

# Challenging Concepts in Oncology

## *Cases with Expert Commentary*

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# FOREWORD

All of the professions involved in providing modern care for cancer patients face an information base which is growing in its volume and complexity at a rate which is both gratifying and alarming. The rapid advances in the basic sciences which underpin our understanding of the biology and pathology of cancer are well recognized. These are feeding through steadily to enhance the scientific basis for the evaluation of the diagnosis, stage, prognosis, and risk factors associated with each individual cancer patient. New treatments, which are increasingly deployed on a personalized or stratified basis, are emerging. We have seen a steady growth in the number of targeted therapies for specific tumour types or subtypes. Perhaps the greatest current excitement results from a significant minority of patients who are achieving durable remissions with new biological and immunological therapies. However, not all of the challenges faced by oncologists arise from science at the international forefront or the need to deploy effective, complex, and novel therapies. We also have to deal with increasing numbers of older cancer patients who may have co-morbidities or frailty which make their choice of therapy, in consultation with their clinicians, especially challenging. Communication skills and time for effective consultations that allow for good choices by patients are at a premium. Wide availability of information through the Internet can also add to the quality, but also sometimes to the challenges presented by consultations. The health care is subject to increasing scrutiny of its quality and must be based on evidence which must be evaluated and absorbed by oncologists, in order to deliver excellence. More than 50% of all cancer patients now survive their disease and live for at least 10 years after their diagnosis. No effort can be spared to ensure that all patients have their best chance to benefit from this opportunity.

Against this background, the text in *Challenging Concepts in Oncology* provides oncologists with a valuable opportunity to stay up to date in their subject, both within their areas of special expertise, but also across the wider range of oncology. The text is strongly learning-orientated. By relating each topic to a case history and bringing out 'clinical tips', 'expert comments', and key 'learning points' in each chapter, the multiple authors are generating a resource which will help oncologists to tackle the many challenges they face. The tips and comments are well chosen to help the busy oncologist update their knowledge and their focus on these important clinical questions. The format is readable, lends itself to the 'occasional' reading session which, for many oncologists, will be early in the morning, late at night, or on a train. By combining authorship between trainees and the experienced consultants, the editors have ensured a balanced approach which will be valuable for learning and teaching, but also valuable for updates and continuing professional development for established consultants and oncologists of all professions.

Professor Peter Selby  
President, Association of Cancer Physicians

# PREFACE

Oncology is a rapidly evolving specialty fundamentally supported by peer-reviewed evidence-based trials. Personalized medicine has already taken a significant foothold in cancer pathways and signals an era of very exciting times ahead. Application of translational work to everyday clinical practice is key to ensuring patients receive the best possible care.

With improvements in cancer outcomes, late effects and survivorship are increasingly important, as many cancers become chronic diseases. The provision of acute oncology services in the UK by oncologists is another recent development. This stems from a national initiative influenced by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) and the National Chemotherapy Advisory Group (NCAG). The recommendations from their reports included the development of dedicated acute oncology services in all trusts involved in reviewing patients presenting with undiagnosed cancer or suspected cancer, complications of chemotherapy, radiotherapy, or with cancer-related complications.

In this book, we have tried to encapsulate the elements of patient-focussed care, principles of acute oncology, and the relevant evidence base. We present 25 clinical cases, written by UK oncology specialty trainees, which have been chosen to provide an overview of the management of the common cancers, with discussion of common complications and acute oncological emergencies. Through the 'learning points', 'clinical tips', 'landmark trials' and 'expert comments', we have discussed the challenges in diagnosis and evidence for current treatments, including some of the molecular and genetic background to the cancer and its treatments. Additionally, we have sought renowned UK experts in the relevant tumour site to provide a peer review commentary throughout each case. The scenarios have been selected to reflect real-life diagnostic and management challenges that would ordinarily generate debate amongst clinicians. In doing so, we have strived to provide a comprehensive textbook, written in a style which is interesting, informative, and, above all, innovative.

We hope the book will appeal to trainees in both medical and clinical oncology. These subspecialties have separate training programmes, although elements of the curriculum are delivered jointly. We feel our concise textbook, covering common problems, treatments, and latest developments in oncology, will be invaluable for both junior oncology trainees and more senior doctors preparing for their postgraduate examinations.

