Abstracts ASCO GU 2015 - Oncologie Journaal

**Part I: Prostate**
Guest speakers: Dr. Gil, Dr. Van den Bergh, Prof. Van Moorselaar

*Topics: Androgen Deprivation Therapy (abstracts: 2 (oral) and 5 (oral)), Markers to predict effectiveness of a therapy (abstracts: 137 (oral) and 138 (oral)), Radiotherapy (abstracts: 4 (oral) and 229 (poster))*

**Part II: Prostate**
Guest speakers: Prof. De Meerleer, Prof. Gerritsen, Prof. Roumeguère

*Topics: Early disease (abstracts: 3 (oral), 40 (poster), 198 (poster)), Combining ADT and docetaxel in mCRPC (abstract 140 (oral)), Immunotherapy (abstracts: 171 (poster), 172 (poster))*

**Part III: GU, non prostate, non renal cell carcinoma**
Guest speaker: Prof. Van Moorselaar, Prof. Roumeguère, Prof. Gerritsen

*Topics: Understanding and Profiling Urothelial Cancer (abstracts: 289 (oral), 290 (oral)), Early-stage Bladder and Urothelial Cancer (abstracts: 292 (poster), 300 (poster), 306 (poster, 331 (poster)), Advanced Urothelial Cancer (abstract: 294 (oral))*

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**Part I: Prostate**
Dr. Gil (oncology), Dr. Van den Bergh (radiotherapy), Prof. Van Moorselaar (urology)

**Abstract 2:**

**Long-term survival update of the Scandinavian Prostate Cancer Group 6 study: Bicalutamide 150 mg daily versus placebo in hormone-naïve, non-metastatic prostate cancer.**

Author(s): Frederik Birkebæk Thomsen, Klaus Brasso, Ib Jarle Christensen, Jan-Erik Johansson, Anders Angelsen, Teuvo L. J. Tammela, Peter Iversen; Copenhagen Prostate Cancer Center, Department of Urology, Rigshospitalet, Copenhagen, Denmark; The Finsen Laboratory, Rigshospitalet and Biotech Research and Innovation Centre, University of Copenhagen, Copenhagen, Denmark; Department of Urology, Örebro University Hospital, Örebro, Sweden; St. Olav's University Hospital, Trondheim, Norway; Tampere University Hospital, Tampere, Finland

Background: The optimal timing of endocrine therapy in non-metastatic prostate cancer (PCA) is not clear. There is a need for more data from randomized trials. Methods: A randomized, double-blind, parallel-group trial comparing bicalutamide 150 mg once daily with placebo in addition to standard of care in patients with hormone-naïve, non-metastatic PCAs. Kaplan-Meier analysis was used to estimate overall survival (OS) and multivariate Cox proportional hazard model was performed to analyse time-to-event (death). Results: 1,218 patients were included into the SPCG-6 study, 607 patients were randomised to bicalutamide and 611 patients to placebo. The majority (81.4%) were managed on watchful waiting. After median 14.6 years follow-up, 866 (71.1%) patients died, 428 (70.5%) in the bicalutamide arm and 438 (71.7%) in the placebo arm, p=0.87. In patients with localised disease (cT1-2, N0/Nx) survival favoured randomisation to the placebo arm (HR=1.19 (95% CI: 1.00-1.43), p=0.056). Bicalutamide significantly improved OS and reduced the risk of death by 23% relative to the placebo arm in patient with locally advanced disease (cT3-4, any N; or any cT, N+) with a median survival difference of 1.8 years (HR=0.77 (95% CI: 0.63-0.94, p=0.01). The survival benefit of bicalutamide in patients with locally advanced PCAs was
present throughout the study period. In multivariate Cox proportional hazard model OS was dependent on age (HR 1.55 (95% CI:1.20-1.85)), baseline PSA (localised PCa HR for 2 x increase in PSA 1.09 (95% CI:1.02-1.16), locally advanced PCa HR 1.23 (95% CI:1.14-1.33)), WHO histological grade (moderate vs. well HR 1.27 (95% CI:1.08-1.49), poor vs. well HR 1.92 (95% CI:1.51-2.45)), and randomisation to placebo in locally advanced disease (HR=0.76 (95% CI: 0.61-0.95)). Conclusions: The addition of early bicalutamide to standard of care resulted in a significant OS benefit in patients with locally advanced PCa, whereas patients with localised PCa derived no survival benefit from early bicalutamide. The survival benefit of bicalutamide therapy increased with higher baseline PSA. Clinical trial information: NCT00672282

Abstract 5:
Place of short-term androgen deprivation therapy in intermediate-risk prostate cancer treated with radiotherapy: A phase III trial.

Author(s): Abdenour Nabid, Nathalie Carrier, Eric Vigneault, Luís Souhami, Céline Lemaire, Marc-André Brassard, Boris Bahoric, Robert Archambault, François Vincent, Thu-Van Nguyen-Huynh; Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; Centre Hospitalier Universitaire de Québec, Québec City, QC, Canada; Centre Universitaire de Santé McGill, Montreal, QC, Canada; Hôpital Maisonneuve-Rosemont de Montréal, Montréal, QC, Canada; Centre de Santé et Services Sociaux de Chicoutimi, Chicoutimi, QC, Canada; Hôpital Général Jui de Montréal, Montréal, QC, Canada; Hôpital de Gatineau, Gatineau, QC, Canada; Centre Hospitalier Régional de Trois-Rivières, Trois-Rivières, QC, Canada; Department of Radiation Oncology, Centre Hospitalier de l’Université de Montréal, Montreal University, Montreal, QC, Canada

Background: The place of short term androgen deprivation therapy (STADT) in combination with radiation therapy (RT) for patients with intermediate risk prostate cancer (IRPC) remains controversial. The purpose of this prospective, randomized trial was to compare outcomes between patients with IRPC treated with different doses of RT with or without STADT, (PCS III trial, Clinical Trials.gov, NCT00223145). Methods: From December 2000 to September 2010, 600 patients with IRPC were randomized to 6 months of STADT and two levels of prostate RT doses of 70 (arm 1) or 76 Gy (arm 2) versus prostate dose-escalated RT alone at 76 Gy (arm 3). STADT consisted of bicalutamide and goserelin for six months. RT (2 Gy per fraction) started four months after the beginning of STADT. Biological failure and disease-free survival (DFS) were primary end-points, with overall survival (OS) as secondary endpoint. DFS and OS rates were estimated with Kaplan-Meier and compared with log rank test and Cox regression. Results: Patient’s characteristics were well balanced among the 3 arms (median age 71 years, median PSA 10 ng/ml, median Gleason score 7). At a median follow-up of 75.4 months, biochemical failure occurred in 84 (14%) patients (arms 1 to 3: 12.5%, 8.0%, 21.5%) with statistical difference between arm 1 and 3 (p = 0.023) and arm 2 and 3 (p < 0.001). There was no significant difference between arm 1 and 2. A total of 113 (19%) patients had died with only 6 deaths (1%) attributed to prostate cancer. The 5-/10-year DFS rates were 93%, 97.5% and 86%, and 77%, 90% and 64.5%, respectively. Significant differences in DFS between the treatment arms were observed at 5 years but at 10 years it was observed only between arm 1 and 3 (p=0.01) and arm 2 and 3 (p<0.001). The 5-/10-year OS rates were 91%, 95% and 93%, and 64%, 70% and 78%, respectively. There was no statistical difference in OS between arms at 5 and 10 years. Conclusions: In patients with IRPC, the use of STADT in association with RT, even at lower doses, leads to a superior biochemical control and DFS as compared to dose-escalated RT alone. These outcomes did not translate into an improved OS. Source of Funding: AstraZeneca Pharmaceuticals Grant. Clinical trial information: NCT00223145
Abstract 137:
Genetic variants of the organic anion transporter SLCO2B1 as pharmacogenomic determinants of response to androgen deprivation therapy (ADT) for prostate cancer.

