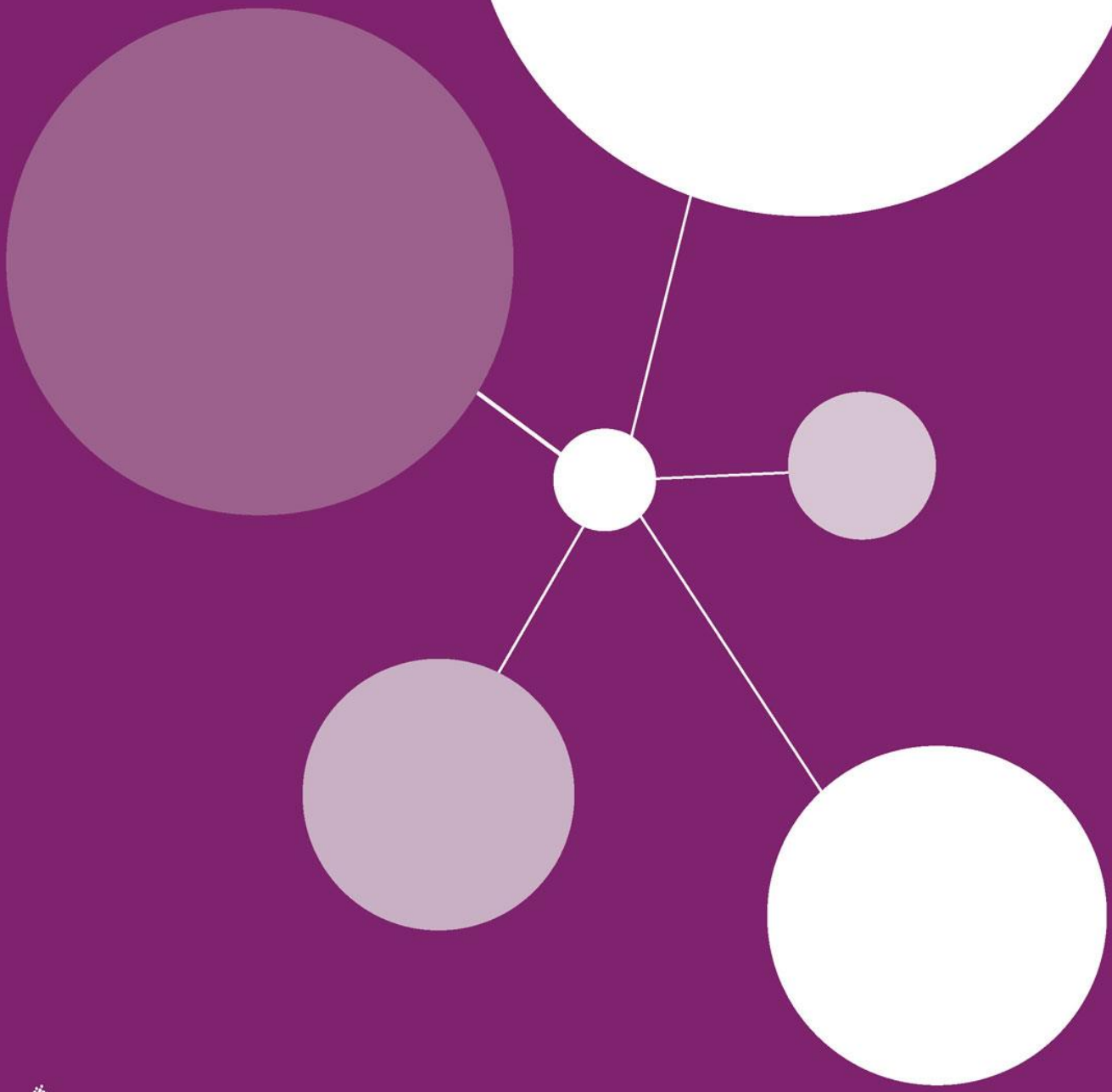
NCRI
National
Cancer
Research
Institute

NCRI Bladder & Renal Group

Annual Report 2018-19



Partners in cancer research

NCRI Bladder & Renal Cancer Group Annual Report 2018-19

1. Top 3 achievements in the reporting year

Achievement 1 A research portfolio across bladder and renal cancer that continues to deliver practice changing studies of international importance. A portfolio that is delivering recruitment for all stages of the diseases with activity across both surgical and non-surgical disciplines.
Achievement 2 Translational output of the highest quality (Tracerx – 3 synchronous Cell papers).
Achievement 3 Continued unification of the Group with a recent strategy meeting that succeeded in setting priorities across all our therapeutic areas. We have re-organised subgroups to better reflect activity and identified the need for working parties to build upon preliminary work by our consumer members that will identify research priorities where future activities will be focussed in areas of unmet need. Our membership has been strengthened to reflect these priorities.

2. Structure of the Group

Dr.Alison Birtle rotated off as Co-Chair of the Group this year. Dr Paul Nathan became Chair and Professor Rob Jones was appointed as Vice Chair of the Group and will succeed Dr Nathan as Chair in the future. Our patient representatives, Rose Woodward and Andrew Winterbottom, have both stepped down from the group. This was a major challenge as both had been exemplars of engaged innovative leaders. We have however made a number of strong appointments and have welcomed Alison Fielding, Salena Mulhere and Henry Scowcroft as consumer members. The Group is well placed to deliver on our strategy for the next reporting cycle. Our trainee representatives have made significant contributions to the group. Dr Sally Appleyard developed funding guidance which clarified funding sources and Dr Arabella Hunt has delivered a GAP analysis in bladder cancer.

We are simplifying the subgroup structure: Bladder cancer and Renal cancer will each have local and systemic treatment subgroups. The Penile Subgroup continues unchanged. We are establishing two working parties: a translational working party and a patient priority working party. The expected outputs from these groups are described below.

The group was deeply saddened to learn of Andrew Winterbottom's death in May 2019. His contribution to bladder cancer research and patient advocacy in research and beyond was immeasurable.

3. Group & Subgroup strategies

Bladder & Renal Group

This report describes:

1. **Our areas of activity during the 2018-2019 reporting year alongside the strategic aims identified in last year's report.**
2. **Our strategic aims following a recent strategy review meeting that has set our priorities for the next reporting cycle.**

1. Strategic Aims and Associated Activity 2018-2019

Develop an increased academic portfolio of high quality interventional systemic treatment studies in RCC The CSG has succeeded in designing and initiating trials that are actively recruiting in the neoadjuvant, adjuvant and advanced disease RCC setting. NAXIVA is investigating the effect of neoadjuvant axitinib in patients having surgery for locally advanced disease involving the IVC. The CSG-designed RAMPART adjuvant IO RCC trial started recruiting in July 2018. PRISM, a randomised phase II study evaluating an alternative combination IO ipi/nivo schedule vs standard schedule is recruiting ahead of forecast. A pipeline of successor studies is in development.
Assess the feasibility of a screening programme for early RCC in higher risk individuals The cost effectiveness analysis work has been completed and submitted for publication. This confirmed that it is likely to be cost effective to screen males (50-70y) and may be cost effective to screen both males and females. Mr Grant Stewart and colleagues at the University of Cambridge, with support of several members of the CSG are developing a programme of research to further evaluate screening for RCC. This includes a feasibility study of recruitment to a screening study prior to a full randomised clinical trial. Targeted screening strategies in identifiable high-risk groups will also be evaluated.
Offer as broad a research portfolio as possible through development of high quality competitive trials suitable for every patient The CSG has an extensive active portfolio of clinical trials across all stages of disease in both bladder and renal cancer. We realise however that there are a significant group of patients who are ineligible for current interventional studies. Our strategy meeting identified planned initiatives to broaden activity that are described in our plans for the reporting period ahead.

Continued liaison with key organisations internationally and nationally

The CSG has highly active relationships with key organisations. CSG members are frequently involved in NICE assessments and are increasingly active in developing a partnership with BAUS to maximise recruitment to clinical trials. A number of CSG members have key relationships with pharma that have enabled and encouraged partnership and development of both pharma sponsored and pharma supported academic clinical trials onto the national portfolio. Members of the Group have been founder members of the new rare urothelial cancers group of the International Rare Cancers Initiative (IRCI), and the Penile Subgroup is an active participant in the penile group of IRCI. During this period the Bladder Group has begun a collaboration with a Canadian group to run adjuvant immunotherapy in bladder cancer, and plans for international collaboration with EORTC, Canadian and Australasian investigators in the planned POUT2 trial (upper tract urothelial cancer) are already advanced.

