^{89}Zr-DFO-girentuximab for PET/CT imaging of clear cell renal cell carcinoma (ccRCC) - results from phase 3 ZIRCON study

AIM: The increasing detection of renal masses presents a challenge as conventional tools (eg, CT, MRI, biopsy) have limitations. Accurate noninvasive techniques to risk stratify patients remains an unmet need.

Girentuximab is a monoclonal antibody that targets carbonic anhydrase IX (CAIX), an enzyme highly expressed in ccRCC. Radiolabeled ^{89}Zr-DFO-girentuximab, highly specific for CAIX, can aid differentiation between ccRCCs and extrarenal lesions. ZIRCON evaluated the performance of ^{89}Zr-DFO-girentuximab PET/CT for detection of ccRCC in patients with indeterminate renal masses (IDRM).

METHODS: Patients with IDRM (≤ 7cm; cT1) scheduled for partial or radical nephrectomy within 90 days from planned ^{89}Zr-DFO-girentuximab administration were enrolled and received 1 dose of ^{89}Zr-DFO-girentuximab IV (37 MBq±10%; 10mg girentuximab) on Day 0 and underwent PET/CT on Day 5 (±2d). Blinded central histology review determined ccRCC status. Coprimary objectives were to evaluate the sensitivity and specificity of ^{89}Zr-DFO-girentuximab PET/CT in detecting ccRCC in patients with IDRM, using histology as standard of truth. Key secondary objectives included sensitivity and specificity of ^{89}Zr-DFO-girentuximab PET/CT in patients with IDRM ≤4cm (cT1a). Other secondary objectives included pos. and neg. predictive values, safety, and tolerability. Wilson 95% CI lower bound for sensitivity and specificity had to be >70% and 68% resp. for ≥2 independent readers to declare the study successful.

RESULTS: 300 patients received ^{89}Zr-DFO-girentuximab (mean age, 62±12y; 71% Males). Of 288 patients with central histopathology, 193 had ccRCC, and 179 had CT1a. Of 284 evaluable patients, average across all 3 readers for sensitivity and specificity was 86% [80%, 90%] and 87% [79%, 92%] resp. for coprimary; and 85% [77%, 91%] and 90% [79%, 95%] resp. for key secondary endpoints. For all readers, lower boundaries of 95% CI for coprimary and key secondary endpoints were >75%. Of 284 patients, pos. and neg. predictive values were ≥91.7% and ≥73.7%, resp. Of 263 treatment-emergent adverse events (TEAEs), 2 were treatment related.

CONCLUSION: ZIRCON confirms ^{89}Zr-DFO-girentuximab PET/CT is well tolerated and can accurately and noninvasively identify/characterize ccRCC, with promising utility for designing best management approaches.