Author(s): Philip W. Kantoff, Xiaodong Wang, Wanling Xie, Mari Nakabayashi, Mark Pomerantz, Gwo-Shu Mary Lee; Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; Dana-Farber Cancer Institute, Boston, MA; Dana-Farber Cancer Institute, Harvard School of Medicine, Boston, MA

Background: Genotypes at three SNPs (rs12422149; rs1789693; rs1077858) within SLCO2B1 were associated with time to progression (TTP) on ADT in the Dana-Farber Cancer Institute (DFCI) Prostate CRIS ADT cohort (J Clin Oncol. 2011 29(18): 2565). Variation at exonic SNP rs12422149 (Gln to Arg) allows more efficient import of DHEAS, enhances AR signaling and cell growth, and as a result, is associated with shorter TTP on ADT. We further externally validated the association of SLCO2B1 variants with TTP on ADT in an independent ADT cohort and estimate their association with overall survival (OS) in both cohorts. Methods: An independent ADT cohort (N=616) was established for validation. TTP was defined using the same criteria as for the original cohort. The associations of genetic variants with TTP on ADT and OS were estimated from multivariable Cox regression and adjusted by known prognostic factors. Effects of one intronic SNP rs1077858 on SLCO2B1 and DHEAS uptake activity were characterized in cell cultures. Results: Association between genotype at rs12422149 and TTP on ADT was confirmed in univariable (P= 0.0187) and multivariable (adjusted HR= 1.31 for GG vs AA/AG, P= 0.0489) analyses. The Median OS from ADT initiation was 6.5 years in all patients (N= 1094, original plus validation cohort). The intronic SNP rs1077858 was significantly associated with the OS from ADT initiation in both univariable (P= 0.0091) and multivariable (adjusted HR= 1.34 for GG vs AA/AG, P= 0.014) analyses. The difference of median OS was 18 months. SLCO2B1 expression in normal prostate tissue carrying the major allele of SNP rs1077858 (AA) was significantly lower than those carrying the risk allele (GG) (Ptrend= 0.0193), suggesting that the association of the SNP rs1077858 with the OS on ADT may be due to its impact on the SLCO2B1 expression. SLCO2B1 knockdown in vitro decreased DHEAS uptake and diminished DHEAS-induced prostate cancer cell growth. Conclusions: Germline variants within SLCO2B1 modulate function or expression of SLCO2B1, subsequently affecting the uptake of androgen precursors and affecting TTP or OS in prostate cancer patients.

Abstract 138:
AR splice variant 7 (AR-V7) and response to taxanes in men with metastatic castration-resistant prostate cancer (mCRPC).

Author(s): Emmanuel S. Antonarakis, Changxue Lu, Yan Chen, Brandon Luber, Hao Wang, Mary Nakazawa, Angelo M. De Marzo, William B. Isaacs, Rosa Nadal, Channing Judith Paller, Samuel R. Denmeade, Michael Anthony Carducci, Mario A. Eisenberger, Jun Luo; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; The James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD; Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD; The Johns Hopkins Medical Institutions, Baltimore, MD

Background: AR-V7 is a truncated form of AR that lacks the ligand-binding domain but remains constitutively active. We previously showed that detection of AR-V7 from circulating tumor cells (CTCs) in men with mCRPC was associated with primary resistance to enzalutamide and abiraterone. Here, we hypothesized that AR-V7[+] patients would retain sensitivity to taxane chemotherapy. Methods: We used a qRT-PCR assay to interrogate CTCs for AR-V7 mRNA in prospectively enrolled patients with mCRPC starting docetaxel or
cabazitaxel. We sought associations between AR-V7 status and PSA response rates (the primary endpoint), PSA progression-free survival (PSA-PFS), and clinical/radiographic progression-free survival (PFS). Multivariable regressions were performed to determine the independent effect of AR-V7 status on clinical outcomes. 36 taxane-treated men were required to produce a 2-sided 95% CI for the difference in PSA response rates (between AR-V7[+] and AR-V7[–] men) with an upper bound of 60%, assuming that 30% of men would be AR-V7[+].

**Results:** 37 taxane-treated patients were enrolled, and 17 (45.9%) had detectable AR-V7 in CTCs. PSA responses were achieved in both AR-V7[+] and AR-V7[–] men (41% vs 65%, P=0.19). Median PSA-PFS was comparable in AR-V7[+] and AR-V7[–] men (4.5 vs 6.2 mo, HR 1.72, P=0.32). Likewise, median PFS was comparable in AR-V7[+] and AR-V7[–] men (5.1 vs 6.9 mo, HR 2.65, P=0.11). After incorporating data from our prior study in 62 abi/enza-treated patients, it was observed that clinical outcomes in AR-V7[+] men were superior with taxanes than with abi/enza, while outcomes did not differ by treatment type in AR-V7[–] men. For example, in AR-V7[+] men, PSA responses were higher in taxane-treated versus abi/enza-treated men (41% vs 0%, P<0.001), and median PSA-PFS and PFS were longer in taxane-treated men (HR for PSA-PFS = 0.19, P=0.001; HR for PFS = 0.21, P=0.003).

**Conclusions:** Detection of AR-V7 in CTCs from men with mCRPC is not associated with primary resistance to taxane chemotherapy, and such patients may retain sensitivity to taxanes. Further, in AR-V7[+] men, taxanes appear to be more efficacious than abi/enza. AR-V7 may represent a treatment-selection marker in mCRPC.

