“PD-1 blockade a common denominator for cancer therapy”

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The PD-1 pathway, including the immune cell receptor Programmed Cell Death 1 (PD-1) and its ligands, PD-L1 (B7-H1) and PD-L2 (B7-DC), mediates immunosuppression in the tumor microenvironment. Drugs that ″release the brakes″ on anti-tumor immunity by blocking PD-1 or PD-L1 have shown substantial and durable activity in multiple cancers, validating them as a ″common denominator″ for cancer therapy. Since September 2014, the US FDA has approved 6 different PD-1/PD-L1 antibodies to treat advanced cancers, including 15 tumor types and the broad genetically-defined MSI-high category. These drugs are now being applied in earlier stages of cancer, in the adjuvant and neoadjuvant settings. Tumor PD-L1 protein expression correlates with enhanced responsiveness of some cancers to anti-PD-1, while tumor mutational burden, reflecting neoantigen load, associates with likelihood of response in additional patients. The continued interrogation of potential biomarkers is expected to further refine the risk:benefit profile for PD-1/PD-L1 antagonists, increase our understanding of the mechanistic underpinnings of this pathway, and guide the development of more effective combination therapies.