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Prostate cancer

Abstract Code: IUCS20693-85

Prostate cancer (PC) and homologous recombination repair genes mutations (HRRm): a retrospective, monocentric, observational study aimed at recording histopathological and clinical data and their associations with oncological outcomes

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Objective: This study aimed to evaluate histopathological and baseline clinical characteristics in PC patients with HRRm, their prevalence, and clinical outcomes.

Methods: From 2019 to 2023, we screened 400 patients with metastatic PC for HRR alterations. HRRm were identified using archival primary or metastatic tumor samples and/or circulating tumor DNA (ctDNA). We retrospectively analysed clinical and tumor characteristics in 45 patients with HRRm, recording histopathological and clinical data and their association with Progression-Free Survival (PFS) in metastatic hormone-sensitive PC (mHSPC) setting as oncological outcome

Results: Out of the 400 screened patients, 45 (11%) had at least one mutation, with BRCA2 being the most commonly altered gene (46.7%), followed by BRCA1 (11.1%) and ATM (11.1%). Other rare HRRm were found in 5 patients (11.1%). Median age was 70 years. HRRm were associated with poorly differentiated PC: about 72% of patients had Gleason score = 8 and, among these, 22.7% had a Gleason score of 10. 58% of patients had metastatic disease at diagnosis, with 40% having High Volume disease. The most common sites of metastasis were bones and lymph nodes, with only 13% having visceral metastasis. In patients with non-metastatic disease at diagnosis, advanced stage (T3-T4) and nodal involvement were frequent, 53% and 35% respectively. 43 patients received medical treatment for mHSPC with androgen deprivation therapy (ADT) alone (37.8%), ADT plus androgen receptor targeting agents (42.2%), or ADT plus chemotherapy (15.5%). 29 patients had disease progression with a median PFS of 16.8 months, regardless of the therapy.

Conclusions: PC with HRRm had more frequently Gleason ⩾ 8, T3/T4 stage, nodal involvement, and metastases at diagnosis, confirming the need to early search for mutations in patients with advanced disease and these characteristics. mHSPC patients had significantly lower PFS compared to the literature, with a median PFS of 16.8 months, suggesting HRRm disease could have worse prognosis. These data support the need for tailoring a specific clinical management of these patients.

Abstract Code: IUCS20709-83

Real-life Analysis of [177Lu]Lu-PSMA-617 on mCRPC Patients cohort treated in France

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Objective: VISION study demonstrated that adding [177Lu]Lu-PSMA-617 to BSoC improved imaging-based progression-free survival and overall survival in patients with PSMA-positive mCRPC. French Health Authorities approved an early access "cohort" for [177Lu]Lu-PSMA-617 in this setting.

Methods: PSMA positive mCRPC patients who had received at least 1 taxane-based chemotherapy and ⩾1 ARPI were included. [177Lu]Lu-PSMA-617 (7.4 GBq) was given up to 6 cycles every 6 weeks. Patients' characteristics and safety data are reported for the whole population. Efficacy was assessed within a sub-population with a minimum of 6 months follow-up after 1st [177Lu]Lu-PSMA-617 injection. AE grading was not performed.

Results: From 1/12/2021 to 31/10/2023, 1340 patients were included, and 696 patients were evaluated for efficacy. At data cut-off, 749 were still on treatment, 591 discontinued treatments including 259 due to disease progression (43.8%), AE (9.8%) or death (6.0%). 210 patients (35.5%) finished all 6 injections.
Patients baseline characteristics: median age 73.4 years; ECOG 0-1: 87.4%; median PSA level 63 ng/ml; metastatic sites: bone 93.4%, lymph node 60.9%, liver 9.3%; prior taxane regimen: 97.4% of which 56.6% had 2; previous ARPI treatment: 100% and 64.3% had 2 or more (median: 2). Concomitant treatment with ARPI was observed in 26.3%.
Regarding efficacy results, the median progression free survival at imaging was determined by investigators (Conventional or TEP imaging) with a median of 7.3 months. The median time to clinical symptoms progression was 7.7 months. 68.4% of patients had a reduction in PSA level at any time point.
Patients received a median of 4 cycles.
12.0 % (n= 159) of patients experienced >1 treatment-related AE(TRAE). Most AE were considered as anticipated (244/344). The most common class of reported TRAE was hematotoxicity (192/344 TRAE).

Conclusions: In this real life cohort of mCRPC treated with [177Lu]Lu-PSMA-617 patients were heavily pretreated, received less concomitant ARPI treatment and higher incidence of 2 prior taxane regimens compared to VISION. Patient profile is evolving with patients in earlier lines after several months of experience. Safety profile of [177Lu]Lu-PSMA-617 remains favorable. The cohort is still ongoing, updated results will be presented at urology summit, including longer follow-up period and higher number of patients who completed treatment

Abstract Code: IUCS20718-83

Southampton experience of prostate specific membrane antigen therapy for metastatic prostate cancer

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Objective: Prostate specific membrane antigen (PSMA) therapy involves the administration of the radiopharmaceutical Lutetium-PSMA, which targets PSMA avid bone and soft tissue metastases in advanced prostate cancer patients. PSMA therapy consists of 6 cycles of IV Lutetium PSMA, delivered in 6 weekly intervals.

Methods: Following participation in clinical trials and early access program, UHS set up a private PSMA therapy service in November 2021. Over a 30-month period, 10 patients referred from the South of England received PSMA therapy at UHS. These patients had disease progression following a range of prior therapies including prostatectomy, Radiotherapy, chemotherapy, enzalutamide and arbiraterone.

Results: Mean age of patients was 73 years (range 48 – 84 years). Of the 10 patients commencing PSMA therapy, 3 have completed the recommended 6 cycles of treatment. All 10 patients initially responded to treatment with a PSA drop. Of the 3 patients who completed all 6 cycles of PSMA therapy the mean average PSA prior to treatment was 117.75 (Range 5.5 - 230) and mean average PSA at the end of treatment was 180 (range 4.7 – 340). To date, 39 treatment cycles have been administered. However, some patients had disease progression whilst on treatment and therefore stopped before completing all 6 cycles. 7 patients have subsequently passed away. The mean average number of cycles completed was 3.9. The mean average time between date of cycle 1 treatment and date of death was 253 days.

Conclusions: From our experience, PSMA is simple to administer, well tolerated with minimal

side effects. Our current patient cohort have demonstrated a positive response to therapy with improving PSA and post therapy imaging.

Abstract Code: IUCS20745-83

Evaluating Outcome and Prognostic Factors in Low-Volume Stage IV Hormone-Sensitive Prostate Cancer (mHSPC)

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Objective: The 8th edition of the AJCC-TNM classification categorizes prostate cancer as stage IV when metastases are present in pelvic lymph nodes (N1) or abdominal lymph nodes (M1a), as well as in the presence of bone metastases (M1b). However, there is a paucity of data on the effectiveness of intensifying treatment with docetaxel and/or androgen receptor targeted agents (ARTA) in addition to androgen deprivation therapy (ADT) for patients with mHSPC who are classified as stage IV due to N1 status. Additionally, the differential benefits of such treatments in M1 low-volume disease, specifically in cases with nodal-only (M1a) or bone (M1b) involvement, are not well understood.