Foster new investigators via CSG and subgroups

Each of our subgroups are vibrant, active and are designed to foster an environment where new investigators at the beginning of their careers can take advantage of an opportunity where their ideas can be tested and where they can obtain support from senior investigators. Trainee members have been active in identifying portfolio gaps in bladder cancer research and in developing new research ideas with more senior members of the groups.

Engage new investigators by offering pragmatic studies to run in cancer units balancing biomarker directed systemic therapy studies

A large number of investigators both experienced and inexperienced contribute to the Groups portfolio activity. Feedback from NIHR research leads suggests a need for simple, pragmatic trials in addition to more complex trials which are more suitable in major cancer centres. Although funding is not yet secured, there are clear plans for such a trial in the surgical management of non-muscle invasive bladder cancer, and an oncological trial of adjuvant therapy in upper tract urological cancer. These trials play to one of the UK's key strengths in delivering practice-changing pragmatic cancer trials. We also recognise the need for a broadening of our activity to include qualitative and semi-qualitative research. This will expand the scope of the research questions we are addressing and enable a greater breadth of investigators to be involved in portfolio studies. This initiative is described below in our forthcoming plans.

Ensure consumer engagement is paramount

The CSG has been fortunate to benefit from highly talented consumers (Rose Woodward and Andrew Winterbottom) who have led novel initiatives that have resulted in exceptional engagement of Bladder and Renal cancer patients with the research community and CSG. The CSG has been fortunate to recruit new consumer leads who, as part of our strategy for the forthcoming reporting period, have started to define areas of consumer priority that will direct CSG activity according to our new strategy for the forthcoming period described below. Our goal is to take consumer input beyond reactive involvement in research proposed by clinicians to a leading role in setting the future research agenda in this area.

Highlight areas of unmet need

Our strategy day identified areas in translational research, patient experience and screening in addition to the obvious area of finding new therapies for disease that is refractory to current treatment. Our patient groups have conducted gap analyses in both bladder and renal cancers.

Use tissue biorepositories

TRACERx Renal continues to be a rich resource for translational research excellence as denoted by 3 papers in Cell in this reporting year. The SOPs developed in TRACERx and other translational strategies such as SCOTRRCC are now being utilised in other clinical trials (i.e. EASE, TransRAMPART, WIRE) to enable harmonised RCC translational work. In bladder cancer, analyses of samples from LAMB have allowed continued hypothesis development for its successor trial, ATLANTIS. As ATLANTIS continues to recruit, we are now collating further genomic data to augment the collection from LAMB. Together, these collections are providing translationally led hypotheses that are being tested in new biomarker driven arms of this adaptive design trial. This has proven a highly attractive feature when engaging with new pharma partners as we can rapidly offer bespoke data from prior patients to support the design of new arms of the study in what has become an iterative process.

The CSG recognises the need to ensure that the highest quality information is gathered from the translational material from our clinical trial activity. We have identified an initiative that focuses on this area in our forthcoming strategy outlined below.

2. Strategic Aims 2019 – 2022

At our 2019 Strategy Day it was agreed that our overall aim will be:

Developing the highest quality clinical and translational research portfolio that integrates patient led priorities, improves patient outcomes and gives new insights into the diseases we treat.

We identified 5 areas that we wish to focus on to deliver this challenge.

1. Engaging with patients and the public in setting the research agenda

The CSG agreed that we should work to ensure that those areas of priority to our patients are reflected in our research development portfolio.

Our Bladder and Renal Group cancer patient representatives (Alison Fielding, Salena Mulhere, Henry Scowcroft) together with our trainee Dr.Arabella Hunt, are building upon an RCC patient RCC gap analysis (led by CSG members Mr Grant Stewart Dr Janet Brown and their teams in Cambridge and Sheffield) to identify patient priorities for research in both bladder cancer and renal cancer.

Preliminary conclusions indicate that patients want research to reveal a greater understanding of disease biology that will lead to novel treatments; develop improved screening, surveillance and diagnostic methods; and identify optimal sequences of treatments. These observations require substantiating in larger studies with broader engagement. We will therefore establish a Patient Priority Working Group to deliver a more data-led robust understanding of patient priorities. These will then instruct initiatives to ensure consumer priorities are reflected in the portfolio.

We are aware that there are many patients who are excluded from interventional clinical trials, frequently due to their co-morbidities or due to resource limitations at their treating centre. There are many issues regarding patient experience before, during and after treatment that we need to understand better. The patient priority working party will develop a program of qualitative research that aims to improve access to clinical trials for the majority of patients who are not able to contribute to current interventional studies.

2. Translational Science

It is a priority for the CSG to ensure that we learn as much as possible from our clinical trial activity about the biology of the diseases we treat as well as the mechanisms of efficacy and toxicity of our treatments. We wish to avoid translational work that pays lip service to the expectation that clinical research requires a translational component. The reality is that a range of pre-clinical expertise will be required across our portfolio and that the breadth of skills required will not be reflected by the CSG membership. We therefore wish to establish a Translational Working Party led by Dr Samra Turajlic that will identify a network of high quality translational scientists working in areas relevant to bladder and renal cancer pre-clinical research. This resource will ensure that relevant pre-clinical scientists are invited to contribute to projects in development at the earliest possible stage. The Working Group will also develop a generic component for trial consent forms, influenced by Dr Turajlic's experience with the TraceRx and PEACE studies, that will ensure future-proofing for biological samples and data generated from our trial activity.

3. Local Treatments

The CSG will be reorganised to have Bladder and Renal Local Treatment Subgroups. These will replace the current Bladder T2 & Below (TABS) and the Renal Surgical Subgroup. They will support study development with surgical and non-surgical local treatments including radiotherapy and other modalities such as RFA and cryotherapy. This clarifies the activities of the subgroups. Local treatments often provide rich opportunity for translational work given that acquisition of tumour material is frequently a standard of care. The membership of each local treatment subgroup will be reviewed to ensure that a translational scientist is a group member.

We believe there is opportunity for the many patients in the country who undergo surgical procedures and who are not eligible for studies on our interventional clinical trial portfolio to contribute to our understanding of their experiences through qualitative and semi-quantitative research. The local treatment subgroups will therefore explore whether there are opportunities with BAUS to develop studies that are relevant for a wider population of patients and the patient priority working party will develop activity in this area.

4. Radiotherapy

Radiotherapy is a mainstay of treatment for many bladder cancer patients. Efficacy needs to continue to be increased and toxicity decreased. Radiotherapy increasingly dovetails with other therapeutic modalities, and with the advent of new systemic therapies the role of combination systemic treatment and radiotherapy needs to be developed. The UK has led the world in the field of chemoradiotherapy in bladder cancer, and we intend to build on this success. The CSG prioritises delivery of radiotherapy research in these areas and therefore will ensure clinical oncology expertise within our local and systemic treatment subgroups in bladder and RCC.

We will develop studies that a) continue to refine methodology with highly technical radiotherapy b) are pragmatic ensuring improvement of radiotherapy regimes that are current standards of care c) explore radiotherapy in combination with systemic treatments and d) address areas of high unmet clinical need including management of brain metastases.

5. Systemic Treatment

The Advanced Bladder Cancer Subgroup has been renamed to the Bladder Systemic Treatment Subgroup and, along with the Renal Cancer Systemic Treatments Subgroup, leads our development of novel systemic therapies and combinations in both diseases. Both groups are productive, have successfully developed potentially practice changing clinical trials that are on the portfolio and meet regularly. We plan to build upon this success with continued development of studies with new agents in areas of unmet clinical need. We also recognise the importance of development of predictive biomarkers of response and toxicity and will ensure activity in this area alongside our interventional studies. We wish to widen access to interventional clinical trials by developing more pragmatic studies that are deliverable in all centres across the network enabling access for a wider patient population.

Advanced Bladder Cancer Subgroup – To be renamed Bladder Cancer Systemic Treatment Subgroup (Chair, Professor Syed Hussain)

Optimise systemic therapy by developing new drug hypotheses to test in MIBC

Efficient delivery of proof of concept studies in advanced disease exemplified by the development of the ATLANTIS precision medicine platform in the maintenance therapy setting (co-CIs Rob Jones & Thomas Powles). New biomarker driven randomised cohorts are being added into this multi arm study successfully, each with a named lead investigator (Rob Jones, Tom Powles, Simon Crabb, Syed Hussain). As the trial develops, we hope to engage with young investigators in this role. Increasing number of centres (currently 29) are recruiting into this national trial.

