Intravesical Therapies

Indications for use

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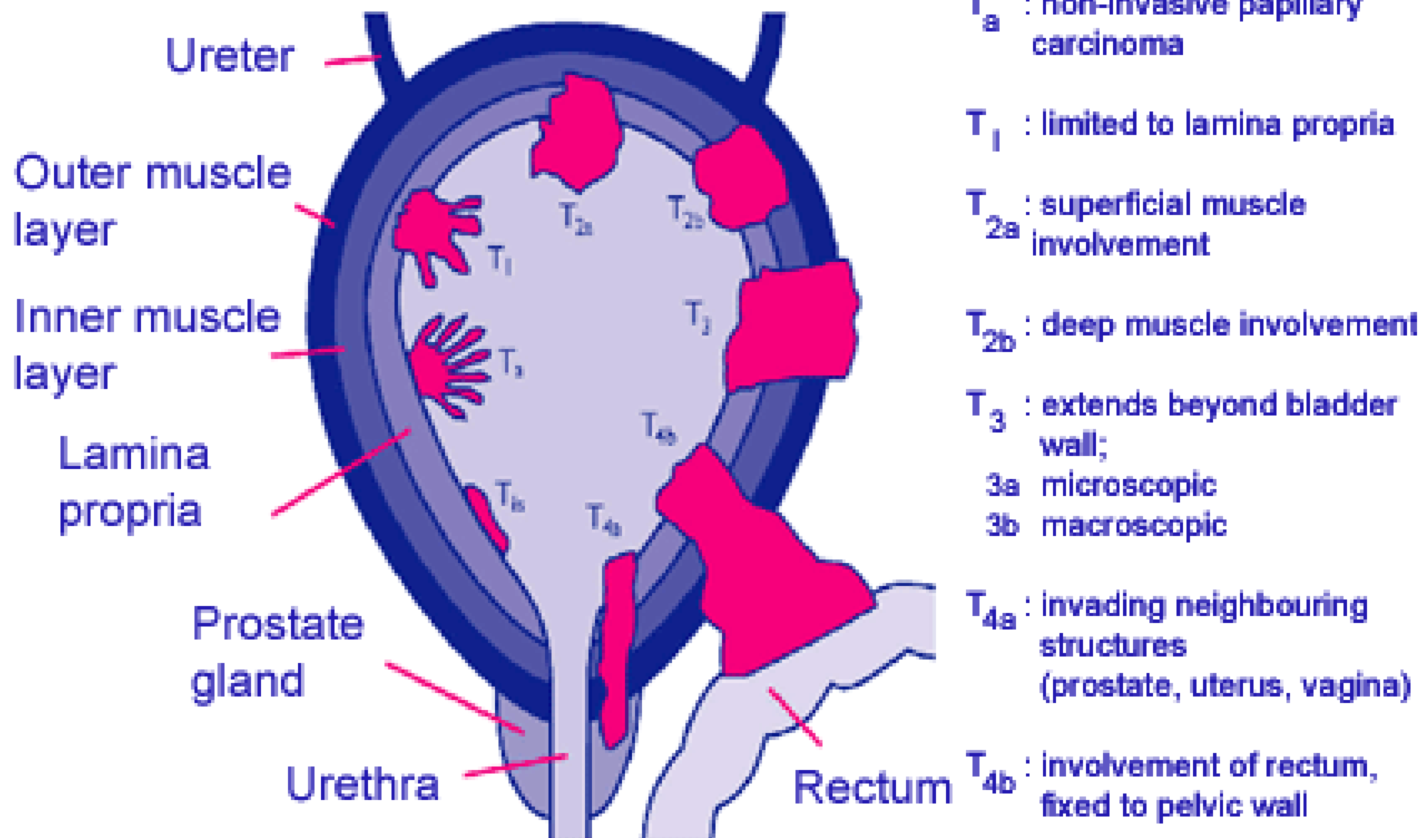
Client/Patient Group

- 2nd most common urological malignancy worldwide
- 11,000 New cases of bladder cancer diagnosed in the UK every year
- 4th most common cancer in men(7,300new cases each year)
- 10th most common cancer in women(3,000 new cases each year)
- 90% of tumours present as superficial
- Not without risk
- 80% treated bladder cancer recur
- In 2011, there were over 5,000 deaths from Bladder cancer in the UK (Cancer Research UK).

