



The Carcinoma of Unknown Primary (CUP) service at Guys and St Thomas' Hospital

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AOS/CUP service lead
LCA pathway chair for AOS- CUP subgroup

+ Format



- How the CUP service at GSTT functions
- Our experience
- Clinical cases CUP
- Learning points



The GSTT MDT

Function

- 'local CUP team'- patients with metastatic malignant disease of undefined primary origin (MUO) patients are initially referred
 - For emergency presentations
 - Patients to be reviewed within 24 hours of referral via AOS (Mon-Fri)
- Specialist CUP (CUP) MDT to which a selected group of provisional CUP cases are referred for further advice on diagnosis and management- from GSTT and network hospitals





The GSTT MDT: Function

- Effective targeting of investigations to confirm treatable disease for MUO at GSTT (Bone only mets- network hospitals)
- Identification of 'treatable syndromes CUP' and refer to specialist MDM (NICE/LCA guidance)
- Management of cCUP: palliative care/ oncology

Treatable syndrome	MDM
Squamous carcinoma (upper/cervical LN)	Head & neck MDM
Adenocarcinoma axillary LN	Breast MDM
Squamous carcinoma inguinal nodes	Colorectal/Gynae MDM
Poorly diff carcinoma with mid-line distribution	Germ cell MDM
Women with predom peritoneal adenocarcinoma	Gynae MDM
Poorly diff neuroendocrine carcinoma	Neuroendocrine MDM
Solitary metastases	liver/lung/RNOH MDM



The GSTT MDT

Aims

- Stopping inappropriate tests for those not fit for treatment
- Streamline patient pathway
- Early oncology and palliative care support
- Key worker, support groups



+ GSTT team members

Meeting weekly with video-links with network hospitals

Weekly oncology/palliative care clinic

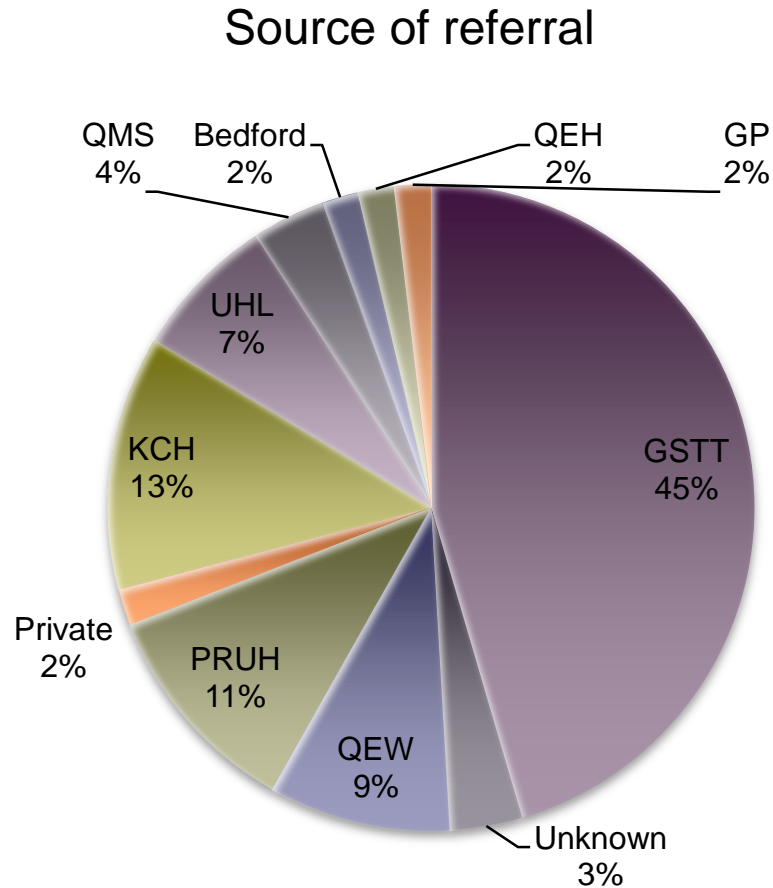
- Medical Oncology: Dr Sarah Ngan, Dr Nick Maisey
- Clinical Oncology : Dr Asad Qureshi
- Imaging specialist: Dr Sofia Gourtsoyianni
- Histopathologist: Dr Giuseppe Culora, Dr Mike Green
- Palliative Medicine: Prof Robert George
- Cancer nurse specialist:
 - Rachel Ingham (CUP CNS)
 - Tina Henry (AOS CNS)
- MDM co-ordinator : Debbie Williams



