Investigational pathway for Bladder carcinoma

Symptoms: Visible and non visible haematuria, passing clots or tissue bits in urine, persistent irritative urinary symptoms

Imaging USS Abdomen and Pelvis (A) Intravenous Urography /CT Urogram (A) MR Urogram (B)

Investigations when muscle invasive bladder tumour is suspected - CT Chest abdomen and Pelvis with contrast (B) FDG PET CT (C) Investigations

-CBP and Renal profile (A)

-Diagnostic Cystoscopy ± biopsy (B)

- Urine cytology (C)

- Advanced vision investigation (Narrow band imaging/ Fluorescent cystoscopy) (C)

Examination under anesthesia and Transurethral resection of Bladder tumour.

TURBT findings should include: Number and size of tumours, relation to ureteric orifices, comment on urethra, Prostate and bladder neck (A).

Following TURBT for suspected non-muscle invasive bladder tumour patients , one dose of Intravesicle Mitomycin at the dosage of 40mg in 50 ml of saline should be administered for Intravesicle treatment within 24hrs of resection (A)



Trans urethral resection of bladder tumour

Examination under anesthesia and Transurethral resection of Bladder tumour. TURBT findings should include: Number and size of tumours, relation to ureteric orifices, comment on urethra, Prostate and bladder neck (A) Following TURBT for low grade NMIBC, one dose of Intravesicle Mitomycin should be administered within the 24hrs of resection (A)







Cisplatin Ineligible is defined as presence of one of the following :

- 1. ECOG PS \geq 2 OR KPS < 60 to 70 %
- 2. Creatinine Clearance < 60 mL/min
- 3. Grade \geq Hearing Loss
- 4. Grade \geq 2 Peripheral Neuropathy
- 5. NYHA Class \geq III Heart Failure

Systemic Treatment For Metastatic Bladder Cancer (Second Line And Subsequent Treatment)

Rechallange with Platin +Gemcitabine (If previous platin based therapy >12 months back) (A)

Weekly paclitaxel (B)

Pemetrexed (B)

Docetaxel (B)

Gemcitabine (B)

Immunotherapy (B/C)

Pembrolizumab

Nivolumab

Atezolizumab

(Optimal (B) only if patient is affordable or there is company insurance cover other wise optional (C)

SUGGESTED REFERENCES:

- 1. G. Jakse, F. Algaba, P.-U. Malmström and W.Oosterlinck, A second-look TUR in T1 transitional cell carcinoma: why?, Eur Urol 45 (2004),pp. 539–546.
- R.T. Divrik, Ü. Yildirim, F. Zorlu and H. Özen, The effect of repeat transurethral resection on recurrence and progression rates in patients with T1 tumours of the bladder who received intravesical mitomycin: a prospective, randomized clinical trial, J Urol 175 (2006), pp. 1641– 1644
- R. Sylvester, W. Oosterlinck and A. van der Meijden, A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a metaanalysis of published results of randomized clinical trials, J Urol 171 (2004), pp. 2186–2190.
- 4. R.J. Sylvester, W. Oosterlinck and J.A. Witjes, The schedule and duration of intravesical chemotherapy in patients with non–muscle-invasive bladder cancer: a systematic review of the published results of randomized clinical trials, Eur Urol 53 (2008), pp. 709–719.
- 5. R.F. Han and J.G. Pan, Can intravesical bacillus Calmette-Guérin reduce recurrence in patients with superficial bladder cancer? A meta-analysis ofrandomized trials, Urology 67 (2006), pp. 1216–1223.
- 6. Böhle A and P.R. Bock, Intravesical bacillus Calmette-Guerin versus mitomycin C in superficialbladder cancer: formal meta-analysis of comparative studies on tumor progression, Urology 63 (2004), pp. 682–. M. Huncharek and B. Kupelnick, The influence of intravesical therapy on progression of superficial transitional cell carcinoma of the bladder: a metaanalytic comparison of chemotherapy versus bacilli Calmette-Guerin immunotherapy, Am J Clin Oncol 27 (2004), pp. 522–528.
- 7. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladdercancer: long-term results in 1,054 patients. J ClinOncol 2001;19:666-675.
- 8. Shariat SF, Karakiewicz PI, Palapattu GS, et al.Outcomes of radical cystectomy for transitional cellcarcinoma of the bladder: a contemporary series from the Bladder Cancer Research Consortium. J Urol 2006;176:2414-2422.
- 9. Zietman AL, Grocela J, Zehr E, et al. Selective bladder conservation using transurethral resection, chemotherapy, and radiation: management and consequences of Ta, T1, and Tis recurrence within the retained bladder. Urology 2001;58:380–5.
- 10. Rodel C, Grabenbauer GG, Kuhn R, et al.Combined-modality treatment and selective organ preservation in invasive bladder cancer: long-term results. J Clin Oncol 2002;20: 3061-3071.
- 11. Shipley WU, Kaufman DS, Zehr E, et al. Selective bladder preservation by combined modality protocol treatment: long-term outcomes of 190 patients with invasive bladder cancer. Urology 2002;60:62–7.

- 12. Neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: a randomised controlled trial. International collaboration of trialists. Lancet 1999; 354:533–40.
- 13. Sternberg CN, de Mulder PH, Schornagel JH, etal., European Organization for Research, Treatment of Cancer Genitourinary Tract Cancer Cooperative Group. Randomized phase III trial of high-doseintensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. J Clin Oncol 2001;19:2638–46.
- 14. Advanced Bladder Cancer Meta-analysis Collaboration. Neoadjuvant chemotherapy ininvasive bladder cancer: a systematic review and meta-analysis. Lancet 2003; 361:1927–34.
- 15. Von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. J Clin Oncol 2005;23:4602–8.
- 16. James ND, Hussain SA, Hall E, Jenkins P, Tremlett J, Rawlings C, Crundwell M, Sizer B, Sreenivasan T, Hendron C, Lewis R, Waters R, Huddart RA; BC2001 Investigators. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer N Engl J Med 2012; 366:1477-1488

17. Kamat AM et al. Society for Immunotherapy of cancer consensus statement on immunotherapy for the treatment of bladder carcinoma. J Immunother Cancer.2017; 5:68

18. Murthy V et al. Clinical outcomes with Dose-escalated adaptive radiation therapy for Urinary Bladder cancer: A Prospective study. Int J Radiat Oncol Phs.2016 Jan 1;94(1):60-66

19. O'Brien T et al. Prevention of bladder tumours after nephroureterectomy for primary upper urinary tract urothelial carcinoma: a prospective, multicentre, randomised clinical trial of a single postoperative intravesical dose of mitomycin C (the ODMIT-C Trial). Eur Urol. 2011 Oct;60(4):703-10