Background
We conducted a phase III randomized open label trial priming the immune system with neoadjuvant nivo prior to nephrectomy followed by adjuvant nivo in pts with high risk RCC compared to surgery alone.

Methods
Entry criteria included patients with clinical stage ≥T2 or TanyN+ RCC planned for nephrectomy (partial or radical). Select oligometastatic disease was permitted if the pt could be rendered ‘no evidence of disease’ within 12 weeks of surgery. In the investigational arm, nivo was administered (480mg IV q4 weeks) with 1 dose prior to surgery followed by 9 adjuvant doses. The control arm was surgery followed by surveillance without a placebo. Baseline tumor biopsy was required only in the nivo arm. Primary endpoint was recurrence free survival (RFS) regardless of histology. Secondary endpoints include clear cell RCC RFS, overall survival (OS), and quality of life measures.

Results
Between 2/2017 and 6/2021, 819 pts were randomized to perioperative nivo (n=404) or surgery alone (n=415). Clinical stage at enrollment was 53% cT2, 47% cT3-4, 17% cN1, and 4% cM1; 83% of pts had clear cell RCC. The trial was stopped early by DSMC due to futility. RFS was similar between the arms (HR: 0.97; 95% CI: [0.74 – 1.28]; P1-sided = 0.43). The median RFS was not reached. OS was not mature at the time of analysis but was not statistically different between study arms (HR: 1.48; 95% CI: [0.89 – 2.48]; P1-sided = 0.93). Similar withdrawal rates occurred in both arms, approximately 12% (48/404 patients in nivo arm vs. 50/415 in surgery alone arm). 20% of patients treated with nivo experienced at least one Grade 3-4 AE that could be attributable to nivo, compared with 6% in the control arm. The most common treatment related grade 3-4 AEs were kidney injury (1% vs. 2%), rash (2% vs. 0%), and elevated lipase (4% vs. <1%). There were 15 (4%) deaths from RCC in the nivo arm and 18 (4%) deaths from RCC in the surgery alone arm.

Conclusions
Perioperative nivo did not improve RFS in RCC patients at high risk for recurrence. OS data remains immature but is not statistically different between arms. Subset analyses including risk stratification by pathologic stage are ongoing.

Clinical trial identification
NCT03055013; Study start date: February 2, 2017.

Legal entity responsible for the study
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This study was conducted by the ECOG-ACRIN Cancer Research Group (Peter J. O'Dwyer, MD and Mitchell D. Schnall, MD, PhD, Group Co-Chairs).

**Funding**
National Cancer Institute of the National Institute of Health and the Canadian Cancer Society.

**Disclosure**
All authors have declared no conflicts of interest.

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