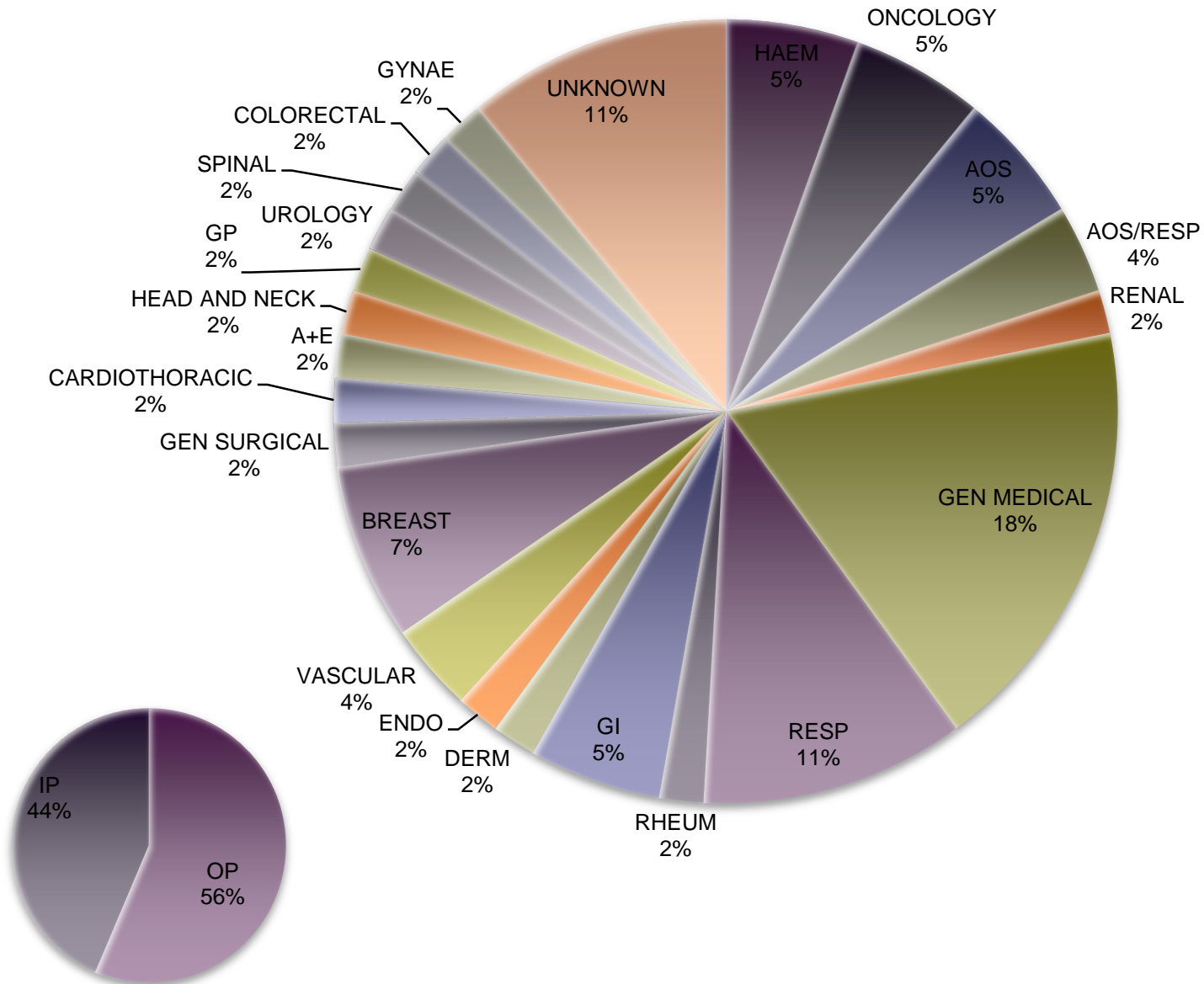
Our experience

GSTT MDM activity: April 13-14

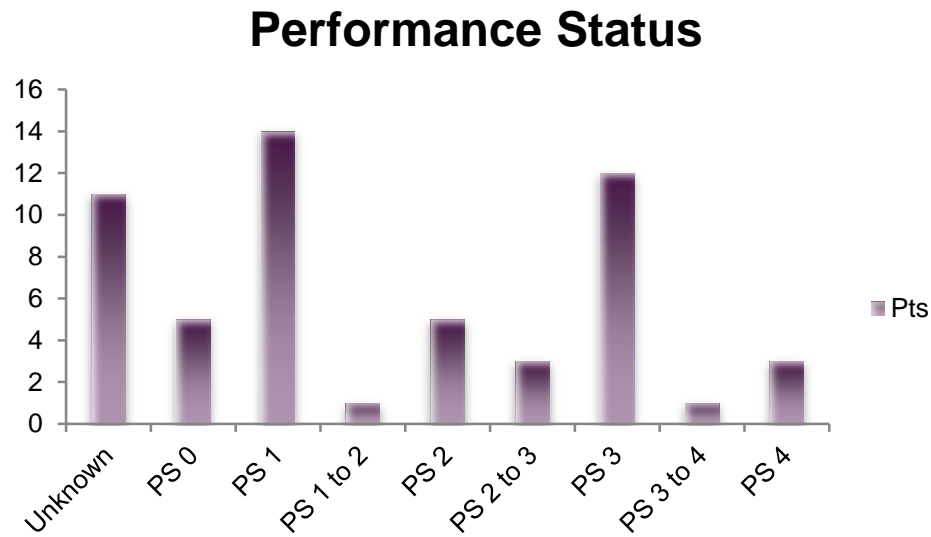
■ 55 new patients



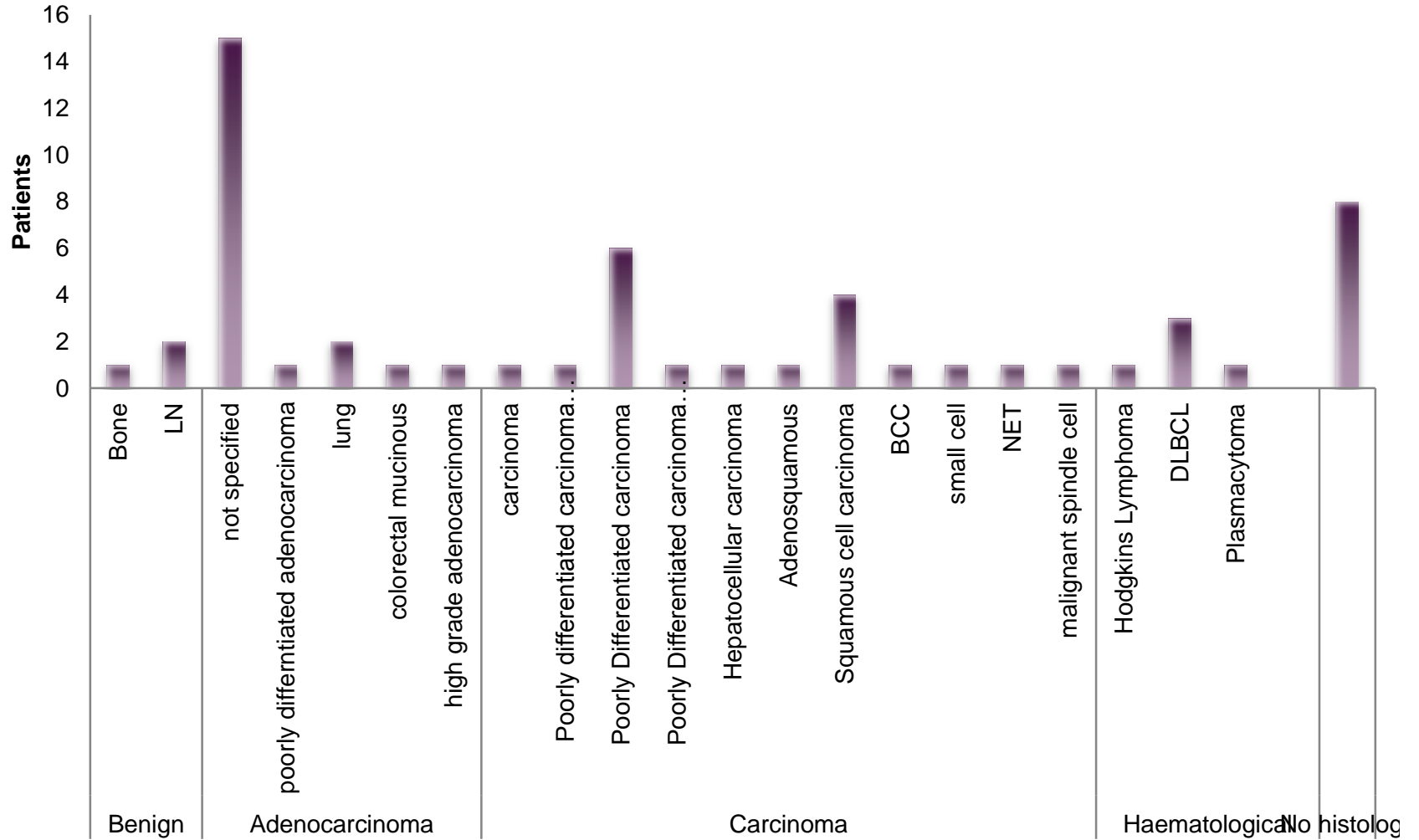
Referral Pathway- Speciality



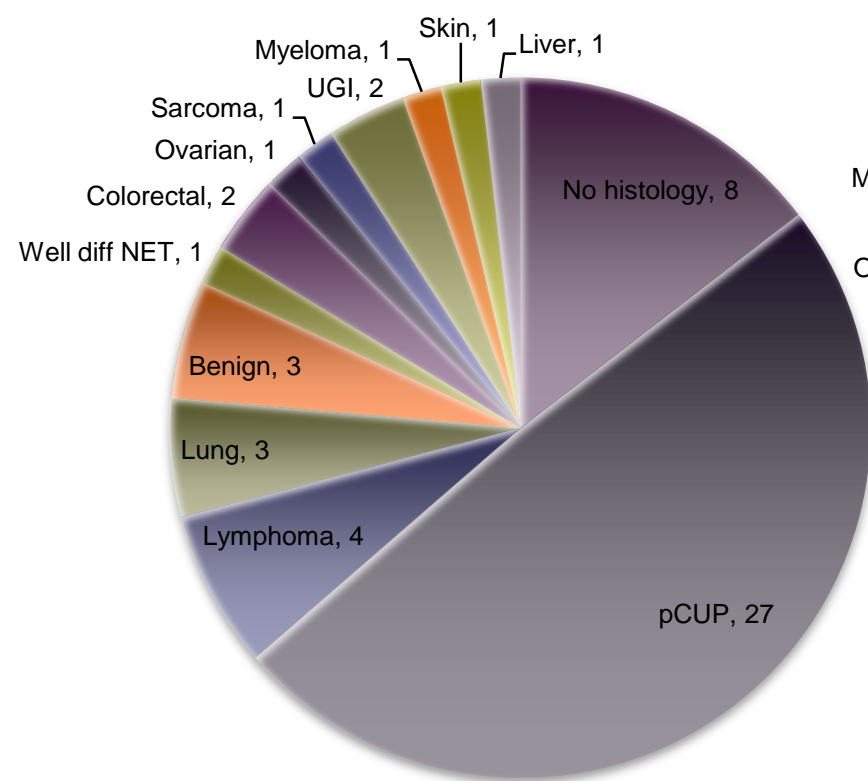
PS- patients referred to CUP MDM



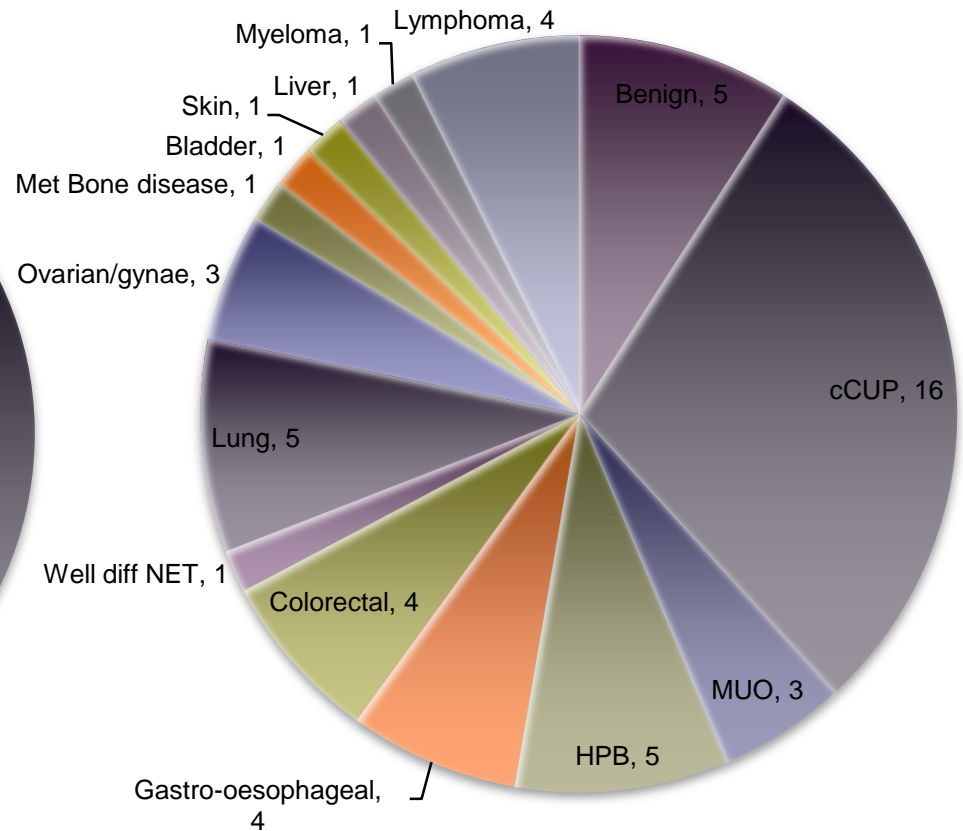
Histology- reviewed at GSTT in MDM



Diagnosis following MDM review

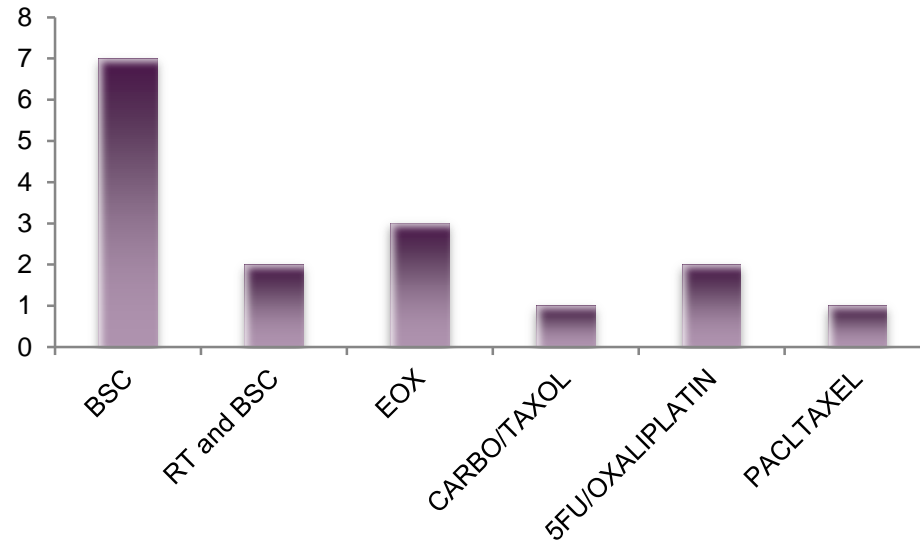


Prior to MDM



Following MDM

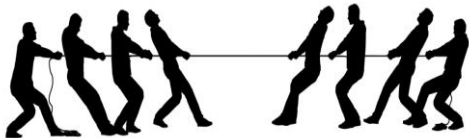
Treatment of cCUP n=16



Challenges for MUO/CUP service:



Challenges