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**Abstract 4:**

**A randomized trial of 79.2Gy versus 70.2Gy radiation therapy (RT) for localized prostate cancer.**

Author(s): Jeff M. Michalski, Jennifer Moughan, James Purdy, Walter Bosch, Jean-Paul Bahary, Harold Y. Lau, Marie Duclos, Matthew Parliament, Gerard Morton, Daniel A. Hamstra, Michael J. Seider, Michael Lock, Malti Patel, Hiram Alberto Gay, Eric Vigneault, James Dignam, Howard Mark Sandler; Washington University in St. Louis, St. Louis, MO; NRG Oncology Statistics and Data Management Center, Philadelphia, PA; University of California, Davis, Sacramento, CA; Department of Radiation Oncology, Centre Hospitalier de l’Université de Montréal, Montreal University, Montreal, QC, Canada; Department of Radiation Oncology, Tom Baker Cancer Center, Calgary, AB, Canada; Centre Universitaire de Santé McGill, Montreal, QC, Canada; Cross Cancer Institute, Edmonton, AB, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada; Department of Radiation Oncology, University of Michigan Health System, Ann Arbor, MI; Akron City Hospital, Akron, OH; London Regional Cancer Program, London, ON, Canada; McMaster University, Hamilton, ON, Canada; Washington University School of Medicine in St. Louis, St. Louis, MO; Centre Hospitalier Universitaire de Québec, Québec City, QC, Canada; Radiation Therapy Oncology Group, Philadelphia, PA; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA

**Background:** RTOG 0126 is a phase III trial for localized prostate cancer (PC) testing whether dose escalation to 79.2Gy with 3DCRT or IMRT will improve overall survival (OS). **Methods:** Stage cT1b-T2b with Gleason Score (GS) 2-6 and PSA ≥ 10 and <20 or GS 7 and PSA <15 were eligible and randomized to receive 79.2Gy or 70.2Gy. No androgen withdrawal was used. Treatment was 3DCRT or IMRT to 79.2Gy in 44 fractions or 70.2Gy in 39 fractions. The objective was to detect a 23% reduction in mortality hazard (HR=0.77) for 79.2Gy. ASTRO and Phoenix definition was used for biochemical failure (BF). Time to local progression (LP), distant metastases (DM), PC death, and late GI/GU toxicity was calculated from date of registration. OS was estimated by Kaplan Meier and arms compared with log rank test. BF, LP, DM, time to late GI/GU, and PC death were estimated by cumulative incidence method and arms compared with Gray’s test. **Results:** 1,532 men were randomized, 763 to 79.2Gy and 769 to 70.2Gy. 1,499 were eligible, 751 and 748 in the 79.2Gy and 70.2Gy arms respectively. Median age was 69, 70% had PSA < 10 ng/ml, 84% with GS 7, 57% had T1 disease, and 66% used 3D-CRT. With a median of 7.0 years follow up, the 5 and 10-yr rates...
of OS are 88% and 67% with 79.2Gy and 89% and 66% with 70.2Gy (p=0.87; HR (95%CI)=0.98 (0.79,1.21)). The ASTRO (Phoenix) BF rates at 5 and 10 yr are 25% (16%) and 30% (26%) with 79.2Gy and 40% (21%) and 45% (43%) with 70.2Gy (both p<0.0001). The 5 and 10-yr rates of LP are 1% and 4% with 79.2Gy and 2% and 8% with 70.2Gy (p=0.0059; HR (95%CI)=0.46 (0.27,0.81)). The 5 and 10 yr rates of DM are 2% and 5% with 79.2Gy and 3% and 8% with 70.2Gy (p=0.026; HR (95%CI)=0.57 (0.35,0.94)). The high dose arm had lower rate of salvage therapy, 13.5% vs 21%, p=0.0002. The 10 yr rates for time to late grade ≥ 2 GI/GU are 22%/15% with 79.2Gy and 16%/10% with 70.2Gy (p=0.0063/p=0.001). Time to late grade ≥ 3 GI was higher for the 79.2Gy arm (p=0.035) but time to late grade ≥ 3 GU toxicity was not (p=0.14). **Conclusions:** Despite significant improvement in BF, DM, and LP rates, dose escalation did not improve OS. Patients receiving high dose radiation experience more late toxicity. Clinical trial information: [NCT00033631](https://clinicaltrials.gov/show/NCT00033631)

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**Abstract 229:**

**Oligometastatic prostate cancer: An evaluation of stereotactic body radiotherapy (SBRT) as an alternative to palliative androgen deprivation therapy.**

**Author(s):** Daniel Robert Henderson, Alison Tree, Helen Taylor, Vincent Khoo, Nicholas John Van As; Royal Marsden NHS Foundation Trust, London, United Kingdom; Royal Marsden NHS Foundation Trust, Surrey, United Kingdom; The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; The Royal Marsden NHS Foundation Trust, London, United Kingdom; Royal Marsden Hospital, London, United Kingdom

**Background:** Oligometastatic prostate cancer (OPC) can be defined as 1-3 sites of metastasis, typically occurring some years after radical treatment for primary disease. Standard treatment is long-term palliative androgen deprivation therapy (ADT). Although effective, this treatment can have a significant impact on quality of life. We hypothesized that ablative treatment with SBRT may delay disease progression, and therefore the need for palliative ADT.

**Methods:** A single-institution case series 2011-present. Eligible patients had metachronous OPC diagnosed by F-choline PET/CT and were ADT-naïve in the palliative setting. Stereotactic body radiotherapy was given to a dose of 30 Gy in 3 fractions using a robotic radiosurgery system (Cyberknife). ADT-free survival was calculated as the time from completion of treatment for oligometastatic disease to initiation of ADT with palliative intent. Follow up with clinical review and PSA was undertaken at four weeks, then three monthly, with F-choline PET/CT restaging as indicated. Palliative ADT was initiated for metastatic disease not amenable to further SBRT. **Results:** Twenty one patients received SBRT for ADT-naïve OPC. Median time from primary treatment to oligometastatic relapse was 59.7 months. Median PSA doubling time was 4.1 months. Six patients received a short course (3-6 months) of ADT with SBRT. Sites treated: bone (8) and lymph node (20). At a median follow up of 16.7 months, 81% (17) remained ADT-free. Median ADT-free survival was 28 months (95% CI: 10 - 43 months). All but one patient had a PSA response, with a median reduction of 84%. There were no local failures. Incidence of grade 1 and 2 CTCAE toxicity was 29% (6) and 5% (1), respectively. No toxicity of grade 3 or above was observed. **Conclusions:** SBRT for OPC is well tolerated. A clinically significant delay in initiation of palliative ADT was observed in patients with ADT-naïve oligometastatic disease. In view of this potential to improve patients’ quality of life, randomised trials against a standard of care are justified.

