Overall Survival Prediction of Docetaxel-Based Second-Line Treatment for Advanced Non-Small Cell Lung Cancer: A Systematic Review and Meta-Analysis

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ABSTRACT

Objectives: Non- small cell lung cancer (NSCLC) accounts for 75 to 85 % of all lung cancer diagnoses. The major outcome of this meta-analysis is overall survival (OS), which is based on 18 randomized control trials, comparing docetaxel to kinase inhibitors, antineoplastic agents, and monoclonal antibodies as second-line chemotherapy for advanced NSCLC.
Methods: In this study, 18 randomized control trials were chosen, wherein, docetaxel was considered as the standard treatment arm and the kinase inhibitor, antineoplastic agent and monoclonal antibody were considered as the experimental arm. The methodologic quality of the trial was classified according to the Modified Jadad score. Several steps were involved in the study plan to reduce publication bias. A Forest plot is used to graphically summarize the meta-analysis. Meta-analysis is performed with R Studio's Meta package.
Results: The Hedge's g value of Antineoplastic agents 0.11(95% CI of – 0.03;0.26), kinase inhibitors 0.04(95% CI of -0.10;0.17), and monoclonal antibodies 0.05(95% CI of -0.02;0.13) were found. Docetaxel's OS was slightly better than that of the antineoplastic agent, kinase

inhibitors, and monoclonal antibodies due to the existence of moderate heterogeneity and less impact. As a result, the forest plot clearly showed that docetaxel's OS was superior; yet, the effect was minor.
Conclusion: In the overall meta-analysis, patients in the standard treatment arm had a slightly better OS than those in the experimental treatment arm. We may infer that docetaxel-based second-line therapy for patients with advanced NSCLC is supported by this meta-analysis. As per the results, docetaxel was more effective in the second-line treatment of advanced NSCLC than antineoplastic agents, monoclonal antibodies and kinase inhibitors.

KEYWORDS: Non- Small Cell Lung Cancer (NSCLC), Meta-analysis, Overall Survival, Docetaxel.

INTRODUCTION

Cancer is a generic term that encompasses a wide range of disorders that can affect any organ in the body.[1] Cancer is a hereditary disease in which some cells in the body proliferate uncontrollably and, in some cases, spread to other parts of the body and invade organs.[2] In every country on the planet, it is a top cause of death and a significant impediment to extending life expectancy. In 2020, an estimated 19.3 million new cancer cases were diagnosed worldwide, with around 10.0 million cancer deaths. India reported around 1.3 million new cancer cases and approximately 0.85 million fatalities.[3]

There are more than 100 different types of cancers that exist. The organs or tissues where tumors originate are generally termed after the cancer types. Cancers can even be categorized based on the cell type that caused them, such as squamous or epithelial cells.[4]

Lung cancer is one of the most frequent cancers in the world, both in terms of mortality and incidence, with approximately one million new cases diagnosed every year.[5] It is the foremost cause of cancer death in both men and women, accounting for over a quarter (27%) of all cancer-related deaths.[6] In 2020, a projected 2.21 million new cases of lung cancer were reported worldwide, which is around 11.4% of the global cancer burden. Lung cancer claimed over 1.8 million lives in 2020.[1]

Non- small cell lung cancer (NSCLC) accounts for 75 to 85 % of all lung cancer diagnoses, which includes adenocarcinoma, squamous cell carcinoma and large-cell carcinoma. The stage, grade, and functional capacity of the patient all influence the treatment options for lung cancer surgery, chemotherapy, and chemoradiotherapy are usually used to treat early- and middle-stage NSCLC. According to reports, stage I NSCLC patients have a 5-year survival rate of 77%, whereas stage IIIa patients have a 5-year survival rate of 23%. Surgery, chemotherapy, immunotherapy, and radiotherapy can all enhance life expectancy in advanced stages of NSCLC.[7]

The majority of patients diagnosed with advance NSCLC estimated that nearly 70% of patients attain disease stabilization or clinical remission with first-line platinum-based treatment, which has a 15% to 30% response rate. Almost everyone has progressed to the point where they require second-line treatment. Monotherapy with docetaxel, erlotinib, or pemetrexed is the currently authorized second-line therapy for NSCLC.[8] Docetaxel is a plant alkaloid that is well tolerated by individuals with metastatic or advanced NSCLC. For patients with advanced NSCLC, it is approved in several countries as first-line therapy in combination with cisplatin, as a second-line monotherapy, or as single-agent maintenance therapy. Also, for such patients, docetaxel in combination with a platinum-based agent (carboplatin or cisplatin) is typically regarded as the first-line therapy.[9]

