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Bristi Basu is a Consultant Medical Oncologist in experimental cancer therapeutics at Cambridge University Hospitals NHS Trust (UK). While undertaking clinical specialty training in medical oncology at Cambridge University (UK), she completed a PhD as a Cancer Research UK Gordon Hamilton-Fairley Clinical Research Training Fellow in cancer cell biology and drug discovery. She has worked with experimental cancer therapy agents in several early-phase trials both at Addenbrooke's Hospital (Cambridge, UK) and at the Drug Development Unit, Royal Marsden Hospital (Surrey, UK).

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Simon Pacey is a Consultant Medical Oncologist in experimental cancer therapeutics at Cambridge University Hospitals NHS Trust. In his current role at the University of Cambridge, he runs a portfolio of early-phase clinical trials for patients with advanced, solid tumors. He has been involved in the clinical studies of several key small antiangiogenic molecules including sorafenib and nintedanib, as well as current clinical studies of agents including vandetanib and pazopanib.

FOREWORD

Antiangiogenesis in cancer therapy

Bristi Basu, Swethajit Biswas & Simon Pacey

Angiogenesis is considered one of the hallmarks of cancer. However, barring a few notable examples of significant success such as in clear-cell kidney cancer, angiogenesis inhibition as monotherapy has failed to make the profound impact on clinical practice that was initially anticipated. Despite being proposed as a therapeutic target by Judah Folkman over 40 years ago [1], it is only in the last decade that scientific knowledge on angiogenesis has been translated into effective inhibitory strategies for patients, with agents such as bevacizumab and VEGF receptor tyrosine kinase inhibitors showing modest clinical benefit across a range of cancers. With increasing experience, we are learning which tumor types may respond to angiogenesis inhibition more than others. We have also

gained knowledge that in the metastatic setting, a major hurdle to clinical effectiveness is the development of resistance through alternative angiogenic pathways. There are, therefore, ongoing efforts to explore angiogenic targets beyond the VEGF ligand and its receptors. It is anticipated that development of relevant predictive biomarkers will permit better patient selection for an antiangiogenic strategy; however, this area of research is still to yield reliable results for mainstream use. This book presents a succinct guide to angiogenesis inhibitors in clinical development and the evidence for angiogenesis inhibition across a broad range of tumors. It presents updates from the clinical research field and opinions on how antiangiogenic strategies may be optimized for therapeutic benefit.

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