Methods: we conducted a retrospective cross-sectional study looking at 126 patients diagnosed with stage IV mHSPC low volume according to the CHAARTED criteria. Patient characteristics and treatment outcomes were analysed, and prognostic factors were evaluated using Cox regression analysis.

Results: Seven patients (6%) had N1, 28 (22%) M1a, and 91 (72%) M1b. The only significant difference in clinical variables among these three patients' categories was found in treatment with ADT only ($p<0.001$). The 5-year progression-free survival (PFS) rate was 63.1% for all patients, 100% for N1, 80.9% for M1a and 54.9% for M1b metastases. High PSA value (>25) and consolidation prostate radiotherapy (cRT) were identified as independent prognostic factors for PFS. Although there was a significant difference in the median follow-up time between patients who received cRT and those who did not receive it (26.8 months vs. 37.7 months, $p=0.03$), cRT was associated with significantly higher 5-year PFS (94.7%, 95% CI, 85.2-100, vs. 55.2%, 95% CI, 40.8-74.8, $p=0.01$).

Conclusions: Despite its limitations, this study suggests a potential role for cRT in patients with low-volume metastatic mHSPC. Additionally, our data indicate that high PSA levels may serve as a valuable prognostic factor for decision-making in this patient population. Further investigation is needed to confirm these findings.

Abstract Code: IUCS20746-84

A case of brain metastasis development despite PSA suppression in a hormone sensitive metastatic prostate cancer patient under apalutamide treatment

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Objective: Prostate cancer (PC) is the most common tumor in older men. The most prevalent sites of metastases are bones, lymphnodes, lungs and liver. Brain involvement by PC is relatively rare. Brain metastases (BM) occur in only 1-2% of patients with metastastic PC. Second-generation androgen receptor-signaling inhibitors (ARSI) are largely used as first-line treatment in metastatic hormone sensitive PC (mHSPC) but they cannot easily penetrate the blood–brain barrier so that they are excluded from Central Nervous System (CNS) or achieve intracerebral concentrations associated with a small risk of seizures (e.g., apalutamide and enzalutamide).

Methods: Here we report a 66-year-old patient with mHSPC who developed BM under apalutamide, started 15 months before and with undetectable PSA.

Results: The patient presented with slowed speech and confusion worsening in 10-15 days. A brain MRI revealed two junctional lesions of repetitive significance, in the right frontal area and left frontal and two further lesions with similar characteristics in the right and left cerebellar hemispheric area. PSA level never increased despite radiological progressive disease. The patient received only best supportive care and did not undergo radiation therapy due to rapid worsening of clinical conditions leading to death after 15 days.

Conclusions: Even though BM are quite rare and more common just in castration resistant prostate cancer, they should be considered as a potential site of disease also for mHSPC under ARSI or chemotherapy treatment because of blood-brain barrier low penetration. BM are associated with poor prognosis and radiological restaging should periodically be performed and include CNS even if PSA value is undetectable.

Abstract Code: IUCS20749-87

Prostate-Specific Membrane Antigen PET-CT findings in biochemical relapse after prostatectomy

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Objective: Surveillance for recurrence of prostate cancer after radical treatment is most often performed by measuring Prostate Specific Antigen (PSA) levels. Prostate-Specific Membrane Antigen (PSMA) PET-CT is increasingly used to assess patients with detectable PSA relapse, identifying sites of persistent or recurrent prostate cancer to inform treatment decisions. We studied PSA levels and PSMA PET-CT results in patients with PSA relapse after radical prostatectomy, to look for patterns of recurrence and at what PSA value this occurred, to inform decision-making on the appropriate PSA threshold to trigger PET-CT imaging.

Methods: A retrospective review of all patients undergoing PSMA PET-CT at the Royal United Hospital, Bath, UK between August 2020 and February 2024. Only patients undergoing PET in the setting of biochemical PSA relapse after prostatectomy were selected. In these patients, data were collected on the interval between prostatectomy and relapse, Gleason score, pT-stage, presence of R0 resection, PSA level to prompt imaging, whether disease was evident on PET-CT and if present, the sites of disease. We also recorded the management plan that was informed by this imaging.

Results: 37 PSMA PET-CT's were performed to look for relapse after radical prostatectomy. The lowest PSA to trigger a scan was <0.1ng/ml and the highest PSA was 9.1. 14 patients had no PET-avid disease on the scan. The lowest PSA level in each recurrence group where avid disease was seen ranged from 0.04 (pelvic nodes) to 0.7 (distant metastases). 19 patients had confirmed PET-avid disease on the scan. 16 of these patients had PET-avid disease in the prostate bed, pelvic nodes or both. 10 out of the 16 patients received salvage radiotherapy, and a further 8 patients received prostate bed radiotherapy on the basis of negative or equivocal PSMA PET-CT results.

Conclusions: PSMA PET-CT was able to detect prostate cancer recurrence even at low PSA values. PET-CT allowed 51% of patients to avoid or delay radiotherapy, either because of non-radically treatable disease or because PSA surveillance could be offered. There was no clear PSA threshold at which PSMA PET-CT scans were unhelpful, so the current practice of scanning when PSA reaches $\geqslant 0.2$ seems appropriate.

Abstract Code: IUCS20752-81

Transcriptomic Analysis of Patients with Metastatic Hormone-Sensitive Prostate Cancer to Identify Genomic Signatures Involved in the Transition from Androgen-Dependent to Androgen-Independent Phenotype

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Objective: The study aims to identify genomic signatures characterizing the transition from androgen-dependent to androgen-independent phenotypes in metastatic hormone-sensitive prostate cancer (mHSPC) patients through comprehensive gene expression analysis of those undergoing doublet therapy (ADT + ARPI).

Methods: Patients with mHSPC treated with ADT plus ARPI was selected for transcriptomic profiling. Total RNA was extracted from Formalin-Fixed Paraffin-Embedded (FFPE) tissue samples using the Maxwell® RSC RNA FFPE Kit. The NanoString Tumor Signaling 360 Panel was employed to profile 780 human genes involved in tumor signaling. Bioinformatics tools were used to identify differentially expressed genes (DEGs), deregulated pathways, and

potential regulatory networks. Key findings will be validated in independent patient cohorts to ensure the robustness and generalizability of the signatures.

