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STAR: A randomised multi-stage phase II/III trial of standard first-line therapy (sunitinib or pazopanib) comparing temporary cessation with allowing continuation, in the treatment of locally advanced and/or metastatic renal Cancer (RCC)

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Background

There is increasing interest in using treatment breaks in oncology, to reduce toxicity without compromising efficacy. STAR was designed to determine if a tyrosine kinase inhibitor drug-free interval strategy (DFIS) was non-inferior to a conventional continuation strategy (CCS) in the first line treatment of advanced RCC. Outcomes were overall survival (OS) and Quality Adjusted Life Years (QALYs).

Methods

STAR is a UK Phase II/III multicentre, randomised controlled trial. Patients were randomised (1:1) to DFIS or CCS. After 24 weeks of sunitinib/pazopanib treatment, DFIS patients took a treatment break, until disease progression, with additional breaks dependent on disease response and patient/clinician choice. Trial strategy continued until intolerance, progression on treatment or death. Both co-primary endpoints (OS and QALYs) must demonstrate pre-defined non-inferiority (NI) (≤7.5% OS; ≤ 10% QALYs) in intention-to-treat (ITT) and per-protocol (PP) analyses for NI to be concluded. An economic evaluation was also conducted.

Results

920 patients were randomised (461 CCS vs 459 DFIS) from 13/01/12 to 12/09/17. 488 (53.0%) patients (240 (52.1%) vs 248 (54.0%)) continued on trial post-week 24. Median treatment break length was 87 days. ITT and PP analyses included 461 vs 458 and 453 vs 418 patients respectively. There was a difference in conclusion in the OS analysis precluding confirmation of NI (HR (95%CI) ITT: 0.97 (0.83, 1.12); PP: 0.94 (0.80, 1.09) NI Margin: 95%CI ≥0.812). However consistent NI conclusions were found for QALYs (Marginal Effect (95% CI) ITT: -0.05 (-0.15, 0.05); PP: 0.04 (-0.14, 0.21) NI Margin: 95%CI ≥-0.156). At two years, DFIS was associated with cost savings (£6,954 per-participant).

Conclusions

Although OS just fell short of overall defined NI using this rigorous approach, probably due to fewer than expected events, QALY NI was demonstrated and a DFIS was seen to be acceptable to patients and clinicians. DFIS also appeared to be highly cost-effective compared to CCS.

Clinical trial identification

EudraCT 2011-001098-16.

Legal entity responsible for the study

University of Leeds.

Funding

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Disclosure

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