Staging of bladder cancer



Clinical staging of Non Muscle Invasive Bladder Cancer

- Low risk - pTaG1/2
- Intermediate risk - pT1G1/2, Primary CIS (indications for use)
- High risk - pTaG3, pT1G3, pT1+CIS (indications for use)

Approximately 75-80% of patients with bladder cancer present with disease confined to mucosa pTa, CIS or sub mucosa pT1

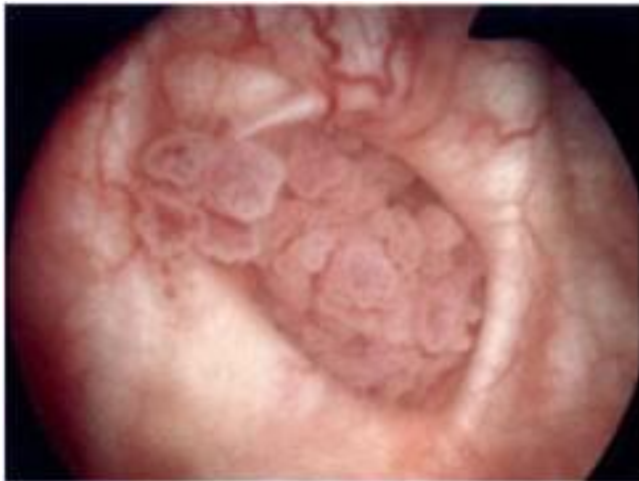
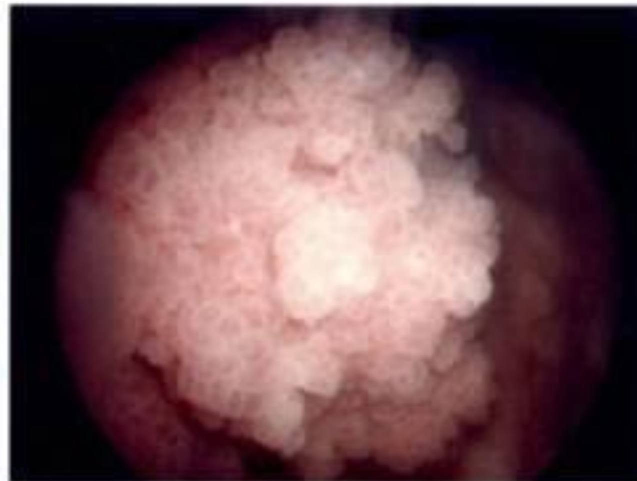
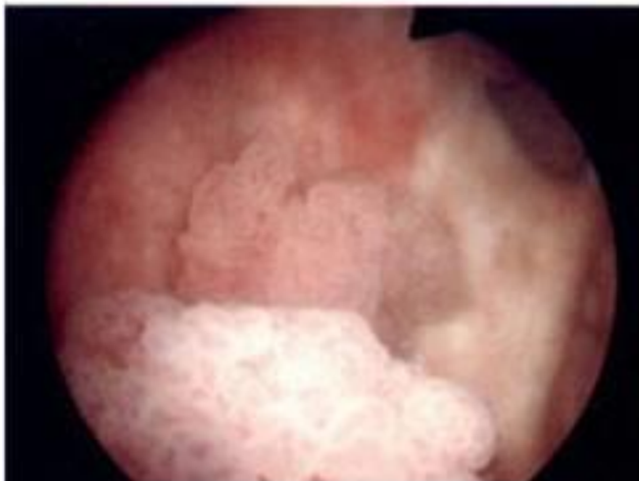
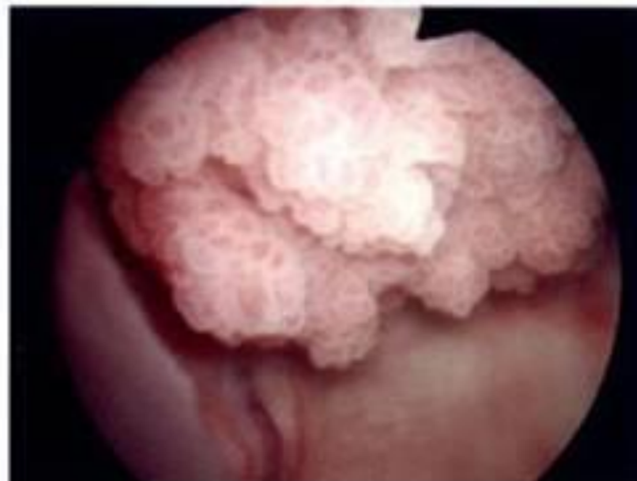
Statistics....

