CheckMate 078.pdf.txt

# 研究患者

progressing during or after one previous platinum- based doublet chemotherapy regimen . Patients were included regardless of tumor PD-L1 expression; pa- tients with EGFR-mutation–positive tumors or known ALK receptor tyrosine kinase (ALK) translocation– positive tumors were excluded. Prior treatment with an EGFR or anaplastic lymphoma kinase inhibitor was not permitted . Eligible patients were 18 years of age or older, had ECOG PS of 0 or 1, and measureable disease per Response Evaluation Criteria in Solid Tumors version 1.

# 样本量

Sample size determination was based on the efﬁcacy results in CheckMate 017 and 057 for patients with squamous and nonsquamous NSCLC, respectively. In the docetaxel treatment group, exponential distribution with a median OS of 10 months for squamous NSCLC and 12 months for nonsquamous NSCLC was assumed, as per historical data in Asian patients.10-15 For the patients with squamous NSCLC in the nivolumab treatment group, exponential distribution with a 16.7-month median OS was assumed providing a hazard ratio (HR) of 0.6. Treatment effect assumption was based on the efﬁcacy results in CheckMate 017 (HR for OS: 0.59; 95% conﬁdence interval [CI]: 0.44–0.79). For the patients with nonsquamous NSCLC in the nivolumab treatment group, nonproportional hazard models were assumed based on the efﬁcacy results in CheckMate 057. For the patients with nonsquamous NSCLC and 1% or greater tumor PD-L1 expression, a two- piece exponential distribution providing an overall 20- month median OS was used. For the patients with non- squamous NSCLC and less than 1% tumor PD-L1 expres- sion, a two-piece exponential distribution was also assumed, providing an overall 13-month median OS. A total sample size of approximately 500 patients randomly assigned to the nivolumab and docetaxel groups in a 2:1 ratio was estimated to provide sufﬁcient power to detect signiﬁcant differences in OS between treatment groups in both a weighted and a standard log-rank test.

# 基线特征

not receive study treatment (Supplemental Fig. 2). The minimum follow-up for this analysis was 8.8 months; median follow-up was 10.4 (range: 0.2 to 21.1) months in the nivolumab arm and 8.8 (range: 0 to 18.7) months in the docetaxel arm. Baseline characteristics of all randomized patients were generally well balanced between treatment groups (Table 1).

# 试验设计

Methods: CheckMate 078 was a randomized, open-label, phase III clinical trial in patients from China, Russia, and Singapore with squamous or nonsquamous NSCLC that had progressed during/after platinum-based doublet chemo- therapy (ClinicalTrials.

# 研究背景

No Match

# 研究结果

Results: OS was signiﬁcantly improved with nivolumab (n ¼ 338) versus docetaxel (n ¼ 166); median OS (95% conﬁdence interval): 12.0 (10.4–14.0) versus 9.6 (7.6–11.2) months, respectively; hazard ratio (97.7% conﬁdence in- terval): 0.68 (0.52–0.90); p ¼ 0.0006. Objective response rate was 17% with nivolumab versus 4% with docetaxel; median duration of response was not reached versus 5.3 months.

# 研究结论

Conclusions: This is the ﬁrst phase III study in a predom- inantly Chinese population reporting results with a pro- grammed death 1 inhibitor.

# 表格相关

not receive study treatment (Supplemental Fig. 2). The minimum follow-up for this analysis was 8.8 months; median follow-up was 10.4 (range: 0.2 to 21.1) months in the nivolumab arm and 8.8 (range: 0 to 18.7) months in the docetaxel arm. Baseline characteristics of all randomized patients were generally well balanced between treatment groups (Table 1)

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patients in the nivolumab group and 23% of patients in the docetaxel group, and approximately half of the delays in each group were 4 to 7 days in duration. At the time of this analysis, 15% of patients treated in the nivolumab group and 1% treated in the docetaxel group were continuing the assigned treatment. Overall, 70% of all treated patients in either treatment group discontinued owing to disease progression (Supplemental Table 1)