The subgroups strategy is to use ATLANTIS to identify new drug signals before developing those signals in the neoadjuvant setting: the setting where the UK previously demonstrated that systemic therapy can improve the cure rate for muscle invasive bladder cancer.

Working towards options of trials of neoadjuvant therapy through successful recruitment in studies in this clinical setting. NeoBlade trial (CI Syed Hussain) and ABACUS (CI Thomas Powles) completed recruitment successfully in 2018. Current examples of recruiting trials include SPIRE (CI Simon Crabb). Current example of study in development in neo-adjuvant setting is GUSTO (CI James Catto, CO-I Simon Crabb, Syed Hussain). This is a phase 2 RCT evaluating the use of genomic profiling in guiding neoadjuvant treatments currently under review (at the Urothelial Cancer NIHR-EME call). The trial, if funded, will investigate real time genomic profiling by randomising 320 patients to either standard care (neoadjuvant chemotherapy and radical cystectomy) or genome stratified care.

Working in collaboration with industry to deliver high quality trials of novel agents in areas of unmet need. In addition to the multiple examples on which we have published (e.g., LaMB, PLUTO; TOUCAN; SUCCINCT; TOTEM; FIESTA) and examples of studies recently completed recruitment successfully include NeoBlade, ABACUS. Current examples of trials in recruitment include ATLANTIS, SPIRE.

We have further trials in development involving collaborations with pharma partners.

- RADio study is combining Durvalumab with Mitomycn C and 5-FU concurrent with radiotherapy (CI Nick James, CO-I Syed Hussain & Maria De Santis)
- EARL trial: A randomised phase II trial of enhancement of efficacy of atezolizumab by radiotherapy in metastatic urothelial cancer (CI Robert Huddart)
- Gareth Griffiths submitted an EOI to create a new Working Group within International Rare Cancer Initiative (IRCI) in non-TCC of the bladder on behalf of the CSG and within it proposed a randomised phase II study utilising IO.
- POUT2. Building on the success of POUT, a further randomised phase III trial investigating the role of IO when added to adjuvant chemotherapy in upper tract urothelial cancer. This trial is also under discussion within the IRCI collaboration with several international parties wishing to take part.

Delivery of potentially practice changing studies Implementing POUT, the first ever randomised phase III trial of adjuvant therapy in upper tract TCC. Trial is in development of a successor study POUT 2
Develop larger translational research programmes Utilisation of the ATLANTIS sample sets to allow generation of data on biomarker rates to facilitate new hypotheses to include in the new comparisons within ATLANTIS and other trials. Developing biomarkers of response utilising BC2001 trial sample set. Entry of bladder cancer patients into the 100,000 Genomes Project and going forward to begin analyses of data emerging from this project. Coordination of a collaborative approach to utilisation of samples sets from the Subgroup's prior and ongoing studies.

Penile Subgroup (Chair, Dr Vincent Khoo)

Develop practice changing trials and optimise current practice procedures.

The past year has been successful with the completion of several clinical studies, maintaining an international randomised phase III trial and further development of new potential studies in this rare cancer entity. We are also pleased to welcome David Wilkinson as our new consumer representative to join Neil Walker.

In the evaluation of penile nodal disease pre-surgery, two studies have been completed.
The first study aims to assess the use of MRI-PET for inguinal nodal staging (Asif Muneer). This study has completed recruitment of 46 cases for impalpable disease and 26 cases for palpable inguinal disease. The results are currently being analysed.
The second study aims to assess the feasibility of Sentimag®/Sienna+® injection for detecting Inguinal Sentinel Node involvement in penile cancer compared to standard of care (SOC) radioactive nanocolloid (Vijay Sangar). This study has also completed recruitment. The preliminary results report good concordance of Sienna with SOC agents which permits this technique to be considered for routine practice and allow units without nuclear medicine facilities to undertake sentinel node biopsy in penile cancers. An abstract is in preparation for 2019.

In the management of morbidity post-inguinal surgery, a randomised controlled phase II study is exploring funding opportunities to assess the efficacy of low-intensity shock wave therapy post inguinal lymph node dissection to lower surgical complications (VS).

In the management of radical penile cancer, the InPACT trial which is a randomised Phase III International Penile Advanced Cancer Trial supported by the International Rare Cancer Initiative, continues to recruit. This trial is ambitious and complex addressing several aspects in the radical management of penile surgery and radiotherapy/chemotherapy. The InPACT trial continues to recruit slowly but steadily worldwide in USA, Europe, Canada and Australia. Involvement of other countries in South America are being explored. In the UK, 4 of 6 centres are open. At the end of 2018, 16/400 patients have been recruited. It is part of the International Rare Cancers Initiative.

In the management of advanced penile cancer, one study (VinCaP) has been fully completed. The VinCaP study was a multi-centre Phase II trial of Vinflunine chemotherapy in locally-advanced and metastatic carcinoma of the penis that reported a clinical benefit rate (CBR) of 45.5% with an objective response rate of 35.5%. This study was awarded both an ASCO GU and ASCO presentation (LP). This study has been written up and will be submitted shortly (SN). Another industry supported study is being developed by AB. This phase II trial of standard of care (SOC) chemotherapy in combination with Immunotherapy (cemiplimab) in locally advanced or metastatic penile carcinoma follows the VinCaP trial design. This study is being finalised and is aimed to open at the end of 2019.

The other strategic plans of the penile subgroup include providing representation from research active penile groups nationally, ensuring efficient communication and information flow to local penile teams, to enable adequate patient advocate representation and to develop and maintain international collaboration for new clinical studies.

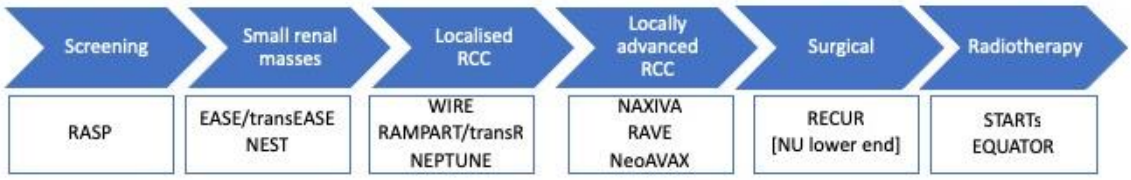
Surgical Subgroup – To be renamed Renal Cancer Local Treatment Subgroup (Chair, Mr Grant Stewart)

Engage with BAUS and BAUS Oncology on promotion of their new trials

BAUS, via President Elect Tim O'Brian, and BAUS Oncology, via Section Chair Ben Challacombe, have pledged to increase their level of support of RCC trials. BAUS have started to allow emails detailing new clinical trials in the field to be circulated e.g. RAMPART. This engagement has allowed new sites to be identified and for surgeons to be educated in the nuances of recruitment of patients within their clinics which is often new to them. The BAUS Nephrectomy Audit will this year evaluate UK cytoreductive nephrectomy practice, there is interest in development of a cytoreductive nephrectomy clinical trial using the evidence from this audit. As such, it is anticipated that there will be greater collaboration between BAUS and CSG in the future.

Develop a range of surgery and radiotherapy relevant studies across all stages of renal cancer i.e. from screening to metastatic disease.

This aim is being achieved as demonstrated in the chart below of clinical studies that are recruiting or in development via the subgroup. This is in contrast to the situation in 2015 where there were 0 surgical trials available.



Deliver and complete feasibility studies in contentious areas to prove recruitment can be achieved

There is international interest in the optimal management of small renal cancers. The NEST study (CI-Miss Maxine Tran) will start recruitment in Q2 2019. This cohort embedded study will evaluate feasibility of randomising patients to ablation or surgery for management of small renal cancers. Initially this will be a single centre study (at Royal Free Hospital, London) with the UK's largest renal cancer practice, as such the ideal centre to determine feasibility.

Dr Vincent Khoo is developing a protocol (EQUATOR), in conjunction with surgeon colleagues, to evaluate stereotactic radiosurgery for oligometastatic RCC. As part of the development of this study Dr Khoo has undertaken extensive scoping of feasibility of delivery be engaging with colleagues across the UK.

Liaise with oncologists for neoadjuvant trials

Surgical Subgroup members have led the development of a range of neoadjuvant trials in close collaboration with oncology colleagues.