*Challenging Concepts* also provides an excellent basis for consultants involved in acute oncology to keep up to date with the latest treatments of a variety of malignancies, as well as their own tumour sites of interest. Allied to this, we hope that this book will be an invaluable reference text for specialist nurses involved in delivering acute oncology services and for the palliative care teams, with whom oncologists work closely.

Management of patients with cancer is multidisciplinary, and the book has been written with this in mind. In addition to the target readership of specialist oncologists, our vision has been to produce a text that will engage and encompass the

interest of associated health care professionals (e.g. palliative care specialists, specialist nurses, and radiographers).

We believe the *Challenging Concepts* series platform has allowed us to produce a book that is unique and innovative in this field and will be a worthwhile contribution to the medical literature.

We, the editors, very much hope you enjoy the book.

Sarah Payne  
Madhumita Bhattacharyya  
Iain McNeish

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We would like to thank all the contributors of the book who have worked very hard together to make it so relevant, inclusive, thorough, and clear.

I would like to say a big thank you to my husband Iain Soulsby and my two wonderful daughters, Emily and Charlotte. Thank you for all your support and patience over the course of this project. Thank you also for ensuring I never ran out of cups of tea.

Sarah Payne

I would like to thank all my family for their support and encouragement, above all, my lovely son Ishaan.

Madhumita Bhattacharyya

With thanks to Geraldine, Angus, and Iona.

Iain McNeish

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# ABBREVIATIONS

°	degree	bd	<i>bis die</i> (twice daily)
°C	degree Celsius	BEP	bleomycin, etoposide, cisplatin
=	equal to	BHIVA	British HIV Association
≥	equal to or greater than	BL	Burkitt's lymphoma
≤	equal to or less than	BMI	body mass index
↓	decreased	BP	blood pressure
↑	increased	BPH	benign prostate hyperplasia
>	greater than	bpm	beat per minute
<	less than	BSA	body surface area
λ	lambda	BTS	British Thoracic Society
%	per cent	CA19.9	carbohydrate antigen 19-9
±	plus or minus	CA125	cancer antigen 125
£	pound sterling	cART	combination antiretroviral therapy
®	registered trademark	CAV	doxorubicin, cyclophosphamide, vincristine
Ab	antibody	cc	cubic centimetre
ABVD	doxorubicin, bleomycin, vinblastine, and dacarbazine	CCC	clear cell carcinoma
ACE	angiotensin-converting enzyme	ccRCC	clear cell renal cell carcinoma
ACTH	adrenocorticotrophic hormone	CCRT	concurrent chemoradiotherapy
ADL	activity of daily living	CEA	carcinoembryonic antigen
AED	anti-epileptic drug	CgA	chromogranin A
AFP	alpha fetoprotein	CHART	continuous hyperfractionated accelerated radiotherapy
AI	aromatase inhibitor	CI	confidence interval
AIDS	acquired immune deficiency syndrome	CINV	chemotherapy-induced nausea and vomiting
AJCC	American Joint Committee on Cancer	CK5/6	cytokeratin 5/6
ALA	5-aminolevulinic acid	CK7	cytokeratin 7
ALK	anaplastic lymphoma kinase	cm	centimetre
ALP	alkaline phosphatase	CMF	cyclophosphamide, methotrexate, and 5-fluorouracil
ALT	alanine aminotransferase	CMV	cytomegalovirus
AOS	acute oncology service	CNS	central nervous system
AR	androgen receptor	CO <sub>2</sub>	carbon dioxide
ARDS	adult respiratory distress syndrome	COG	Children's Oncology Group
ARSAC	Administration of Radioactive Substances Advisory Committee	COX	cyclo-oxygenase
ASC	active symptom control	CR	complete remission
ASCO	American Society of Clinical Oncology	CRC	colorectal carcinoma
AST	aspartate aminotransferase	CRM	circumferential margin
AUC	area under the curve	CRP	C-reactive protein
AVP	arginine vasopressin	CRT	chemoradiotherapy
BAP1	BRCA1-associated protein 1	CSF	cerebrospinal fluid
BCLC	Barcelona-Clinic Liver Cancer	CT	computerized tomography
BCT	breast-conserving therapy		