The major outcome of this analysis is overall survival (OS), which is based on 18 randomized control trials (RCT). The number of months between randomization and mortality for any reason is referred to as the OS.[10] Most medical therapies are evaluated using randomized trials, which are regarded as the most suitable and accurate method of determining their efficacy and safety. Randomized studies can help researchers learn more about the effects of docetaxel in combination with antineoplastic drugs, kinase inhibitors, and monoclonal antibodies on patients.[11] Although docetaxel has proved to be good second-line therapy, the overall survival benefit is modest. When antineoplastic drugs, kinase inhibitors, and monoclonal antibodies were compared to docetaxel as a second-line therapy, no survival benefit was seen.[12]

METHODOLOGY

Source of literature search

Google Scholar, Science Direct, Scopus, PubMed, and the Cochrane library databases were used to conduct an extensive literature search for articles published between 2010 and 2021. Advanced NSCLC, randomized control trial, chemotherapy, docetaxel, and second-line treatment were among the terms included in the search.

Selection criteria

The study's major criteria were randomized trials comparing docetaxel to kinase inhibitors, antineoplastic agents, and monoclonal antibodies as second-line chemotherapy for advanced NSCLC. Based on some inclusion criteria, the applicable clinical trials were manually chosen. The first inclusion criterion was the trial should be a randomized control trial and should contain patients with clinically proven NSCLC. The other criteria included the standard

treatment should be a docetaxel-based second-line treatment, should be a phase II or phase III trial and the chief outcome should be OS. Similarly, Studies that compared docetaxel to other drug classes were excluded, also early studies published as a series of articles by the same author with overlapping data that could lead to publication bias, as well as editorials, case reports, conference articles, experimental studies, and other related studies that failed to deliver comprehensive results. The first author, year of publication, trial information, demographic parameters, histology characteristics, smoking status, treatment for each group, and adverse events were all extracted using a fixed standardized procedure. In this study, Docetaxel was considered as the standard treatment arm and the kinase inhibitor, antineoplastic agent and monoclonal antibody were considered as the experimental arm.

Quality assessment

The methodologic quality of the trial was classified according to the Modified Jadad score. Several steps were involved in the study plan to reduce publication bias. Considerably large search strategy, selection of publications based on some inclusion criteria and exclusion of publications strictly according to the exclusion criteria were the important steps involved in the study plan to avoid publication bias. Several strategies were used to detect publication bias which was proved by the funnel plot.

Statistical methods

The effect size is calculated using the standardized mean difference (SMD) and then corrected using Hedge's approach. Hedge's g value is then used to symbolize it. The Random-effect model is used to pool the effect sizes. Higgins and Thompson's I^2 statistics were used for heterogenicity estimation. A Forest plot is used to graphically summarize the meta-analysis. Meta-analysis is performed with R Studio's Meta package.

RESULTS

The flow chart for study inclusion and exclusion criteria in the meta-analysis of drug intervention prevalence is shown in Figure 1. The database search yield 1009 publications retrieved from Google Scholar, PubMed, Science Direct, Scopus and Cochrane databases. After removing duplicate results, 984 papers remained, and 435 were retained after removing articles related to non-randomized control trials. Because of phase 1 randomized control trials, 36 were ruled out, while 53 were ruled out because of NSCLC. Following the screening process, 278 articles were left for full-text examination. 156 articles were removed from the

study due to the absence of docetaxel in the treatment arm, and 101 publications were excluded due to the absence of monoclonal antibodies, kinase inhibitors, and antineoplastic drugs in the experiment arm. Finally, for the study, 18 randomized control trials were chosen.