1. NEOAVAX: Neoadjuvant axitinib+avelumab in localised RCC (CI-Mr Axel Bex; recruiting)

2. NAXIVA: Neoadjuvant axitinib in patients with IVC tumour thrombi (CI-Mr Grant Stewart; recruiting)
3. WIRE: Window-of-opportunity platform for novel drug combinations in surgical RCC patients (CI-Mr Grant Stewart; IRAS submission stage)
4. RAVE: TKI loaded embolization beads for selective embolization of patients with locally advanced RCC prior to surgery with the aim of assessing the immune stimulation following this process (CI-Prof David Nicol; protocol development)

Systemic Treatments Subgroup – To be renamed Renal Cancer Systemic Treatment Subgroup (Chair, Dr Naveen Vasudev)

Generate internationally competitive trials for all patients with advanced disease

The treatment landscape in patients with metastatic RCC (mRCC) continues to evolve rapidly, presenting opportunities and challenges in study development.

1) The potentially practice-changing PRISM trial, examining alternative scheduling of combination ipilimumab plus nivolumab, has been highly successful, with recruitment ahead of target and is an exemplar of developing the right study at the right time.
2) What to do following failure on IO is a key question and the group have successfully developed the CAPER trial (led by Dr Tom Waddell) that is currently in set-up, exploring the addition of cyclophosphamide to pembrolizumab following IO failure.
3) There is a significant unmet need for better treatment options for patients with non-clear cell RCC and this is a focus for the group moving forwards.

Develop a multi-arm platform second-line study

This is an ambitious but important strategic aim for the group. The past year has seen significant progress in the development of this concept (led by Dr Stefan Symeonides) with an intention to explore biomarker-driven stratification and would be internationally competitive. Study design has been agreed and initial arms have been identified

Develop high quality translational biobanks

No biomarkers are in routine clinical use in patients with RCC. The establishment of high quality sample banks in the context of a changing treatment landscape is a priority.

1) The TRIBE study (led by Dr Fiona Thistlethwaite) is a biomarker driven study to understand the influence of VEGF TKI on the immune environment prior to starting IO.
2) A pilot study (led by Dr Natalie Charnley) exploring the potential for PET as an early biomarker of response to nivolumab has recently opened to recruitment.

3) PRISM incorporates a robust translational component, with longitudinal sample collection strengthened by collaboration for incorporation of cfDNA with Dr Samra Turajlic at the Crick Institute.

4) The NIHR funded, portfolio adopted, multi-centre prospective RCC Biobank study represents a tremendous UK resource for diagnostic and prognostic biomarker studies, with collection of blood and tissue from >700 patients with newly diagnosed suspected RCC. The first manuscript from this study has recently been submitted for publication to Eur Urol Oncol.

Having a talented ambitious group membership consisting of experienced and lesser experienced investigators

The group's membership has continued to expand over the past twelve months, with involvement of a consumer member (Salena Mulhere), a trainee member (Dr Manon Pillai) and other medical oncologists with broad representation from across the UK. The group maintains a balance of experienced members who are able to support and nurture more junior members, as exemplified by the number of new CIs currently leading their own studies. The group continues to engage by monthly hour-long teleconferences.

T2 & Below (TABS) Subgroup – To be renamed Bladder Cancer Local Treatment Subgroup (Chair, Mr Param Mariappan)

Enhance the outcomes of patients with high risk NMIBC (HR-NMIBC)

The TABS subgroup aspires to have 'a study for every patient' – with the vast majority of cancers being within the surgical remit. Our strategy includes enhancing engagement with urologists in pragmatic trial development by emulating trials like PHOTO and HIVEC II.

Whilst intravesical BCG remains the Standard of Care (SoC) in HR-NMIBC, recent threats of global shortage and the need to embrace stratified medicine consequent to heterogeneity, several avenues have been explored.

The strongly supported HIVEC III proposal (Heated Mitomycin V BCG) failed to receive funding from the HTA and industry. The lessons learnt have now helped the team (with support from ICR-CTSU) explore a MAMS-style trial allowing for several experimental arms (novel and future) to be evaluated against SoC while ensuring a pragmatic approach.

There are several industry-driven I/O trials in HR-NMIBC where UK centres have opened to recruitment recently:
(a) POTOMAC - phase 3 RCT evaluating the safety and efficacy of Durvalumab+BCG V BCG.
(b) CheckMate 9UT - Nivolumab Vs Nivolumab+experimental medication (BMS-986205) +/- BCG in BCG un-responsive HR-NMIBC.

Trials in development - En-Bloc TURBT V standard TURBT could reduce the risk of recurrence and improve staging - CSG has given recommendations and awaits further details.

Develop improved bladder sparing approaches in muscle invasive bladder disease

The recent call from the EME programme for studies in Urothelial Carcinoma (UC) was discussed by TABS and proposals for 4 studies were submitted.

GUSTO, a randomised phase 2 trial employing stratified medicine in MIBC by identifying patients suitable for neo-adjuvant chemotherapy and/ or I/O prior to radical surgery or radiotherapy on the basis of genomics has been successful through the first stage of the selection process. Consequent to the recognition that not all MIBC patients respond to the standard-of-care neo-adjuvant chemotherapy, the trial is designed to introduce targeted treatment based on translational work demonstrating that tumours which are of basal-type are likely to respond to neo-adjuvant chemo while luminal-type tumours might respond to I/O.

The Bladder & Radiotherapy workshop in 2018 revealed a desire for 'platform type trials' as the preferred model and to evaluate radiotherapy in MIBC alongside biomarkers. Hypoxia markers were felt to be the most relevant - following submission to the EME, the team from The Christie are applying to the NIHR to fund development of the biomarker before re-submission for clinical trial funding.

The RAIDER trial (Phase 2 RCT comparing adaptive image-guided standard radiotherapy V dose escalated tumour boost) is expected to complete recruitment soon.

Work with the Systemic Treatments Renal Cancer Working Party Strategy to improve neo-adjuvant, concomitant and adjuvant therapies for patients with invasive urothelial cancer

The hugely successful POUT trial is to be published soon, representing a good example of surgical and oncological collaboration in the Urothelial Carcinoma - a successor trial proposal is currently under review by CRUK CRC and an industry partner. The trial has been accepted into the portfolio of the newly formed IRCI group on rare urothelial cancers, with interest for collaboration from Australasia and Europe.

NEOBLADE, a phase 2 UK RCT of neoadjuvant treatment (comparison between Gem-Cis neoadjuvant chemotherapy and combination of chemotherapy and the Tyrosine Kinase Inhibitor, Nintedanib in MIBC) was supported by the CSG and we are pleased to note has closed to recruitment in 2018.

There are several industry-driven I/O trials in MIBC where UK centres have opened to recruitment recently/ in setup:
(a) NIAGARA - Phase 3 global RCT evaluating efficacy and safety of combined neoadjuvant Gem-Cis chemotherapy and Durvalumab with adjuvant Durvalumab V neoadjuvant Gem-Cis chemotherapy alone prior to radical surgery.
(b) CheckMate 274 - phase 3 RCT evaluating DFS following adjuvant treatment with Nivolumab V placebo in patients with high risk of recurrence following radical surgery for bladder or upper tract urothelial carcinoma.

Trials in development that were presented to the CSG - evaluation of Urinary Derived Lymphocytes (UDLs) as surrogates of the bladder immune TME could be used to predict response to IO drugs and prognosis - CSG was supportive and has sought more details of the proposal.

Seek to understand better and then improve, factors that impact on patient quality of life and experience of bladder cancer treatment

The Life in Bladder Cancer study, funded by Yorkshire Cancer Research is evaluating the QoL in patients diagnosed with bladder cancer over the past 10 years using a questionnaire - recruitment is good following recent protocol amendments. Likewise, the Q-ABC study, evaluating QoL in patients undergoing treatment for MIBC, supported by the CSG and developed by a trainee member opened to recruitment in 2018.

TABS have felt that Bio-marker development is essential to replace QoL-affecting surveillance cystoscopy - a proposal was submitted following the EME call. This proposal was based on the UroMark and AmpseqUR urine-based tests with high levels of accuracy - unfortunately the submission was unsuccessful, and feedback will be shared with the CSG. Nonetheless, DETECT II trial (using UroMark) should be completing recruitment soon.

The TABS members have been working on the research gap analysis for the Strategy Day meeting in May 2019. Support was received from the epidemiological researchers at KCL who have already performed the gap analysis using input from BAUS, BUG, charities and patient representatives. The TABS trainee member (with a mentor CSG member) have been tasked to produce the details of the research gaps prior to the next TC on the 5th April 2019.