Author(s): W. James Morris, Scott Tyldesley, Howard H Pai, Ross Halperin, Michael R. McKenzie, Graeme Duncan, Gerard Morton, Nevin Murray, Jeremy Hamm; BC Cancer Agency, Vancouver, BC, Canada; BC Cancer Agency, Victoria, BC, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada; Vancouver Cancer Centre, British Columbia Cancer Agency, Vancouver, BC, Canada; BC Cancer Research Centre, Vancouver, BC, Canada

**Background:** This trial compared the efficacy of DE-EBRT and LDR-B for National Comprehensive Cancer Network (NCCN) high and intermediate-risk disease. **Methods:** A planned sample size of 400 patients were randomized to one of two treatment arms and stratified by risk group. Both arms received 12 months of androgen deprivation therapy (ADT) with luteinizing hormone releasing hormone (LHRH) agonist plus a non-steroidal anti-androgen for at least 1 month. After 8 months of neo-adjuvant ADT, both arms received whole pelvis EBRT (46Gy/23#). Patients assigned to DE-EBRT (standard arm) then received a conformal EBRT boost (32Gy/16#). Patients assigned to LDR-B (experimental arm) received an Iodine-125 LDR boost prescribed to a minimum peripheral dose of 115Gy. The primary endpoint was relapse free survival (RFS) defined by biochemical criteria using the nadir+2 ng/mL threshold. Time zero was the date of the first LHRH injection. **Results:** Between Dec 2002 and Sep 2011, 276 high-risk and 122 intermediate-risk patients were accrued at 6 cancer treatment centers. 200 men were assigned to DE-EBRT and 198 to LDR-B. The treatment arms were well balanced in terms of age and known prognostic factors. Median follow up (FU) is 6.5 years; 65 men have >9 years FU. There were 12 major protocol violations in each arm. By intent-to-treat analysis, the 3-, 5-, 7-, and 9-year Kaplan-Meier RFS estimates are 94% vs 94%, 77% vs 89%, 71% vs 86%, and 63% vs 83% for DE-EBRT and LDR-B respectively (hazard ratio = 0.473; 95% CI 0.292 – 0.765; P = 0.0022). Randomization (p<0.001), percent positive cores (p=0.005), initial PSA (p=0.006) and clinical T-stage (p=0.013) were predictive of RFS in a multivariable Cox model. The median PSA at latest FU for non-relapsing patients assigned to LDR-B is 0.02 vs 0.24 ng/mL for DE-EBRT. **Conclusions:** In a randomized trial, an Iodine-125 LDR boost was much more effective than an EBRT boost in rendering unfavorable-risk prostate cancer patients biochemically disease free.

*ASCENDE-RT- Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy is an NCI registered trial (NCT00175396). Clinical trial information: NCT00175396

Abstract 40: Outcomes following immediate versus delayed radical prostatectomy among men on active surveillance for prostate cancer.

Author(s): Christopher James Welty, Pauline Fillipou, Janet E. Cowan, Peter Carroll; University of California, San Francisco, San Francisco, CA

**Background:** Little is known about the risk of delaying radical prostatectomy (RP) until biopsy progression following active surveillance (AS) for prostate cancer. This study examines the pathological outcomes associated with surgery following AS compared to
immediate treatment of prostate cancer with similar grades. **Methods:** Men who underwent RP between 1997-2013 at University of California San Francisco were included. The first comparison consisted of men who met strict AS inclusion criteria (Gleason Score ≤ 6, PSA ≤ 10, clinical stage <T3, ≤ 33% biopsy cores positive, and ≤ 50% of any single core positive) at diagnosis and underwent AS prior to RP (AS+RP) compared to men who met strict AS criteria and underwent RP within 6 months (immediate RP). The second comparison consisted of men who met strict AS criteria and were upgraded on follow-up biopsy compared to a cohort of men matched on the basis pre-treatment biopsy pathology. Logistic regression was used to determine associations of RP group with adverse pathology (stage ≥pT3/N1, positive margins, and/or upgrade to Gleason ≥4+3), adjusting for clinical and demographic factors. **Results:** We identified 241 men who underwent RP after a period of AS, 157 of whom initially met strict AS criteria. The median time to RP was 20 months (IQR 14-36). Men who met strict criteria and underwent immediate RP were less likely to have unfavorable pathology than those who underwent AS+RP (OR 0.39, 95% CI 0.24-0.62). Fifty-four of the men who underwent AS+RP did so have upgrading to Gleason 3+4 disease. These patients were matched with 154 men based on their pre-treatment biopsy features. After appropriate matching, the timing of RP was not associated with adverse pathology (OR 1.27, 95% CI 0.65-2.49). **Conclusions:** Men who undergo surgery following AS are a selected subset of men with low risk prostate cancer. The surgical pathology features of these patients are more similar to men undergo surgery after diagnosis with intermediate risk prostate cancer than those diagnosed with very low risk disease. Additional follow-up of this and other cohorts is needed to assess long term clinical outcomes following delayed RP.

**Abstract 198:**
Androgen deprivation with or without radiation therapy for clinically node-positive prostate cancer.

Author(s): Jason Alexander Efstathiou, Chun Chieh Lin, Phillip John Gray, Ahmedin Jemal; Massachusetts General Hospital, Harvard Medical School, Boston, MA; American Cancer Society, Atlanta, GA; Massachusetts General Hospital, Boston, MA

**Background:** Clinically lymph node positive (cN+) prostate cancer (PCa) is an often fatal disease. Its optimal management remains largely undefined given a lack of prospective, randomized data to inform practice. We sought to describe modern practice patterns in the management of cN+ PCa and assess the effect of adding radiation therapy (RT) to androgen deprivation therapy (ADT) on survival using the National Cancer Data Base. **Methods:** Patients with cN+ PCa with no distant metastases diagnosed between 2004-2011 were included. Five-year overall survival for patients diagnosed between 2004-2006 and treated with ADT alone or ADT+RT were compared. Propensity score (PS) matching was used to balance baseline characteristics and Cox multivariate regression analysis was used to estimate hazard ratios (HRs) for all-cause mortality. **Results:** 3,540 patients were included. 32.2% were treated with ADT alone and 51.4% received ADT+RT. Patients aged <65, those with private insurance, lower comorbidity scores, higher Gleason scores, and lower PSA values were significantly more likely to receive ADT+RT (p<.05). After PS matching, 318 patients remained in each group. Compared to ADT alone, ADT+RT was associated with a 50% decreased risk of five-year mortality (HR: 0.497, 95% CI: 0.37-0.67, p<.001). **Conclusions:** Using data recorded in a large national database, we have identified a significant survival benefit for patients with cN+ PCa treated with ADT+RT. These data, if appropriately validated, suggest that a significant proportion of such patients at high risk for
prostate cancer death may be undertreated warranting a re-evaluation of current practice guidelines.

Abstract 140:
Androgen deprivation therapy (ADT) plus docetaxel (D) versus ADT alone for hormone-naïve metastatic prostate cancer (PCa): Long-term analysis of the GETUG-AFU 15 phase III trial.

