

available at www.sciencedirect.comjournal homepage: www.eu-openscience.europeanurology.com

European Association of Urology



Brief Correspondence

Major Urological Cancer Surgery for Patients is Safe and Surgical Training Should Be Encouraged During the COVID-19 Pandemic: A Multicentre Analysis of 30-day Outcomes

Wei Shen Tan^{a,b,c,*}, Rajan Arianayagam^c, Pramit Khetrapal^{a,c}, Edward Rowe^d, Samantha Kearley^d, Ahmed Mahrous^d, Raj Pal^d, William Fowler^e, Rakesh Heer^{e,f}, Mohamed Elajnaf^g, Jayne Douglas-Moore^g, T.R. Leyshon Griffiths^g, James Voss^h, Daniel Wilby^h, Omar Al Kadhiⁱ, Jonathan Noel^j, Nikhil Vasdev^{j,k}, Alastair McKay^l, Imran Ahmad^{l,m}, Islam Abu-Naylaⁿ, Benjamin Lambⁿ, George T. Hill^o, Krishna Narahari^o, Howard Kynaston^o, Arzu Yousuf^p, Venkata R.M. Kusuma^p, Jo Cresswell^p, Pete Cooke^q, Aniruddha Chakravarti^q, Ravi Barod^b, Axel Bex^{a,b}, John D. Kelly^{a,c} on behalf of a multicentre collaborator group[†]

Article info

Article history:

Accepted January 5, 2021

Associate Editor:

Silvia Proietti

Keywords:

COVID-19
Cystectomy
Mortality
Nephrectomy
Prostatectomy
Outcomes

Abstract

COVID-19 has resulted in the deferral of major surgery for genitourinary (GU) cancers with the exception of cancers with a high risk of progression. We report outcomes for major GU cancer operations, namely radical prostatectomy (RP), radical cystectomy (RC), radical nephrectomy (RN), partial nephrectomy (PN), and nephroureterectomy performed at 13 major GU cancer centres across the UK between March 1 and May 5, 2020. A total of 598 such operations were performed. Four patients (0.7%) developed COVID-19 postoperatively. There was no COVID-19–related mortality at 30 d. A minimally invasive approach was used in 499 cases (83.4%). A total of 228 cases (38.1%) were described as training procedures. Training case status was not associated with a higher American Society of Anesthesiologists (ASA) score ($p = 0.194$) or hospital length of stay (LOS; $p > 0.05$ for all operation types). The risk of contracting COVID-19 was not associated with longer hospital LOS ($p = 0.146$), training case status ($p = 0.588$), higher ASA score ($p = 0.295$), or type of hospital site ($p = 0.303$). Our results suggest that major surgery for urological cancers remains safe and training should be encouraged during the ongoing COVID-19 pandemic provided appropriate countermeasures are taken. These real-life data are important for policy-makers and clinicians when counselling patients during the current pandemic.

Patient summary: We collected outcome data for major operations for prostate, bladder, and kidney cancers during the COVID-19 pandemic. These surgeries remain safe and training should be encouraged during the ongoing pandemic provided appropriate countermeasures are taken. Our real-life results are important for policy-makers and clinicians when counselling patients during the COVID-19 pandemic. © 2021 The Author(s). Published by Elsevier B.V. on behalf of European Association of Urology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.euro.2021.01.005>2666–1683/© 2021 The Author(s). Published by Elsevier B.V. on behalf of European Association of Urology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1 – Patient characteristics stratified by type of surgery

	All patients (n = 598)	RP (n = 282)	RC (n = 104)	RN (n = 124)	PN (n = 52)	RNU (n = 36)
Median age, yr (IQR)	65.1 (58.5–71.3)	64.1 (59.0–68.6)	70.4 (60.4–75.4)	65.9 (58.5–73.4)	59.4 (52.1–68.5)	61.8 (62.5–75.4)
ASA score, n (%)						
I	83 (13.9)	47 (16.7)	11 (10.5)	13 (10.5)	8 (15.3)	4 (11.2)
II	393 (65.7)	212 (75.1)	58 (55.8)	74 (59.7)	33 (63.5)	16 (44.4)
≥III	122 (20.4)	23 (8.2)	35 (33.7)	37 (29.8)	11 (21.2)	16 (44.4)
Surgical technique, n (%)						
Open	99 (16.6)	1 (0.4)	39 (39.4)	46 (37.1)	7 (13.5)	6 (16.7)
Robotic	418 (69.9)	280 (99.3)	65 (62.5)	12 (9.7)	43 (82.7)	18 (50.0)
Laparoscopic	81 (13.5)	1 (0.4)	0 (0)	66 (53.2)	2 (3.8)	12 (33.3)
Training case, n (%)						
No	370 (61.9)	173 (61.3)	69 (66.3)	68 (54.8)	34 (65.4)	26 (72.2)
Yes	228 (38.1)	109 (38.7)	35 (33.7)	56 (45.2)	18 (34.6)	10 (27.8)
Mean EOT ± SD (min)						
Training cases		174.0 ± 63.5	334.3 ± 79.1	162.7 ± 44.4	207.0 ± 70.0	197.1 (56.2)
Non-training cases		159.6 ± 59.5	255.7 ± 80.3	145.1 ± 60.4	181.9 ± 63.9	209.5 (47.1)
Median LOS, d (IQR)	3.0 (1.0–5.0)	1.0 (1.0–2.0)	7.5 (6.0–11.8)	4.0 (3.0–6.0)	3.0 (2.0–4.0)	4.0 (3.0–5.0)
Developed COVID-19, n (%)	4 (0.7)	0 (0)	3 (2.9)	1 (0.8)	0 (0)	0 (0)