4. Task groups/Working parties

The Bladder & Renal Cancer Group had no task groups or working parties during the reporting year.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)					
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**
May 2018					
Tracking urine derived lymphocytes (UDLs) in predicting response and resistance to immunotherapy in bladder cancer	Biomarker Project Award	Dr Sergio Quezada	Not Supported	Support solicited prior to grant application. Presented at group meeting.	
TransRAMPART: Renal Adjuvant MultiPle Arm Randomised Trial – translational	Sample Collection	Dr Angela Meade	(Preliminary – invited to resubmit)	Developed with multiple members of the surgical subgroup and main CSG. Resubmitted to CRC, decision awaited May 2019	535,000
November 2018					
A randomised phase II trial assessing trimodality therapy with or without adjuvant durvalumab to treat patients with muscle-invasive bladder cancer	Clinical Trial Award - Endorsement	Professor Gareth Griffiths/ Prof Rob Jones	Endorsed. Industry partner subsequently withdrew support.	Developed by the advanced disease subgroup.	
Risk stratification biomarkers in Wilms tumour	Biomarker Project Award	Professor Kathy Pritchard-Jones	Not Supported		
Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**

6. Consumer involvement

The 2018/19 consumer team of Henry Scowcroft for Bladder and Alison Fielding and Salena Mulhere for RCC were newly recruited in the summer of 2018 and have a background of both being a patient and a partner of someone with cancer. Each also brings a useful background of knowledge and contacts gained from their work with Cancer Research UK and the Kidney Cancer Support Network. They have spent the first year getting up to date with the group priorities and in the UK research environment. Henry sits on both Bladder Subgroups (TABS and Advanced bladder cancer), Alison on the Renal Surgical Subgroup and Salena on the Systemic Therapy Subgroup.

One joint piece of work has been to help ensure the Group's strategy is aligned to the priorities of patients and consumers. This involved collation of previous research, incorporating the 'Living with and beyond cancer' NCRI James Lind Alliance Priorities, identifying possible gaps, and seeking wider input from the relevant communities. Initial results from an online survey of people affected by both bladder and kidney cancer were presented at the Group's Strategy Away Day in May 2019, and helped shape discussions around future priorities.

Each has also engaged in particular projects to further the Group's work programme.

Henry Scowcroft has fed into the funding submission on the Re-ARM and Durance studies, including both the patient information leaflet and study design, and has been invited to participate in POUT2. The Re-ARM study proposal subsequently received positive comments at CRUK's committee. He has also been developing links with Fight Bladder Cancer, and research groups at Kings College London, Birmingham and UCL, and facilitated dialogue between Fight Bladder Cancer and CRUK with the aim of future collaboration in the areas of policy, early diagnosis and research prioritisation. His role at CRUK has also enabled him to provide useful contacts in basic science and primary care research which have the potential to enrich the CSG work.

Alison Fielding spoke at the NCRI Conference in the co-morbidities session. This has high relevance to the Group particularly due to the common risk factors of smoking and obesity for bladder and kidney cancer alongside heart disease, diabetes and COPD. The toxicity profile of TKIs and Immunotherapies means that the Group and its consumer representatives wish to keep a focus on how best to minimise harms and improve quality of life. Alison has also contributed to the development of the NAXIVA and WiRE trials.

Salena Mulhere is collaborating with the University of Surrey on the development and co-design of a Patient Reported Outcome Measure (PROM) to assess adverse events in people with renal and melanoma cancers treated with immunotherapy, which is currently being considered by the NIHR Research for Patient Benefit programme and the Macmillan Scientific Research Committee. Salena is also a member of the Trial Management Group for the RAMPART trial and providing support with the development of patient focused communications.

The team are looking forward to engaging further with clinical colleagues in future to influence study design at an early stage and support patient enrolment.

7. Priorities and challenges for the forthcoming year

Priority 1

Engaging with patients and the public in setting the research agenda

It is increasingly essential to demonstrate patient involvement beyond simple tick box exercise in order to secure new research funding. Building on the work of previous consumer members, our new team will work to broaden PPI engagement and to find new ways of setting the research agenda for the future.

Priority 2

Translational science

Gap analyses reveal how important it is to better understand the diseases we seek to treat. The group has already strengthened its membership to reflect this activity, and we seek to strengthen it still further in the coming year.

Priority 3

To develop new pragmatic trials which can be run in all research active hospitals. POUT2 and a new trial in non-muscle invasive bladder cancer are key priorities this year.

Challenge 1

Funding. It is becoming increasingly difficult to obtain research funding for high quality, academically sponsored trials. In particular, the funding streams around tissue collections and translational research have become harder to access as seen by the premature withdrawal of funding for the translational sub study underpinned by the practice-changing POUT trial.

Challenge 2

Increasing difficulties with trial delivery in within the NHS. In England and the devolved states, resources to support trial participation are growing ever thinner. As the regulatory and protocol demands continue to expand, this poses a major threat to our ability to deliver practice changing trials in a timely manner.

Challenge 3

Continued development of the group since integration. We believe that the group has made significant progress in this direction, but, as very few clinicians treat any two or more of the three disease covered in our remit, it will remain a constant challenge to draw these three disparate research areas together in a way that continues to drive the research agenda for all.

8. Collaborative partnership studies with industry

The Group has a strong recent track-record of engagement with the pharmaceutical industry. Ongoing examples of collaboration include the RAMPART trial of adjuvant immunotherapy in renal cancer (AstraZeneca), the presurgical renal cancer study NAXIVA (Pfizer), and the ATLANTIS signal-searching molecular platform trial in urothelial cancer (Exilixis, Astellas, Clovis). Recent successes include the completion of the neoadjuvant bladder cancer trial ABACUS (Roche). The POUT2 trial is in advanced discussions with a major pharma partner (withheld for confidentiality reasons), and the advanced disease subgroup (bladder) is also negotiating with new partners for future cohorts within ATLANTIS. The systemic therapies subgroup (renal) is developing a similar platform phase II study which will enable multiple industry partners to participate with several partners already in advanced discussion.

The Group's portfolio reflects a healthy balance of industry-sponsored and investigator sponsored clinical trials.

9. Appendices

Appendix 1 - Membership of the Bladder & Renal Group and subgroups

Appendix 2 – Bladder & Renal Group and Subgroup strategies

- A – Bladder & Renal Group Strategy
- B – Advanced Bladder Cancer (ABC) Subgroup Strategy
- C – Penile Subgroup Strategy
- D – Surgical Renal Cancer Subgroup Strategy
- E – Systemic Treatments Subgroup Strategy
- F – T2 & Below (TABS) Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

- *This section is currently outstanding and will be added as an amendment to the report*

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Dr Paul Nathan (Bladder & Renal Cancer Group Chair)
Professor Rob Jones (Bladder & Renal Cancer Group Vice Chair)

Appendix 1

Membership of the Bladder & Renal Cancer Group

Name	Specialism	Location
Dr Kate Fife	Clinical Oncologist	Cambridge
Dr Ann Henry	Clinical Oncologist	Leeds
Professor Peter Hoskin	Clinical Oncologist	Middlesex/ Manchester
Dr Vincent Khoo	Clinical Oncologist	London
Dr Arabella Hunt*	Clinical Research Fellow	London
Ms Alison Fielding	Consumer	Surrey
Mrs Salena Mulhere	Consumer	London
Mr Henry Scowcroft	Consumer	London
Mr Andrew Winterbottom	Consumer	High Wycombe
Professor Janet Brown	Medical Oncologist	Sheffield
Professor Syed Hussain	Medical Oncologist	Sheffield
Professor Robert Jones (Vice Chair)	Medical Oncologist	Glasgow
Dr Paul Nathan (Chair)	Medical Oncologist	Middlesex
Dr Lisa Pickering	Medical Oncologist	London
Dr Samra Turajlic	Medical Oncologist	London
Dr Naveen Vasudev	Medical Oncologist	Leeds
Dr Manon Pillai*	Medical Oncology Specialist Trainee	Manchester
Dr Anne Warren	Pathologist	Cambridge
Professor Emma Hall	Statistician	London
Mr Christopher Blick	Surgeon	Oxford
Professor James Catto	Surgeon	Sheffield
Mr Param Mariappan	Surgeon	Edinburgh
Professor David Nicol	Surgeon	London
Mr Grant Stewart	Surgeon	Cambridge

* denotes trainee member

Membership of the Subgroups

Advanced Bladder Cancer Subgroup		
Name	**Specialism**	**Location**
Dr Maria de Santis	Associate Clinical Professor	Warwick
Dr Ananya Choudhury	Clinical Oncologist	Manchester
Dr Alison Birtle	Clinical Oncologist	Preston
Professor Robert Huddart	Clinical Oncologist	London
Dr Sundar Santhanam	Clinical Oncologist	Nottingham
Mr Andrew Winterbottom	Consumer	High Wycombe
Professor John Chester	Medical Oncologist	Cardiff
Professor Syed Hussain (Chair)	Medical Oncologist	Plymouth
Professor Robert Jones	Medical Oncologist	Glasgow
Professor Thomas Powles	Medical Oncologist	London
Professor Maggie Knowles**	Pathologist	Leeds
Professor Gareth Griffiths	Statistician	Southampton

