KEYNOTE-042-全球研究.pdf.txt

# 研究患者

Methods This randomised, open-label, phase 3 study was done in 213 medical centres in 32 countries. Eligible patients were adults (≥18 years) with previously untreated locally advanced or metastatic non-small-cell lung cancer without a sensitising EGFR mutation or ALK translocation and with an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, life expectancy 3 months or longer, and a PD-L1 TPS of 1% or greater.

# 样本量

Findings From Dec 19, 2014, to March 6, 2017, 1274 patients (902 men, 372 women, median age 63 years [IQR 57–69]) with a PD-L1 TPS of 1% or greater were allocated to pembrolizumab (n=637) or chemotherapy (n=637) and included in the intention-to-treat population.

# 基线特征

Table 1: Baseline characteristics  
patient demographics and disease char acteristics were similar between groups and across the TPS populations at baseline (table 1).

# 试验设计

26 Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med 2006; 355: 2542–50. 27 Zinner RG, Obasaju CK, Spigel DR, et al. PRONOUNCE: randomized, open-label, phase III study of first-line pemetrexed + carboplatin followed by maintenance pemetrexed versus paclitaxel + carboplatin + bevacizumab followed by maintenance bevacizumab in patients with advanced nonsquamous non-small-cell lung cancer.

# 研究背景

Background First-line pembrolizumab monotherapy improves overall and progression-free survival in patients with untreated metastatic non-small-cell lung cancer with a programmed death ligand 1 (PD-L1) tumour proportion score (TPS) of 50% or greater. We investigated overall survival after treatment with pembrolizumab monotherapy in patients with a PD-L1 TPS of 1% or greater.

# 研究结果

results of clinical trials not yet published in full. We applied no other search parameters.

# 研究结论

Findings From Dec 19, 2014, to March 6, 2017, 1274 patients (902 men, 372 women, median age 63 years [IQR 57–69]) with a PD-L1 TPS of 1% or greater were allocated to pembrolizumab (n=637) or chemotherapy (n=637) and included in the intention-to-treat population. 599 (47%) had a TPS of 50% or greater and 818 patients (64%) had a TPS of 20% or greater. As of Feb 26, 2018, median follow-up was 12·8 months. Overall survival was significantly longer in the pembrolizumab group than in the chemotherapy group in all three TPS populations (≥50% hazard ratio 0·69, 95% CI 0·56–0·85, p=0·0003; ≥20% 0·77, 0·64–0·92, p=0·0020, and ≥1% 0·81, 0·71–0·93, p=0·0018). The median surival values by TPS population were 20·0 months (95% CI 15·4–24·9) for pembrolizumab versus 12·2 months (10·4–14·2) for chemotherapy, 17·7 months (15·3–22·1) versus 13·0 months (11·6–15·3), and 16·7 months (13·9–19·7) versus 12·1 months (11·3–13·3), respectively. Treatment-related adverse events of grade 3 or worse occurred in 113 (18%) of 636 treated patients in the pembrolizumab group and in 252 (41%) of 615 in the chemotherapy group and led to death in 13 (2%) and 14 (2%) patients, respectively.  
Interpretation The benefit-to-risk profile suggests that pembrolizumab monotherapy can be extended as first-line therapy to patients with locally advanced or metastatic non-small-cell lung cancer without sensitising EGFR or ALK alterations and with low PD-L1 TPS.

# 表格相关

patient demographics and disease char acteristics were similar between groups and across the TPS populations at baseline (table 1)

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In the PD-L1 TPS 50% or greater population, 118 (39%, 95% CI 34–45) of 299 patients in the pembrolizumab group and 96 (32%, 27–38) of 300 patients in the chemotherapy group had an objective response to treatment. The values in the TPS 20% or greater and 1% or greater populations were 138 (33%, 29–38) of 413 versus 117 (29%, 25–34) of 405 and 174 (27%, 24–31) of 637 versus 169 (27%, 23–30) of 637, respectively (appendix). The median duration of re sponse was 20·2 months in the pembrolizumab group in all TPS populations and was 10·8 months, 8·3 months, and 8·3 months, respectively, in the TPS 50% or greater, 20% or greater, and 1% or greater populations in the chemotherapy group (appendix). In the as-treated population, the median number of doses administered was nine (range one to 36) in the pembrolizumab group and six (one to 42) in the chemo- therapy group. Treatment-related adverse events of any grade occurred in 399 (63%) of 636 patients in the pembrolizumab group and 553 (90%) of 615 patients in the chemotherapy group (table 2)

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. Treatment-related adverse events of grade 3 or worse severity occurred in 113 (18%) of 636 patients in the pembrolizumab group and 252 (41%) of 615 patients in the chemotherapy group. Treatment-related adverse events led to death in 13 (2%) and 14 (2%) patients in the pembrolizumab and chemotherapy groups, respectively, and treatment discontinuation in 57 (9%) and 58 (9%), respectively. The most common treatment-related adverse event was hypothyroidism (69 [11%] of 636) in the pembrolizumab group and anaemia (229 [37%] of 615) in the chemo- therapy group (table 2, appendix)

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. Treatment-related adverse events of grade 3 or worse severity that occurred in 20 or more patients were pneumonitis in the pembrolizumab group and anaemia, decreased neutrophil count, neutropenia, decreased white blood cell count, and decreased platelet count in the chemotherapy group (table 2, appendix)

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. Adverse events of interest (events judged likely to be immune mediated and infusion reactions) occurred in 177 (28%) of 636 patients (51 [8%] grade ≥3) in the pembrolizumab group and 44 (7%) of 615 patients (9 [1%] grade ≥3) in the chemotherapy group (table 3)

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. The only grade 3 or worse immune-mediated events that occurred in five or more patients in the pembrolizumab group were pneumonitis, severe skin reactions, and hepatitis (table 3)

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