EOT = estimated operating time; IQRg = interquartile range; LOS = length of stay; PN = partial nephrectomy; RC = radical cystectomy; RN = radical nephrectomy; RNU = radical nephroureterectomy; RP = radical prostatectomy; SD = standard deviation.

The coronavirus disease 2019 (COVID-19) pandemic has resulted in deferment of between 29% and 53% of genitourinary cancer surgeries globally [1]. Initial reports suggest that 30-d mortality among patients who contracted COVID-19 in the perioperative period was 23.8% [2]. Despite the catastrophic effects of COVID-19, it remains necessary to provide prompt cancer surgery with curative intent for selected patients.

International societies and national bodies have produced guidelines aimed at minimising the risk of contracting COVID-19 while balancing treatment options, although these recommendations have been based on limited evidence (Supplementary Table 1). The British Association of Urological Surgeons (BAUS) recommended deferring surgery for T1 kidney cancer and intermediate- and high-risk prostate cancer, and referring patients with muscle-invasive bladder cancer (MIBC) for radical radiotherapy over radical cystectomy (RC) [3]. Initial guidance from the Royal College of Surgeons (RCS) suggested that laparoscopy should not be used owing to the risk of aerosol formation [4]. The European Association of Urology (EAU) recommends that minimally invasive procedures should be performed by experienced surgeons, which would limit training opportunities [5]. As further peaks of COVID-19 infection are anticipated, we sought to explore the impact of recommendations in the context of surgery for major genitourinary (GU) malignancy to provide an evidence base for policy makers.

In this retrospective study, we report outcomes for major GU cancer operations, namely radical prostatectomy (RP), RC, radical nephrectomy (RN), partial nephrectomy (PN), and nephroureterectomy, performed at 13 UK major cancer referral centres between March 1 and May 6, 2020. Early in the study, all hospitals adopted standard perioperative assessments and precautions. The reduction in operations carried out was due to the deferment of cases deemed “less urgent” in view of the competing risk of contracting COVID-

19 as well as the requirement for nursing and medical staff to work in expanded intensive care units across the UK.

For patients undergoing surgery at hot sites, operations were performed in theatres purely reserved for elective non-COVID-19 patients, which in most cases, are in a separate area of the hospital away from patients admitted with COVID-19 infections. Postoperatively, patients were allocated to COVID-19-free wards (green zone) and swabs were taken for SARS-CoV-2 detection if there was a clinical suspicion of COVID-19. Additional COVID-19 safety precautions are described in the Supplementary material. Adherence to guidelines was variable between hospitals and the decision to perform surgery was based on risk assessment at a local level. Institutional review boards exempted this work from ethical approval as it represents an audit of clinical practice.

Patient and hospital characteristics recorded include age, American Society of Anesthesiologists (ASA) score (1, 2, ≥3), surgical approach (open, robotic, laparoscopic), hospital length of stay (LOS), and whether an operation was a training case, defined as a urology resident performing part or all of the operation. COVID-19 infection was defined as patients with a positive polymerase chain reaction swab or clinical features consistent with COVID-19 infection. The primary endpoint was 30-d all-cause mortality and COVID-19-related death.