CTCAE	common terminology criteria for adverse events	ESR	erythrocyte sedimentation rate
CT CAP	computerized tomography of the chest, abdomen, and pelvis	EUS	endoscopic ultrasound
CTV	clinical target volume	FBC	full blood count
CTZ	chemoreceptor trigger zone	FDA	Food and Drug Administration
CUP	carcinoma of unknown primary	FDG	fluorodeoxyglucose
CXR	chest X-ray	FEV <sub>1</sub>	forced expiratory volume in 1 second
3D	three-dimensional	FGFR	fibroblast growth factor receptor
DCIS	ductal carcinoma <i>in situ</i>	FIGO	<i>Fédération Internationale de Gynécologie et d'Obstétrique</i>
DFS	disease-free survival	FISH	fluorescence <i>in situ</i> hybridization
dL	decilitre	fL	femtolitre
DLBCL	diffuse large B-cell lymphoma	FLIPI	Follicular Lymphoma International Prognostic Index
DNA	deoxyribonucleic acid	FNA	fine-needle aspiration
DPD	dihydropyrimidine dehydrogenase deficiency	FOLFIRINOX	5-fluorouracil, folinic acid, irinotecan, and oxaliplatin
DRE	digital rectal examination	FSH	follicle-stimulating hormone
DVT	deep vein thrombosis	FTR	free/total ratio
EASL	European Association for the Study of the Liver	5-FU	5-fluorouracil
EBCTCG	Early Breast Cancer Trialists' Collaborative Group	FVC	forced vital capacity
EBRT	external beam radiotherapy	g	gram
EBUS	endobronchial ultrasound	GBM	glioblastoma multiforme
EBV	Epstein–Barr virus	GBM-O	glioblastoma with oligodendroglioma component
ECF	epirubicin, cisplatin, and 5-fluorouracil	GBq	giga becquerel
ECG	electrocardiogram	GC	gemcitabine and cisplatin
ECOG	Eastern Cooperative Oncology Group	GCS	Glasgow coma score
ECX	epirubicin, cisplatin, and capecitabine	G-CSF	granulocyte colony-stimulating factor
ED	emergency department	GEP	gastroenteropancreatic
ED-SCLC	extensive-disease small cell lung cancer	GFR	glomerular filtration rate
EEG	electroencephalography	GI	gastrointestinal
EGCCCG	European Germ Cell Cancer Consensus Group	GOJ	gastro-oesophageal junction
EGF	epidermal growth factor	GP	general practitioner
EGFR	epidermal growth factor receptor	G6PD	glucose-6-phosphate dehydrogenase
EIA	enzyme immunoassay	GTV	gross tumour volume
EMA	European Medicines Agency	GU	genitourinary
EMG	electromyography	Gy	gray
ENETS	European Neuroendocrine Tumor Society	HAART	highly active antiretroviral therapy
ENT	ear, nose, and throat	Hb	haemoglobin
EP	cisplatin and etoposide	HBV	hepatitis B virus
EPP	extra-pleural pneumonectomy	HCC	hepatocellular carcinoma
ER	oestrogen receptor	HCG	human chorionic gonadotrophin
ERCP	endoscopic retrograde cholangiopancreatography	HCV	hepatitis C virus
ESMO	European Society for Medical Oncology	HDGC	hereditary diffuse gastric cancer
		HDR	high-dose rate
		HER2	human epidermal growth factor receptor 2
		HGF	hepatocyte growth factor
		HGSC	high-grade serous ovarian carcinoma