- ‘ Surely you need to start this patients chemotherapy treatment while you find the primary’

‘I cannot decide on behalf of my medical oncology colleagues how or by whom she should be treated (lung, H&N, Gynae, CUP.....) but I would have thought the tumour should have been analysed by now for driver mutations and treated accordingly’

‘It is TTF-1 negative it can’t be lung cancer’

- ‘ When we see a patient who is not right and we are worried may have cancer we need a service to refer them to’
- ‘ The patient clearly has cancer- what difference is it going to make as to where it is from?’



Building Relationships



+ Relationships within the MDM





Relationships within the MDM

- MDM co-ordinator:
 - MUO/CUP referral form clinical data, electronic MDM- data collection, investigations
- Histopathology/ Radiology:
 - Update on investigations between MDMs
 - Regular e-mail/ phone contact
 - Depth of specialist histol/radiology specialist interest
- AOS/CUP CNS:
 - patient investigations, information, telephone monitoring
- Palliative care:
 - Community team, palliative care clinic, in-patient review,
- Medical and clinical oncology:
 - Joint clinic, differing view points
 - Screening of referrals/ pre-MDM work-up, redirecting to appropriate MDM
- Video-link with AOS network teams:
 - Clinical information, educational, immediate feedback- point of contact





Relationships with other teams/ MDM

- Links with diagnostic services:
 - IR, bronchoscopy, EBUS, endoscopy, ENT, Gynae
- Site-specific MDM
 - Links: clinical, MDM co-ordinator
 - Education:
 - Increased treatment options for ' Probable primary' versus CUP
 - Role of IHC in clinical and radiological context





Relationships with other teams/ MDM



- Referring teams
 - Patients must be informed of probable cancer diagnosis
 - Minimal diagnostics prior to referral:
 - MUO GSTT: CT scan (CAP)
 - pCUP: CT scan (CAP) and tissue biopsy
 - Patients without a treatable syndrome and unfit for systemic treatment- better suited to local palliative care input
 - Education
- MUO/CUP service
 - Responsive- in-pt review, patient communication, escalation decisions
 - MUO out-patient clinic- earlier discharge



Relationship with patients

■ MUO

- Engagement patient & family
 - Regarding appropriate investigations
 - Role of biopsy
 - Clear contact information
 - CUP CNS- role
 - Importance of palliative care involvement

■ pCUP/ cCUP

- Role of further investigations
- Benefits of treatment
- Role of palliative care
- Holistic assessment
- Managing uncertainty
 - Patient support, written information