We included 598 patients in the current analysis (Table 1, Supplementary Table 2). Figure 1 illustrates the weekly cumulative tally of operations performed across all sites. There was a notable decline in the number of operations when the UK-wide confirmed COVID-19 deaths peaked. Four patients (0.7%) developed COVID-19 postoperatively ($n = 3$ at hot sites; $n = 1$ at a cold site), of whom three were discharged from hospital and one remains an inpatient because of postoperative complications. There was no COVID-19-related mortality at 30 d. Two patients (0.3%; RC and PN) died from sepsis and multiorgan failure postoperatively which were

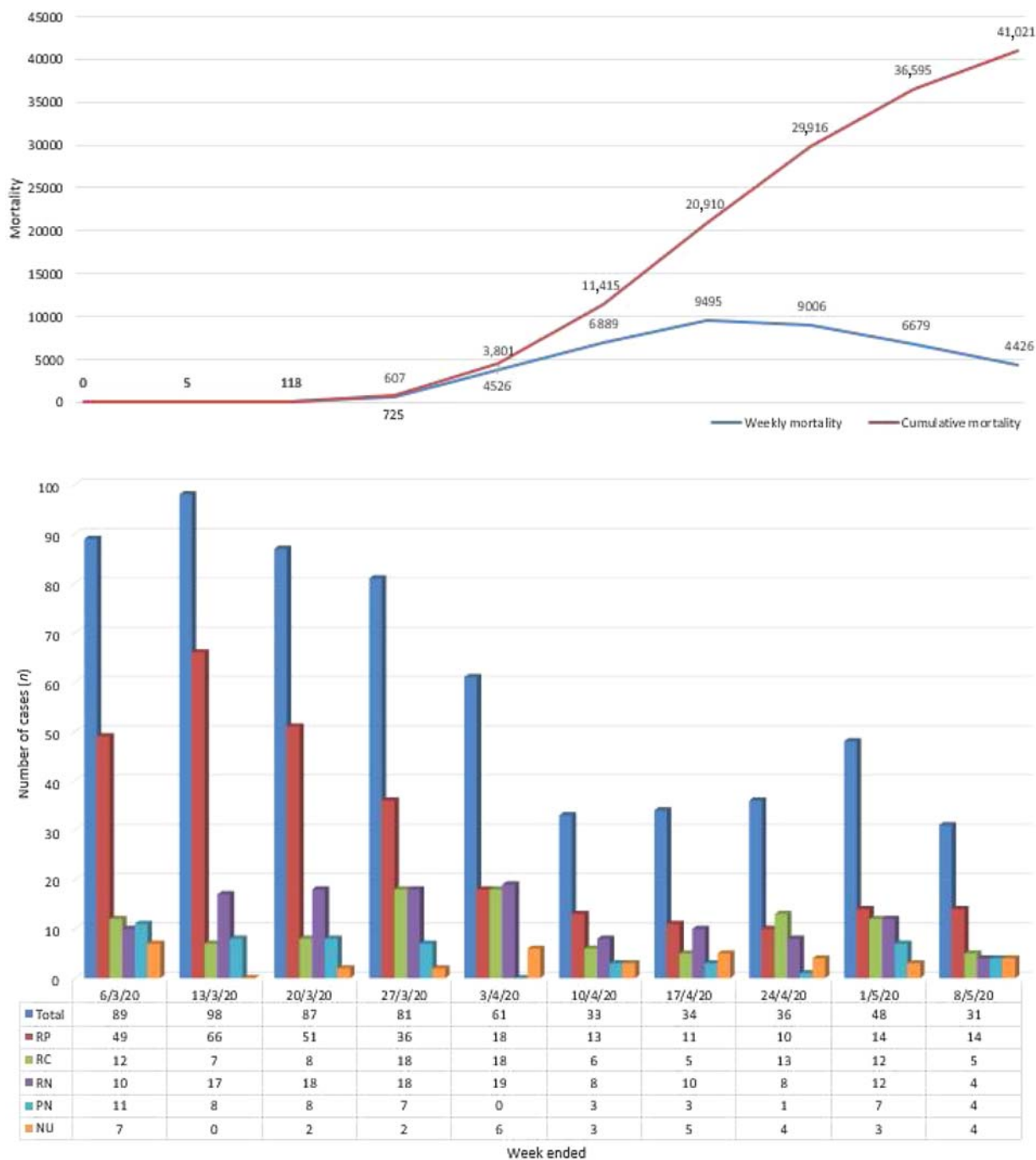


Fig. 1 – Number of weekly and cumulative UK COVID-19-related deaths and number of surgical operations performed on a weekly basis across all 13 hospitals. NU = nephroureterectomy; PN = partial nephrectomy; RC = radical cystectomy; RN = radical nephrectomy; RP = radical prostatectomy.

deemed not COVID-19-related. None of the medical teams who cared for the four patients who tested positive for COVID-19 developed the infection.

