Background

Nivolumab is approved at a fixed dose of 240 mg every 2 weeks (Q2W) across multiple tumor types in several countries, including non-small cell lung cancer (NSCLC) in the USA and Canada.1

Nivolumab is also approved at 480 mg every 4 weeks (Q4W) for multiple tumor types in several countries, including non-small cell lung cancer (NSCLC) in the USA and Canada.2

For 480 mg Q4W dosing were based on pharmacokinetic modeling and limited clinical safety data (n = 61), which predicted that the exposure, safety, and efficacy of this dose would be similar to that of the body weight–based 3 mg/kg Q2W.3

Decreasing the frequency of nivolumab administration may improve convenience while maintaining efficacy and safety.4

Here we present an interim analysis of CheckMate 384, a study evaluating 480 mg Q4W nivolumab dosing in patients with previously treated advanced NSCLC with disease control on nivolumab.

Methods

Study design

CheckMate 384 (NCT02713867) was a phase 3/4, open-label, randomized study investigating2 2 approved doses of nivolumab (480 mg Q4W vs 240 mg Q2W) in patients with previously treated advanced NSCLC following up to 12 months of prior treatment with nivolumab 3 mg/kg or 240 mg, each Q2W (Figure 1).

Patients were required to have 2 consecutive assessments of complete response (CR), partial response (PR), or stable disease (SD) on prior nivolumab treatment.

Patients were stratified by tumor histology (squamous vs non-squamous) and response to prior nivolumab therapy at randomization (CRFV vs SD).

Assessments

Tumor response: assessed using RECIST v1.1 every 8 weeks for the first year after randomization, then every 3 months for the second year.

Safety: adverse events (AEs) were assessed continuously through 100 days after the last dose of study therapy; select AEs are those with potential impact on drug development.

Statistical considerations

CheckMate 384 was originally designed as a non-inferiority study (N = 600 planned) to evaluate the efficacy and safety of nivolumab 480 mg Q4W vs 240 mg Q2W in patients with previously treated advanced NSCLC. Enrollment was stopped early and the sample size was reduced to N = 363.

With this reduction in sample size, there was insufficient power to conduct the non-inferiority analyses. Therefore, the statistical plan was changed to include descriptive analyses only, with one-sided 95% CI.

Data presented here are from an interim analysis (N = 329). A total of 34 additional patients have been enrolled after this analysis was performed and a final analysis will be conducted when all patients have a minimum of 12 months follow-up.

Results

Patients and disposition

Patients (N = 329) were randomized at 48 sites in 7 countries (Australia, Canada, France, Germany, Italy, Japan, and the USA) (Table 1).

Baseline characteristics were generally balanced between treatment arms.

In either group.

Conclusions

In this descriptive analysis, nivolumab 480 mg Q4W appeared to show similar efficacy and safety to 240 mg Q2W in patients with advanced NSCLC following disease control with prior nivolumab.

Post-randomization PFS at 6 months appeared similar in both treatment arms.

No new safety signals were observed with either dose, and trends in TRAEs were similar compared to both arms.

This study offers support for the use of nivolumab 480 mg as a more convenient dosing option compared to advanced NSCLC with response or stable disease on nivolumab (≤ 12 months).

Overall, these clinical data are in agreement with pharmacokinetic modeling analyses and further evidence supporting a 480 mg Q4W nivolumab dosing regimen.

Efficacy

Post-randomization PFS rates at 6 months appeared similar between treatment arms (Figure 2).

Post-randomization PFS with nivolumab 480 mg Q4W vs 240 mg Q2W.

$s_{\text{480 mg (n = 166) }}$ $s_{\text{240 mg (n = 163) }}$

None of the differences were statistically significant (HR 0.96, 95% CI 0.62–1.51). Median PFS was 8.8 months in the 480 mg Q4W arm and 8.4 months in the 240 mg Q2W arm. The difference in median PFS was not statistically significant (−0.4 months, 95% CI −0.1, +7.0).

$s_{\text{Post-randomization PFS with nivolumab 480 mg Q4W vs 240 mg Q2W.}}$

$s_{\text{480 mg Q4W (n = 164)}}$ $s_{\text{240 mg Q2W (n = 163)}}$

$s_{\text{Non-squamous}}$

$s_{\text{Post-randomization PFS with nivolumab 480 mg Q4W vs 240 mg Q2W.}}$

$s_{\text{Patients with an event (%)}}$

$s_{\text{Age, median (range), years}}$

$s_{\text{Number of post-hoc subgroup}}$

$s_{\text{Percent change from baseline, pooled results}}$

$s_{\text{From 480 mg Q4W (n = 166) vs 240 mg Q2W (n = 163) to maximum clinical benefit.}}$

$s_{\text{Non-squamous (n = 215)}}$ $s_{\text{Squamous (n = 114)}}$

$s_{\text{Sex (n = 231)}}$

$s_{\text{Nivolumab is approved at a fixed dose of 240 mg every 2 weeks (Q2W) across multiple tumor types in several countries, including non-small cell lung cancer (NSCLC) in the USA and Canada.}}$

$s_{\text{Nivolumab is also approved at 480 mg every 4 weeks (Q4W) for multiple tumor types in several countries, including non-small cell lung cancer (NSCLC) in the USA and Canada.}}$

$s_{\text{For 480 mg Q4W dosing were based on pharmacokinetic modeling and limited clinical safety data (n = 61), which predicted that the exposure, safety, and efficacy of this dose would be similar to that of the body weight–based 3 mg/kg Q2W.}}$

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