## xviii Abbreviations

HHV-8	human herpesvirus-8	kCO	transfer coefficient
HIA	hepatic intra-arterial	kg	kilogram
5-HIAA	5-hydroxyindoleacetic acid	kPa	kilopascal
HIF	hypoxia-inducible factor	KS	Kaposi's sarcoma
hIL-6	human interleukin-6	KSHV	Kaposi's sarcoma-associated herpesvirus
HIV	human immunodeficiency virus	L	litre
HNPCC	hereditary non-polyposis colorectal cancer	LANA-1	latent nuclear antigen-1
HNSCC	head and neck squamous cell carcinoma	LC	local control
HPB	hepatopancreaticobiliary	LCIS	lobular carcinoma <i>in situ</i>
HPF	high power field	LCNEC	large cell neuroendocrine carcinoma
HPV	human papillomavirus	LDH	lactate dehydrogenase
HR	hazard ratio	LDR	low-dose rate
HRD	defective homologous recombination	LD-SCLC	limited-disease small cell lung cancer
HRT	hormone replacement therapy	LEMS	Lambert–Eaton myasthenic syndrome
Hsp90	heat shock protein 90	LFT	liver function test
HSV	herpes simplex virus	LH	luteinizing hormone
5HT3	5-hydroxytryptamine-3	LHRH	luteinizing hormone-releasing hormone
HTLV	human T-lymphotropic virus	LMWH	low-molecular-weight heparin
IASLC	International Association for the Study of Lung Cancer	LND	lymph node dissection
IBS	irritable bowel syndrome	LoDLIN	longest diameter of the largest involved node
ICP	intracranial pressure	LVEF	left ventricular ejection fraction
ICU	intensive care unit	LVSI	lymphovascular space invasion
IDH1	isocitrate dehydrogenase 1	m	metre
IFN	interferon	mAb	monoclonal antibody
IGCCC	International Germ Cell Consensus Classification	MAC	<i>Mycobacterium avium</i> complex
IGF	insulin-like growth factor	MAP	methotrexate, cisplatin, and Adriamycin®
IgG	immunoglobulin G	MCD	multicentric Castleman disease
IHC	immunohistochemistry	mCi	millicurie
IL	interleukin	mCRC	metastatic colorectal carcinoma
IM	intramuscular	M, C & S	microbiology, culture, and sensitivity
IMRT	intensity-modulated radiotherapy	MCV	mean corpuscular volume
INR	international normalized ratio	MDT	multidisciplinary team
IPI	International Prognostic Index	MEN	multiple endocrine neoplasia
IPS	International Prognostic Score	MET	mesenchymal–epithelial transition factor
irAE	immune-related adverse event	mg	milligram
irCR	immune-related complete response	MGMT	methyl guanine methyl transferase
irPD	immune-related progressive disease	MHRA	Medicines and Healthcare products Regulation Agency
irPR	immune-related partial response	MIBC	muscle-invasive bladder cancer
irRC	immune-related response criteria	MIBG	meta-iodobenzylguanidine
irSD	immune-related stable disease	min	minute
ISH	<i>in situ</i> hybridization	mIU	milli international unit
ITT	intention-to-treat	mL	millilitre
IU	international unit	mm	millimetre
IV	intravenous	mmHg	millimetre of mercury
K	potassium		

mmol	millimole	PARP	poly (adenosine diphosphate-ribose) polymerase
mOsm	milliosmole	PBL	plasmablastic lymphoma
MRI	magnetic resonance imaging	PCI	prophylactic cranial irradiation
MSCC	metastatic spinal cord compression	PCL	primary central nervous system lymphoma
MSI	microsatellite instability	PCOS	polycystic ovary syndrome CH5; Prostate Cancer Outcomes Study
MSKCC	Memorial Sloan Kettering Cancer Center	PCP	<i>Pneumocystis jirovecii</i> pneumonia
mTOR	mammalian target of rapamycin	PCV	procarbazine, CCNU, and vincristine
MTP	muramyl tripeptide	PD-1	programmed death-1
MU	million unit	PDAC	pancreatic ductal adenocarcinoma
MUGA	multigated acquisition	PDGF	platelet-derived growth factor
MVAC	methotrexate, vinblastine, adriamycin, cisplatin	PDGFR	platelet-derived growth factor receptor
Na	sodium	PE	pulmonary embolism
nab	nanoparticle albumin-bound	PEG	percutaneous endoscopic gastrostomy
NANETS	North American NeuroEndocrine Tumor Society	PEI	percutaneous ethanol injection
NB	<i>nota bene</i> (take note)	PEL	primary effusion lymphoma
NCAP	computerized tomography scan of the neck, chest, abdomen, and pelvis	PET	positron emission tomography
NCCN	National Comprehensive Cancer Network	PF	performance status
NCRI	National Cancer Research Institute	PFS	progression-free survival
NET	neuroendocrine tumour	PICC	peripherally inserted central catheter
ng	nanogram	PLD	pegylated liposomal doxorubicin
NG	nasogastric	Plt	platelet
NHL	non-Hodgkin's lymphoma	pmol	picomole
NHS	National Health Service	PNET	pancreatic neuroendocrine tumour
NICE	National Institute for Health and Care Excellence	PO	<i>per os</i> (taken orally)
NK1	neurokinin 1	PPE	palmar–plantar erythrodysesthesia
NMBIC	non-muscle-invasive bladder cancer	PR	progesterone receptor
nmol	nanomole	PRN	<i>pro re nata</i> (as required)
NNRTI	non-nucleoside reverse transcriptase inhibitor	PS	performance status
NRTI	nucleoside reverse transcriptase inhibitor	PSA	prostate-specific antigen
NSAID	non-steroidal anti-inflammatory drug	PTV	planning target volume
NSCLC	non-small cell lung cancer	PV	portal vein
NTS	nucleus tractus solitarii	qds	<i>quater die sumendum</i> (four times daily)
NYHA	New York Heart Association	QoL	quality of life
OAR	organs at risk	RAI	radioactive iodine ablation
od	<i>omne in die</i> (once daily)	RANKL	receptor activator of nuclear factor kappa B ligand
OGD	oesophagogastroduodenoscopy	RCC	renal cell carcinoma
OGJ	oesophagogastric junction	RCT	randomized controlled trial
OI	opportunistic infection	R-CVP	rituximab, cyclophosphamide, vincristine, and prednisolone
OPG	orthopantomogram	RECIST	Response Evaluation Criteria in Solid Tumours
OS	overall survival	RFA	radiofrequency ablation
		rhTSH	recombinant human thyroid-stimulating hormone
		RIG	radiologically inserted gastrostomy

