Tumour Markers

Introduction

Tumour marker levels are expensive and relatively non-specific biochemical tests which need to be used selectively and responsibly in the management of patients. Tumour markers should not be used to screen, diagnosis or exclude malignancy. This document was produced in order to provide guidance on the appropriate use of tumours markers, a summary of which has been given the in the table overleaf. The document was written in consultation with the oncologists at the Cancer centre, Royal Surrey County Hospital.

Frequency of Testing

1. Chemotherapy

The recommended frequency of testing during chemotherapy (CT) varies with the tumour type. For most tumours this will be prior to each cycle (i.e. every 3-4weeks). Myelomas require monthly paraprotein levels (serum free light chains in the case of BJP-only myeloma). For testicular teratomas, markers should be measured weekly post-orchidectomy until normal. No marker levels are required during CT for lung tumours.

2. Radiotherapy

For most tumours, tumour marker levels are rarely required in the context of radiotherapy (RT). In the case of prostate cancer it is appropriate to measure PSA pre- and six weeks post-RT.

3. Remission

For many tumours, marker measuring is rarely required during remission. Testing is appropriate in the case of:

- Prostate tumours (PSA 3 monthly in first year, thereafter frequency depends on grade. In general once every doubling time of the tumour. If low grade, 6 months then annually).
- Haematological tumours (3 monthly)
- Marker-positive breast cancer (3-6 monthly)
- Testicular tumours (monthly surveillance for first year ect. As per regional protocol)

Tumour Marker 'screens'

1. **Patients with metastases but unknown primary tumour**

In the case of patients presenting with metises, tumour markers requests are appropriate as results may help indicate the primary site. When considered in conjunction with immunohistochemistry and clinical picture, the levels of tumour markers may assist in the choice of chemotherapy. Only those markers which are elevated should continue to be measured, except in the case of testicular tumours, the nature of which can change. Suggested tumour marker screens are given below:

Situation	Appropriate Screen
Histologically proven undifferentiated adenocarcinoma	CEA, CA19-9, CA125 and CA15-3 (women)
Suspected prostate cancer	PSA
Suspected hepatoma	AFP
Suspected germ cell tumour in young adult	AFP, hCG, LDH
Bone disease or elevated ESR	Serum/urine electrophoresis.

2. **Patients with symptoms but no known malignant disease**

In the case of patients presenting with non-specific symptoms (e.g. tiredness) but no other evidence of a tumour, it is inappropriate to request tumour marker levels. Due to their non-specific nature, tumour markers should not be used to screen, diagnosis or exclude malignancy.

Appropriate use of Tumour Markers

The table below summarises appropriate use of tumour markers in different tumour types (adapted from the summary of current National Academy of Clinical Biochemistry recommendations).

	Screening/Early detection	Diagnosis/Case-finding	Staging/Prognosis	Detecting recurrence	Monitoring Therapy
Bladder cancer	NR	NR	NR	NR	If metastatic disease, screen pre-chemotherapy, follow markers which are raised.
Breast cancer	NR	NR	HER-2	CA15-3, CA125, CEA (if suspicion of recurrence)	CA15-3, CA125, CEA (monitoring of advanced disease)
Cervical cancer	NR	SCC (possibly in SCCC)	SCC (possibly in SCCC)	SCC (possibly in SCCC)	SCC (possibly in SCCC)
Colorectal cancer	FIT (if they meet the criteria stated in NICE DG30)	NR	CEA	CEA	CEA
Gastric cancer	NR	NR	NR	NR	NR
Lung cancer	NR	NSE may be used as an aid to the diagnosis of SCLC and in prognosis and monitoring CEA may be helpful in prognosis and monitoring of NSLSC.			
Lymphomas	LDH	LDH	LDH	LDH	LDH
Melanoma	NR	LDH	LDH	NR	NR
Monoclonal gammopathies	Serum paraprotein (PP) every 3/12 in asymptomatic myeloma. Confirmation of complete remission requires that there is no detectable PP by immunofixation (IF). IF should be performed if no detectable PP on electrophoresis. MGUS: serum PP 3/12 after diagnosis then every 6-1/12 thereafter if no evidence of progression.				
Ovarian cancer	CA125 (in combination with TVUS for early detection in hereditary syndromes only)	CA125 (post-menopausal women only)	CA125	CA125	CA125
Pancreatic cancer	NR	CA19-9 (if used, only with CT or EUS and in an appropriate clinical context)	CA19-9	NR	CA19-9 (during palliative therapy with imaging tests or after potentially curative surgery)
Parathyroid gland tumours	PTH and serum calcium should be measured 6 monthly in asymptomatic with primary hyperparathyroidism who are not treated surgically and at least 6 monthly post-operatively in those treated surgically.				
Primary liver cancer	AFP (in high risk subjects)	AFP	AFP	AFP	AFP
Prostate cancer	NR	PSA (with DRE)	PSA (with DRE & biopsy Gleason Grade)	PSA	PSA If aggressive tumour heaving oddly (e.g. visceral metises and PSA falling), NSE if need to exclude small cell transformation
Testicular tumours	NR	AFP, hCG, LDG	AFP, hCG, LDG	AFP, hCG, LDG	AFP, hCG, LDG
Thyroid cancer	NR	NR	NR	Tg, Tg antibodies	Tg, Tb antibodies

Key: CT, computed tomography; DRE, digital rectal examination; EUS, examination under ultrasound; FIT, faecal immunochemical testing; IF, immunofixation; LDH, lactate dehydrogenase; MGUS, monoclonal gammopathy of uncertain significance; NR, no tumour markers recommended; PP, paraprotein; PTH, parathyroid hormone; SCLC, small cell lung cancer; NSCLC, non-small cell lung cancer; SCCC, squamous cell cervical carcinoma; Tg, thyroglobulin; TVUS, transvaginal ultrasound.

References:

1. National academy of clinical biochemistry guidelines: practie guidelines for use of tumour markers in the clinic, 2006.
2. NICE DG30, Quantitative FIT to guide referral for colorectal cancer in primary care, July 2017.