- pTaG1/G2 5% risk of progression
- pT1G1/G2 10% risk of progression
- Primary CIS 12% risk of progression
- pTaG3 or pT1G3 30% risk
- Any G3+CIS 50% risk

(EORTC)

Re resection Indications

- Initial resection is incomplete. E.g. when multiple or large tumours are present
- When pathology reports that the TUR specimen does not contain muscle tissue
- When high grade non muscle invasive tumour or pT1 tumour has been identified at initial TUR
- Demonstrates that 2nd TUR can increase recurrence free survival
- Resection should be carried out 2-6 weeks post initial TUR
- Should include a resection of the primary tumour site
- Treatment for pT1 high grade tumours and pT2 tumours are completely different, therefore correct staging is important
- 'We do not want to under stage the patient's disease'

Why Intravesical Therapy?

- High percentage of patients recur and progress to muscle invasive disease
- Necessary to consider adjuvant therapy in all patients
- To treat residual TCC post resection
- Reduces recurrence by >50%
- Prophylaxis post resection to reduce incidence of recurrence
- To increase the disease free interval
- To preserve the bladder
- One immediate instillation of chemotherapy post TUR decreases percentage of recurrence by 12% (48.4% to 36.7%) and the odds of recurrence by 39%

Benefits of Intravesical Administration

- Easy to administer/catheterisation
- Contained within the bladder sparring other organs from systemic effects/ differs from intravenous
- Easier to tolerate/ small doses
- High levels of compliance/ tolerance

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Intravesical chemotherapy

- Mitomycin C
- Dose 40mgs/40mls Normal Saline (Mito-in)
- Chemically stable for 24 hours following reconstitution
- When ? Post resection/single instillation
- Timing critical 6-24hours
- Treatment of choice
- One post op instillation should be given to all patients after TUR of presumably NMIBC
- Considered cost effective
- Destroys circulating tumour cells/ablative effect (chemo resection) of residual tumour cells at the resection site
- Course of six administered weekly for multiple recurrences

Drug characteristics

- Isolated from Streptomyces Bacterium
- Anti-biotic with anti-tumour properties
- Alkylating agent which interferes with cross linking of DNA (inhibits DNA synthesis)
- High molecular weight/little systemic absorption
- Protects against tumour implantation
- Mops up residual cells

Potential side effects

- Bladder irritation
- Frequency and dysurea
- Skin rash

- Principle - the drug should come into contact with the entire bladder urothelium

Intravesical chemotherapy

- Epirubicin/Anthracycline anti tumour antibiotic
- Inhibits DNA replication and repair
- Dose 50mgs/50mls Normal Saline
- Used for NMIBC since 1970's
- Very low absorption 80-90% recovered from urine
- Course of 6/52 for high grade tumours
- Utilized as an alternative to BCG
- Used in Newcastle as 2nd line to MMC

Potential side effects

- Urinary frequency
- Chemical cystitis
- Dysurea

- Systemic toxicity is rare!

