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Anti PD-1/anti PD-L1 in digestive cancers

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Abstract

Human tumors tend to activate the immune system regulatory checkpoints as a means of escaping immunosurveillance. For instance, interaction between PD1 and PD-L1 will lead the activated T cell to a state of anergy and PD-L1 is upregulated on a wide range of cancer cells. Anti-PD1 (Program Death 1) and anti-PD-L1 monoclonal antibodies (mAbs), called immune checkpoint inhibitors (ICls), have consequently been designed to restore T cell activity.

Accumulating data are in favor of an association between PD-L1 expression in tumors and response to treatment. A PD-L1 expression is present in 30 to 50% of digestive cancers. Multiple anti-PD1 (nivolumab, pembrolizumab) and anti-PD-L1 mAbs (MPDL3280A, Medi4736) are under evaluation in digestive cancers, Preliminary results in metastatic gastric cancer with pembrolizumab are highly promising and phase II will start soon. In metastatic colorectal cancer, a phase III trial of MPDL3280A as maintenance therapy will shortly be initiated. Trials are also ongoing in metastatic colorectal cancer with high immune T cell infiltration (i.e. microsatellite instability).

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