Abstract citation ID: oyaf276.037

36

International neoadjuvant kidney cancer consortium guidelines on assessing pathological response after neoadjuvant therapy in kidney cancer

James Jones[1], James Blackmur[2], Koen van der Mijn[3], Anne Warren[4], Lisa Browning[5], Femke Burgers[3], Michelle S. Hirsch[6], Payal Kapur[7], Rohit Mehra[8], Priya Rao[9], Sabina Signoretti[6], Axel Bex[10], Grant Stewart[11], Maurits van Montfoort[12], On behalf of the INKCC members

[1]University of Cambridge, Department of Oncology, [2]Western General Hospital, Edinburgh, [3]Netherlands Cancer Institute, Department of Oncology, [4]Cambridge University Hospitals NHS Foundation Trust, [5]University of Oxford, [6]Brigham and Women's Hospital, [7]UT Southwestern Medical Center, Department of Pathology, [8]University of Michigan, Department of Pathology, [9]MD Anderson, Department of Pathology, [10]Royal Free London NHS Foundation Trust, UK & The Netherlands Cancer Institute, Netherlands, [11]University of Cambridge, Department of Surgery, [12]Netherlands Cancer Institute, Department of Pathology

Background: Despite effective surgery and adjuvant immunotherapy, 1/3 of patients with initially localised renal cell carcinoma (RCC) will go on to develop relapse. Neoadjuvant therapy might improve outcomes for some of these patients; however, the approach has not been widely adopted due to a lack of prospective randomised trial data. Designing prospective neoadjuvant studies for RCC depends on properly defined clinicopathological endpoints. Pathological response is a surrogate marker of efficacy for neoadjuvant therapy in many non-renal tumour types. However, there are no standard guidelines on pathological response reporting for RCC, and correlation between pathological response following neoadjuvant therapy and survival has not been established. This study aimed to assess the status of pathological response reporting in RCC and develop a recommendation on tissue preparation and reporting for neoadjuvant RCC clinical trials.

Methods: A systematic review of the PubMed and Web of Science databases was conducted to identify manuscripts reporting response to pre-surgical therapy in RCC. Guidelines for tissue preparation and pathological response reporting were reviewed at a workshop of the International Neoadjuvant Kidney Cancer Consortium (INKCC) held at the Netherlands Cancer Institute in October 2024, and further developed through expert discussions involving pathologists, surgeons, oncologists and patient advocates.

Results: 119 eligible papers were identified. Of these, 27 were prospective neoadjuvant studies, 81.5% of which included a systematic assessment of pathological response across participants. However, methods varied widely between studies. Across all papers, ypT stage post treatment was reported in 34.5%, grade in 22.7%, and a quantitative assessment of residual tumour in 6.7% of manuscripts. Only 4.2% of papers provided specific methodology on tumour sampling for pathological response assessment.

Key points from the INKCC guideline on pathological response assessment include:

1. One tissue section every 10mm should be submitted for masses with grossly viable tumour, with consideration of increased sampling to identify microscopic residual viable tumour foci in selected cases.

2. Areas of residual viable tumour, fibroinflammatory regression, necrosis, and haemorrhage should be quantified by microscopic assessment and reported in 10% intervals. The largest viable tumour measurement should also be reported.
3. Until prospective evidence is generated, suggested response cut offs for percentage residual viable tumour are: >50%—non-response, <50%—partial response, <10%—major response, 0%—complete response.
4. Extent of viable tumour in venous tumour thrombus and metastatic lesions should be reported separately using the same methods as the primary tumour.

Academic studies assessing neoadjuvant response should report a core set of information including neoadjuvant treatment details, macroscopic and microscopic extent of viable tumour, and linked oncological outcome data. We recommend that sampling for correlative studies is embedded in study design, including comparison to pre-treatment biopsy features, so that we can understand neoadjuvant therapy response and identify the patients that benefit from this approach.

Conclusions: Current reporting of pathological response to neoadjuvant therapy in RCC is highly variable, without defined guidelines. We have provided a standardised method for assessment and reporting pathological response, initially for use in clinical trials or research settings. We anticipate that based on application of this method, a streamlined approach can be developed for use in standard clinical care. Critically, future neoadjuvant trials in RCC should assess whether the degree of pathological response is linked to survival outcomes, to refine the cut-off levels for response and validate pathological response as a surrogate endpoint in RCC.

Keywords: neoadjuvant; pathological response; clinical trials; pathology; surgery