Clinical outcomes of patients with BRAFV600 mutated metastatic NSCLC (mNSCLC) receiving first-line (1L) dabrafenib+trametinib vs other standard of care in real-world practice

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RESULTS

• After weighting, baseline weighting covariates were balanced across each treatment comparison (Table 1).
• Efficacy outcomes for noS and neP were summarized in Table 2, with km noS and neP curves shown in Figure 1.
• A Kaplan-Meier analysis of dab-tram vs ICI was performed.
• Data were analyzed in all treated patients.
• To the number of patients with PD-L1 TPS ≥50% (dab-tram, n = 15).
• The effectiveness of dab-tram vs ICI by PD-L1 expression levels could not be reliably assessed owing to the small number of patients with PD-L1 TPS ≥50%.

Figure 1: Patient Attrition from Flatiron Health NSCLC Database

Figure 2. noS with A) Dab-tram vs ICI + PDC, B) Dab-tram vs ICI, and c) Dab-tram vs PDC in Weighted Analyses

Figure 3. neP with A) Dab-tram vs ICI + PDC, B) Dab-tram vs ICI, and c) Dab-tram vs PDC in Weighted Analyses

Table 1. Baseline Characteristics After Weighting

Table 2. Efficacy Outcomes After Weighting

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• Methodological assistance was provided by Isabella Khachik, Isabelle L., and Thomas H. K. with Novartis Pharmaceuticals Corporation
• Data were analyzed in all treated patients
• The Flatiron Health NSCLC database is representative of the wider real-world oncology community in the USA and includes patients unlikely to participate in clinical trials
• This retrospective study compared the effectiveness of 1L dab-tram vs other standard of care (SoC) in mNSCLC (BRAFV600 mutated NSCLC)
• Patients with BRAFV600 mutated mNSCLC are a rare population for whom targeted treatments are sparse and evidence on their efficacy is limited or unavailable

INTRODUCTION

• Patients with BRAFV600 mutated mNSCLC are a rare population for whom targeted treatments are sparse and evidence on their efficacy is limited or unavailable
• The combination of dabrafenib (dab-tram) inhibition of BRAFV600 and MEK, respectively, was approved for BRAFV600 mutated, mNSCLC based on a single-arm phase 2 study (NCT02200641) showing clinically meaningful efficacy and a manageable safety profile in both treatment-naïve and treatment-experienced patients
• This retrospective study compared the effectiveness of 1L dab-tram vs other standard of care in NSCLC (BRAFV600 mutated-mNSCLC treatable/widely used patients from a de-identified database

METHODS

• Patients with BRAFV600 mutated mNSCLC received dab-tram from the US nationwide, electronic health record (EHR) derived, de-identified Flatiron Health NSCLC database (anonymous patients). Dab-tram was compared with ICI, including pembrolizumab (ICI; pembrolizumab) + platinum-doublet chemotherapy (PDC), ICI alone, or PDC alone
• The Flatiron Health database is longitudinal, comparing de-identified patient-level structured and electronicized data, current on technology-enhanced approaches
• During the study period, the cohort included patients originated from approximately 200 US cancer centers (~600 sites of care)
• Patients received 1L therapy with either dab-tram, or one of the 3 SoC therapies: immune-checkpoint inhibitor (ICI; pembrolizumab) + platinum-doublet chemotherapy (PDC), ICI alone, or PDC alone
• Additional inclusion and exclusion criteria are shown in Table 1
• For each comparison, each patient was assigned a weight using propensity score weighting method based on baseline characteristics (age, gender, race, stage at initial diagnosis, smoking status, ECOG status, and histology).
• Histology was only considered in dab-tram vs PDC comparison due to the lack of sample size in each subsampling histology comparison
• Efficacy outcomes for rwOS and rwPFS were statistically significantly longer with dab-tram than with ICI (p < 0.001), and with dab-tram vs PDC (p = 0.001)
• Endpoints included overall survival (OS) assessed from start of 1L therapy to death or censoring, and progression-free survival (PFS) assessed from start of 1L therapy to progression occurring within 14 days after treatment start, death, or censoring
• TheFlatiron Health commercially composite variable™ neP was assessed retrospectively based on data abstracted from EHRs

KEY FINDINGS AND CONCLUSIONS

• Median noS was numerically longer, and neP was similar with dab-tram vs ICI + PDC in unweighted and weighted analyses
• Median noS and neP were numerically longer with dab-tram vs ICI in unweighted and weighted analyses
• Median noS was numerically longer, and neP was similar with dab-tram vs PDC in unweighted analyses; both noS and neP were statistically significantly longer with dab-tram vs ICI in weighted analyses
• Median neP and noP estimated in the present study with 1L dab-tram, ICI, or PDC are in line with those previously observed in patients with mNSCLC receiving these agents
• The findings support the use of dab-tram for patients with BRAFV600 mutated mNSCLC in the 1L setting

The landmark flatiron has been used to support the noS model

The landmark flatiron has been used to support the neP model

Figure 3. Kaplan-Meier of Overall Survival (OS) in Dab-tram vs Other Standard of Care in Weighted Analyses

Figure 4. Kaplan-Meier of Progression-Free Survival (PFS) in Dab-tram vs Other Standard of Care in Weighted Analyses

References