非小細胞肺癌免疫治療新進展

The evolving role of immunotherapy in non-small cell lung cancer

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In 2015, nivolumab was approved for the treatment of advanced NSCLC based on CheckMate 057 and 017 which exhibited the overall survival (OS) advantage over docetaxel in the second line setting. After these trials, other CPIs (check-point inhibitors; pembrolizumab and atezolizumab) have also shown OS improvement in the second line setting. Since CPIs also provided the better toxicity profile over cytotoxic agents and only about half patient received second-line chemotherapy, it was appealing to relocate them in the frontline setting. Pembrolizumab was approved by the FDA in October 2016 for the front-line treatment of patients with advanced NSCLC with tumor PD-L1 expression more than 50%. And for tumoral PD-L1 status expression less than 50%, the combination of immunotherapy with platinum-based chemotherapy (KEYNOTE-189) or plus angiogenesis inhibitors (IMpower150) became the first-line setting. And result from CheckMate 227 and CheckMate 9LA demonstrated the benefits of combination therapy with CTLA-4 plus PD-1 blockers. Stage III NSCLC is a heterogeneous disease which should be treated after multidisciplinary team (MDT) discussion. A landmark study, the PACIFIC trial, published in 2017, demonstrated the benefit in both PFS and OS using durvalumab as consolidation treatment after completion of concurrent chemoradiotherapy in unresectable stage III NSCLC compared with placebo. Five-year survival outcomes published this year at ASCO, showing 42.9% of patients who received durvalumab remained alive and approximately a third remained free of disease progression. Novel therapeutic strategies are poised to expand CPI in adjuvant settings for patients with early-stage disease facing recurrence risks. The FDA has approved atezolizumab as an adjuvant treatment after surgery and chemotherapy for patients with stage II to IIIA NSCLC with tumors expressing PD-L1 on 1% or more. The approval is based on results from the IMpower010 clinical trial in which atezolizumab reduced the risk of disease progression or death by 34%

versus best supportive care. And the median disease-free survival was not reached in the atezolizumab group versus 35.3 months for best supportive care group. In this review, we discuss recently reported and ongoing studies that are designed to define the role of immunotherapy in patients with advanced stage NSCLC to those with non-metastatic NSCLC.