PEMBROLIZUMAB ACHIEVES SURVIVAL IMPROVEMENTS ACROSS PD-L1 STATUS IN KEYNOTE-407 TRIAL

Adding pembrolizumab to chemotherapy boosts survival of patients with treatment-naïve, squamous non-small-cell lung cancer that has metastasised, regardless of PD-L1 tumour proportion score

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medwireNews: Phase III trial findings support the use of the programmed cell death protein 1 (**PD-1**) inhibitor pembrolizumab for patients with stage IV squamous non-small-cell lung cancer (**NSCLC**) who are receiving their first systemic chemotherapy for metastatic disease.

For the KEYNOTE-407 trial, patients were randomly assigned to receive pembrolizumab 200 mg or placebo every 3 weeks for up to 35 cycles, explain Luis Paz-Ares, from Hospital Universitario 12 de Octubre in Madrid, Spain, and co-investigators.

Additionally all patients received four cycles of carboplatin on day 1 plus physician's choice of paclitaxel or nab-paclitaxel on days 1, 8 and 15.

At a median of 7.8 months of follow-up, median overall survival (OS) was 15.9 months for the 278 patients given pembrolizumab and 11.3 months for the 280 participants using placebo, with a significant hazard ratio (**HR**) for death of 0.64.

OS was better with pembrolizumab across all patient subgroups, the researchers say. This included an OS benefit of "consistent magnitude" regardless of whether patients had a programmed cell death ligand 1 (**PD-L1**) tumour proportion score (TPS) of less than 1% (64.2 vs 43.3%, HR=0.61), 1– 49% (65.9 vs 50.0%, HR=0.57) and 50% or greater (63.4 vs 51.0%, HR=0.64), albeit that the upper limit of the 95% confidence interval in the latter group exceeded 1.

Progression-free survival was a median of 6.4 months for the pembrolizumab arm and 4.8 months for controls, giving a significant HR for disease progression or death of 0.56. Again, **PFS** was better with pembrolizumab across the patient subgroups, with "incremental improvements" noted with increasing PD-L1 TPS.

A treatment response was reported for 57.9% of the patients using pembrolizumab and 38.4% of controls, with a median duration of 7.7 months and 4.8 months, respectively, at the time of data cutoff. And response rates were higher for the pembrolizumab arm than the controls regardless of PD-L1 TPS, say Luis Paz-Ares et al.

Overall, grade 3 or more severe adverse events were reported for a comparable 69.8% of the pembrolizumab-treated patients and 68.2% of those given placebo, although patients in the pembrolizumab group were more likely to require a dose reduction of chemotherapy (22.7 vs 17.5%) or discontinue treatment (23.4 vs 11.8% because of adverse events.

This may be “in part because of the longer duration of treatment in this group”, the investigators comment.

Pembrolizumab was associated with more frequent occurrence of grade 3 or worse pneumonitis and autoimmune hepatitis than placebo, and immune-mediated events and infusion reactions at this grade were also more common with the PD-1 inhibitor. There was one death from pneumonitis in both arms.

“The results of the current trial and of three other phase 3 trials suggest that pembrolizumab has a role in the first-line treatment of metastatic NSCLC, regardless of histologic subtype or PD-L1 tumor proportion score”, the KEYNOTE-407 investigators conclude.

They summarise that pembrolizumab plus chemotherapy shows a “high level of activity as compared with chemotherapy alone” for patients with PD-L1-negative tumours but that data do not yet show whether the combination is better than pembrolizumab alone for those with PD-L1-positive disease.

“Therefore, the treatment decision should be made on an individual basis after a discussion of the relative risks and benefits and consideration of patient-specific factors”, the team recommends.

The results of the KEYNOTE-407 trial were reported at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer in Toronto, Ontario, Canada, and simultaneously published in The New England Journal of Medicine.

Reference

Paz-Ares L, Luft A, Vicente D, et al. **Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer** . N Engl J Med; Advance online publication 25 September 2018.
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