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Neoadjuvant treatment for solid tumors—the earlier, the better

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Administering adjuvant systemic treatment following local therapy aiming to reduce recurrence rates and mortality is a standard approach in many common malignancies such as breast, colorectal, or lung cancer. Of note, administering systemic treatment already before surgery offers potential additional advantages such as downstaging and downsizing of the primary tumor and regional lymph nodes, in vivo sensitivity testing, earliest possible treatment of potential micrometastatic disease, and response-adapted tailoring of further postoperative therapy.

In breast cancer, neoadjuvant treatment is today regarded as the preferred approach in aggressive disease subtypes for the majority of patients. The addition of HER2-directed monoclonal antibodies to chemotherapy in HER2-positive breast cancer have vastly increased pathologic complete remission (pCR) rates, a surrogate endpoint indicating improved long-term outcome. More recently, in triple-negative breast cancer, the combination of the immune checkpoint inhibitor pembrolizumab with chemotherapy improved pCR rates and event-free survival (EFS) over chemotherapy alone. In patients not achieving pCR, recurrence risk may be reduced by response-adapted postoperative treatment such as T-DM1 in HER2-positive disease. These data are reviewed in detail by Dr. Pusch in her article [1]; in addition, the important field of de-escalating treatment intensity and the role of preoperative endocrine therapy are discussed.

Things are slightly different in gastric cancer, where perioperative chemotherapy may still be underutilized in UICC stage II and III disease as reviewed by Sonnweber et al. [2]. In addition, the potential role of HER2-directed drugs in the neoadjuvant treatment of HER2-positive gastric cancer as well as the role of immune checkpoint inhibitors as a component of neoadjuvant treatment currently remain ill-defined. In locally advanced esophageal cancer, neoadjuvant chemoradiotherapy is the standard of care; in this setting, additional postoperative immunotherapy with nivolumab has significantly improved disease-free survival, defining a novel standard of care.

Terbuch et al. report on the CheckMate 816 trial, a randomized phase III trial evaluating the addition of nivolumab to preoperative platinum-base chemotherapy in non-small cell lung cancer (NSCLC) [3]. Resulting outcome improvements in terms of EFS and pCR rates have meanwhile led to US Food and Drug Administration (FDA) approval of this combination regimen. In addition, promising data on preoperative treatment with small molecule tyrosine kinase inhibitors in patients with EGFR-mutant or ALK-positive NSCLC are also discussed.

Finally, Kosma et al. discuss the role of preoperative chemotherapy in pancreatic cancer, a malignancy still associated with extremely poor outcome [4]. While the role of adjuvant chemotherapy is well established, the role of neoadjuvant treatment remains ill-defined. Data generally point toward a benefit of upfront systemic therapy; still the optimal chemotherapy regimens and the appropriate patient population remain elusive. Authors therefore encourage neoadjuvant treatment within the context of clinical trials.

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In summary, these reviews show the clinical relevance of neoadjuvant treatment and further developments in this field are eagerly awaited.

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