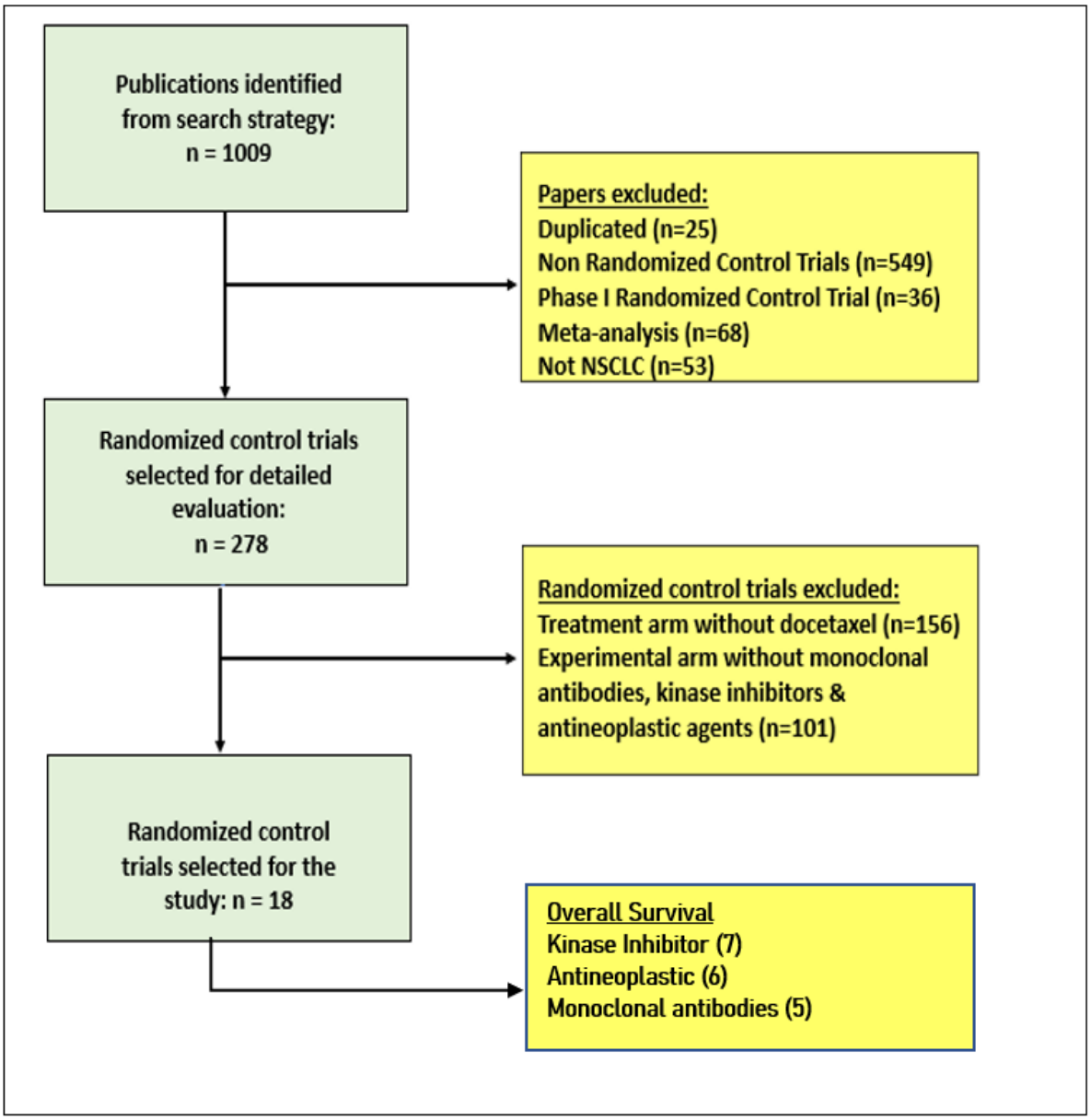

Figure 1: The flowchart summarizing the steps of study selection

Table 1 shows the baseline characteristics of 18 RCTs, including study name, first author, publication year, phase trial, number of recruited patients, experimental intervention and control groups, and outcome data. This meta-analysis includes 6 RCTs involving 2160 patients in an antineoplastic agent (experiment arm). 7 RCTs with 4090 patients in the kinase inhibitor

(experiment arm) and 5 RCTs with 3488 patients in the monoclonal antibodies (experiment arm) were compared to docetaxel (treatment arm).

Table 1: Characteristics of the selected Randomized controlled trials for meta-analysis

Sl. No	Study Reference	No. of Patients	Drug class-intervention	Intervention and dosage	Treatment and dosage	Jadad score
1	Barlesi F et al. (2018)[13]	792	3	Avelumab 10mg/kg/2W	Docetaxel 75mg/m^2/3W	5
2	Fehrenbacher L et al. (2016)[14]	287	1	Atezolizumab 1200mg/3W	Docetaxel 75mg/m^2/3W	5
3	Garassino M C et al. (2013)[15]	219	2	Erlotinib 150mg/D	Docetaxel 75mg/m^2/3W	6
4	Garon E B et al. (2014)[16]	1253	3	Ramucirumab 10mg/kg/3W + Docetaxel 75mg/m^2/3W	Placebo + Docetaxel 75mg/m^2/3W	6
5	Gerber D E et al. (2018)[17]	597	3	Bavituximab 3mg/kg/W + Docetaxel 75mg/m^2/3W	Placebo + Docetaxel 75mg/m^2/3W	6
6	Herbst R S et al. (2015)[18]	689	3	Pembrolizumab 10mg/kg/3W	Docetaxel 75mg/m^2/3W	7
7	Jänne P A et al. (2017)[19]	510	2	Selumetinib 75mg/0.5D + Docetaxel 75mg/m^2/3W	Placebo + Docetaxel 75mg/m^2/3W	5
8	Kawaguchi T et al. (2014)[20]	301	2	Erlotinib 150 mg/D	Docetaxel 75mg/m^2/3W	5
9	Kubota k et al. (2015)[21]	596	1	S-1 80mg/m^2/D + cisplatin 60mg/m^2/W	Docetaxel 60mg/m^2/3W + Cisplatin 80mg/m^2/3W	6

