What is a useful biomarker for advanced gastric cancer (AGC)?

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In advanced gastric cancer (AGC), most of clinical trials have been designed based on immunohistochemistry (IHC)/in situ hybridization (ISH) for some tyrosine kinase receptors (RTKs; HER2, EGFR, MET, FGFR2). However, currently, the molecular aberrations to target without HER2 are unclear in most cases. Indeed, unfortunately, the other drugs without trastuzumab or ramucirumab did not result in significant benefit in the phase III clinical trial. On the other hand, recently, next-generation sequencing (NGS) allowed us to comprehensively profile tumor gene status. In addition, the Cancer Genome Atlas (TCGA) project proposed a molecular classification dividing gastric cancer into four subtypes. However, the efficacy of therapies against detected targeted gene in AGC is not known enough, and furthermore it is difficult to enrich patient population now. We performed comprehensive analyses by both NGS and IHC to design the optimal therapy with which to treat the right population of AGC patients, because AGC contained a complicated arrangement of protein expression and gene alterations. On the other hand, antibody-mediated blockade of the programmed death 1 protein (PD-1) and its ligand (PD-L1) resulted in potent and durable tumor regression and prolonged stabilization of disease in patients with advanced solid tumors recently. A phase IB study of pembrolizumab in AGC patients with PD-L1 tumor positivity by IHC was presented at ESMO 2014. However, we do not yet enrich the right population for immunotherapy in AGC. We need to find biomarkers such as virus infection or MSI status for immunotherapy in future clinical trial and pre-clinical research. In this session, we will present biomarkers in AGC that may be usefulness in the future clinical trial from previous reports and our research.