A minimally invasive approach was used in 499 cases (83.4%). A total of 228 cases (38.1%) were described as training procedures (Table 1). There was no significant association between training case status and higher ASA score ($p = 0.194$) or hospital LOS ($p > 0.05$ for all operation types). The patient risk of contracting COVID-19 was not associated with longer hospital LOS ($p = 0.146$), training

case status ($p = 0.588$), higher ASA score ($p = 0.295$), and type of hospital site ($p = 0.931$). The median operating time was longer for training cases than for non-training cases; however, with the exception of radical cystectomy ($p < 0.001$), there were no significant differences in mean operating time between the two groups (Table 1).

Our findings suggest that major GU cancer surgery can be safely performed if appropriate countermeasures are taken. We report no 30-d COVID-19-related mortality, with a minimal risk of contracting COVID-19 of 0.7%. While we

acknowledge that early reports suggest that patients who contract COVID-19 perioperatively have a high risk of mortality, our data suggest that the risk of COVID-19 infection is minimal with safety precautions [2]. In addition, training should be encouraged, as this had no impact on the risk of COVID-19 transmission and hospital LOS.

It is established that a delay in radical treatment for localised cancer carries the risk of disease progression to the point at which such treatment may no longer be curative [6,7]. Early in the pandemic, there was an emphasis on minimising the competing risk of death due to COVID-19 infection. Patients with cancer are often older, making them more susceptible to COVID-19. In the case of RC in particular, concerns about prolonged operating times, potential admission to the intensive care unit, and prolonged hospital stay increasing the risk of COVID-19 transmission appear to be unproven provided adequate precautions are taken (Supplementary material) [8].

Critics of surgery during the COVID-19 pandemic often cite alternatives such as radiation therapy. Radiotherapy with or without hormones is a valid alternative in the case of prostate cancer. However, there is a scarcity of data regarding the competing risk of COVID-19 transmission during attendance at a radiotherapy facility up to 37 times for treatment when compared to an overnight hospital admission. Furthermore, it has been reported that the requirement for androgen deprivation therapy increases cardiovascular risk [9]. In the case of RC, while selected MIBC patients experience a good outcome from bladder-sparing approaches, oncological equivalence cannot be guaranteed [10]. Our results suggest that a significant number of UK centres did not adhere to recommendations and continued to offer RC, probably because of oncological concerns regarding radiotherapy. For $\geq T2$ kidney cancer, surgery remains the only viable option. Equally important is patient choice, and patients often have a preference for one treatment over another. We believe that after proper counselling, referral for surgery should be an option for patients.

There is no doubt that COVID-19 has significantly impacted training. Our results suggest that cases performed by trainees under supervision have no bearing on the risk of COVID-19 transmission. Hence, our data support the continuance of training, particularly because COVID-19 transmission is likely to persist.

We acknowledge limitations of the study. The cohort described represents a well-selected patient group who were deemed suitable for surgery by their urologist following multidisciplinary team review during the COVID-19 pandemic. We have attempted to generalise our results to UK hospitals by performing a multicentre study, but acknowledge that our experience may not be generalisable to other countries. Finally, there remained variability over timing of the peak incidence of COVID-19 deaths across the country, although the peak for COVID-19 deaths experienced by each contributing hospital was captured during the study period.

Our results suggest that major surgery for urological cancers remains safe and that training should be encouraged

during the ongoing COVID-19 pandemic provided appropriate countermeasures are taken. These real-life data are important for policy-makers and clinicians when counselling patients during the current pandemic.

Author contributions: Wei Shen Tan had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Tan, Kelly.

Acquisition of data: Tan, Arianayagam, Khetrapal, Kearley, Fowler, Elajnaf, Voss, Al Kadhi, Noel, McKay, Abu-Nayla, Hill, Yousuf, Cooke, Chakravarti, Barod, Bex.

Analysis and interpretation of data: All authors.

Drafting of the manuscript: Tan, Kelly.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Tan.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: Kelly.

Other: None.

Financial disclosures: Wei Shen Tan certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: Wei Shen Tan is funded by the Urology Foundation.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.euros.2021.01.005>.

