# Testicular cancer and other germ cell tumours

# London Cancer 2018

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# Background

- Testicular germ cell tumours are the commonest cancers of young men
- Overall they are curable but long term side effects of treatment are well recognised
- Over the last 30-40 years treatment has been refined – patients who do well with treatment have benefitted from randomised controlled trials which have allowed treatment to be shortened without compromising efficacy

# Background

- Patients who have done less well ( because of extensive metastatic disease) have had treatment intensified
- Smaller phase 2 studies have identified candidate therapies which are able to cure patients who relapse- even patients who relapse after 2 lines of therapy may be still curable with 3rd line treatment
- Surgical excision of metastases seems important in achieving these outcomes

# Backround

- Ovarian germ cell tumours have often had similar approaches but whilst some have clear malignant potential that is amenable to chemotherapy – many the so called immature teratomas are less responsive and are probably being subjected to unnecessary chemotherapy rather than having surgery to remove metastases
- The approach in the paediatric oncology community has been rather different – here germ cell tumours are managed with less chemotherapy
- Ovarian immature teratomas tend to have surgical resection when metastatic rather than chemotherapy

# Backround

- Large projects of data collection ( MaGIC)- have demonstrated that around the age of 11 – germ cell tumours become les chemosensitive  and regimens considered less toxic and easier to administer than adult therapies  appearl to be less effective
- To improve therapies  we need to improve data collection and ensure that input into new regimens comes from the paediatric and adult oncologists

# Mutidiscipilinary working – the Anglian germ cell multidisciplinary team

- Network hosted at Barts covering an area of 7 million people
- Based around various hospitals – including all of East Anglia including Cambridge and parts of Kent ( through Guys and St Thomas' hospitals)
- All patients are presented through this forum including the teenage cases –in the last 3 years the ovarian germ cell tumours have also been presented

# The supra regional MDT

- Early stage cases are monitored locally – but all histology and scans are centrally reviewed
- Poor prognosis patients are referred to one of 3 hospitals ( Barts or Addenbrooke's or Guys)
- Surgery for metastatic residual disease is carried out at designated hospitals ( RPLND- Addenbrooke's or Guys)
- Neurosurgery – Addenbrooke's or Bart's health
- Lung surgery- Papworth , Guys , Bart's

# The supra regional MDT

- Salvage chemotherapy ( following failure of first line therapy ) is carried out at St Bartholomew's or Addenbrooke's
- High dose chemotherapy and stem cell transplantation is carried out at Barts
- Audit results

# Evolving approaches

- Stage 1 disease- generally offered surveillance if low risk of relapse ( ovarian and testicular)
- Stage 1 high risk – have option of adjuvant chemotherapy ( testicular)
- Tumours in solitary testis – offered the option of chemotherapy – if testis is producing adequate hormones with or without partial orchidectomy-
- Avoidance of unnecessary orchidectomy in patients with small lesions in the testis

# Good risk metastatic disease-95% cure rate

- Normally treated with 3 cycles of cisplatin, etoposide and bleomycin
- Good delivery of this therapy with maintenance of dose intensity and minimising treatment delay thought to be essential in improving outcome
- Sometimes this therapy is in appropriate – poor renal function or poor respiratory function
- Avoiding stopping bleomycin unnecessarily – best approaches to screening for toxicity
- A trial to assess the role of carboplatin in combination in patients up to 25 is due to start – should reduce hearing/ renal and neuropathic damage

# Good risk metastatic disease

- Post treatment surgery for residual masses is important in preventing late relapse
- Increasingly RPLND using robotic approaches is being offered
- MDT influence- reduction in overtreatment – some patients with minimally enlarged nodes are being observed in the first instance – many do not relapse  and thus avoid chemotherapy

# Metastatic seminoma

- More chemo-sensitive
- ? Can be managed with monotherapy – using carboplatin AUC10

| 199 patients | PFS | OS |
|---|---|---|
| BARTS | 96% | 98% |
| OTHER SITES | 86% | 94% |

# Intermediate-risk – 80% cure rate

- Currently our standard therapy is 4 cycles of BEP
- Participation in international trial of dose dense BEP ( 2 weekly rather than 3 weekly administration-P3BEP)

# Poor Risk – 60% cure rate

- Many patients are quite ill – may have evidence of renal obstruction, brain metastases – some delay diagnosis
- Many may not have a large testicular mass at all
- Treatment has been individualised – often induction chemotherapy then  either an intensive regimen ( e.g GAMEC) or conventional BEP
- Intensive therapies provide an increased chance of disease control first time round

# Comparison of outcome  Barts vs the rest

- Poor prognosis disease (97 patients)

| | PFS | OS | |
|---|---|---|---|
| Barts | 65% | 69% | |
| Other sites | 44% | 64% | |

# RELAPSED GCT

- Long History of treatment at Barts
- Sequence of phase 2 studies has allowed us to shorten therapy for relapse ( 6-weeks for some patients – normal LDH, < 35 y)
- Dose dense therapy – GAMEC has been the main second line therapy
- Non cisplatin- based therapy IPO ( irinotecan, oxaliplatin and weekly paclitaxel)- use as 3$^{rd}$ line therapy or where second line cisplatin based therapy is contra indicated

# Overall outcomes

- Using GAMEC as second line therapy overall 49% are progression free

Using High dose chemotherapy as 3rd line therapy approximately 25% will be cured

Overall cure rate for relapsed disease is around 60%

# High dose chemotherapy and stem cell transplantation

- This has been part of our integrated approach for many years
- Currently we use it as 3rd line therapy in relapsed gonadal germ cell tumours
- We use it on 1st relapse in mediastinal non-seminomatous germ cell tumours
- Patients remain under medical oncology – we have good working relationships with haematology who facilitate stem cell collection
- Mortality <5%

# Special Situations

- Brain metastases- use of GAMEC – which includes high dose methotrexate has allowed the avoidance of radiotherapy
- 71% are progression free in the first line setting
- 27% of those who relapse with brain metastases are rendered progression-free

# Incremental changes

- Use of low dose induction chemotherapy in patients with renal obstruction, shortness of breath etc
- Move to out patient monitoring in patients receiving intensive chemotherapy
- Reducing haematological thresholds to start chemotherapy to neut> 0.5 and platelets> 75
- Prophylactic antibiotics
- Use of olanzapine as antiemetic and reduction in steroid use

# Incremental changes – the effects

- Safer treatment- reduction in treatment related deaths
- Reduction in length of stay
- Reduced treatment related mortality

# Trials in relapsed GCT

- Local studies – GAMMA for relapsed GCT
- International studies – TIGER- due to open – randomiseng patients between conventional cisplatin-based therapy on 1st relapse or triple HDCT with stem cell transplantation

# Future areas of research

- CVS
- Studies of follow up
- Studies to reduce hearing damage
- Closer working with paediatric oncology partcularly in management of ovarian GCT

# Potential threats to the future

- Inadequate resource for the service – esp in terms of clinical nurse specialist support
- Inability to admit complications of treatment to Barts because of bed pressures
- Changes to the training environment making looking after of ill people more difficult
- Lack of pharmaceutical company interest in this disease