Results: A comprehensive transcriptomic analysis was conducted on samples from 24 mHSPC patients treated with doublet therapy (ADT+ ARPI). The study focused on identifying differentially expressed genes (DEGs) between non-responder (NR) and responder (R) patients. These genes were significantly involved in various pathways that contribute to therapeutic resistance. At the stromal level, NR patients exhibited a marked increase in ligands known to activate metastasis-promoting receptors. These receptors play a crucial role in the tumor microenvironment by facilitating cancer cell migration, invasion, and ultimately metastasis. Genes involved in cell-cycle progression were also up-regulated in NR patients, promoting unchecked cellular proliferation. Additionally, there was a notable up-regulation of genes associated with androgen receptor (AR) signaling, a key driver of prostate cancer growth and progression. The concurrent increase in metastasis-promoting ligands and the dysregulation of cell-cycle progression suggest a multifaceted mechanism of resistance to hormonal therapy in NR patients. This suggests that combining hormonal therapy with chemotherapy, which can target rapidly dividing cells, could potentially overcome this resistance and improve treatment efficacy.

Conclusions: The study identified key genomic signatures and pathways involved in the transition from androgen-dependent to androgen-independent mHSPC. These findings provide insights into the molecular mechanisms driving resistance to androgen receptor-targeted therapies and highlight potential biomarkers for early detection of therapy resistance. The identified signatures may serve as therapeutic targets for developing novel treatment strategies aimed at delaying or preventing the onset of castration resistance in prostate cancer patients.

Abstract Code: IUCS20755-84

Serum levels of Thymidine Kinase 1 correlate with PSA and tumour shrinkage in metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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Objective: Thymidine kinase-1 (TK1) is a cell cycle-dependent cytosolic enzyme involved in DNA synthesis, and its levels rise during cellular proliferation or cell repair following DNA damage. In healthy subjects, levels of TK1 are low to absent, with elevated levels being observed in patients affected by solid malignancies. As recent evidence suggests serum TK1 activity to correlate with tumour response to treatment, our objective was to investigate serum TK1a in advanced prostate cancer and its correlation with PSA.

Methods: From January 2023 we collected blood samples from 27 patients of three oncological units. All patients were diagnosed with advanced prostate cancer, 9 of them having received previous therapies for localized disease, and were treated with androgen deprivation therapy plus androgen-receptor signalling inhibitors (ARSI). After collecting informed consent, serum samples were collected at the baseline (T0), after 1 month (T1) of treatment and at 3 months (T3), 6 months (T6), until disease progression (PD). Subsequently, TK1 serum activity (sTK1a) was assessed using Divitum® assay (Biovica), a refined ELISA-based assay. Prostate-specific antigen (PSA) was collected as well, along with clinical and imaging data. Finally, a correlation analysis was performed.

Results: Up to date, we evaluated sTK1a and PSA levels in 19 patients at T1, T3 and T6 and compared to baseline. Serum TK1a levels decreased in 14 out of 19 patients, rose in 2 cases and were steady in 3. On the other hand, PSA levels decreased in 17 out of 19 patients. Interestingly, five of the 6 patients who did not showed decrease of sTK1a levels had already been treated for localized prostate cancer and experienced disease relapse. Therefore, in 14 out of 19 tested blood samples a positive correlation trend between fold change of PSA and sTK1a compared to baseline levels was found, whereas no correlation was deemed for pre-treated patients.

Conclusions: sTK1a showed as a potential prognostic marker in mHSPC patients who received ARSi plus ADT for mHSPC. The assessment of correlation between baseline sTK1a dosage and its dynamic changes in peripheral blood could represent a non-invasive biomarker to assess

patients' response to therapy and for the early detection of the oligo-metastatic disease.

Abstract Code: IUCS20761-81

Remote Consultation in Prostate Cancer Clinics: Impact on Carbon Footprint and Patient Satisfaction

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Objective: Healthcare contributes around 4-5% of total UK carbon emissions. The National Health Service (NHS) in England alone is responsible for 40% of the public sector's emissions. During and after Covid, remote consultations were started in the NHS. These remote consultations reduce the travelling time and cost for the patients but how does these affect our environment has not been investigated thoroughly. Quantify the reduction in carbon emissions achieved by implementing remote consultations in our Prostate Cancer clinics. Calculate the environmental benefit in terms of reduced patient travel and associated CO2 emissions. Assess patient perceptions of remote consultations, including preference and overall satisfaction.

Methods: One month of prospective data collection from our Prostate Cancer Clinics. Patients who had Telephone consultation during that clinic were interviewed after seeking their permission. Their usual mode of travel and distance was documented. Patient preference was asked about Telephone consultation compared with Remote Video and Face-to-Face clinic review. Patient satisfaction with regards to the Telephone consultation was documented on a scale of 0-10.

Results: 61 patients were interviewed in one month. 55 out of the 61 were Prostate Cancer patients, one was Penile Cancer and 5 Endometrial Cancer. The average distance from the hospital was 40.1Km. Total Carbon dioxide (CO2) emission saved for all 61 patients: 811Kg. Average CO2 emission saved per patient per visit: 13.3Kg. Total CO2 emission saved for all 61 patients for one year: 3707Kg. Average CO2 emission saved per patient for one year: 60.8Kg. 15% and 84% of the patients preferred a Face-to-Face and Telephone consultation respectively. 29.5% and 57.3% of the patients gave a score of 9 and 10 respectively for "Patient satisfaction" with the Telephone consultations.

Conclusions: Our findings suggest Telephone consultation have significant positive impact on the CO2 emissions and for one patient that has been reviewed remotely we have saved around 44.5 home deliveries by an average Mail company. Therefore, Telephone consultations should be encouraged where appropriate as patients are also satisfied with these in the right setting.

Testicular cancer

Abstract code: IUCS20769-89

Carboplatin AUC10 in metastatic Seminoma (Topic: "Real world evidence (except case studies)")

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Objective: Carboplatin monotherapy has been evaluated as a treatment option for patients with metastatic seminoma exhibiting a good prognosis according to IGCCCG criteria. Results from a phase II study, reported in 2010, demonstrated that the treatment was both tolerable and effective. These outcomes instilled confidence in the collaborative group to recommend carboplatin as a viable management strategy.

Methods: Data were collected on 61 patients diagnosed with good prognosis seminoma. The cohort was comprised of 46% with stage IIA/IIB disease and 54% with stage >IIB. Patients received either 3 or 4 cycles of carboplatin depending on their initial response to the first cycle. The endpoints evaluated included complete response (CR), partial response (PR), stable disease, and progressive disease (PD), alongside overall survival (OS) and progression-free survival (PFS) rates over a three-year period.

Results: Out of the 61 patients, 20 (33%) achieved a CR following the first cycle and subsequently received 2 cycles of carboplatin, while the remaining patients received 4 cycles. At the conclusion of the treatment, 31 patients (51%) had a CR, 27 (44%) had marker-negative PR, 2 (3%) had marker-negative stable disease, and 1 patient (2%) exhibited PD. The 3-year OS was 96%, and the PFS was 93%. Notably, the patient with PD eventually progressed through BEP and died 13 months post-diagnosis. However, two other patients who initially had marker-negative SD were successfully salvaged with BEP, remaining disease-free subsequently.

Conclusions: Carboplatin monotherapy demonstrates significant efficacy in the management of metastatic seminoma with good prognosis. The favorable survival rates, combined with the convenience and reduced acute toxicities associated with carboplatin, support its consideration as a standard treatment option in this patient population.

