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IMPACT OF TUMOR-INFILTRATING LYMPHOCYTES AND FUTURE IMMUNE STRATEGIES IN BREAST CANCER

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Background: The role of TILs in BC is still an issue for clinical research, albeit results of neoadjuvant and adjuvant clinical trials already now highlight the crucial impact of TILs on therapy response and survival. Methods: Evaluation of related publications (pubmed) and meeting abstracts (ASCO, SABCS). Results: Increased stromal TILs are found in 30% of TNBC and in 19% of HR-,HER2+BC. The percentage of TILs is a significant independent parameter for pCR after neoadjuvant chemotherapy (NAC). Lymphocyte-predominant BC (LPBC) respond with higher pCR-rates than non-LPBC or tumors without any TILs. Increased TILs in TN and HR-, HER2+ subtypes predict benefit from addition of carboplatin to NAC. TILs are also associated with improved DFS and OS among patients with TNBC and HR-, HER2+ BC. Conversly and interestingly increased TILs in patients with HR+, HER2-(luminal) BC are associated with a 10% higher risk of death per 10% increase of TILs. Interactions between immune system and cancer are complex. The cancer-immunity cycle characterizes these interactions. BC subtypes with higher number of mutations such as TNBC and HR-, HER2+BC are considered to provide a raising number of tumor-associated antigens, thereby capable to build up a higher endogenous immune response. TILs may serve as surrogate marker of both an existing endogenous immune response and the probability to respond to cancer immune therapies. As cancer co-opt immune checkpoint-pathways as a major mechanism of immune resistance, in particular, against cytotoxic T-cells, blockades of checkpoint-pathways by antibodies are one of the goals of the current cancer immunotherapy studies. Therapy studies with antigene-based strategies (vaccines) and antibodies against the immune checkpoints PD-1 and CTLA-4 and their inhibitory pathways in order to enhance cytotoxic T-cell activities against cancer cells with or without chemotherapy are underway. Conclusions: Integration of TILs as immunological biomarker after their evaluation has been standardized, might be helpful to identify patients with benefit from addition of carboplatin to taxan –anthracykline-based chemotherapy. As crosstalks of various lymphocyte subsets are shaping the tumor-microenvironment and thereby driving anti- or protumor activities, oncologists need raising information from this space adjacent to the tumor. To date, only a few small studies of BC immunotherapy have been reported, but the preliminary results are encouraging.

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