Author(s): Gwenaelle Gravis, Jean-Marie Boher, Florence Joly, Stephane Oudard, Laurence Albiges, Franck Priou, Igor Latorzeff, Remy Delva, Ivan Krakowski, Brigitte Laguerre, Frederic Rolland, Christine Theodore, Gael Deplanque, Jean-Marc Ferrero, Damien Pouessel, Loïc Mourey, Philippe Beuzeboc, Muriel Habibian, Michel Soulie, Karim Fizazi; Department of Medical Oncology, Institut Paoli Calmettes, Marseille, France; Biostatistic, Institut Paoli-Calmettes, Aix-Marseille Université, Marseille, France; Department of Medical Oncology, Centre François Baclesse, Caen, France; Department of Medical Oncology, Hôpital Européen Georges Pompidou, René Descartes University, Paris, France; Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France; Centre Hospitalier Départemental Les Oudairies, La Roche sur Yon, France; Clinique Pasteur, Toulouse, France; Institut de Cancérologie de l’Ouest, Angers, France; Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France; Centre Eugène Marquis, Rennes, France; Centre René Gauducheau, Saint-Herblain, France; Hospital Foch, Suresnes, France; Groupe Hospitalier St. Joseph, Paris, France; Department d’Oncologie Medicale, Centre Antoine Lacassagne, Nice, France; Department of Medical Oncology, Hôpital Saint-Louis, Paris, France; Institut Claudius Regaud, Toulouse, France; Medical Oncology Department, Institut Curie, Paris, France; UNICANCER, Paris, France; Centre Hospitalier Universitaire Rangueil, Toulouse, France; Institut Gustave Roussy, University of Paris Sud, Villejuif, France

Background: ADT is standard treatment for metastatic PCa. Recently, the E3805 trial reported a survival benefit for (ADT+D) in high volume disease (HVD) patients, whereas the GETUG-15 trial did not demonstrate a survival improvement among a less selected group of patients (pts) with hormone-naïve metastatic PCa. We report an updated analysis of overall survival (OS) of the GETUG 15 trial and aligned the definition of HVD and low volume disease (LVD) subgroups.

Methods: Long-term OS was analyzed in the intention-to-treat population (n=385 pts). Additionally, we retrospectively assessed the tumor volume as defined per E3805 criteria in all patients enrolled in GETUG 15. Results: See Table. With a median follow-up of 82.9 months (95%CI [80.5-84.3]) (vs 50 months (95%CI [80.5-84.3] in the original analysis), 212 patients (55%) have died. The median OS is 46.5 [39.1-60.6] and 60.9 months [46.1-71.4] in the ADT and in the ADT + D arms, respectively (HR: 0.9 [95%CI: 0.7-1.2]). In HVD patients (n=183, 47.5%), median OS rates were 35.1 months [29.9-44.2] in the ADT alone arm and 39 months [28-52.6] in the ADT+D arm (HR: 0.8 [0.6-1.2]). Conclusions: With longer follow-up, the addition of docetaxel to ADT did not significantly improve OS in patients with hormone-naïve metastatic prostate cancer. In the retrospective analysis using aligned definition of volume of metastasis as E3805, the HVD outcomes were similar to E3805 for ADT alone and there was a non-significant 4 months increase in OS with ADT+D, in this underpowered subset. Clinical trial information: 00104715.
* HVD: visceral (lung or liver) metastases and/or 4 or more bone metastases with at least 1 beyond the pelvis and the vertebral column.

Abstract 171:
Antigen-specific immune responses through 24 months in the STAND trial: A randomized phase 2 study evaluating optimal sequencing of sipuleucel-T (sip-T) and androgen deprivation therapy (ADT) in biochemically-recurrent prostate cancer (BRPC).

Author(s): Emmanuel S. Antonarakis, Adam S. Kibel, George W. Adams, Lawrence Ivan Karsh, Aymen Elfiky, Neal D. Shore, Nicholas J. Vogelzang, John M. Corman, Robert Claude Tyler, Candice McCoy, Todd Devries, Nadeem A. Sheikh, Charles G. Drake; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; Urology Centers of Alabama, Homewood, AL; The Urology Center of Colorado, Denver, CO; Brigham and Women’s Hospital, Harvard University, Boston, MA; Carolina Urologic Research Center, Myrtle Beach, SC; US Oncology Research, Comprehensive Cancer Centers of Nevada, Medical Oncology, Las Vegas, NV; Dendreon Corporation, Seattle, WA

Background: Sip-T is an autologous cellular immunotherapy targeting prostatic acid phosphatase (PAP), approved for treatment of asymptomatic/minimally symptomatic metastatic castration-resistant prostate cancer. STAND evaluates sequencing of sip-T and ADT in men with BRPC at high risk of metastases. Here we report interim assessments of cellular and humoral responses through 24 mos. Methods: Men (n=68) were randomized 1:1 to sip-T followed by ADT (2 wks after 3rd infusion; Arm 1) or ADT (3-mo lead-in) followed by sip-T (Arm 2). Product parameters (total nucleated cell [TNC] count, antigen presenting cell [APC] count, APC activation) were determined with each product manufacture. Cellular and humoral immune responses were analyzed through 24 mos with a repeated measures statistical model. Results: Sample size ranged 8–28 for cellular responses and 34–64 for humoral responses. PA2024 ELISPOT count increased vs baseline at most timepoints (p<0.05) and was lower in Arm 2 vs Arm 1 (p=0.015). PA2024 antigen-specific T-cell proliferation increased from baseline at all timepoints (p≤0.001) and was lower in Arm 2 vs Arm 1 (p<0.001). PA2024 antibody titers were similar between treatment arms (p=0.976). PA2024 antibody titer was significantly higher at the 3rd sip-T infusion visit and remained elevated at 24 mos (23 times higher on average vs baseline; p<0.001). A similar antibody titer profile was reported for PAP but of lesser magnitude. The number of immune responders (post-baseline antibody titer ≥25,600) was similar at any timepoint between arms (Arm 1: 30/34, 88.1%; Arm 2: 32/34, 94.1%; p=0.673). Higher cumulative TNC and baseline hemoglobin positively correlated with maximum PA2024 antibody titer response (p<0.05). Conclusions: Sip-T induced a robust immune response sustained to 24 mos in men with BRPC. Cellular response appeared to differ according to treatment sequence; humoral response was similar between treatment arms. Given its consistent association with the humoral response, cumulative TNC count may be a potential biomarker of response to sip-T.

Clinical trial information: NCT01431391

Abstract 172:
Combining active immunotherapy and immune checkpoint inhibitors in prostate cancer.