Renal cancer

Abstract Code: IUCS20726-82

Real word data of first-line metastatic renal cell carcinoma (mRCC) treatment choice in a tertiary centre in the UK

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Objective: To review the first-line treatment choices for mRCC in a tertiary hospital.

Methods: Retrospective data analysis of 131 patients who received treatment at University Hospitals of Leicester NHS Trust from 2018-2024. Data included gender, prior nephrectomy, histology, IMDC score and survival outcomes. Analysis was conducted using SPSS version 29. Patient demographics are detailed in Table 1.

Results: Most common regimen was Ipilimumab+nivolumab (IN) 26%, followed by Avelumab+axitinib (AA) and pazopanib (P) 25.2% each. Other regimens were Sunitinib (S) 13%, Cabozantinib (C) 8.4% & Lenvatinib+ Pembrolizumab (LP) 2.3%.
The mPFS for IN (7.7 months), LP (17 months), AA (10.2 months), S (24.7 months), P (18.2 months) and C (8.4 months); p=0.093. The mOS for IN (22 months), LP (19.48 months), AA (26.5 months), S (21.6 months), P (60 months) and C (27.7 months); p=0.186.
As expected, the poor risk IMDC group had the worst mOS (13.7 months), while there was minimal disparity between favorable (35 months) and intermediate (37.8 months); p=0.001.
Of the 90 patients who progressed after the first line, 65% (n=58) received second-line treatment. The remaining did not get additional treatment due to clinical decline (22%), toxicities (10%) and death (3.3%). Most patients received TKI in the second line after IO or TKI progression (67.2%). Few patients received Nivolumab (32.7%) after TKI progression.

Conclusions: TKIs demonstrated the highest PFS and OS in our population signifying that this remains a valid option for patients in the first-line setting. Only 65% received second-line therapy and these findings are similar to the recently published UK multicentric review on SACT dropout rates (1). This study highlights the importance of using the most effective treatments sooner. Significant OS differences were seen amongst IMDC risk groups.

Table 1. Patient demographics.

Gender	**No. (%)**
Male	92 (70.2%)
Female	39 (29.8%)
Nephrectomy	**No. (%)**
Yes	71 (54.2%)
NO	60 (45.8%)
Histology	**No. (%)**
Clear cell type	118 (90.1)
Papillary	7 (5.3%)
Chromophobe	1 (0.8%)
Other (No histology/unclassified)	5 (3.8%)

Abstract Code: IUCS20751-80

The prognostic impact of the metastatic pattern in advanced Renal Cell Carcinoma (aRCC): a retrospective analysis of 306 patients (pts) treated with compassionate ipilimumab and nivolumab (IPI+NIVO)

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Objective: The combination of IPI+NIVO is a first line option for IMDC intermediate-poor risk disease aRCC. Factors for risk stratification and pts selection remain, however, unmet clinical need. We assessed the different prognostic impact of

pattern of metastases in aRCC that could be potential biomarker for IPI+NIVO treatment choice.

Methods: aRCC who received IPI+NIVO among the Expanded Access Program available in Italy between April and October 2019 were included in the analysis. Clinical data were retrospectively collected. Statistical analyses were conducted with Software Stata 16. Univariable (UNV) and Multivariable (MLV) Cox regression analyses were conducted.

Results: Among 86 Italian centers, 306 pts with aRCC were included. Pts were mostly males (74%), with a median age of 62 and prevalent clear cell tumor histology (86%). The most frequent sites of metastases (mts) were lung (70%), bone (31%), liver (18%), brain (8%) and pancreas (5%). One-year Overall Survival (OS) was 67%. Half of the pts had only 1 mts site, 26% had 2 mts sites and 9% had $\geqslant$ 3 mts sites. A higher number of mts sites directly correlated with worse OS. In MLV analysis, the prognostic factors associated with worse OS were poor IMDC (HR 2.94; $p<0.001$), non-clear cells histology (HR 2.20; $p=0.001$), brain mts (HR 1.96; $p=0.033$) and the presence of both lung and bone mts (HR 2.11; $p=0.026$). In terms of risk of progression, the presence of bone and liver mts together appeared the most impactful factor (HR 3.12; $p<0.001$).

Conclusions: Our findings confirm that brain and bone mts, alone or in combination, may negatively affect OS in aRCC treated with first line IPI+NIVO. Despite the known favorable prognostic factor of lung mts alone, when associated with bone mts they unfavorably impact on OS. Number of mts and the type of mts sites should be considered in the risk stratification of aRCC pts.

Abstract Code: IUCS20753-82

Adopting the Sectra Lesion Tracking Tool for RECIST 1.1 in Renal Cell Cancer patients: First in the UK Pilot Study

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Objective: RECIST 1.1 is the standard systematic radiological response evaluation criteria used in cancer clinical trials. Sectra is the leading medical imaging enterprise spanning 1/3rd of acute and specialist UK NHS trusts. Sectra Lesion Tracking (SLT) is an integrated advanced visualisation surveillance tool, tracking the number and size of lesions with dynamic disease monitoring. Launched in 2016, it is currently installed in 39/45 trust Sectra systems.

Methods: Seven metastatic renal cell cancer patients recruited on 2 randomised controlled trials from 2015 to 2021 were retrospectively evaluated at our district general hospital. They had radiologist lesion tracked, manually calculated RECIST 1.1 outcomes for restaging/response assessment CT scans. We used the SLT to track lesions and generate output via its embedded RECIST 1.1 calculator. Performance wise, concordance percentage of target lesion and overall response amongst two modalities was calculated. Time distribution wise, nonparametric central tendencies i.e., median was used to compare.

Results: All 7 patients had a baseline and first restaging CT scan for trial intervention. 5/7 had second restaging CT scan. 1/7 had no identifiable target lesion. Concordance percentage for target lesion and overall response was 66.7% and 71.4% respectively in the first restaging whereas 75% and 80% in the second restaging CT scan respectively. The median time lag during first and second restaging CT for manual RECIST was 5760- and 2400-minutes vs 10 and 4 minutes for SLT RECIST respectively. Massive outlier delays were noted for manual RECIST i.e., 20 and 21 days for first and restaging CTs respectively.

Conclusions: The significant time savings and reasonably higher accuracy of SLT over existing standard creates higher radiologist reporting capacity to eliminate the NHS cancer report backlog. Till date, we have nil published or presented evidence in the UK. Our results not only warrant national adoption but also invites deployment in real world practice with promising time to cancer treatment reductions.

Abstract Code: IUCS20754-83 – Merit Award

External validation of the GRade, Age, Nodes and Tumor (GRANT) score for patients with surgically treated papillary renal cell carcinoma

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Objective: Stratifying the risk of recurrence for surgically treated papillary renal cell carcinoma (pRCC) could be challenging. Prognostic models are crucial for patient counselling, individualized surveillance, and identifying potential candidates for adjuvant therapy. The GRANT score is one of the models suggested by European Association Urology (EAU) guidelines to predict prognosis of surgically treated pRCC. This study aims to externally validate the GRANT score using a three-risk group stratification in a large cohort of pRCC patients.