## XX Abbreviations

RMI	risk of malignancy index	TKI	tyrosine kinase inhibitor
RNA	ribonucleic acid	TLS	tumour lysis syndrome
RPA	recursive partitioning analysis	TNM	tumour–node–metastasis
RPS	radiation protection supervisor	TPF	taxane, cisplatin, and 5-FU
RR	relative risk	TRUS	transrectal ultrasound
RT-PCR	reverse transcriptase polymerase chain reaction	TSH	thyroid-stimulating hormone
SALT	speech and language therapy	TTF-1	thyroid transcription factor-1
s/c	subcutaneously	TURBT	transurethral resection of bladder tumour
SCC	squamous cell carcinoma	TURP	transurethral resection of the prostate
SCLC	small cell lung cancer	TVUS	transvaginal ultrasound
SEER	Surveillance, Epidemiology, and End Results	TYA	teenage young adult
SIADH	syndrome of inappropriate anti-diuretic hormone	U&Es	urea and electrolytes
SIRT	selective internal radiation therapy	UK	United Kingdom
SLE	skeletal-related event	UKI	NETS UK and Ireland Neuroendocrine Tumour Society
SMA	superior mesenteric artery	ULN	upper limit of normal
SMV	superior mesenteric vein	US	United States
SPARC	secreted protein acidic and rich in cysteine	USS	ultrasound scan
SPF	sun protection factor	UVA	ultraviolet A
SRE	skeletal-related event	UVB	ultraviolet B
SVC	superior vena cava	VALSG	Veterans Administration Lung Study Group
SVCO	superior vena cava obstruction	VBT	vaginal vault brachytherapy
T3	tri-iodothyronine	VEGF	vascular endothelial growth factor
T4	thyroxine	VEGFR	vascular endothelial growth factor receptor
TACE	trans-arterial chemo-embolization	VeIP	cisplatin, ifosfamide, and vinblastine
TAH-BSO	total abdominal hysterectomy with bilateral salpingo-oophorectomy	VHL	von Hippel–Lindau
TBNA	transbronchial needle aspiration	vIL-6	viral interleukin-6
TBNK	T-cells, B-cells, and natural killer cells	VIP	etoposide, ifosfamide, and cisplatin;
TCC	transitional cell carcinoma		vasoactive intestinal polypeptide
tds	<i>ter die sumendum</i> (three times daily)	VTE	venous thromboembolism
tFL	transformed follicular lymphoma	WBC	white blood count
Tg	thyroglobulin	WCC	white cell count
TGF	transforming growth factor	WHO	World Health Organization
TIP	paclitaxel, ifosfamide, cisplatin	WLE	wide local excision







Table 0.2 (continued)

10.12 Management of sarcoma			X
10.13 Management of leukaemia and plasma cell dyscrasia			
10.14 Management of prostate cancer		X	
10.15 Management of immunosuppression-associated malignancies			X
10.16 Management of urothelial cancer		X	
10.17 Management of cervical cancer			
10.18 Management of head and neck cancer			X
10.19 Management of central nervous system malignancy			X
10.20 Management of renal cell cancer		X	
10.21 Management of tumours affecting the endocrine organs			X
10.22 Management of tumours of the thoracic cavity	X		
10.23 Management of teenagers and young adults with cancer			X X

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