Author(s): Harpreet Singh, Ravi Amrit Madan, William L. Dahut, Geraldine Helen O’Sullivan Coyne, Myrna Rauckhorst, Sheri McMahon, Christopher Ryan Heery, Jeffrey Schlim, James L. Gulley; Genitourinary Malignancies Branch, National Cancer Institute at the National Institutes of Health, Bethesda, MD; National Cancer Institute at the National Institutes of Health, Bethesda, MD; Medical Oncology Branch, National Cancer Institute at the National Institutes of Health, Bethesda, MD; Laboratory of Tumor Immunology and Biology, National Cancer Institute at the National Institutes of Health, Bethesda, MD
Background: Results of recent clinical trials have intensified interest in immunotherapy in oncology. A number of cancer immunotherapies have been approved recently, while others are in late stage clinical development. The poxvirus-based active immunotherapy, PROSTVAC is generally well tolerated and is currently being evaluated in a global Phase 3 randomized, placebo-controlled trial. Ipilimumab, an approved immune checkpoint inhibitor in melanoma, is also being evaluated in a Phase 3 trial in chemo-naïve mCRPC. Methods: Results of two Phase 2 trials in men with mCRPC who were treated with PROSTVAC alone were compared with results from a Phase 1 combination study in mCRPC patients treated with PROSTVAC plus escalating doses of ipilimumab. Patients were enrolled in the Phase 1 combination study when docetaxel was the only FDA-approved mCRPC treatment that improved overall survival (OS). Results: In a multicenter Phase 2 trial, 125 men were randomized 2:1 to receive PROSTVAC or placebo. Patients treated with PROSTVAC had improved OS compared to placebo (25.1 vs 16.6 months; HR 0.56; 95% CI 0.37-0.85). Similar data was seen in a second phase 2 trial of PROSTVAC, where 32 patients with mCRPC had a median OS of 26.6 months (predicted median OS by the Halabi nomogram was 17.4 months). In a Phase 1 combination study of 30 mCRPC patients with similar baseline characteristics (predicted median OS of 18.5 months), patients were treated with PROSTVAC plus escalating doses of ipilimumab. The observed median OS was 31.3 months for all dose cohorts and 37.2 months for patients treated at 10 mg/kg based on updated overall survival data. Furthermore, there appears to be a tail on the curve with approximately 20% of patients at 10 mg/kg alive at 80 months. Conclusions: The comparison of data from three independent trials of PROSTVAC active immunotherapy in three similar patient populations provides hypothesis-generating data that the addition of an immune checkpoint inhibitor may have a positive effect on overall survival through a potential synergy in mechanism of action. The updated long term survival data is further evidence of improved OS with PROSTVAC. Future randomized trials are being planned to prospectively evaluate this hypothesis. Clinical trial information: NCT00113984

Abstract 289:

Comprehensive genomic profiling urinary bladder urothelial carcinoma (UC) to reveal frequency of clinically relevant genomic alterations.

Author(s): Jeffrey S. Ross, Siraj M. Ali, Julia Andrea Elvin, Juliann Chmielecki, Roman Yelensky, Doron Lipson, Vincent A. Miller, Philip J. Stephens, Kai Wang; Albany Medical College, Albany, NY; Foundation Medicine, Inc., Cambridge, MA

Background: Clinically advanced UC is a devastating disease lacking effective therapies. We present a comprehensive genomic profile-based (CGP) study of UC designed to detect clinically relevant genomic alterations (CRGA) that could inform the selection of established and novel targeted therapies. Methods: DNA was extracted from 40 microns of FFPE sections from 295 consecutive cases of relapsed/metastatic UC. CGP was performed on hybridization-captured, adaptor ligation based libraries to a mean coverage depth of 688X for 3,230 exons of 182 cancer-related genes plus 37 introns from 14 genes frequently rearranged in cancer. The CGP assay included base substitutions (SUB), INDELs, copy number alterations (CNA) and fusions/rearrangements. CRGA were defined as GA linked to drugs on the market or under evaluation in mechanism driven clinical trials. Results: There were 75%...
male and 25% female patients with a mean age of 66 years. 295/295 (100%) of UC were high grade and advanced stage (III and IV). 294/295 (99.7%) UC had at least 1 GA on CGP with a mean of 6.4 GA/UC with 61% SUB + INDEL, 37% CNA and 2% fusions. 275 (93%) UC had at least 1 CRGA involving 75 individual genes with a mean of 2.6 CRGA/UC. The most common CRGA involved CDKN2A (34%), FGFR3 (21%), PIK3CA (20%) and ERBB2 (16%). FGFR3 GA were of diverse type and included 10% fusions. ERBB2 GA were equally divided between amplifications (CNA) and SUB. ERBB2 SUB were predominantly in the extracellular domain and were highly enriched in the micropapillary UC subgroup. Multiple clinical antitumor responses to therapies targeting FGFR3 and ERBB2 will be presented. Conclusions: Using a CGP assay capable of detecting all classes of GA simultaneously, an extraordinary high frequency of CRGA were identified in a large series clinically advanced UC. More than one-third of these relapsed/refractory cases of UC harbored alterations in FGFR3 and ERBB2 that are showing active responses to targeted therapies. Continued evaluation of CGP for UC and the development of genomic-based clinical trials designed to employ targeted agents potentially in combination with cytotoxic drugs for this challenging disease appears warranted.

Abstract 290:
Clonal heterogeneity in platinum-resistant metastatic urothelial cancer.

Author(s): Bishoy Faltas, Himisha Beltran, Kenneth Eng, Chantal Pauli, Brian D. Robinson, Juan Miguel Mosquera, David M. Nanus, Scott T. Tagawa, Olivier Elemento, Mark A. Rubin; New York-Presbyterian Hospital, New York, NY; Weill Cornell Medical College, New York, NY; Department of Medicine, Institute for Precision Medicine, Weill Cornell Medical College and New York-Presbyterian Hospital, New York, NY

Background: Beyond platinum-based chemotherapy, there are currently no approved therapies for advanced PRUC. Our objective was to generate the first detailed genomic profile of metastatic PRUC to identify molecular changes critical to platinum-resistance and metastasis development. Methods: Following informed consent, we collected 50 urothelial cancer (UC) tissue samples, from 23 patients. Metastatic tumor samples were obtained from biopsies or metastatectomy. Germline samples were prospectively collected and matched archival formalin-fixed paraffin-embedded primary tumors from the same patients were retrieved. Our cohort comprises 23 metastatic samples, 37 PRUC samples and 18 trios of matched primary, metastatic and germline samples including 2 rapid autopsies yielding tumor samples from multiple sites. We performed whole exome sequencing of all tumor and germline samples followed by integrated analysis of somatic single nucleotide variants and copy-number alterations and to analyze clonality. We utilized DAVID bioinformatic tool for pathway analysis. Results: Advanced PRUC samples were enriched for several molecular alterations, we identified 414 recurrently mutated genes including common genes such as TP53 (45%) as well as actionable alterations in PIK3CA (11%) and TSC1 (19%). We also identified frequent alterations in novel genes such as DPCR1 (38%) and NIN (28%). Frequent copy number alterations included CDKN2A deletion (33%), E2F3 amplification (10%) and ERBB2 amplification (7%). Pathway analysis showed enrichment of mutations in the apoptosis (p=1.0E-7) and cell cycle regulation (p=1.6E-2) pathways compared to TCGA primary UC dataset. We reconstructed phylogenetic trees from matched primary, metastatic and germline trios. Variant allele frequencies of certain shared mutations increased from primary tumors to lymph node and visceral metastases revealing clonal selection of mutations present in primary tumors. Conclusions: This study generates a detailed profile of the genomic landscape of advanced PRUC revealing extensive heterogeneity and clonal selection underlying platinum-resistance and metastatic spread.
Abstract 292:

Comparative effectiveness of adjuvant chemotherapy (AC) versus observation in patients with ≥ pT3 and/or pN+ bladder cancer (BCa).