Methods: The present analysis utilized retrospective data from pRCC patients who underwent radical or partial nephrectomy, as collected by Wagener et al. [PMID: 28934212]. The GRANT score parameters included tumor grade, age, pathological T-stage, and N-stage. Patients were stratified into three risk groups (0-1 *vs.* 2 *vs.* 3-4 risk factors). Cancer-specific survival (CSS) was assessed using the Kaplan-Meier method, and differences between groups were evaluated using the log-rank test. Harrell's c-index was used to measure model accuracy, and restricted mean survival time (RMST) was calculated for up to 120 months.

Results: A total of 1,942 patients were analysed. The median follow-up was 64.6 months. Patients aged > 60 years comprised 58% of the population, and 75.6% were male. At 60 months, CSS was 93.2% (95%CI 91.7%-94.6%) for group 1, 60.8% (95%CI 54.0%-78.6%) for group 2, and 26% (95%CI 15.7%-42.9%) for group 3, with significant differences between each group ($p < 0.001$). The median CSS was not reached for group 1 (95%CI NR-NR), 86.0 months in group 2 (95%CI 65-NR), and 22.8 months in group 3 (95%CI 16.4-48.0), **Figure 1**. The c-index for CSS was 0.732. The RMST at 120 months was 113.3 months for group 1, 75.9 months for group 2, and 56.6 months for group 3, resulting in a statistically significant difference ($p < 0.001$).

Conclusions: The GRANT score effectively stratified surgically treated pRCC patients into three risk groups with significant differences in CSS, demonstrating good prognostic accuracy. This validation supports the GRANT score's utility as a reliable and easy-to-use tool for predicting prognosis in surgically treated pRCC patients.

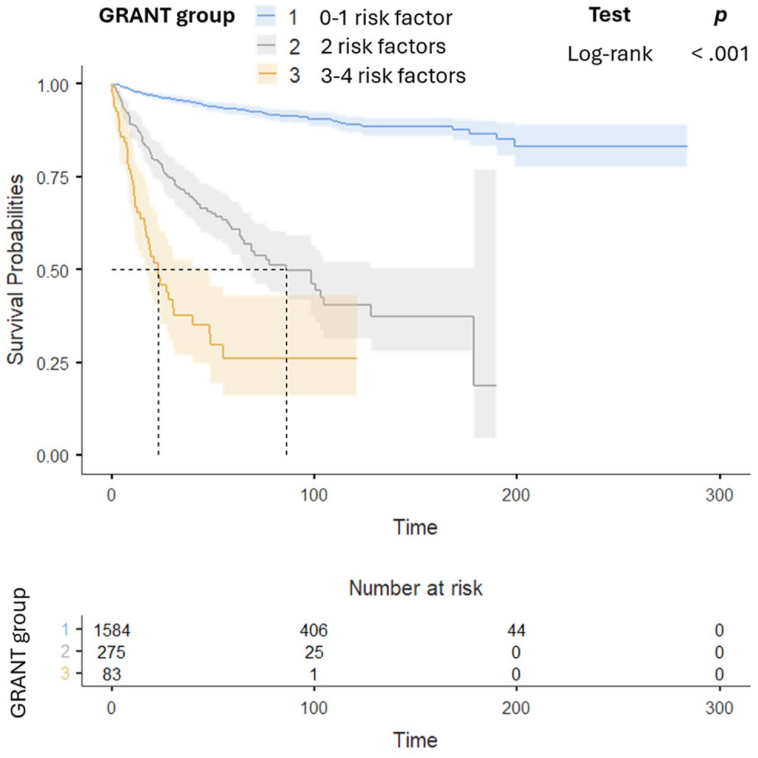

Figure 1. Kaplan–Meier curves for cancer-specific survival in each GRANT group.

Abstract Code: IUCS20757-86

Clinical response of advanced renal carcinoma's patients treated with small immunomodulatory proteolipid particle

I. Caballero Aguirrechu[1], C. Mesa[2], R. Alvarez[2], L. Oliver[2], D. Gomez[1], R. Rodriguez[1], A. Rosales[1], G. Vega[1]

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[2]Molecular Inmunology Center, La Habana - Cuba

Objective: Renal cancer is a tumor with high immunogenicity and resistance to systemic chemotherapy; in the metastatic condition, surgery alone does not show high survival rates. The main therapeutic strategies are directed at molecular targets. Objectives: Characterize patients according to clinical-epidemiological data, risk group, survival and safety of the treatment administered, as well as the kinetics of peripheral myeloid populations.

Methods: A descriptive, retrospective, cross-sectional study was carried out with 30 patients with metastatic or recurrent renal cell carcinoma who received treatment with very small proteolipid particle immunomodulator of the tumour microenvironment (natural NAcetyl GM3/VSSP). Survival was estimated with Kaplan Meyer curves, clinical benefit analysis (p=0.05) with non-parametric methods.

Results: The average age was 62 years, the male sex predominated (76.7%), the presence of lung metastases (60%), and tumour in the right kidney (40%). The median progression-free survival was 42.6 months and overall survival was not reached, with a better response for patients in the favourable and intermediate risk groups and those who received more than 5 doses of VSSP. No grade 3-4 adverse events were reported.

Conclusions: Young patients with CRC with lung metastases, from the intermediate risk group and with tumor in the right kidney predominated. Survival rates with the use of natural VSSP correspond to those reported with other immunotherapy drugs in this setting and the administration of the product was safe. Myeloid cell population determinations were elevated at inclusion and their decrease was observed with the administration of VSSP.

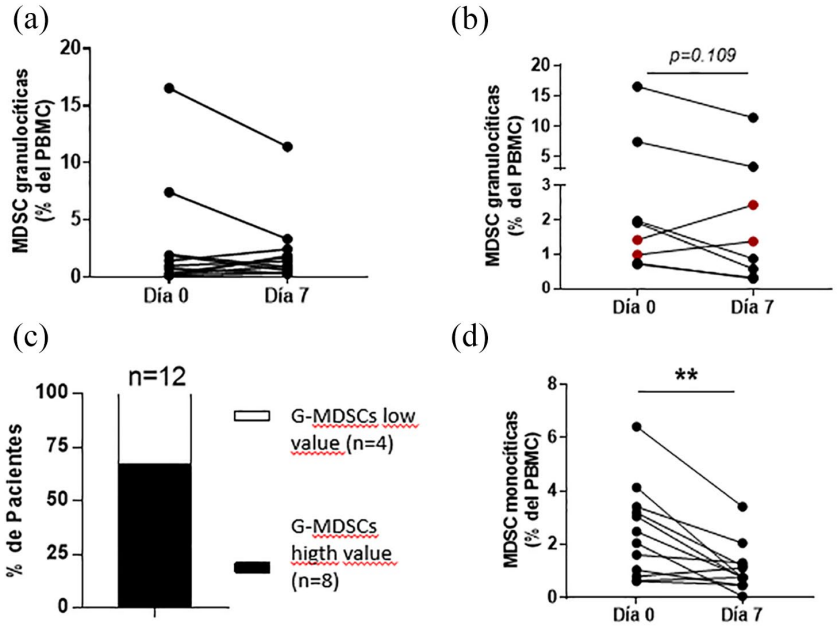

Figure 1. Serological peripheral myeloid cell's kinetics in patients with metastatic renal carcinoma.
OS risk group PFS risk group