+ MUO/CUP: Challenging cases

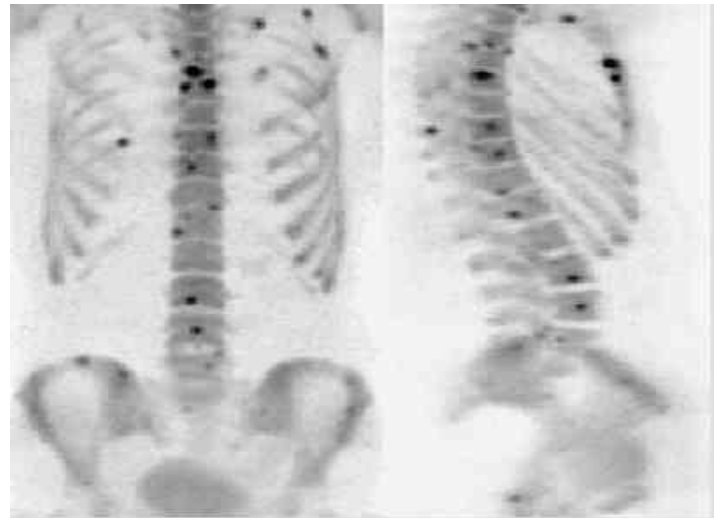
? Failure



? Success



Bone metastases





Clinical case

40yr old male- referred for a second opinion as cCUP



- September 2014:
 - Presented with chest pain, 10kg wt loss
 - Poor appetite
 - PS0
 - GP: CXR- normal
 - Self referred to doctors in Romania for further investigations

PMH: Nil

SH: Romanian- Lorry driver, Lived with wife in UK for 5 yrs, smoker 15/day, no ethol

FH: Nil

+ Investigations: letters



- Romania:
 - 'OGD/ colonoscopy: normal'
 - 'CT : multiple metastatic lesions'
 - Liver biopsy- 'carcinoma'

- Care transferred to Turkey
 - Pathology review ' poorly differentiated adenocarcinoma'
 - PET-CT: multiple lytic skeletal lesions, para-caval LN, right para-tracheal LN, left kidney lesion
 - cCUP

+ Treatment (1)

- December 2014-Turkey
 - Palliative XRT to spine and sacrum (30gy/12 fractions)
 - 1st line: Carboplatin/ paclitaxel chemotherapy, zolendronic acid (C3-progressive disease within the liver)
 - 2nd line: Gemcitabine/ Cisplatin C1
 - Transferred care back to UK: continued imaging in Turkey
 - Histopathology review: no report 'block difficult to interpret'
 - Genotyping requested; No residual cancer cells- recommended repeat biopsy
 - completed C6
 - C6 neutropenic sepsis, thrombocytopenia

+ Treatment (2)

- June 2015:
 - PET- CT: response in bone lesions, new nodal disease
 - Referred for phase 1 study
 - Agreed to repeat biopsy for molecular testing
 - Second opinion GSTT





MDM review (July 2015 GSTT)

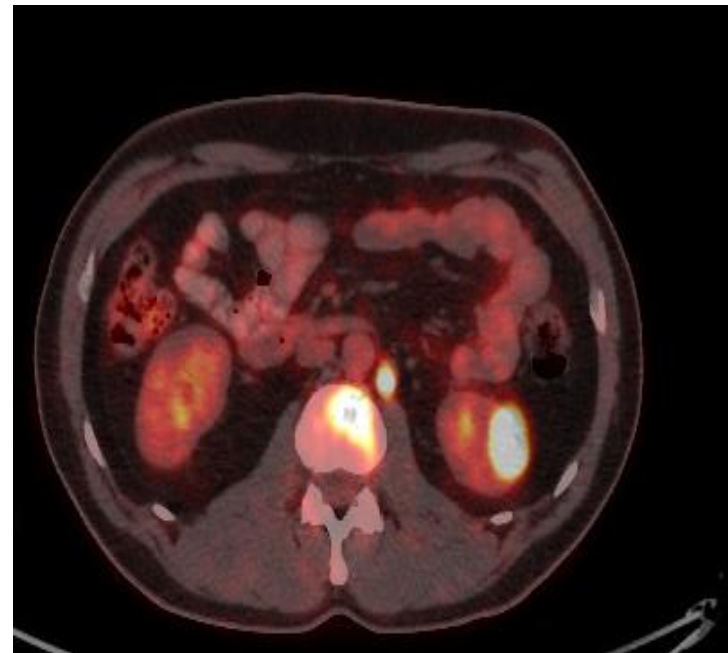
Clinical review:

- Lower back pain- controlled with co-codamol
- PS0
- No wt loss, good appetite, no other symptoms
- O/E: 2cm axillary LN, no skin lesions
- LDH 237, PSA 2.32, CEA <1, CA 19.9 3.9,