Author(s): Matt D. Galsky, Kristian Stensland, Erin L. Moshier, John Sfakianos, Russell Bailey McBride, Che-Kai Tsao, Martin Francis Casey, Simon J Hall, Paolo Boffetta, William K. Oh, Juan P. Wisnivesky; The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY; Lahey Clinic, Burlington, MA; Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY; Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, NY; Department of Urology, Icahn School of Medicine at Mount Sinai, New York, NY; Ichan School of Medicine at Mount Sinai, New York, NY

Background: Though Level I evidence supports the use of neoadjuvant chemotherapy (NAC) in BCa, the data supporting AC has been mixed. Experience suggests an adequately powered trial to definitively assess the role of AC is unlikely to be completed. Alternative approaches to evidence development are necessary.

Methods: Patients who underwent cystectomy for ≥pT3 and/or pN+ M0 BCa were identified from the National Cancer Database. Patients who received NAC and/or diagnosed after 2006 (most recent year with survival data) were excluded. Logistic regression was used to calculate propensity scores representing the predicted probabilities of assignment to AC versus observation based on: age, demographics, year of diagnosis, pT stage, margin status, lymph node density, distance to hospital, hospital cystectomy volume, and hospital type and location. A propensity score-matched cohort of AC versus observation (1:2) patients was created. Stratified Cox proportional hazards regression was used to estimate the hazard ratio (HR) for overall survival for the matched sample while propensity score adjusted and inverse probability of treatment weighted proportional hazards models were used to estimate adjusted HR for the full sample. A sensitivity analysis examined the impact of comorbidities.

Results: 3,294 patients undergoing cystectomy alone and 937 patients undergoing cystectomy plus AC met inclusion criteria. Patients receiving AC were significantly more likely to: be younger, have more lymph nodes examined and involved, have higher pT stage, have positive margins, reside in the Northeast and closer to the hospital, and have private insurance. AC was associated with improved overall survival (Table). The results were robust to sensitivity analysis for comorbidities.

Conclusions: AC was associated with improved survival in patients with ≥pT3 and/or pN+ BCa in this large comparative effectiveness analysis.

HR for overall survival with AC versus observation.

<table>
<thead>
<tr>
<th>Model</th>
<th>HR [95% CI]</th>
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<tbody>
<tr>
<td>Cox model adjusted for propensity score</td>
<td>0.78 [0.71-0.86]</td>
</tr>
<tr>
<td>Cox model weighted by the inverse probability of treatment</td>
<td>0.79 [0.75-0.83]</td>
</tr>
<tr>
<td>Matched sample (Cox model stratified)</td>
<td>0.69 [0.60-0.78]</td>
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Abstract 300:

PDL1 status in muscle-invasive urothelial carcinoma in the context of neoadjuvant cisplatin-based chemotherapy.

Author(s): Jen-Jane Liu, Alexander S Baras, Nilay M Gandhi, Gunes Guner, Enrico Munari, Sheila Faraj, Janis M. Taube, Mark Schoenberg, Noah M. Hahn, Charles G. Drake, George J. Netto, Trinity Bivalacqua; The James Buchanan Brady Urological Institute, The Johns Hopkins Medical Institutions, Baltimore, MD; The Johns Hopkins Medical Institutions, Baltimore, MD; Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD; The Johns Hopkins University School of Medicine, Baltimore, MD; Montefiore Medical Center, Baltimore, MD; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD
Background: Although complete and partial response rates to cisplatin-based neoadjuvant chemotherapy (cNAC) are 40-50% in patients with muscle-invasive urothelial carcinoma (MIUC), post-cystectomy cancer specific survival (CSS) for patients who fail to respond to cNAC is poor (5-y CSS = 27%). Therefore, up to half of MIUC could be amenable to alternative systemic therapies. Anti-programmed death ligand (PDL1) has shown promising results in tumors with proven PDL1 expression, including advanced stage MIUC. We evaluated PDL1 expression in MIUC in a cohort categorized by pathologic response to cNAC to test the hypothesis that anti-PDL1 therapy is a rational therapeutic option for patients non-responsive to cNAC. 

Methods: We studied 150 patients who received cNAC followed by open radical cystectomy (RC) from 2000-2013. Pathologic response (<pT1 N0 at RC) and CSS were compared to patients who had RC without cNAC. Tissue microarrays of MIUC specimens representing patients with and without response to cNAC were stained with PD-L1 (Cell-Signaling, E1L3N, 1:100) and FOXP3 (eBioscience, 236A/E7, 1:250). The degree of tumoral PDL1 and tumoral lymphocyte FOXP3 staining was manually scored. Tumors with 5% and >15/hpf staining were considered positive for PDL1 and FOXP3, respectively. Percentage of non-responders to cNAC staining positive for PDL1 was the primary outcome of our study. 

Results: The rate of PDL1 positivity in MIUC cNAC non-responders was 47% which was similar to the 43% rate in responders. There was a strong positive correlation of tumoral PDL1 staining with tumoral lymphocytes FOXP3 staining, Goodman-Kruskal gamma=0.71 (p<0.0001), which was independent of cNAC responder status (Table). 

Conclusions: Patients with MIUC that are non-responders to cNAC have poor long term CSS. Our results demonstrate that cNAC non-responders exhibit frequent PDL1 tumoral staining, suggesting that neoadjuvant or adjuvant anti-PDL1 therapy represents an attractive therapy worthy of prospective clinical trial testing in MIUC patients whose tumors do not respond to or in patients who cannot tolerate cisplatin based chemotherapy.

Abstract 306: Concurrent gemcitabine (GEM) and radiotherapy (XRT) as organ-sparing treatment for muscle-infiltrating bladder cancer (MIBC): Preliminary results of a patient-based cumulative analysis of seven phase I-II trials.

Author(s): Orazio Caffo, Catherine Thompson, Maria De Santis, Borut Kragelj, Daniel A. Hamstra, David Azria, Giovanni Pappagallo, Giovanni Fellin, Ananya Choudhury; Santa Chiara Hospital, Trento, Italy; The Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; LBI-ACR & ACR-ITR Vienna/CEADDP, KFJ-Spital, Wien, Austria; Institute of Oncology, Ljubljana, Slovenia; Department of Radiation Oncology, University of Michigan Health System, Ann Arbor, MI; Institut Régional du Cancer Montpellier, Montpellier, France; Azienda ULSS 13, Mirano, Italy; Ospedale Santa Chiara, Trento, Italy

Background: GEM is a highly effective radiosensitiser and has been combined with XRT in MIBC after transurethral resection (TUR) to achieve bladder preservation. Several phase I-II trials confirmed that concurrent GEM and XRT is a feasible treatment able to achieve good disease control and a high rate of organ preservation. We performed a patient-based cumulative analysis of the published trials with concurrent GEM/XRT in MIBC. 