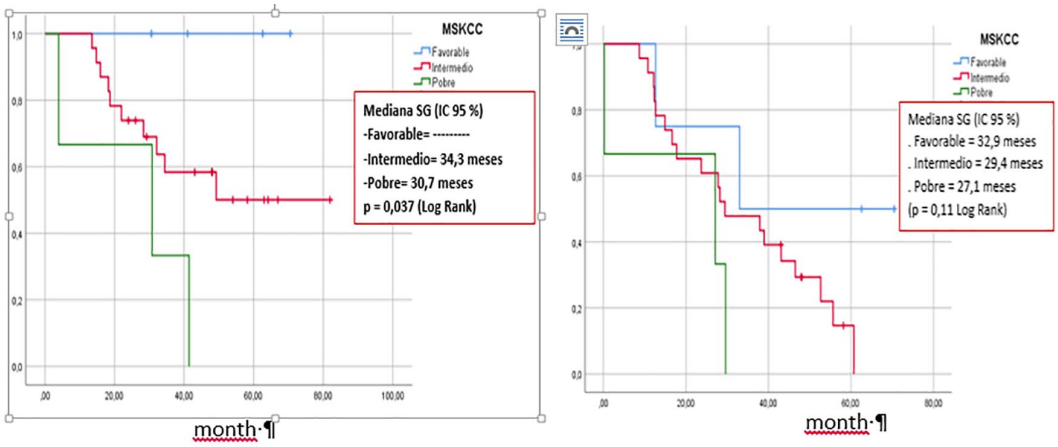

Figure 2. OS and PFS according to MSKCC risk groups (Kaplan-Meyer)

Abstract Code: IUCS20759-88

Baseline characteristics as parameters of choice of first-line therapy in metastatic renal cell carcinoma (mRCC) patients (pts): the Meet-URO 33 study

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Objective: Despite many first-line therapeutic options in mRCC, no formal comparisons and no standard parameters are available to guide the treatment choice. The ongoing Meet-URO 33 study will recruit up to 80 Italian centres to answer many clinical unmet needs.

Methods: The Meet-URO 33 study is a multicenter prospective/retrospective registry of a real-world mRCC population receiving first-line therapy from January 2021. As of April 2024, 421 pts from 25 Italian centers were assessed. We investigated which clinical/tumoral characteristics (age, ECOG PS, type/number of comorbidities, steroids, primary tumor surgery, histology, sarcomatoid features, type/number of metastases, IMDC and Meet-URO scores) influenced the choice among IO-IO, IO-TKI and TKI.

Results: Overall, 263 pts (62.5%) received IO-TKI, 81 (19.2%) IO-IO and 77 (18.3%) TKI. At the univariate analysis, the IMDC and Meet-URO scores, age, bone/pancreatic metastases, high-dose steroids, renal/cardiac/hematological/metabolic/gastroenteric comorbidities and ⩾2 comorbidities significantly correlated with the therapeutic choice ($p<0.05$). At the multivariate analyses, in the IO-IO vs IO-TKI comparison, a higher IMDC score and metabolic comorbidities correlated with IO-IO ($p<0.001$ and $p=0.005$), while the presence of bone metastases with IO-TKI ($p=0.024$); in the IO-IO vs TKI comparison, a higher IMDC score was associated with IO-IO ($p<0.001$) and a higher age with TKI ($p=0.09$); in the IO-TKI vs TKI comparison, a higher number of metastases correlated with IO-TKI ($p=0.037$) while a higher age, gastroenteric/renal comorbidities and ⩾2 comorbidities with TKI ($p<0.001$, $p=0.024$, $p=0.024$ and $p=0.046$).

Conclusions: The results of this preliminary data of the ongoing Meet-URO 33 study showed a real-world scenario of the current first-line setting in mRCC pts. Despite some well-known prognostic factors (e.g. ECOG PS, sarcomatoid features, lung/liver metastases) seems not be relevant parameters of therapeutic choice, others

were confirmed to direct our therapeutic choices (IMDC score, bone metastases, number of metastases, age, comorbidities). These findings are food for thought for further analyses with a larger sample size.

Abstract Code: IUCS20760-80

Clinical parameters for first-line immuno-combinations choice in metastatic renal cell carcinoma (mRCC) patients (pts): the Meet-URO 33 study

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Objective: Despite several first-line immuno-combinations in mRCC, there are no formal comparisons or biomarkers to guide the treatment choice. In this context, the ongoing Meet-URO 33 study will recruit pts in up to 80 Italian centers to answer many clinical unmet needs.

Methods: The Meet-URO 33 study is a multicenter prospective/retrospective registry of a real-world mRCC population receiving first-line therapy from January 2021. As of April 2024, 421 pts from 25 Italian centers were included. We investigated which clinical parameters (age, ECOG PS, type/number of comorbidities, steroids, primary tumor surgery, histology, sarcomatoid features, type/number of metastases, IMDC and Meet-URO scores) influenced investigators' choice.

Results: Overall, 344 (81.7%) pts received an immuno-combo: 160 (46.5%) Pembro + Axi (P+A), 81 (23.6%) Nivo + Ipi (N+I), 63 (18.3%) Nivo + Cabo (N+C), 40 (11.6%) Pembro + Lenva (P+L). At univariate analysis, the IMDC and Met-URO scores, histology, bone and pancreatic metastases, and metabolic comorbidities significantly associated with an immuno-combo choice. Specifically, N+I population had a higher percentage of IMDC intermediate-risk pts while P+L poor-risk pts (p=0.002). According to the Meet-URO score, the worst prognostic group (group 5) was predominantly treated with P+A and N+C (p=0.043). Metabolic comorbidities correlated with a more frequent choice of N+I and less of P+L (p=0.019). P+L was significantly preferred in clear-cell histology, while N+C with the higher percentage of papillary histology (p=0.047). Bone metastases correlated with N+C and less with N+I and P+L (p=0.021), while pancreatic metastases were associated with P+L and less with N+I and N+C (p=0.006).

Conclusions: Despite the bias linked to the different prescription indications over time, the associations observed from this real-world scenario confirmed the consideration of well-known prognostic factors in the therapeutic choice; these findings should be also interpreted as a general reflection of the oncologists experience. Associations of clinical parameters will be assessed within a larger sample size.

