SUPPLEMENTARY MATERIAL

Plain Language Summary

The CASPIAN clinical trial compared three different treatments (durvalumab plus chemotherapy, durvalumab plus tremelimumab plus chemotherapy, or chemotherapy alone) for patients with small-cell lung cancer (SCLC) that has spread beyond a single area (extensive-stage SCLC; ES-SCLC) and who had not received any previous treatment. Durvalumab and tremelimumab are both types of medicine called immunotherapy: treatments that target the immune system to help the body fight cancer. Immunotherapy works better in some people more than others. Predictive biomarkers are molecules that can help identify people who are more likely to respond to a particular treatment, but these are not well established in ES-SCLC.

PD-L1 and tumor mutational burden (TMB) have previously been shown to be biomarkers of response to some immunotherapies used to treat patients with non-small cell lung cancer. PD-L1 is the target that durvalumab binds to in the tumor. TMB is the total number of mutations found in cancer cells. Using samples taken from a subset of patients participating in CASPIAN, we investigated the link between the length of time participants lived after starting treatment and either the amount of PD-L1 present in the tumor or the TMB score.

We found that patients treated with durvalumab plus chemotherapy had a better chance of living longer than those treated with chemotherapy alone whatever the amount of PD-L1 in the tumor. However, among patients treated with durvalumab plus tremelimumab plus chemotherapy, the chance of living longer than patients treated with chemotherapy alone was increased in patients with higher amounts of PD-L1 in the tumor relative to those with lower amounts. We also found that TMB made no difference to how much longer patients lived when treated with either durvalumab plus chemotherapy or with durvalumab plus tremelimumab plus chemotherapy, compared with chemotherapy alone.

Our results strongly suggest that neither PD-L1 nor TMB can predict response to durvalumab plus chemotherapy in patients with ES-SCLC. PD-L1 seemed better at predicting response in patients treated with durvalumab plus tremelimumab plus chemotherapy, but these results need to be confirmed in a larger study designed to investigate this. Other biomarkers such as molecular subtypes of SCLC (types of SCLC identified by genetic differences in tumor cells) may prove more useful than PD-L1 and TMB in predicting response to treatment in patients with ES-SCLC.