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# 研究患者

Patients  
Eligible pat ients had histologically or cytologi- cally documented stage III, locally advanced, un- resectable NSCLC according to the Staging Manual in Thoracic Oncology, version 7, of the Internat ional Association for the Study of Lung Cancer.

# 样本量

\* The intention-to-treat population included all patients who underwent randomization. Randomization was stratified according to age at randomization (<65 vs. ≥65 years of age), sex, and smoking history (current or former smoker vs. never smoked). There were no significant (P<0.05) between-group differences in the baseline characteristics listed here. Percentages may not total 100 because of rounding or because some categories occurred with very low frequency and therefore are not shown here. A complete listing of baseline characteristics is provided in Table S1 in the Supplementary Appendix. † Race was reported by the patients. ‡ Patients with other disease stages included 12 patients in the durvalumab group (4 with stage IV, 4 with stage IIB, 3 with stage IIA, and 1 with stage IA) and 5 patients in the placebo group (2 with stage IIB, 1 with stage IIA, and 2 with stage IB).

# 基线特征

The coprimar y end points were progression-free sur vival (according to the Response Evaluat ion Criteria in Solid Tumors [RECIST], version 1.1, as assessed by means of blinded independent central review) and overall survival. Progression-free sur- vival was def ined as the time from randomization (which occurred up to 6 weeks after chemoradio- therapy) to the date of the f irst documented event of tumor progression or death in the absence of disease progression. Overall survival was def ined as the time from randomization until death from any cause. Progression-free survival was assessed by the investigators, according to RECIST, version 1.1, as a predef ined sensitivity analysis. The secondar y end points were the percent- age of pat ients who were alive without disease progression at 12 and 18 months, the object ive response rate, the durat ion of response, and the t ime to death or distant metastasis (all assessed by means of blinded independent central review); and overall survival at 24 months, the safety and side-ef fect prof ile (graded with the use of the CTCAE, version 4.03), health-related quality of life, pharmacokinetic characteristics, and immunoge- nicity.

# 试验设计

R e fe r enc e s 1. Aupérin A, Le Péchoux C, Rolland E, et a l. Meta-ana lysis of concomitant versus sequent ia l rad iochemotherapy in loca l ly advanced non-sma l l-cel l lung cancer. J Clin Oncol 2010; 28: 2181-90. 2 . Yoon SM, Shaikh T, Ha llman M. Ther- apeut ic management opt ions for stage III non-sma ll cell lung cancer. World J Clin Oncol 2017; 8: 1-20. 3. Ahn JS, Ahn YC, K im JH, et a l. Mult i- nat iona l randomized phase III t ria l with or without consolidat ion chemotherapy using docetaxel and cisplat in af ter con- current chemoradiat ion in inoperable stage III non-sma ll-cell lung cancer: KC- SG-LU05-04. J Clin Oncol 2015; 33: 2660-6. 4. Et t inger S, Wood DE, A isner DL, et a l.

# 研究背景

BACKGROUND  
Most patients with locally advanced, unresectable, non–small-cell lung cancer (NSCLC) have disease progression despite def init ive chemoradiotherapy (chemotherapy plus concurrent radiat ion therapy). This phase 3 study compared the ant i–programmed death ligand 1 antibody durvalumab as consolidation therapy with placebo in patients with stage III NSCLC who did not have disease progression after two or more cycles of plat inum-based chemoradiotherapy.

# 研究结果

RESULTS  
Of 713 pat ients who underwent randomizat ion, 709 received consolidat ion therapy (473 received dur valumab and 236 received placebo). The median progression-free survival from randomization was 16.8 months (95% conf idence interval [CI], 13.0 to 18.1) with durvalumab versus 5.6 months (95% CI, 4.6 to 7.8) with placebo (stratif ied hazard rat io for disease progression or death, 0.52; 95% CI, 0.42 to 0.65; P<0.001); the 12-month progression-free survival rate was 55.9% versus 35.3%, and the 18-month progression-free survival rate was 44.2% versus 27.0%.

# 研究结论

CONCLUSIONS  
Progression-free survival was signif icantly longer with durvalumab than with placebo.