Abstract Code: IUCS20761-50 – Merit Award

External validation of the novel prognostic Meet-URO score in Metastatic Renal Cell Carcinoma on First Line Immune-combination therapy

Aruni Ghose[1], Alessio Signori[2], Nicholas Brown[3], Sophia Haywood[4], Jose Tapia[5], Anupama Vijay[6], Michael Cheung[7], Ishika Mahajan[8], Ondrej Fiala[9], Ritika Abrol[10], Vishwani Chauhan[1], Yamin Shwe Yee Soe[11], Anum Zargham[12], Sophie Ashley[13], Michelle Smith[14], Orla Hardy[15], Emma Johnston[16], Abdullah Sarwer[17], Kyaw Kyaw Tun[18], Amarnath Challapalli[19], Roshani Shrestha[20], Yüksel Ürün[21], James Meegan[22], Pasquale Rescigno[23], Joanne Parkes[24], Benjamin Smalley[25], Shobana Anpalakhan[26], Francesco Buono[27], Alexandr Poprach[28], Jeremy Yuen Chun Teoh[29], Veronica Murianni[30], Fabio Catalano[30], Davide Bimbatti[31], Sebastino Buti[32], Giuseppe Fornarini[30], Giuseppe Banna[25], Sara Elena Rebuzzi[33]

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Trust, Cardiff, UK, [6]Leicester Cancer Research Centre, University Hospitals of Leicester NHS Trust, Leicester, UK, [7]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK, [8]United Lincolnshire Hospitals NHS Trust, Lincoln, UK, [9]Department of Oncology and Radiotherapeutics, Faculty of Medicine, University Hospital in Pilsen, Charles University Prague, Czech Republic, [10]Royal Wolverhampton NHS Trust, Wolverhampton, UK, [11]St Luke's Cancer Centre, Royal Surrey NHS Foundation Trust, UK, [12]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, [13]Rosemere Cancer Centre, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK, [14]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK, [15]St George's University Hospitals NHS Foundation Trust, London, UK, [16]Northern Ireland Cancer Centre, Belfast Health and Social Care Trust, Belfast, UK, [17]Weston Park Cancer Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, [18]Royal Stoke Cancer Centre, University Hospitals of North Midlands NHS Trust, Stoke-on-Trent, UK, [19]Bristol Haematology and Oncology Centre, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK, [20]Kent Oncology Centre, Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK, [21]Ankara University School of Medicine, Ankara, Turkey, [22]Shrewsbury and Telford Hospital NHS Trust, Shrewsbury, UK, [23]Translationsal and Clinical Research Institute, Centre for Cancer, Newcastle University, Newcastle Upon Tyne, UK, [24]Worcestershire Oncology Centre, Worcestershire Acute Hospitals NHS Trust, Worcester, UK, [25]Department of Oncology, Portsmouth Hospitals University NHS Trust, Faculty of Science and Health, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, UK, [26]University Hospital Southampton NHS Foundation Trust, Southampton, UK, [27]Leeds Cancer Centre, Leeds teaching Hospitals NHS Trust, Leeds, UK, [28]Department of Comprehensive Cancer Care and Faculty of Medicine, Masaryk Memorial Cancer Institute and Masaryk University, Brno, Czech Republic, [29]Department of Surgery, S.H. Ho Urology Centre, The Chinese University of Hong Kong, Hong Kong, [30]Medical Oncology Unit 1, IRCCS Ospedale Policlinico San Martino, Genova, Italy, [31]Oncology 1 Unit, Veneto Institute of Oncology, IOV - IRCCS, Padua, Italy, [32]Medical Oncology Unit, University Hospital of Parma, Department of Medicine and Surgery, University of Parma, Parma, Italy, [33]Medical Oncology Unit, Ospedale San Paolo, Savona, Italy.

Objective: First-line immune-combination therapy based on immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs) are the new mainstay in metastatic renal cell cancer (mRCC). In this setting, there is a dearth of standard prognostic/predictive parameters to guide treatment choice. The novel prognostic Meet-URO score (IMDC score + bone metastases and neutrophil-to-lymphocyte ratio - NLR) showed a higher prognostic accuracy than IMDC in 306 patients on first-line nivolumab + ipilimumab in the Italian Expanded Access Program (PMID: 36493602). Hence, the necessity to externally validate and expand to other first-line immune-combination settings.

Methods: Twenty-seven European centres were included. Baseline patient and tumour characteristics were collected, including the IMDC score along with the presence of pre-treatment bone metastases, neutrophils, and lymphocytes for calculating the Meet-URO score. The prognostic performance of Meet-URO and IMDC scores were compared and defined by the Harrell's c-index.

Results: 1174 mRCC patient data was retrospectively collected. The median age was 64. 72.8% were male, 54.2% received nephrectomy, 62% were metastatic at diagnosis and 86.7% had clear-cell histology. 35% had bone metastases and 51.6% had NLR $\geqslant$ 3.2. 672 (57.2%) patients received ICI-ICI (nivolumab + ipilimumab) whereas 502 (42.8%) an ICI-TKI combination, mainly avelumab + axitinib (27.1%) and pembrolizumab + lenvatinib (14.3%).

Overall, median overall survival (mOS) was 36.2 months (95% CI 31.1 – 38.5) with a median follow up of 15.5 months. The c-index of Meet-URO resulted higher than IMDC score (0.68 vs 0.65). In particular, the mOS resulted more distinctive within the Meet-URO prognostic groups: 45.8 months for group 1 (12.9% of patients), 55.0 for group 2 (25.7%), 38.1 for group 3 (23.5%), 20.9 months for group 4 (29.6%) and 10.4 for group 5 (8.2%). On the other hand, mOS was 45.8 months for IMDC favorable-risk (19.5% of patients), 38.2 for intermediate-risk (53.7%) and 16.2 for poor-risk (26.8%).

Conclusions: In this large-scale real-world external validation analysis on mRCC patients receiving first-line immune-combinations, Meet-URO confirmed higher prognostic accuracy compared to IMDC. A further validation is planned in the ongoing Italian prospective Meet-URO 33 (REGAL) study (PMID: 38914928).

Bladder cancer

Abstract Code: IUCS19584-92

Efficacy and toxicity of half dose BCG therapy in bladder cancer

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Objective: Bacillus Calmette–Guérin (BCG) has been successfully used as immunotherapy to treat non-muscle invasive bladder cancer (NMIBC) for more than four decades. BCG is the only intravesical agent shown to reduce the risk of progression of NMIBC to muscle-invasive disease. Unfortunately, BCG therapy is not a universal panacea and it still fails in up to 40% of patients. This prospective cohort study was designed to document efficacy and toxicity of half dose (40 mg) BCG.

Methods: Eligibility criteria include intermediate and high-grade NMIBC and carcinoma in situ after 3 weeks of TURBT. Weekly BCG therapy (40 mg, half dose) was given for 6 weeks as induction and a weekly dose for 3 weeks at 3, 6, 9 and 12 months was given as maintenance therapy. The entire procedure was done as an outdoor procedure.

