消化系癌免疫治療的新進展

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Immuno-oncology (IO) has made major advances for the treatment of digestive cancers since 2012.

Gastric Cancer (GC) & Gastroesophageal Junction (GEJ) Adenocarcinoma

Immune checkpoint inhibitors (ICIs), anti-PD-1 (pembrolizumab, nivolumab) and anti-PD-L1 (avelumab, durvalumab) antibodies [Ab] are under active evaluation in GC. Pembrolizumab has shown encouraging objective response rates (ORRs) of 22% in the 3rd-line treatment of GC. Nivolumab ± ipilimumab (a CTLA-4 Ab) demonstrated encouraging antitumor effects (with ORRs of 14-26%, 14% (N3), 26% (N1+I3)) and survival in the 3rd-line treatment of metastatic GC. Avelumab maintenance after 1st-line chemotherapy achieved an ORR of 7.3% (1 CR, 3 PR in 55 evaluable patients). In the 2nd-line setting, avelumab demonstrated an ORR of 15%.

Colorectal Cancer (CRC)

ICI monotherapy, such as pembrolizumab, has shown promising antitumor effects with objective response rates, ORRs, of 40-57% in mismatch repair-deficient (dMMR) with high-microsatellite instability (MSI-H) CRC patients. Pembrolizumab has been granted breakthrough therapy designation for treatment of MSI-H CRC by US FDA in Nov., 2015. Nivolumab ± ipilimumab were well tolerated and demonstrated encouraging antitumor effects (with ORRs of 25.5-33.3%) and survival in MSI-H metastatic CRC. However, MSI-H only accounts for about 2% of mCRC patients. Huge unmet needs do exist.

Hepatocellular Carcinoma (HCC)

Nivolumab has demonstrated encouraging antitumor effects (with ORRs of 14%, 3CR, 4PR in 48 evaluable patients) and survival in the 2nd-line (73% had prior sorafenib) treatment of HCC.

Future Perspectives

In addition to the *above* mentioned cancer types, immuno-oncology (IO) still actively investigates the potentials in the treatment of other digestive cancers, such as cancers of esophagus, anus, biliary tract, pancreas, etc. Currently, IO/IO combinations [e.g., nivolumab + ipilimumab, durvalumab +

tremelimumab (a CTLA-4 Ab)], or combinations of immunogenic chemotherapy or targeted therapies with ICIs (or other IO agents) warrant active studies in the treatment of digestive cancers. To identify valid *predictive* biomarkers for *precision oncology* is also crucial.