Penile Subgroup		
Name	**Specialism**	**Location**
Dr Jim Barber	Clinical Oncologist	Cardiff
Dr Tony Elliot	Clinical Oncologist	Manchester
Dr Vincent Khoo (Chair)	Clinical Oncologist	London
Dr Anita Mitra**	Clinical Oncologist	London
Dr Heather Payne**	Clinical Oncologist	London
Mr Neil Walker	Consumer	Bristol
Dr Steve Nicholson**	Medical Oncologist	London
Dr Lisa Pickering**	Medical Oncologist	London
Dr Mark Callaway	Radiologist	Bristol
Dr Miles Walkden**	Radiologist	London
Ms Clare Cruickshank**	Statistician	London
Professor Emma Hall	Statistician	London
Mr Pradeep Bose**	Surgeon	Swansea
Mr David Dickerson**	Surgeon	Somerset
Mr Asaf Muneer	Surgeon	London
Mr Matthew Perry**	Surgeon	London
Mr Vijay Sangar	Surgeon	Manchester
Mr Duncan Summerton	Surgeon	Leicester
Dr Nick Watkin**	Surgeon	London
Mr Roland Donat**	Urologist	Edinburgh
Mr Aditya Manjunath**	Urologist	Bristol
Mr Suks Minhas**	Urologist	London
Dr Cathy Corbishley**	Uropathologist	London
Ms Stephanie Burnett **		London
Mr Wayne Lam**		

Surgical Subgroup		
Name	**Specialism**	**Location**
Dr Kate Fife	Clinical Oncologist	Cambridge
Dr Vincent Khoo	Clinical Oncologist	London
Mrs Alison Fielding	Consumer	Surrey
Mr Axel Bex	Surgeon	London
Mr Christopher Blick	Surgeon	Oxford
Mr Stephen Bromage	Surgeon	Manchester
Mr Tobias Klatte	Surgeon	Bournemouth
Mr Tom Mitchell	Surgeon	Cambridge
Mr Pieter Le Roux	Surgeon	London
Professor David Nicol	Surgeon	London
Mr Grenville Oades	Surgeon	Glasgow
Miss Maxine Tran	Surgeon	London
Mr Grant Stewart (Chair)	Surgeon	Cambridge
Mr Mark Sullivan	Surgeon	Oxford
Mr Ravi Barod	Surgeon	London
Mr Satish Maddineni	Surgeon	Manchester
Mr Alex Laird	Surgeon	Edinburgh
Mr Simon Williams	Surgeon	Derby

Systemic Treatments Subgroup		
Name	**Specialism**	**Location**
Dr Natalie Charnley	Clinical Oncologist	Preston
Mrs Salena Mulhere	Consumer	
Dr Richard Griffiths	Medical Oncologist	Liverpool
Dr James Larkin	Medical Oncologist	London
Dr Paul Nathan	Medical Oncologist	Middlesex
Dr Lisa Pickering	Medical Oncologist	London
Professor Thomas Powles	Medical Oncologist	London
Dr Christy Ralph	Medical Oncologist	Leeds
Dr Stefan Symeonides	Medical Oncologist	Edinburgh
Dr Fiona Thistlethwaite	Medical Oncologist	Manchester
Dr Samra Turajlic**	Medical Oncologist	London
Dr Naveen Vasudev (Chair)	Medical Oncologist	Leeds
Dr Balaji Venugopal	Medical Oncologist	Glasgow
Dr Tom Waddell	Medical Oncologist	Manchester
Dr Manon Pillai*	Medical Oncology Specialist Trainee	Manchester
Mr Grant Stewart**	Surgeon	Cambridge

T2 & Below Subgroup		
Name	**Specialism**	**Location**
Dr Alison Birtle**	Clinical Oncologist	Preston
Dr Ann Henry	Clinical Oncologist	Leeds
Dr Ashok Nikapota	Clinical Oncologist	Brighton
Dr Yvonne Rimmer	Clinical Oncologist	Cambridge
Dr Arabella Hunt*	Clinical Research Fellow	London
Dr Anne Warren	Pathologist	Cambridge
Mr Henry Scowcroft	Consumer	London
Mr Andrew Winterbottom	Consumer	High Wycombe
Dr Sally Appleyard*	Specialist Registrar Clinical Oncology	Sussex
Professor Emma Hall	Statistician	London
Professor James Catto	Surgeon	Sheffield
Mr Mark Johnson	Surgeon	Newcastle
Mr Param Mariappan (Chair)	Surgeon	Edinburgh
Dr Rik Bryan	Urologist	Birmingham
Miss Alexandra Colquhoun	Urologist	Cambridge

* denotes trainee member

**denotes non-core member

Appendix 2

Bladder & Renal Group & Subgroup Strategies

A – Bladder & Renal Group Strategy

The main CSG strategy remains to offer as broad a research portfolio as possible, ideally to develop a high quality competitive trial suitable for every patient. This requires a combination of pragmatic trials allowing smaller clinical sites to actively participate in bladder and renal trials, balanced with more complex interventional studies.

To do this, an optimal skill mix is required on the CSG and there is a need to plan succession carefully. Whilst the CSG membership, and that of the Subgroups, has been refreshed, it is important to highlight that the pool of research active clinicians in these tumour types is significantly smaller than in some others, e.g. breast cancer, and thus it is important to retain as well as refresh membership, particularly where members continue to make a significant contribution to the Group and portfolio activities.

Immunotherapies have an increasing role in the management of both bladder and renal cancer and have become a standard of care in both diseases. The CSG membership contains international leaders in this area and the Subgroups aim to use their experience to maximal effect. We therefore aim to continue to develop immunotherapy studies in both diseases that explore novel combinations and clinical settings.

The role of patients as research champions is paramount and our consumers, together with KCSN and FBC, continue to work with the CSG to train patient representatives as research experts to liaise with other patients and to exert pressure on research inactive clinicians. All current portfolio interventional trials collect quality of life data where appropriate and there are a number of studies with a primary qualitative endpoint to allow us to better inform patients on the optimum choice of radical treatment. The CSG has particularly strong consumer input and there is an opportunity to build upon their already excellent work and to consider opportunities in PROM research.

The use of and challenges in expanding the translational work of the CSG has been highlighted already, with premature withdrawal of funding from POUT-T and unsuccessful applications for tissue collection for two other portfolio interventional trials. Given the already successful work from LAMB in informing the biomarker directed Rucaparib and Enzalutamide arms of ATLANTIS, the CSG will need to consider other funding sources to continue this component of its portfolio. NAXIVA and A-PREDICT both have rich translational components and information from these studies will inform the development of future studies. TRACERx Renal is an Internationally leading translational research programme resulting in several high impact publications this annum in RCC. The CSG will use the experience gained from TRACERx to instruct high quality translational research in other studies across both diseases.

Several years ago, the Bladder CSG conducted a national audit of surgical barriers on recruitment into bladder trials and has attempted to act on the feedback. One key message to develop pragmatic trials deliverable in smaller units has been rectified, yet some CRNs and urologists continue to fail to engage. Working with the SSLs, together with a direct approach from the CSG Co Chairs and BAUS Oncology, the Group will continue to try to overcome this issue. The

work of the Surgical Subgroup directly addresses the barriers to engagement of the renal surgical community and it is of strategic importance to us that this issue is addressed.

There is an unmet need for patients with node positive bladder cancer; previous attempts to design a study for this patient group have been unsuccessful but there is now momentum to achieve this. In addition, the interface between systemic therapies and radiotherapy has been identified as a key research area.

