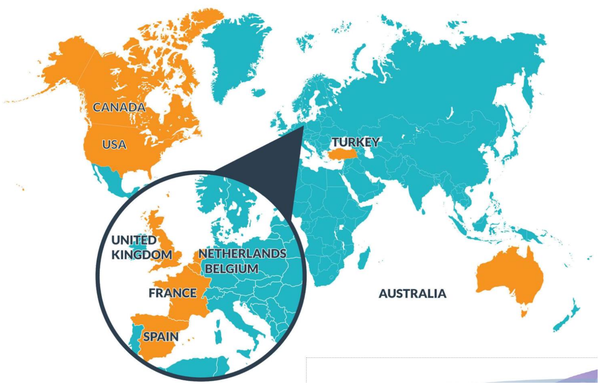
- Biopsy procedure only (no partial or total nephrectomy) planned for histological species delineation of IRM
- Renal insufficiency with GFR ≤ 45 mL/min/ 1.73 m²
- Renal mass known to be a metastasis of another primary tumor.
- Active non-renal malignancy requiring therapy during the time frame of the study participation
- Chemotherapy, radiotherapy, or immunotherapy within 4 weeks prior to the planned administration of TLX250-CDx or continuing adverse effects (> grade 1) from such therapy ([CTCAE] v5.0)
- Planned antineoplastic therapies (for the period between administration of TLX250-CDx and imaging)

Trial Schema



Enrollment

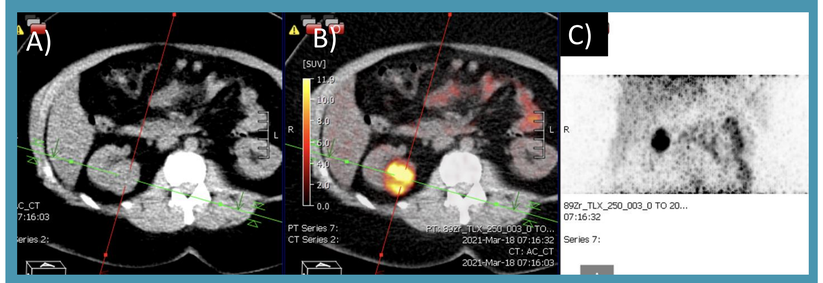
252 patients, international multi-center with 35 sites in 9 countries.



Sites in USA
UCLA
City of Hope
AMIT
Karmanos
Seattle Cancer Alliance
Emory
Johns Hopkins
Washington Univ, St. Louis
MSKCC

Image

ZIRCON Imaging Study



65 year old male with a 4.2 cm enhancing right renal mass

RENAL score 2+2+3+3= 10 treated with a partial nephrectomy. A) cross sectional imaging B) fused imaging with PET C) PET Imaging

^{89}Zr-girentuximab PET/CT:

- ✓ **High accumulation of girentuximab**
- ✓ **No other suspicious sites of disease**

Disclosures

This study is funded and sponsored by Telix Pharmaceuticals.

BS and AP has received research funding from Telix Pharmaceuticals. CH is employee of Telix Pharmaceuticals.

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[1]Stewart, GD et al., Eur. Urol. 2014, 5, 956-63 [2]Van Kuijk, SJA et al. Front. in Onc. 2016, 6, 1-16 [3]Stillebroer, AB et al., Rev. Kidney Can. 58, 1, 75-83
2clinicaltrials.gov/ct2/show/NCT03849118

TLX250-CDx has not received a marketing authorisation in any jurisdiction