Contents

Edit	ors	xii
Con	tributors	xvi
Rev	iewers	xxii
Abb	reviations	XXV
Ack	nowledgements	xxxiii
Pref	ace	xxxiv
	Section 1: Introduction to immunology and immunotly	nerapy
1.1	Immune Checkpoints	3
	Definition	3
	Immune Synapse	4
	Technical Procedures	7
	Predictive and/or Prognostic Biomarkers of (Potential)	
	Clinical Relevance	8
	Clinical Results	10
	Potential Future Developments	13
	Further Reading	14
1.2	Adoptive T Cell Therapy	15
	Naturally Occurring Tumour-specific T Cells	15
	Genetically Modified T Cells	17
	Concluding Remarks	22
	Further Reading	22

1.3	Vaccines (Dendritic Cell Vaccines, Peptide Vaccines, DNA	
	Vaccines, RNA Vaccines, Oncolytic Viruses)	23
	Definition (Introduction to the Concept and Development	
	of Cancer Vaccine Strategies)	23
	Essential Processes Involved	26
	Dendritic Cell Vaccines	27
	Peptide Vaccines	31
	DNA Vaccines	34
	RNA Vaccines	35
	Oncolytic Viruses	36
	Predictive and/or Prognostic Biomarkers of (Potential)	
	Clinical Relevance	37
	Potential Future Developments	37
	Further Reading	40
1.4	Biomarkers for Immunotherapy	43
	Introduction	43
	Biological Background for Biomarkers in Immunotherapy	43
	Future Immuno-oncology Biomarker Strategies	53
	Conclusion	53
	Further Reading	54
1.5	Resistance to Immunotherapy	56
	Introduction	56
	Tumour-intrinsic Mechanisms of Immune Checkpoint	
	Inhibitor Resistance	57
	Tumour-extrinsic Mechanisms of Immune Checkpoint	
	Inhibitor Resistance	63
	Environmental Host Factors	64
	Unmet Needs	66
	Further Reading	67
传统	Section 2: Immunotherapies in specific disease groups –	
VELTON.	State of the art	
2.1	Melanoma	73
	Overview of Immunotherapy in Melanoma	73

	Immunotherapy in Metastatic/Unresectable Melanoma	74
	Adjuvant Immunotherapy in Melanoma	79
	Immunotherapy Versus Targeted Therapy	81
	The Endless Search for a Biomarker	82
	Future Perspectives	83
	Further Reading	85
2.2	Merkel Cell Carcinoma	87
	Overview	87
	Introduction	87
	Immunology of MCC	88
	Immunotherapy of MCC	90
	Unmet Needs and Future Directions	94
	Conclusion	96
	Further Reading	96
2.3	Thoracic Malignancies	
	2.3.1 Non-small Cell Lung Cancer	99
	Current Scope of Immunotherapy of NSCLC	99
	Predictive Biomarkers of Immunotherapy Response of	
	Clinical Relevance	100
	Immunotherapy of Locally Advanced NSCLC	105
	Immunotherapy of Early-stage NSCLC	105
	Potential Future Developments	107
	Further Reading	111
	2.3.2 Small Cell Lung Cancer	112
	Introduction	112
	Rationale for Immunotherapy in SCLC and	
	Predictors of Response	114
	Clinical Results	115
	Future Developments	118
	Further Reading	123
	2.3.3 Mesothelioma	125
	Definition	125
	Predictive and/or Prognostic Biomarkers of	
	Clinical Relevance	125