References

- [1] JY-C Teoh, Ong WLK, Gonzalez-Padilla D, et al. A global survey on the impact of COVID-19 on urological services. *Eur Urol* 2020;78:265–75. <http://dx.doi.org/10.1016/j.eururo.2020.05.025>.
- [2] COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet* 2020;396:27–38.
- [3] British Association of Urological Surgeons. About coronavirus & COVID-19. BAUSLondon, UK www.baus.org.uk/about/coronavirus_covid-19.aspx, 2020.
- [4] Royal College of Surgeons of England. Updated intercollegiate general surgery guidance on COVID-19. RCSLondon, UK www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v2, 2020.
- [5] Ribal MJ, Cornford P, Briganti A, et al. European Association of Urology Guidelines Office Rapid Reaction Group: an organisation-wide collaborative effort to adapt the European Association of Urology guidelines recommendations to the coronavirus disease 2019 era. *Eur Urol* 2020;78:21–8.
- [6] Cancer Research UK. Cancer statistics for the UK. Cancer Research UKLondon, UK www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk#heading-Zero, 2020.
- [7] Richards M. The national awareness and early diagnosis initiative in England: assembling the evidence. *Br J Cancer* 2009;101:S1.

- [8] Mossanen M, Krasnow RE, Zlatev DV, et al. Examining the relationship between complications and perioperative mortality following radical cystectomy: a population-based analysis. *BJU Int* 2019;124:40–6.
- [9] Levine GN, D'Amico AV, Berger P, et al. Androgen-deprivation therapy in prostate cancer and cardiovascular risk: a science advisory from the American Heart Association, American Cancer Society, and American Urological Association: endorsed by the American Society for Radiation Oncology. *Circulation* 2010;121:833–40.
- [10] Witjes JA, Lebre T, Compérat EM, et al. Updated 2016 EAU guidelines on muscle-invasive and metastatic bladder cancer. *Eur Urol* 2017;71:462–75.

^aDivision of Surgery and Interventional Science, University College London, London, UK

^bSpecialist Centre for Kidney Cancer, Royal Free London NHS Foundation Trust, London, UK

^cDepartment of Uro-Oncology, University College London Hospitals NHS Foundation Trust, London, UK

^dDepartment of Urology, Southmead Hospital, North Bristol NHS Trust, Bristol, UK

^eTranslational and Clinical Research Institute, Newcastle University Centre for Cancer, Newcastle University, Newcastle upon Tyne, UK

^fDepartment of Urology, Freeman Hospital, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK

^gDepartment of Urology, Leicester General Hospital, University Hospitals of Leicester NHS Trust, Leicester, UK

^hDepartment of Urology, Queen Alexandra Hospital, Portsmouth Hospital NHS Trust, Portsmouth, UK

ⁱDepartment of Urology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK

^jDepartment of Urology, Lister Hospital, East and North Hertfordshire NHS Trust, Stevenage, UK

^kSchool of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK

^lDepartment of Urology, Queen Elizabeth University Hospital, NHS Greater Glasgow and Clyde, Glasgow, UK

^mBeatson Institute for Cancer Research, Glasgow, UK

ⁿDepartment of Urology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

^oDepartment of Urology, University Hospital of Wales, Cardiff & Vale University Health Board, Cardiff, UK

^pDepartment of Urology, The James Cook University Hospital, South Tees Hospitals NHS Foundation Trust, Middlesbrough, UK

^qDepartment of Urology, New Cross Hospital, Royal Wolverhampton NHS Trust, Wolverhampton, UK

*Corresponding author. Division of Surgery and Interventional Science, University College London, 43–45 Foley Street, London W1W 7TY, UK. E-mail address: wei.tan@ucl.ac.uk (W.S. Tan).

[†]The other collaborators were Senthil Nathan, Tim Briggs, Ashwin Sridhar, Prasanna Sooriakumaran, Greg Shaw, Prabhakar Rajan, Anand Kelkar, Raj Pal, Salah Albuheissi, Jonathan Aning, Frank Keeley, Anthony Koupparis, Raj Persad, Tim Whittlestone, Naeem Soomro, Toby Page, Bahvan Rai, Mark Johnson, David Thomas, Edgar Paez, Rajan Veeratterapillay, David Rix, John Kilian Mellon, Roger Kockelbergh, Paul Butterworth, John Beatty, Ben Jackson, Richard Robinson, Lemke Solomon, Simon Wilkinson, Omer Karim, Mark Rochester, Robert Mills, Vivekanandan Kumar, Petre Ilie, Ben Pullar, Jim Adshead, Tim Lane, Lorenzo Dutto, Jaimin Bhatt, Abdullah Zreik, David Hendry, Khaver Qureshi, Nkem Umez-Eronini, Alexandra Colquhoun, Nimish Shah, Grant D. Stewart, Thomas Mitchell, James Armitage, Tev Aho, Antony Riddick, Keval Patel, Saiful Miah, Brian Chaplin, Simon Fulford, Raj Gowda, Ashok Sakhtivel, Maxine Tran, Prasad Patki, and Faiz Mumtaz.