

New response criteria for immunotherapy to capture response patterns in advanced melanoma patients treated with ipilimumab: Results from two phase II trials

Jedd Wolchok

Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Abstract

Ipilimumab is a monoclonal antibody directed against cytotoxic T lymphocyte antigen-4 (CTLA-4). Previous reports have noted that modified World Health Organization (mWHO) criteria may not fully capture ipilimumab clinical benefit. Here we present response and survival data, analyzed by mWHO or proposed novel efficacy endpoints, from 227 previously-treated patients with advanced melanoma enrolled in 2 Phase II trials. Patients received 10 mg/kg ipilimumab every 3 weeks (Q3W) X 4; eligible patients received 10 mg/kg ipilimumab maintenance therapy Q12W starting at Week 24. Response was assessed by Independent Review Committee (IRC) using mWHO criteria (complete response [CR], partial response [PR], stable disease [SD], and progressive disease [PD]) starting from Week 12. Follow-up was obtained in some patients after PD if they did not receive other therapies. Best overall response rate (BORR, CR+PR), disease control rate (DCR, CR+PR+SD), overall survival (OS) and 1-year survival were determined. Novel response endpoints, termed immune-related response criteria (irRC), were designed (using mWHO as a foundation) to systematically capture patterns of clinical activity and characterize changes in total measurable tumor burden over time (index + new lesions, when present) before and after mWHO PD. Survival was analyzed by DCR according to mWHO or novel efficacy endpoints. Overall, 4 response patterns were observed: 2 conventional (response in baseline lesions and 'stable disease', often with slow, steady decline in total tumor burden) and 2 novel (response after initial increase in total tumor burden and response in index and new lesions after the appearance of new lesions). The mWHO BORR was 7.5% (17/227). The median OS was 10.7 months (95% CI 7.8, --) and 1-year survival rate was 48.6% (95% CI 40.6, 54.9) with 0.2-18.7 months of follow-up. The median OS for patients with mWHO CR/PR/SD and for those with responses captured by the novel efficacy endpoints (mWHO PD followed by tumor shrinkage) were comparable and have not yet been reached. These data suggest that mWHO-classified PD may not always be a surrogate for drug failure in ipilimumab-treated melanoma patients. Novel response criteria such as irRC, which track tumor burden (including new lesions, when present) before and after mWHO PD, may better characterize the clinical activity of ipilimumab and other immunotherapies. Survival follow-up is ongoing.