	Clinical Results	126
	Potential Future Developments	129
	Further Reading	131
	2.3.4 Other Thoracic Malignancies: Thymic Malignancies	
	and Others	133
	Thymic Malignancies	133
	Other Rare Thoracic Malignancies	138
	Further Reading	140
2.4	Genitourinary Malignancies	
	2.4.1 Renal Cancer	142
	Introduction	142
	Clinical Results	143
	Potential Future Developments	148
	Conclusion	151
	Further Reading	152
	2.4.2 Bladder Cancer	154
	Introduction and Context	154
	Introduction and Context Clinical Results	
	Clinical Results Potential Future Developments	154
	Clinical Results	154 156
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies	154 156 161
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high	154 156 161 164
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability	154 156 161 164
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To?	154 156 161 164
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in	154 156 161 164 166 167 168
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in Detection of Mismatch Repair Deficiency	154 156 161 164 166 167 168
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in Detection of Mismatch Repair Deficiency Historical Prognostic and Predictive Value of MSI	154 156 161 164 166 167 168
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in Detection of Mismatch Repair Deficiency Historical Prognostic and Predictive Value of MSI Clinical Rationale of Using MSI as a Predictive Biomarker	154 156 161 164 166 167 168 169 171
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in Detection of Mismatch Repair Deficiency Historical Prognostic and Predictive Value of MSI Clinical Rationale of Using MSI as a Predictive Biomarker for Programmed Cell Death Protein 1 Antibody Response	154 156 161 164 166 167 168 169 171
2.5	Clinical Results Potential Future Developments Further Reading Gastrointestinal Malignancies 2.5.1 Microsatellite Instability-high Pathogenesis of Microsatellite Instability Who Does This Apply To? Clinical, Pathological and Genetic Criteria Involved in Detection of Mismatch Repair Deficiency Historical Prognostic and Predictive Value of MSI Clinical Rationale of Using MSI as a Predictive Biomarker	154 156 161 164 166 167 168 169 171

	2.5.2 Gastric and Oesophageal Malignancies	178
	Introduction	178
	The Immune Environment in Gastro-oesophageal Cancer	178
	Immune Checkpoint Blockade in Gastro-oesophageal Cancer	179
	Squamous Oesophageal Cancer	187
	Conclusions and Future Directions	188
	Further Reading	189
	2.5.3. Hepatocellular Carcinoma	191
	Introduction	191
	HCC Immunobiology	192
	Current Landscape of Immune Checkpoint Inhibition in HCC	193
	Alternative Immunotherapeutic Strategies	198
	Future Directions and Issues Specific to HCC	199
	Conclusions	201
	Further Reading	202
2.6	Immunotherapy in Head and Neck Tumours (HPV+ and HPV-	203
	Immunotherapy in Head and Neck Cancer – the Rationale	203
	Immunotherapy for Locally Advanced Head and Neck	
	Squamous Cell Carcinoma	205
	Immunotherapy in Recurrent/Metastatic Head and	
	Neck Cancer – Evidence and Future Directions	208
	Immuno-oncology in Head and Neck Cancer:	
	Predictive Biomarkers?	210
	Conclusion	214
	Further Reading	214
2.7	Immunotherapies in Lymphoma	217
	Introduction	217
	Monoclonal Antibodies	217
	Interferons	219
	Vaccination	220
	Immune Checkpoint Inhibitors	221
	Chimeric Antigen Receptor-T cell Therapy	224
	Bispecific Antibodies	227
	Further Reading	228

2.8	Gynaecological Malignancies	230
	The Role of Immunotherapy in Ovarian Cancer	230
	The Role of Immunotherapy in Cervical Cancer	235
	The Role of Immunotherapy in Endometrial Cancer	238
	Further Reading	241
	Section 3: Implications for clinical practice	
3.1	Management of Adverse Events Related to Immune	
	Checkpoint Blockade	245
	Definition	245
	Processes Involved	245
	Global Management	246
	Clinical Results	247
	Further Reading	256
3.2	Immune Checkpoint Blockade: Response Patterns and	
	Assessment of Response	258
	The Problem	258
	Response Patterns in Immunotherapy	258
	Criteria for Response	261
	Potential Future Developments	264
	Further Reading	266
3.3	Immunotherapy in Special Populations	267
	Introduction	267
	Clinical Results/Patient Groups	268
	Potential Future Developments	275
	Further Reading	276
3.4	Cancer Immunotherapy Trials: Challenges	
	and Opportunities	278
	Introduction	278
	Lessons from Pre-checkpoint Inhibitor Immunotherapy	280
	Optimising Contemporary Immunotherapy Clinical Trials	282
	Summary	285
	Further Reading	286

3.5	Future Perspectives	287
	Introduction	287
	Precision Immunotherapy	288
	Conclusions	294
	Further Reading	295
Index		296