# 表格相关

Between May 2014 and April 2016, a total of 709 of 713 pat ients who underwent randomizat ion (99.4%) received at least 1 dose of study drug as consolidat ion therapy (473 pat ients received dur- valumab and 236 received placebo) (Fig. S1 in the Supplementar y Appendix). Baseline charac- terist ics were well balanced in the two groups (Table 1, and Table S1 in the Supplementar y Appendix)

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. The median age of all pat ients was 64 years, and the majorit y were men (70.1%) and current or former smokers (91.0%); 45.7% had a squamous histologic t ype of tumor. The previ- ous use of chemotherapy was also well balanced between the two groups (Table S2 in the Supple- mentar y Appendix)

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; in addit ion, 25.8% of the pat ients in the dur valumab group and 28.7% of those in the placebo group had received induc- t ion chemotherapy before def init ive chemoradio- therapy. The response to previous chemoradio- therapy was similar in the two groups (complete response, 1.9% in the dur valumab group and 3.0% in the placebo group; part ial response, 48.7% and 46.8%, respect ively). According to the assessment of archived tu- mor samples obtained before chemoradiothera- py, PD-L1 expression of 25% or more on tumor cells occurred in 22.3% of pat ients (24.2% in the dur valumab group and 18.6% in the placebo group) and PD-L1 expression of less than 25% on tumor cells occurred in 41.0% of the pat ients (39.3% in the dur valumab group and 44.3% in the placebo group); 36.7% of the pat ients in both groups had unknown PD-L1 status (Table S3 in the Supplementar y Appendix)

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placebo group), whereas 67.3% of the pat ients’ tumors were EGFR-negat ive or wild-t ype (66.2% in the dur valumab group and 69.6% in the pla- cebo group). The EGFR mutat ion status was un- known in 27.7% of the patients in the durvalumab group and 24.5% of the patients in the placebo group (Table S3 in the Supplementar y Appen- dix)

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. No signif icant (P<0.05) between-group dif- ferences were noted in either PD-L1 expression or EGFR mutat ion status. As of Februar y 13, 2017 (the data cutof f point for this interim analysis), 371 pat ients had dis- ease progression (214 in the dur valumab group and 157 in the placebo group). The overall me- dian follow-up was 14.5 months (range, 0.2 to 29.9). The median number of infusions received was 20 (range, 1 to 27) in the dur valumab group and 14 (range, 1 to 26) in the placebo group; 6.3% and 5.1% of the pat ients, respect ively, were st ill receiving the study drug at the data cutof f point (Table S4 in the Supplementar y Appendix)

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. The median relat ive dose intensit y was 100% in each group (range, 29 to 100 in the dur valumab group and 50 to 100 in the placebo group). Se- rum trough concentrat ions of dur valumab were similar at weeks 24 and 48 (177.00 and 189.00 μg per milliliter, respect ively) (Table S5 in the Sup- plementar y Appendix)

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\* The intention-to-treat population included all patients who underwent randomization. Randomization was stratified according to age at randomization (<65 vs. ≥65 years of age), sex, and smoking history (current or former smoker vs. never smoked). There were no significant (P<0.05) between-group differences in the baseline characteristics listed here. Percentages may not total 100 because of rounding or because some categories occurred with very low frequency and therefore are not shown here. A complete listing of baseline characteristics is provided in Table S1 in the Supplementary Appendix. † Race was reported by the patients. ‡ Patients with other disease stages included 12 patients in the durvalumab group (4 with stage IV, 4 with stage IIB, 3 with stage IIA, and 1 with stage IA)

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dur valumab (5.5% vs. 11.0%) (Table S6 in the Supplementar y Appendix)

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. The object ive response rate, as assessed by means of blinded independent central review, was signif icant ly higher with dur valumab than with placebo (28.4% vs. 16.0%; P<0.001) (Ta- ble 2); 16.5% of pat ients who received dur va lu- mab and 27.7% of those who received placebo had disease progression (Table 2)

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. The median dura- t ion of response was longer with dur va lumab than with placebo (Table 2, and Fig. S4 in the Supplementary Appendix)

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. Of the pat ients who had a response to dur valumab, 72.8% had an ongoing response at both 12 and 18 months as compared with 56.1% and 46.8%, respect ively, of patients in the placebo group who had an ongoing response (Table 2)

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(Table 3)

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; grade 3 or 4 adverse events occurred in 29.9% and 26.1%, respect ively. The most com- mon grade 3 or 4 adverse event was pneumonia (in 4.4% of pat ients in the dur valumab group and 3.8% of pat ients in the placebo group). Dis- cont inuat ion due to adverse events occurred in 15.4% of pat ients in the dur valumab group and 9.8% of pat ients in the placebo group, and seri- ous adverse events occurred in 28.6% and 22.6%, respect ively (Table S7 in the Supplementar y Ap- pendix)

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. Death due to adverse events occurred in 4.4% of pat ients in the dur valumab group and 5.6% of pat ients in the placebo group (Table 3)

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6.8%), high-dose glucocorticoids (8.8% and 5.1%), endocrine therapy (11.6% and 1.3%), and other immunosuppressive agents (0.4% of both groups). Immune-mediated adverse events of any grade, regardless of cause, were reported in 24.2% of pat ients in the dur valumab group and 8.1% of pat ients in the placebo group; grade 3 or 4 im- mune-mediated adverse events were reported in 3.4% and 2.6% of pat ients, respect ively (Table S9 in the Supplementar y Appendix)

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