Results: 18 patients were included in the study from 2018 to 2021. All patients had T1 disease, 6 had low grade (Intermediate risk) and 12 had high grade (High risk without very high-risk features) cancer. Cystitis is the most common symptom experienced by all patients to varied extent but fortunately all are self-limiting. 2 patients had fever which subsided with paracetamol. No serious adverse effect observed in any of the 18 patients, and all were discharged on the same day of admission. After 36 months of mean follow up period, 8 patients had recurrence.

Conclusions: BCG therapy is an effective treatment in intermediate and high-grade NMIBC and carcinoma in situ after TURBT. With half-dose of BCG the toxicity is low and the cost of treatment is just over 20$ for each session.

Abstract Code: IUCS20697-89

Novel prognostic score for patients with metastatic bladder cancer on immunotherapy using real-world data

V. Chauhan[1], *S. Silva Diaz*[2], *P. Jara Martin*[3], *A. Gurung*[4], *M. Young*[1], *C. Wells*[1], *E. Nally*[1], *B. Szabados*[1], *F. Jackson-Spence*[1], *T. Powles*[1]
[1]Barts Cancer Institute, Centre for Experimental Cancer Medicine, London - United Kingdom, [2]University Hospital A Coruna, Medical Oncology Department, A Coruna - Spain, [3]University Hospital Marqués de Valdecilla, Medical Oncology Department, Santander - Spain, [4]Queen Mary University of London, Barts and The London School of Medicine and Dentistry, London - United Kingdom

Objective: Some patients with metastatic bladder cancer (mBC) have durable responses to immune checkpoint inhibitors (ICIs); others progress early while suffering from autoimmune toxicity. Currently there is no prognostic score or tumour marker to predict who will benefit from ICIs in bladder cancer. We designed a novel prognostic score to stratify response to ICIs in patients with mBC.

Methods: We analysed data from patients with mBC receiving ICIs as second- or later-line treatment between 2013–2023. We assessed key patient characteristics and their impact on progression-free survival (PFS) and overall survival (OS) using Kaplan-Meier and Cox-regression methods (retained if $p<0.05$). Variables independently correlated with OS and PFS on multivariate analysis were selected to create a new score. Radiological response to ICIs was assessed. C-statistic was calculated to assess the model's fit. SPSS and Stata software were used.

Results: Between 2013–2023, 149 patients received ICIs for mBC previously treated with at least one line of platinum chemotherapy. Median OS was 9.3 months (IQR2.7–21.4) and median PFS 2.5 months (IQR1.6–6.2). On multivariate analysis, variables independently correlating with improved OS and PFS were absent liver and bone metastases, haemoglobin$\geqslant$100g/L, alkaline phosphatase$\leqslant$130unit/L, neutrophil-to-lymphocyte ratio$>$5, and time from last therapy$\geqslant$6 months.

Equal weighting was given to each variable to create a new score for stratifying patient outcomes. This 3-tier model that strongly correlated with OS (HR 2.0, 95% CI 1.4–2.4, p<0.001) and PFS(HR 1.7, 95% CI 1.2–2.0, p<0.001). Median OS for patients with 0-1, 2 and 3-5 risk factors was 24.2, 6.7, and 2.4 months, respectively, and complete or partial response was seen in 45.8%, 21.2%, and 6.5%, respectively. This model achieved a C-statistic of 0.70(95% CI 0.65-0.75), which is comparable to those of previous studies.

Conclusions: We used routinely available metrics from real-world data to develop a new model that stratifies outcomes of patients with mBC receiving post-chemo ICIs. Certain variables suggested by literature, such as ECOG PS, were not found to correlate with survival in our data. The model requires further validation.

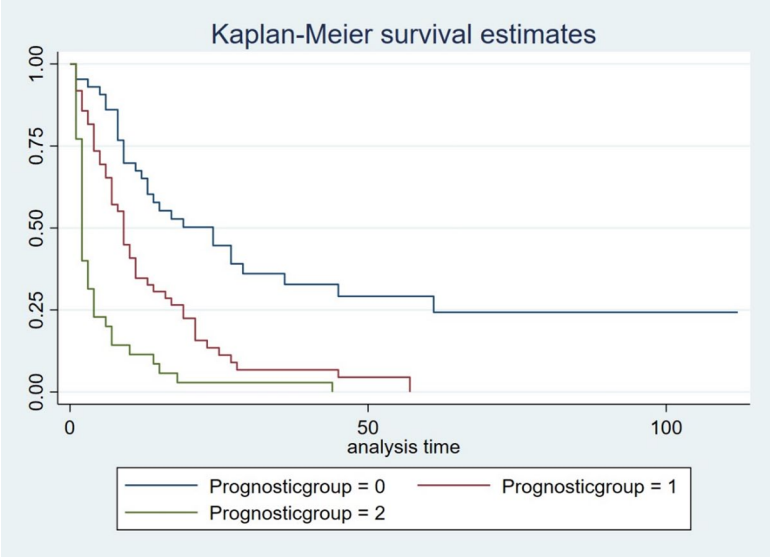

Figure. Stratification of overall survival across grouped risk factors to create 3-tier model.

Abstract Code: IUCS20464-81

SunRISe-5 Trial In Progress: A phase 3, randomized, open-label study of TAR-200 compared with intravesical chemotherapy after Bacillus Calmette-Guérin in recurrent high-risk non–muscle-invasive bladder cancer

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Objective: Efficacious therapies for patients with high-risk non–muscle-invasive bladder cancer (HR NMIBC) whose disease recurs after bacillus Calmette-Guérin (BCG) therapy are limited. TAR-200 is a novel intravesical drug delivery system designed to provide local, sustained release of gemcitabine within the bladder. SunRISe-5 (NCT06211764) is a randomized, open-label, multicenter phase 3 study that evaluates the safety and efficacy of TAR-200 compared with intravesical chemotherapy in patients with papillary-only HR NMIBC that recurs within the first year of BCG treatment who either refuse or are ineligible for radical cystectomy (RC).

Methods: Eligible patients are aged ⩾18 years, have an ECOG performance status of 0-2, and were diagnosed within ⩽90 days of informed consent with histologically confirmed recurrent, papillary-only HR NMIBC (defined as high-grade Ta or any T1, no carcinoma in situ) with a last dose of BCG ⩽12 months, who are ineligible for or who have elected not to undergo RC. Patients

will be stratified based on T stage and prior BCG. 250 patients will be randomized 1:1 to receive TAR-200 every 3 weeks for an induction phase and every 12 weeks during a maintenance phase or to receive investigator's choice of mitomycin C or gemcitabine weekly during induction and monthly during the maintenance phase. The primary end point is disease-free survival. Secondary end points include recurrence-free survival, time to next intervention, time to disease worsening, time to progression, overall survival, safety and tolerability, and patient-reported health-related quality of life outcomes. This trial is enrolling patients across 4 sites in the UK.

Funding: Janssen Research & Development.

Previously presented at AUA Annual Meeting; May 3-6; San Antonio, TX, USA by S.Porten et al. – Reused with permission

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