







Sanjay Popat Royal Marsden Hospital

Immune checkpoint inhibitor therapy has revolutionized out comes for stage 4 non-small cell lung cancer (NSCLC). This therefore begs the question on its utility in patients with radically treatable NSCLC. In patients with inoperable stage 3 NSCLC, the PACIFIC trial demonstrated that consolidation durvalumab for 1 year following radical chemoradiotherapy significantly improved progression-free survival (PFS) and overall survival (OS), and increased the absolute 5-year PFS from 19% to 33% and OS from 33% to 44%. For resected NSCLC, in the adjuvant setting, data from immunotherapy-only trials (without a neoadjuvant component) have reported mixed outcomes, and all trials are continuing follow-up. The first trial to report was IMpower-010. All patients were mandated to have adjuvant chemotherapy, and then randomized to one year of adjuvant atezolizumab or not. Here, in the subset of stage IIA-IIIA(v7) patients, the primary endpoint of disease-free survival (DFS) was met and was significantly improved in tumour proportion score (TPS) 1% or more tumours (HR=0.66). Overall survival (OS) at first interim analysis was exploratory and demonstrated a marked OS benefit in PD-L1 1% or more tumours, but driven by those with TPS 50% or more, no benefit in those with PD-L1 1-49% and potential inferior OS in PD-L1 negative tumours. The second trial to report was PEARLS/KEYNOTE-091. In this trial, adjuvant chemotherapy was not mandated. Patients were randomized to one year of pembrolizumab or placebo. The trial met one of the dual primary endpoints of DFS, significantly improved (HR=0.76), in the IB-IIIA(v7) population. However, did not meet the second of the dual primary endpoint of DFS in the PD-L1 50% or more subgroup. This biologically unexpected subset result limits additional interpretation of other subsets. OS remained immature and non-significant. The third trial to report was BR.31. Here, after mandatory adjuvant chemotherapy, patients with stage IB-IIIA(v7) were randomized to one year of durvalumab or placebo. Unfortunately, the primary endpoint of DFS in the PDL-L1 25% or more was not met (HR=0.935). Taken together, while these trials indicate that adjuvant immunotherapy enhances DFS in early NSCLC, uncertainties remain regarding OS benefits and the optimal PD-L1 patient selection criteria.