B – Advanced Bladder Cancer Subgroup Strategy

The Subgroup strategy works towards a central objective 'to increase cure rates by improving systemic therapy as a component of multimodality therapy' in the following ways:

- Optimising systemic therapy by developing new drug hypotheses to test in MIBC
    - Efficient delivery of proof of concept studies in advanced disease exemplified by the development of the ATLANTIS precision medicine platform in the maintenance therapy setting.
    - Working towards options for practice changing trials of neoadjuvant therapy through initiation of studies in this clinical setting. Current examples of recruiting trials include NeoBLADE, ABACUS and SPIRE.
    - Working in collaboration with industry to deliver high quality trials of novel agents in areas of unmet need. In addition to the multiple examples on which we have recently published (e.g., LaMB, PLUTO, ABACUS), current examples of trials in recruitment include ATLANTIS, SPIRE, NeoBLADE. We have further emerging trials in development involving collaborations with pharma partners
- Delivery of potentially practice changing studies
    - Implementing POUT, the first ever randomised phase III trial of adjuvant therapy in upper tract TCC, and development of a successor study POUT 2.
- Development of a larger translational research programme
    - Utilisation of the LaMB and ATLANTIS sample sets to allow generation of data on biomarker rates to facilitate new hypotheses to include in the latter trial.
    - Entry of bladder cancer patients into the 100,000 Genomes Project and going forward to begin analyses of data emerging from this project.
    - Coordination of a collaborative approach to utilisation of samples sets from the Subgroup's prior and ongoing studies.

C – Penile Subgroup Strategy

In order to deliver its strategy, the Penile Subgroup will:

- Hold six-monthly meetings with the opportunity of joining in person or by teleconference.
- Provide opportunities for advice and support of applications for grants.
- Increase engagement in clinical trials through promotion of clinical trials and regular engagement with supraregional teams.
- Regularly review Subgroup membership and widening of the membership base to increase contribution to future trials development.
- Ensure consumer involvement in all projects.
- Ensure trainee involvement in the Subgroup to promote development of future researchers.

D – Surgical Subgroup Strategy

The Surgical Subgroup strategy is:

- Develop a range of surgery and radiotherapy relevant studies across all stages of renal cancer i.e. from screening to metastatic disease.
- Engagement with BAUS Oncology and BAUS academic section on promotion of new trials at their meetings and newsletters.
- Ensure strong background information (literature review, BAUS database analysis, canvassing urologist opinion) before new trial plans developed more formally.
- Delivery and completion of feasibility studies in contentious areas to prove recruitment can be achieved, i.e. NAXIVA in IVC tumour thrombus, NEST- RCT of ablation vs surgery for SRMs.
- Embedding translational research as much as possible, urologists are well placed to deliver on this as demonstrated in the past (A-PREDICT, NAXIVA, TRACERx Renal, SCOTRRCC).

- Regular meetings every 3 months (up to 1 face to face per year, other teleconference) to facilitate rapid development of trial ideas to design and delivery.
- Involvement of each member of the Subgroup with a specific study within our portfolio.
- Use the Subgroup as a proving ground for members of the main CSG and also new trial CIs. Invitation of selected subgroup members to the main CSG to consider applying for membership.
- Regular review of Subgroup membership to ensure all members are contributing.
- Close liaison with oncologists for neoadjuvant and adjuvant trials, with greater engagement of urologists in the TDG/TMG of these studies and also providing information to the urological community during development phase.

E – Systemic Treatments Subgroup

The newly formed RCC systemic treatment subgroup aims to generate internationally competitive interventional studies across all stages of the disease by:

- Having a talented ambitious group membership consisting of experienced and lesser experienced investigators in a supportive and co-operative environment.
- Having an explicit expectation that all members take ownership for developing at least one study whilst on the group
- Monthly teleconference meetings. This frequency was found to be necessary in the development of the PRISM and TRIBE studies
- Using pharma contacts of experienced group members to bring investigational products to the group.

F – T2 & Below Subgroup Strategy

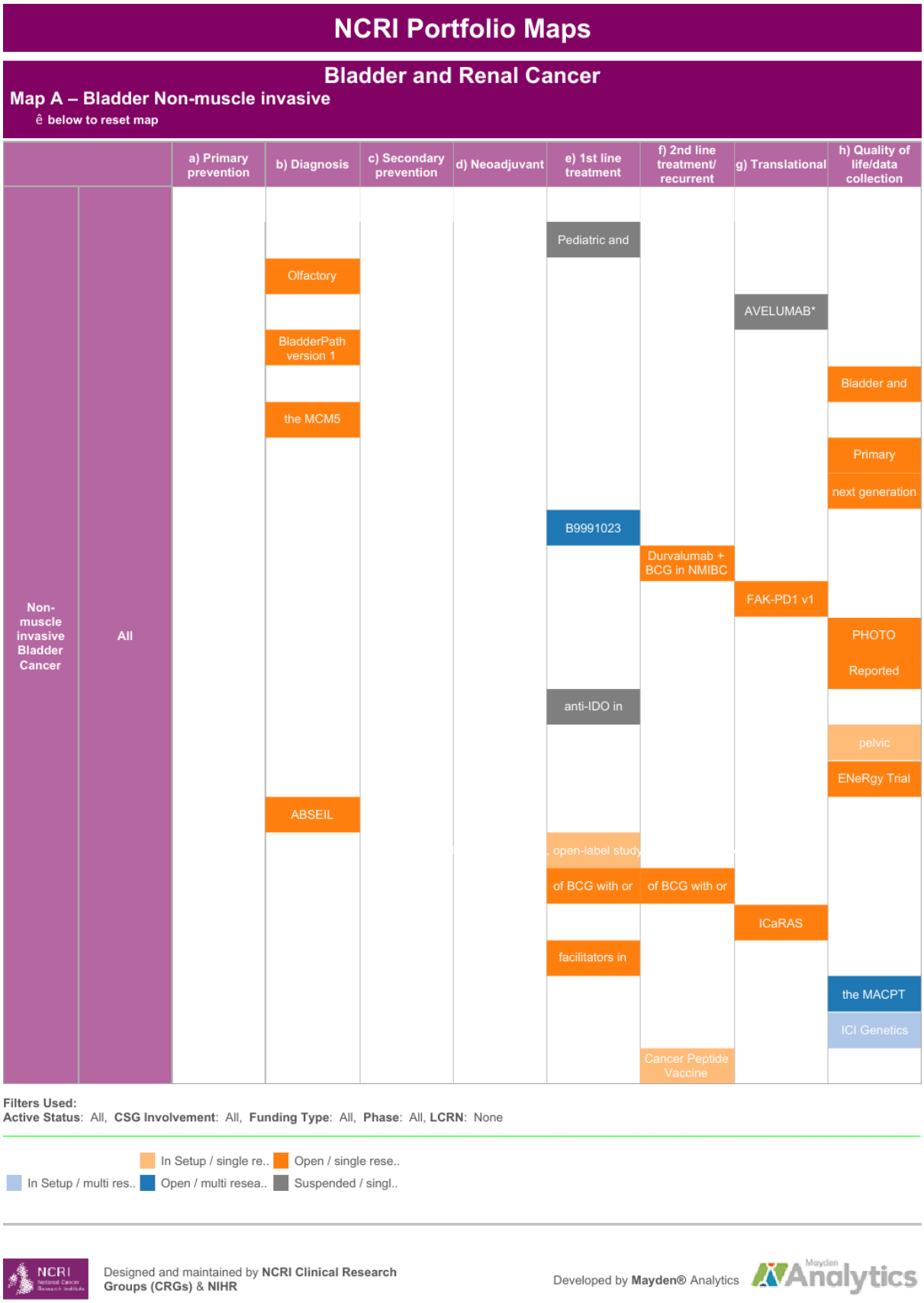
The Subgroup aims to develop and support studies aiming to enhance the care of patients with non-metastatic bladder cancer. We will seek to improve the patient experience through enhancing cancer control and maximising quality of life. Key targets areas of the Subgroup include:

- To enhance the outcomes of patients with high risk NMIBC through
    - Improved diagnostics utilising developments and knowledge in genomics and gene profiling.
    - Optimised adjuvant therapies both intravesical and systemic.
    - Exploration of the optimal approach to the use of radical surgery.
- To develop improved bladder sparing approaches in muscle invasive bladder disease.
- To work with the Systemic Treatments Renal Cancer Working Party Strategy to improve neo-adjuvant, concomitant and adjuvant therapies for patients with MIBC.
- To seek to understand better, and then improve, factors that impact on patient quality of life and experience of bladder cancer treatment.

We will seek to achieve these goals by utilising improved knowledge of tumour biology from translational research projects and through advances in drug development leading to enhanced treatment personalisation.