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. Of all randomized patients, 42% in either treatment group received subsequent systemic therapy (Supplemental Table 2)

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; 5% in the docetaxel group received subse- quent immunotherapy, including nivolumab (3%) and pembrolizumab (1%). Nivolumab showed superior OS compared with doce- taxel (Fig. 1A). In all randomized patients, the median OS was 12.0 months with nivolumab versus 9.6 months with docetaxel (HR: 0.68; 97.7% CI: 0.52–0.90; p ¼ 0.0006), and estimated 1-year OS rates were 50% and 39% with nivo- lumab and docetaxel, respectively. HR for death was less than 0.855, thus meeting the criterion for consistency in OS beneﬁt with CheckMate 017 and 057. Improved OS with nivolumab was observed across most pre-speciﬁed subgroups, including patients from China (Fig . 1B) . Among those with squamous histology , median OS was 12 .3 months with nivolumab versus 7 .9 months with docetaxel (HR: 0 .61; 95% CI: 0 .42– 0 .89) (Supplemental Fig . 3); for patients with non- squamous histology , median OS was 11 .9 months with nivolumab and 10 .2 months with docetaxel (HR: 0.76; 95% CI: 0 .56–1 .04). In the subgroup of patients with 1% or greater tumor PD-L1 expression , median OS was 12 .3 months with nivolumab and 7 .9 months with docetaxel (HR: 0 .62; 95% CI: 0.45–0.87); in the sub- group with less than 1% tumor PD-L1 expression , median OS was 11.4 months with nivolumab and 10.2 months with docetaxel (HR: 0 .75; 95% CI: 0 .52–1 .09) (Supplemental Fig . 4) . The ORR among all randomized patients was 16 .6% for nivolumab compared with 4 .2% for docetaxel (odds ratio: 4 .4; p < 0 .0001) (Table 2)

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, with similar results in patients with squamous and nonsquamous histology (Supplemental Table 3)

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. Response could not be determined in 9.8% of patients in the nivolumab arm and in 15 .7% of patients in the docetaxel arm , owing to death prior to disease assessment (n ¼ 29), patients never receiving treatment (n ¼ 11) , or other reasons (n ¼ 19) . The median time to response was 2.6 months with nivolumab and 1 .4 months with doce- taxel . The median duration of response was not reached with nivolumab and 5 .3 months with doce- taxel (Table 2)

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Although the median PFS in all randomized patients was identical for nivolumab and docetaxel (2.8 months), the PFS curves began to separate at 3 months, resulting nivolumab (HR: 0.77; 95% CI: 0.62–0.95; p ¼ 0.0147) in a signiﬁcant PFS advantage for patients treated with (Fig. 2). The estimated 6-month PFS rate was 29% in the nivolumab arm and 23% in the docetaxel arm. PFS was more favorable with nivolumab than docetaxel regard- less of tumor histology or PD-L1 expression. PFS in pre- speciﬁed subgroups is detailed in Supplemental Figure 5. Treatment-related AEs of any grade were less frequent with nivolumab (64%) than docetaxel (83%). The most common treatment-related AEs were rash (12%) and fatigue (10%) among patients treated with nivolumab, and anemia and decreased white blood cell count (26% each) among those treated with docetaxel (Table 3)

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. The percentage of patients with grade 3 or greater treatment-related AEs was 10% with nivolumab and 48% with docetaxel, including one patient with a grade 5 treatment-related event (circulatory collapse) in the docetaxel group. Any-grade and grade 3 or greater treatment-related serious events were reported in 9% and 5% of patients, respectively, in the nivolumab group and in 16% and 15% of patients, respectively, in the docetaxel group (Supplemental Table 4)

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. The majority of select AEs (deﬁned as AEs of poten- tial immunologic causes) were grade 1 to 2, and most were considered drug-related by the investigator. The most frequently reported any-grade, treatment-related, select AE categories with nivolumab treatment were skin (21%), hepatic (18%), and endocrine (9%) (Supplemental Table 5)

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