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Revival of anti-angiogenic therapies in cancer—news on an old therapeutic concept

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Inhibition of angiogenesis became clinical reality in 2004 with the approval of bevacizumab in metastatic colorectal cancer and we are now approaching the expiration dates of the patents for bevacizumab in the US in July 2019 and in Europe in January 2022. From the historical view on anti-angiogenic drug development, mainly targeting the vascular endothelial growth factor (VEGF) pathway, there were several ups and downs with the use of these agents, and the first euphoric view on the concept to starve tumors by blocking angiogenesis has many parallels with the enthusiasm we are facing at the moment with immune checkpoint inhibitors. As endothelial cells and not cancer cells are the main targets of anti-angiogenic drugs the scientific focus moved on the investigation and characterization of the tumor microenvironment (TME). These investigations led to the description of the complex and highly plastic TME, which finally led to the identification of new therapeutic concepts. Approved anti-angiogenic agents either neutralizing VEGF or blocking the VEGFR now form the backbone treatment of several cancer entities and will be used as combinational partners for new therapeutic strategies like immune checkpoint inhibitors or other new therapies in the future. In this special issue of *MEMO*, we are happy to offer the readers five articles written by experts in their respective fields presenting the current knowledge of anti-angiogenic therapies in different cancer entities and their future developments.

We are glad to present two state-of-the-art reviews of role-model cancer entities for angiogenesis inhibition including colorectal cancer by Stragier et al. [1] and metastatic renal cell cancer (mRCC) by Pichler et al. [2]. In both cancer entities anti-angiogenic drugs are successfully used; however, there is still a high medical need for biomarker identification and optimal patient selection. Also in other urological malignancies besides mRCC anti-angiogenic therapies pose an attractive therapeutic strategy and Haidl et al. [3] summarize the first evidence to use to use anti-angiogenic drugs in prostate, bladder, testicular as well as penile cancer patients. Gampenrieder et al. [4] describe the roller-coaster experience of anti-angiogenic drugs in breast cancer and discusses critically their current role and future aspects in breast cancer. The article by Young et al. [5] reports on the rare but biologically highly interesting use of anti-angiogenic strategies in angiosarcomas, which represent the malignant differentiation of endothelial cells and mechanistically seen "real" endothelial tumor and how these tumors respond on anti-angiogenic drugs.

All five articles provide an up-to-date review of the research and literature about anti-angiogenic therapies in these tumor entities. We therefore hope that this special issue will help the readers to understand the underlying complex biology and challenges in developing successful anti-angiogenic therapies and future perspectives of combinational therapy approaches, which will soon become clinical reality.

Conflict of interest A. Pircher declares that he has no competing interests.

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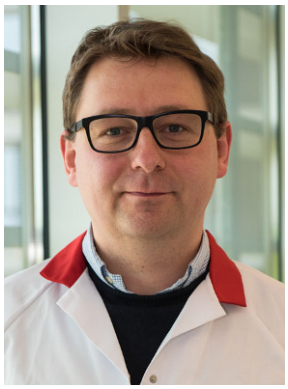

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