Appendix 3

Portfolio maps



NCRI Portfolio Maps

Bladder and Renal Cancer

Map B – Bladder Muscle invasive, urothelial cell carcinoma, penile

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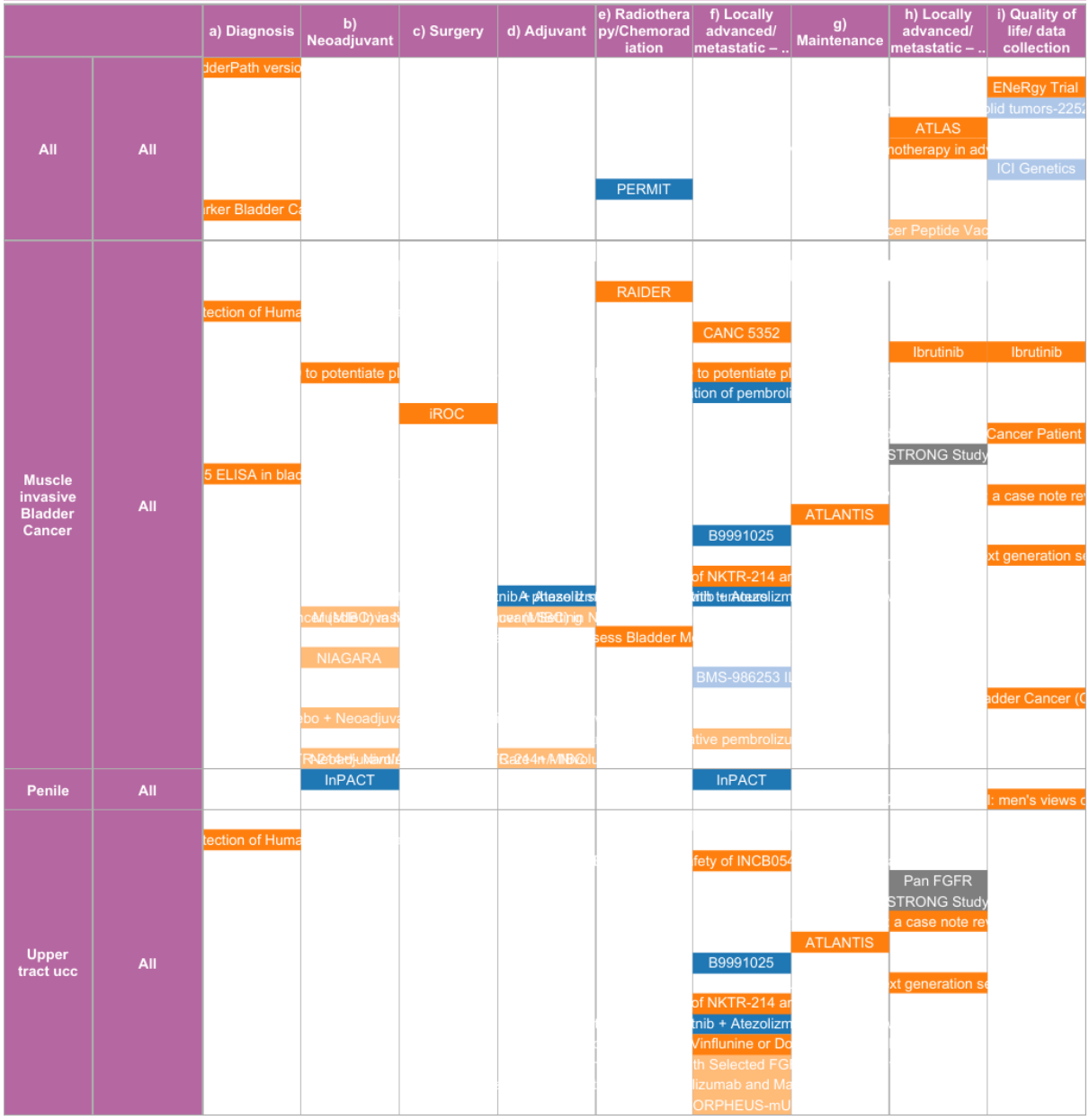

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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NCRI Portfolio Maps

Bladder and Renal Cancer

Map C – Renal clear cell, non-clear cell, adrenal

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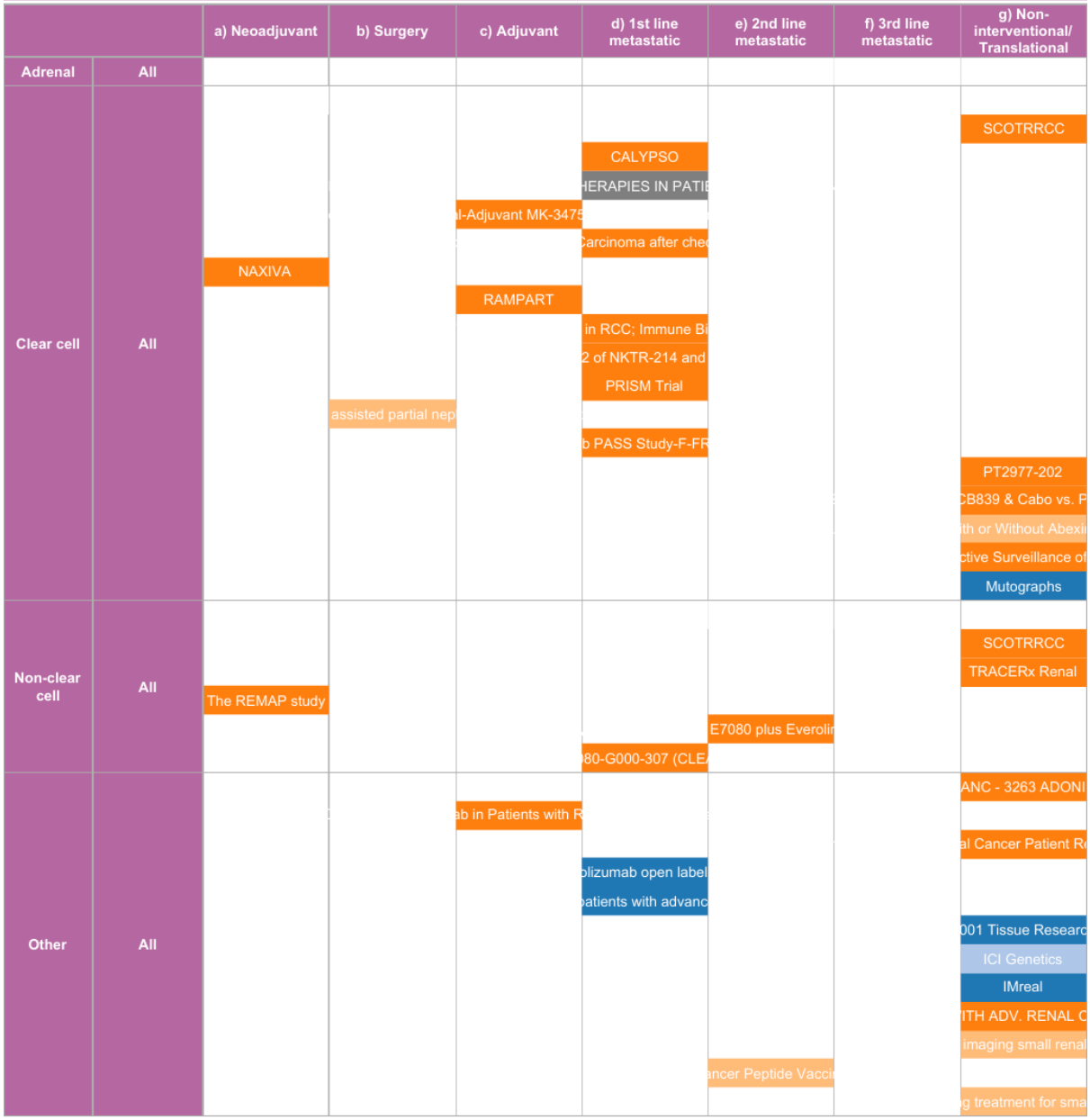

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Appendix 4

Top 5 publications in the reporting year

- *This section is currently outstanding and will be added as an amendment to the report*

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1.		
2.		
3.		
4.		
5.		

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Bladder & Renal Cancer Group portfolio, 28 trials closed to recruitment and 36 opened.

Summary of patient recruitment by Interventional/Non-interventional

Bladder

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2014/2015	69	262	69	262	0.7	2.5
2015/2016	763	604	649	604	6.20	5.77
2016/2017	5827	948	5624	948	53.70	9.05
2017/2018	3351	1176	3311	1166	31.61	11.13
2018/2019	1066	1158	982	1127	9.65	11.08

Renal

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2014/2015	154	255	130	255	1.6	3.1
2015/2016	61	399	61	378	0.75	4.64
2016/2017	148	315	148	315	1.82	3.87
2017/2018	170	323	170	318	2.09	3.91
2018/2019	154	397	154	397	1.23	3.16