Methods:
Primary data for patients (pts) enrolled in all published studies on GEM/XRT were provided from the institutions. **Results:** A total of 190 pts were treated in seven phase I-II GEM/XRT trials. The median age was 70 yrs (range 42-87 yrs). The histology was pure transitional in 79% and mixed with squamous features in 21% of the cases. Clinical stage was T2 in 70%, T3 in 21%, and T4 in 8% of the cases, respectively. After TUR, pts received a median XRT dose of 55.5 Gy (range 45-64 Gy) with standard and hypo-fractionated regimes used in 68% and 32% of the cases, respectively. GEM was administered on a weekly or twice-weekly basis, with doses ranging from 10 mg/sqm to 500 mg/sqm; a concurrent administration of cisplatin was planned in 38 pts (20%). Grade ≥ 3 acute and late urinary toxicities were recorded in 7 (4%) and 5 (3%) pts, while grade ≥ 3 acute and late intestinal toxicities were recorded in 20 (10%) and 1 (0.5%) pts, respectively. The complete remission rate was 93.3%. Thirty-six pts (18.9%) experienced a bladder recurrence with 14 pts undergoing cystectomy. The 3- and 5-year survival rates calculated by Kaplan-Meier methods are reported in the table. **Conclusions:** From this pooled analysis of the clinical outcomes of the pts enrolled in phase I-II studies it appears that GEM/XRT is a treatment with mild toxicity profile, able to achieve a high rate of bladder preservation and producing favorable outcomes compared to other published series for organ-sparing therapy for MIBC. Prospective studies are ongoing to confirm these findings.

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<thead>
<tr>
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<th>3-year</th>
<th>5 year</th>
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<tr>
<td>Bladder intact survival</td>
<td>65.8%</td>
<td>61.1%</td>
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<tr>
<td>Distant free survival</td>
<td>85.7%</td>
<td>85.7%</td>
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<tr>
<td>Overall survival</td>
<td>69.1%</td>
<td>65.1%</td>
</tr>
<tr>
<td>Disease specific survival</td>
<td>84.3%</td>
<td>82.6%</td>
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**Abstract 331:**
Assessing the impact on morbidity and mortality of neoadjuvant chemotherapy in patients with high-risk and muscle invasive bladder cancer eligible for radical cystectomy.

**Author(s):** Ettore Di Trapani, Rafael Sanchez-Salas, Lorenzo Rocchini, Giorgio Gandaglia, Marco Moschini, Daphne Lizee, Eric Barret, Francois Rozet, Marc Galliano, Renzo Colombo, Alberto Briganti, Francesco Montorsi, Xavier Cathelineau; Division of Oncology/Unit of Urology, Urological Research Institute, IRCCS Ospedale San Raffaele, Milan, Italy; Institut Mutualiste Montsouris, Paris, France; Department of Urology, A.O. Papa Giovanni XXIII, Bergamo, Italy

**Background:** Despite the increasing number of studies confirming the importance of neoadjuvant chemotherapy in patients addressed to radical cystectomy (RC) for bladder cancer (BC), its association remains controversial. We aimed to test the safety and the efficacy of neoadjuvant chemotherapy in pts underwent RC for BC in a multistitutional retrospective study. **Methods:** We analyzed 768 pts who underwent RC and PLND with / without neoadjuvant chemotherapy in two European high volume centers between 2007 and 2013. Complete demographic, pre and postoperative functional data and oncologic outcomes were collected. T-tests and Chi-square analyses were used to evaluate the differences between the groups. Kaplan-Meier curves were used to assess time to cancer specific mortality (CSM) free and overall mortality (OM) free survival. Univariable (UVA) and multivariable (MVA) logistic and Cox regression analyses were developed to address predictors of perioperative complications and CSM- and OM-free survival. **Results:** The mean follow up was 20 months (range 1-24). Mean age at surgery was 67 yrs (median 67 yrs). Patients had mainly pT2 disease (79,6%). Overall, 14% of pts had preoperative cisplatinum
based neoadjuvant chemotherapy. We did not find any difference in pre-operative and post-operative blood tests assessment (all p>0.1). Intraoperative blood loss was higher in patients who went directly to surgery (mean 1.200 vs 740 cc; p<0.001) but the number of transfusions was similar (p=0.77) as well as the hospital stay (p=0.8). The complication rate was not significant at the MVA logistic regression analysis (p=0.74) even after evaluating per Clavien-Dindo groups (p=0.11). Neoadjuvant chemotherapy showed a better CSM-free survival at UVA (p=0.035) and at MVA (p= 0.043; OR 0.44). Then a nomogram was developed to predict the 60 months CSM-free rate showing an accuracy of 72.6%. Conclusions: Neoadjuvant chemotherapy is associated with a better CSM-free survival in patients with high-risk bladder cancer eligible for RC and it’s not linked with perioperative morbidity. We finally developed the first nomogram predicting the CSM-free rate in these patients.

Abstract 294: Phase II study of pazopanib with weekly paclitaxel in refractory urothelial cancer.

Author(s): Sandy Srinivas, Sujata Narayanan, Lauren Christine Harshman, Russell Kent Pachynski, Anthony P. Lam, Alice C. Fan, Shermeen Poushnejad, Denise Haas, Ulka N. Vaishampayan; Stanford University Medical Center, Stanford, CA; Stanford University, Stanford, CA; Dana-Farber Cancer Institute, Boston, MA; Washington University School of Medicine in St. Louis, St. Louis, MO; Stanford Cancer Institute, Stanford, CA; Karmanos Cancer Institute, Wayne State University, Detroit, MI

Background: Currently, there are no standard treatments for relapsed or refractory urothelial carcinoma (UC). Discouraging results have been observed in trials evaluating established chemotherapeutics as single agents or in combination regimens. Paclitaxel has moderate activity when used alone and in combination in UC. Pazopanib is active in other solid tumors secondary to its potent anti-angiogenic effects. We report the results of a multi-center phase II study evaluating the combination of paclitaxel with pazopanib in refractory UC. Methods: Eligible patients (pts) had histologically confirmed UC, with disease that progressed on upto 2 chemotherapeutic regimens. Pazopanib (800 mg) was administered daily, with weekly paclitaxel (80mg/m2) for 3 weeks in a 28 day cycle. Treatment was continued until disease progression or unacceptable toxicity. The primary endpoint of the study was response-rate (RR) based on RECISTv 1.1 criteria. Secondary endpoints included safety, and progression free-survival (PFS). Results: From April 2010 to September 2014, 32 patients were enrolled. Median age was 67 years (29-89) and median ECOG performance status was 1 (0-2). 17 pts (54%) had UC of the upper urinary tract disease and 15(47%) had primary bladder tumors. All pts had multiple metastatic sites, including 9 (28%) with liver metastases. Median number of prior cytotoxic regimens was 2, and 50% were considered cisplatin responsive. Objective responses were observed in 58% with 3 (12%) complete responses (CR), and 12 pts (46%) with partial responses (PR). Another 9 (35%) acheived stable disease (SD). High grade toxicities included grade 3 hypertension (n=2), grade 3 fatigue (n=4), grade 3 thrombosis (n=2) and grade 4 neutropenia (n=2). Nearly half of the patients( n= 14 ) required growth factor support. Conclusions: Our phase II study combining paclitaxel and pazopanib demonstratedsignificant anti-tumor activity in relapsed/refractory UC. This combination is safe, effective and is worthy of evaluation in randomized phase 3 study. Clinical trial information: NCT01108055