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Efficacy of dual checkpoint-blockade in solid tumors, part 1

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Checkpoint inhibition is one of the most important medical discoveries of the 21st century. Not without reason James P. Allison and Tasuku Honjo received the Nobel Prize in medicine 2018 for their work in this field. The idea to fight cancer by activating immune response, e.g., by cytokines or IL-2, has been around for decades with limited success. In contrast to these unspecific approaches, the idea of checkpoint inhibition (CPI) is to enhance T-cell activation, leading to tumor elimination. Apart from CPI monotherapy, there is evidence for synergistic efficacy of combination strategies using inhibitors of the PD-L1/PD-1 axis plus CTLA4, LAG3, and TIGIT, respectively. There is, however, quite variable efficacy of these combinations across many solid tumor entities, which might be due to differences in tumor heterogeneity and resistance mechanisms.

In this edition of *memo*, the new series "Efficacy of dual checkpoint blockade in solid tumors" begins with two excellent reviews on two highly aggressive solid tumors with poor outcome.

First, Dr. Mayerhofer [1] shows in his review "Dual checkpoint-blockade in urothelial carcinoma—it's time" that not only single PD-1/PDL1 inhibitors, which are already routinely used in urothelial cancer, but also dual CPI combinations show encouraging activity in this highly aggressive tumor.

Thereafter, Dr. Ilhan-Mutlu [2] gives us hope in her review "Dual immune checkpoint blockade in gastroesophageal tumors: never say never", which shows that dual checkpoint inhibition can be also effective in gastroesophageal tumors, an entity in which checkpoint inhibition has so far not show as much benefit compared to other tumor entities.

I hope you will enjoy these two excellent reviews.

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Conflict of interest D. Niedersüß-Beke declares that she has no competing interests.

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