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Primary efficacy analysis results from the SORCE trial (RE05): Adjuvant sorafenib for renal cell carcinoma at intermediate or high risk of relapse: An international, randomised double-blind phase III trial led by the MRC CTU at UCL

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Abstract

Background

SORCE is a randomised, double-blind trial of sorafenib after surgical excision of primary renal cell carcinoma (RCC) at intermediate or high risk of recurrence (Leibovich classification).

Methods

We recruited patients from 147 sites in the UK, Australia, France, Belgium, Denmark, The Netherlands and Spain and randomised them (2:3:3) between three years of placebo (A), one year of sorafenib followed by two years of placebo (B) and three years of sorafenib (C). The initial sorafenib dose was 400mg twice per day orally, amended during trial recruitment to a reduced starting dose of 400mg daily. The primary outcome is investigator-reported disease-free survival (DFS). Given the results of the ASSURE and S-TRAC trials, and blinded to SORCE outcomes, we revised the primary analysis to compare three years of sorafenib (arm C) vs placebo (arm A) to focus on the question of longer exposure to sorafenib.

Results

Between July 2007 and April 2013, we randomised 1711 patients; 430, 642, and 639 to arms A, B, and C respectively. Median age was 58 years; 71% male, 84% clear cell histology, 53% at intermediate risk of recurrence and 47% at high risk of recurrence. We observed no differences in DFS or OS in any of our pre-planned and pre-powered analyses: all randomised patients, high-risk patients only, and patients with clear cell RCC only. Median DFS was not reached for three years sorafenib or for placebo (HR 1.01, 95% CI 0.83 -1.23, p=0.95). We observed non-proportional hazards: restricted mean survival time (RMST) was 6.81 years for three years of sorafenib and 6.82 years for placebo, RMST difference 0.01, 95% CI -0.49 – 0.48, p=0.99. Despite offering treatment adaptations, over half of patients stopped treatment early. Grade 3 hand-foot syndrome was reported in 24% of patients on sorafenib.

Conclusions

Sorafenib should not be used as adjuvant therapy for RCC. Active surveillance remains the standard of care for patients at intermediate or high risk of recurrence following nephrectomy; it is the appropriate control of our current international adjuvant RCC trial, RAMPART.

Clinical trial identification

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Legal entity responsible for the study

University College London (UCL).

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Disclosure

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