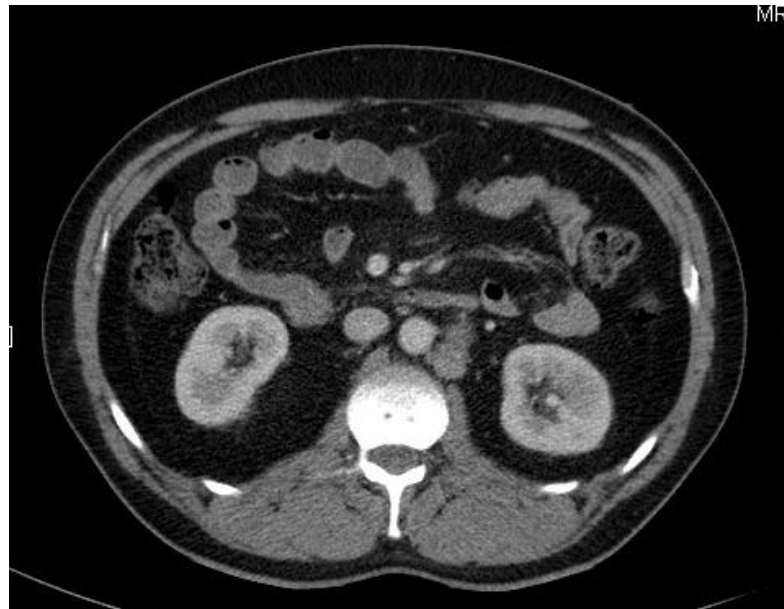
+ MDM review (July 2015 GSTT)

- Radiology (no imaging available prior to Jan 2015)
- Jan 2015 C3 carbo/tax:
 - PET-CT: Right SCF LN, left para-aortic LN, left lower pole kidney lesion, multiple bone mets
 - Reported as PD from previous imaging: increased metabolic response in some LN, reduced in others: SD based on RECIST
 - MRI liver: small benign liver lesion
 - March/June 2015
 - PET-CT: Stable disease



+ MDM review (July 2015 GSTT)

- July 2015 CT CAP GSTT:
 - Right SCF LN 1.3 cm, 1.3cm fluid dense lesion in axilla with appearance of cyst, new right lung consolidation, no liver lesions, left 3.2cm renal lesion lower pole, increase size of left para-aortic LN 2.6x 1.9cm, multiple sclerotic bone mets-vertebrae, stream, ribs, pelvis
- Conclusion: Left renal lesion may represent a metastasis or site of primary, immediately adjacent left para-aortic LN suggest a primary more likely



+ MDM review (July 2015 GSTT)

■ Histopathology

- September 2014: Unable to obtain original 'liver biopsy'
- August 2015: Right SCF LN biopsy (6 weeks from biopsy to CUP MDM review)
- Compact papillary and solid architecture, deep eosinophilic cytoplasm and moderate nuclear pleomorphism with prominent nucleoli
- IHC (performed externally and reviewed in MDM)
 - Positive: MNF116+, Vimentin +,
 - Negative: CK7, CK20, TTF1, CDX2, CD10, Thyroglobulin, PSA, s100, CD56, p63, CD117, e-cadherin, CD31, CD34, PLAP, AFP, CD99, desmin, SMA
- Although CD10-, MNF116+, vimentin+ support profile support the features of a papillary renal cell cancer type 2



Renal MDM



Referral to renal MDM:

- Metastatic papillary renal cell cancer- type 2
- Clinical trial sarah cannon research institute: cMet inhibitor in papillary renal cell cancer

+ Learning points

- Multiple centers navigating information- far from ideal
- Need for all clinical information
- CUP MDM
 - Review of all clinical material
 - Importance of tissue
 - Interpretation of histopathology with clinical and radiological findings
 - Team working- intra and inter-MDM
- CNS support
 - Regular contact with CNS to provide clinical update on MDM review, biopsy results and psychological support



Thank You