TUR and Adjuvant treatment

- Up to 80% of treated superficial cancers recur
- Require regular cystoscopy surveillance/+ resection
- Propensity to recur and the possibility of disease progression makes bladder carcinomas one of the most expensive malignancies to be treated

Intravesical Immunotherapy

- Bacillus Calmette-Guerin is an attenuated strain of the living bovine tubercle bacillus, macro bacterium bovis
- 1921 Albert Calmette and jean Camille Guerin developed BCG as a vaccination for TB
- 1929 -TB post-mortems
- 1935 first tumours treated with BCG (cancer vaccine)
- 1976 Morales treated 1st bladder tumour with BCG
- Lamm reduction in recurrence in 1 year
- To date 6 strains of BCG
- Connaught used in Newcastle/Oncotice at present
- Oncotice licence for 1 year-treatment change due to shortage in Connaught
- ? More patients having radical surgery for HG NMIBC
- Robotic surgery at Freeman

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BCG

- Proven immunotherapy to prevent progression of NMIBC
- Treats tumours by immunostimulating
- BCG is a live attenuated mycobacterium
- BCG+maintanenence is critical for preventing progression
- Proven to reduce progression by 37%
- Average of 77 months recurrence free compared to 36
- Reduces likelihood of recurrence by 58%
- 3 year programme endorsed by British association of Urological Surgeons (BAUS) and British Uro-oncology Group (BUG)
- SWOG regime

BGC contraindications

- Haematuria or traumatic catheterisation
- TUR<10 days
- Patients who are immunocompromised
- Active TB- danger of exacerbation
- Pregnancy
- Caution with
  - patients with auto-immune diseases
  - prostheses
  - other live vaccines
  - UTI- don't give until infection resolved

Common side effects

- Cystitis, irrititive bladder
- Haematuria 11-19%
- Transient fever, rigors 31%
- Malaise
- Dysuria 46%
- Frequency 34%

Less common systemic effects

- Arthralgia
- Myalgia
- Conjunctivitis / urethritis
- BCG infection
- Sepsis
- Hepatitis
- Pneumonitis

Less common local side effects

- Bladder contracture
- Prostatitis
- Epididymo-orchitis
- Ureteric obstruction
- Renal abscess

Administration

- Reconstitution
- Communication – in both directions
- Catheterisation
- Administration
- Disposal of waste

- Advise -

  Men to use condoms to avoid infection from BCG in semen or vaginal fluid

  Give up smoking-higher risk of cancer returning after treatment

  Smokefree.nhs.uk

  Alcohol in small amounts to prevent dehydration

  Healthy diet and adequate exercise

Challenges

- Referral procedures-vigorous follow up regime/nurse led
- Follow ups - particularly for BCG patients
- Health & Safety
- Communication
    - internal
    - with patients and carers
    - with community service
    - Home treatments in Newcastle

Research

- BOXIT- A randomised phase III placebo controlled trial evaluating the addition of celecoxib to standard treatment of transitional cell carcinoma of the bladder
- HYMN- A randomised controlled phase III trial comparing hyperthermia plus mitomycin to a second course of mitomycin alone in patients with recurrence of non-muscle invasive bladder cancer following induction or maintenance bacillus Calmette-Guerin therapy
- Ofloxacin antibiotics with BCG
- Maintenance Mitomycin-C

(continued)

Research continued

- Hexvix study called PHOTO. A multi centre randomised clinical control study looking at the effectiveness of using blue light in day to day management of patients undergoing resection for HR NMIBC.
- Main objectives to see reduction of bladder cancer recurrence compared to white light

References

- European Association of Urology 2009
- British Association of Urology Nurses-Intravesical guidelines 2011
- BRITISH Uro-oncology Group (BUG)

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Thank you to BAUN for inviting me!!