



## Development of chemotherapeutics in oncology: is there anything new?

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In a decade where the dynamic development of targeted therapies and modulation of the immune system for treating cancer has dramatically changed and dominates the armamentarium of an oncologist, the topic the authors of this minireview series have been confronted was challenging: is there anything new in the development of classical cytostatic drugs and their indications?

Despite living in the area of “modern oncology”, there are indeed indications where chemotherapy remains the mainstay of treatment in all stages of the disease. Examples are pancreatic or gastric cancer, where many efforts of testing modern treatment strategies failed. On the other hand, there are entities like lung cancer, where chemotherapy has been significantly replaced by targeted or immunological treatment approaches.

Nevertheless, the use of chemotherapy has not remained static and there are some developments with clinical impact for several indications. One of the major issues of chemotherapeutic substances is their toxicity. With the development of new antiemetic drugs the tolerability has been improved significantly, as is reviewed here. This is accompanied by using chemotherapeutic regimen in a de-escalated manner by retaining its efficacy. One example is the use of shortened weekly paclitaxel in combination with trastuzumab in low-risk, Her2-positive breast cancer. In addition, we could realize the more “specific” application of chemotherapeutic drugs. This has been

achieved by the regional application of chemotherapy, for example Hepatic Artery Infusion (HAI) in colorectal cancer, on the one hand or by the tricky binding of the well-known anti-microtubule substance emtasine to the antibody trastuzumab, which specifically targets Her2-positive cancer cells on the other hand. For some indications, like pancreatic cancer or colorectal cancer, it could be shown that “more aggressive is more effective”. The combination of oxaliplatin, irinotecan and 5-Fluorouracil (5FU) in the FOLFIRINOX or the FOLFOXIRI regimen increased efficacy in colorectal and pancreatic cancer. In the latter, this combination indeed represents one of the most significant steps forward despite modern therapeutics. A very interesting topic covers the conversion of “old” to “modern” chemotherapeutics. First, classical paclitaxel was bound to nanoparticle-albumin, resulting in nab-paclitaxel. The aim was to reduce solvent-caused toxicity. It also showed enhanced efficacy for example in breast cancer. Nowadays, it is also a standard of care in the treatment of pancreatic cancer. Another example is nanoliposomal irinotecan, which offers a new and the first standard based on phase III evidence in second-line treatment of pancreatic cancer. Other examples are liposomal-bound doxorubicin, or a novel oral formulation of vinorelbine, which enhances patient autonomy during treatment. But not only has old been turned into new: with eribulin, for example, a new drug has been invented and is frequently used in breast cancer or sarcoma. There are other examples, like trabectedin, which are not discussed here.

Development of chemotherapeutic regimens has possibly not been as dynamic as compared to targeted agents and immunotherapeutics. However, sophisticated use by de-escalation strategies, the careful combination of substances for specific indications, the development of new formulations of older drugs, and the

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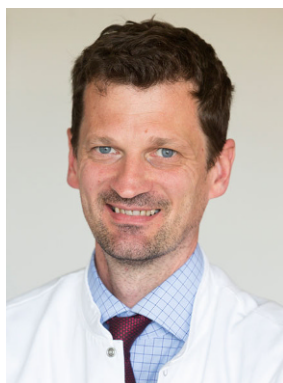
development of, although few, new drugs clearly contributes to the overwhelmingly improved outcome of cancer patients nowadays. Chemotherapy will remain a mainstay in the treatment of cancer, whereas one of the major issues will be to determine its role, in combination or in sequence, within the huge number of new substances. Finally, we should always keep in mind that decades of treatment with cytotoxic chemotherapy has also helped to improve our understanding of malignant diseases. This knowledge significantly contributed to the development of modern substances and the clinical experience of oncologists.

The authors of this minireview series have to be congratulated for mastering a difficult task in a far-sighted manner.

**Conflict of interest** H. Rumpold and T. Winder declare that they have no competing interests.



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