# Contents

**Author biographies** vii

1 **Introduction and background biology** 1
   - Introduction 1
   - Epidemiology 1
   - HER2 primary structure 2
   - Signal transduction through receptor tyrosine kinases 4
   - Receptor tyrosine kinases: site of therapeutic intervention 5
   - Signaling through HER-receptor family dimers leads to the activation of downstream cascades 5
   - Conclusions 10
   - References 10

2 **HER2 testing** 13
   - Introduction 13
   - Pre-analytic phase: sample handling 14
   - Analytic phase: HER2 testing methodologies 15
   - Post-analytic phase: screening and interpretation 17
   - Alternate HER2 testing methodologies 22
   - References 23

3 **HER2-positive breast cancer: adjuvant and neoadjuvant therapy** 25
   - Adjuvant setting 25
   - Neoadjuvant therapy 33
   - Current therapy standards for HER2-positive early breast cancer 38
   - Future directions and ongoing trials 38
   - References 39

4 **HER2-positive metastatic breast cancer: first-line treatment** 43
   - Introduction 43
Trastuzumab-based therapy
Pertuzumab
Ongoing first-line studies
HER2/hormone receptor co-positive tumors
Conclusions
References

5 HER2-positive metastatic breast cancer: second-line treatment
Introduction
Trastuzumab emtansine
Lapatinib in the metastatic setting
Investigations of trastuzumab-lapatinib combination therapy
Conclusions
References

6 Emerging targeted agents for HER2-positive breast cancer
Challenges and unmet needs in HER2-positive breast cancer
Novel HER2 tyrosine kinase inhibitors
PI3K/Akt/mTOR inhibition
Other signaling pathways
Boosting immunological response to HER2 blockade
Vascular endothelial growth factor inhibition
Conclusions
References
Handbook of HER2-targeted agents in breast cancer
Alvarez, R.H.; Cortés, J.; Mattos-Arruda, L.; Falzon, M.;
Fasolo, A.; Gandy, M.; Gianni, L.; Harbeck, N.; Piccart,
M.; Zambelli, S.; Zardavas, D.
2013, XI, 96 p. 13 illus., Softcover
ISBN: 978-1-907673-93-1