10	Lee D H et al. (2010)[22]	161	2	Gefitinib 250mg/D	Docetaxel 75mg/m^2/3W	7
11	Manegold C et al. (2013)[23]	70	1	Cilengitide 600mg/m^2/0.5D	Docetaxel 75mg/m^2/3W	5
12	Ramlau R et al. (2012)[24]	913	2	(Ziv-)aflibercept 6mg/kg/3W + Docetaxel 75mg/m^2/3W	Placebo + Docetaxel 75mg/m^2/3w	6
13	Reck M et al. (2014)[8]	1314	2	Docetaxel 75mg/m^2/3W + Nintedanib 200mg/0.5D	Docetaxel 75mg/m^2/3W	6
14	Rittmeyer A t al. (2016)[25]	850	1	Atezolizumab 1200mg/3W	Docetaxel 75mg/m^2/3W	7
15	Rodrigues-Pereira J et al. (2011)[26]	211	1	Pemetrexed 500mg/m^2/3W + Carboplatin 5mg/ml/min	Docetaxel 75mg/m^2/3W + Carboplatin 5mg/ml/min	5
16	Socinski M A et al. (2010)[27]	146	1	Pemetrexed 500mg/m^2/3W + Carboplatin 6mg/ml/min	Docetaxel 75mg/m^2/3W + Carboplatin 6mg/ml/min	6
17	Yoh K et al. (2016)[28]	157	3	Ramucirumab 10mg/kg/3W + Docetaxel 60mg/m^2/3W	Placebo + Docetaxel 75mg/m^2/3W	5
18	Pillai R N et al. (2019)[29]	672	2	Ganetespib 150mg/m^2/2W + Docetaxel 75mg/m^2/3W	Docetaxel 75mg/m^2/3W	7
Drug class of intervention: 1- Antineoplastic agents, 2- Kinase inhibitors,3- Monoclonal antibodies, Treatment and dosage: W- Week, D-day						

For advanced NSCLC, platinum-based chemotherapy is the conventional first-line treatment. However, Patients who get first-line chemotherapy, almost always progress. Docetaxel was the conventional second-line treatment for advanced NSCLC at the time, but the benefit was minimal. The literature search identified eighteen randomized control trials comparing antineoplastic agents, kinase inhibitors and monoclonal antibodies-based chemotherapy versus docetaxel-based chemotherapy as second-line treatment for advanced NSCLC, based on individual patient data from patients enrolled in randomized control trials.
A total of 9738 patients from 18 clinical studies were analyzed for the second-line treatment of advanced NSCLC. From eighteen RCT's 6 antineoplastic agents-based therapy,7 kinases inhibitors-based therapy and 5 monoclonal antibodies-based therapy are retrieved to compare with docetaxel-based therapy.

A forest plot was used to summarize the pooled effect of OS for an antineoplastic agent (Figure 2), kinase inhibitors (Figure 3), and monoclonal antibodies (Figure 4) against docetaxel. The Hedge's g value of Antineoplastic agents 0.11(95% CI of – 0.03;0.26), kinase inhibitors 0.04(95% CI of -0.10;0.17), and monoclonal antibodies 0.05(95% CI of -0.02;0.13) were found. The effect was clearly less because the hedge's g was less than 0.20. The meta-analysis indicates moderate heterogeneity in both kinase inhibitor (I^2 =42%,$\tau^2 = 0.0163, p = 0.11$) and antineoplastic agent therapy(I^2=45%,$\tau^2 = 0.0100, p = 0.11$) and there is no heterogeneity in monoclonal antibodies(I^2=0, $\tau^2 = 0.0011, p = 0.69$). Docetaxel's OS was slightly better than that of the antineoplastic agent, kinase inhibitors, and monoclonal antibodies due to the existence of moderate heterogeneity and less impact. As a result, the forest plot clearly showed that docetaxel's OS was superior; yet, the effect was minor.

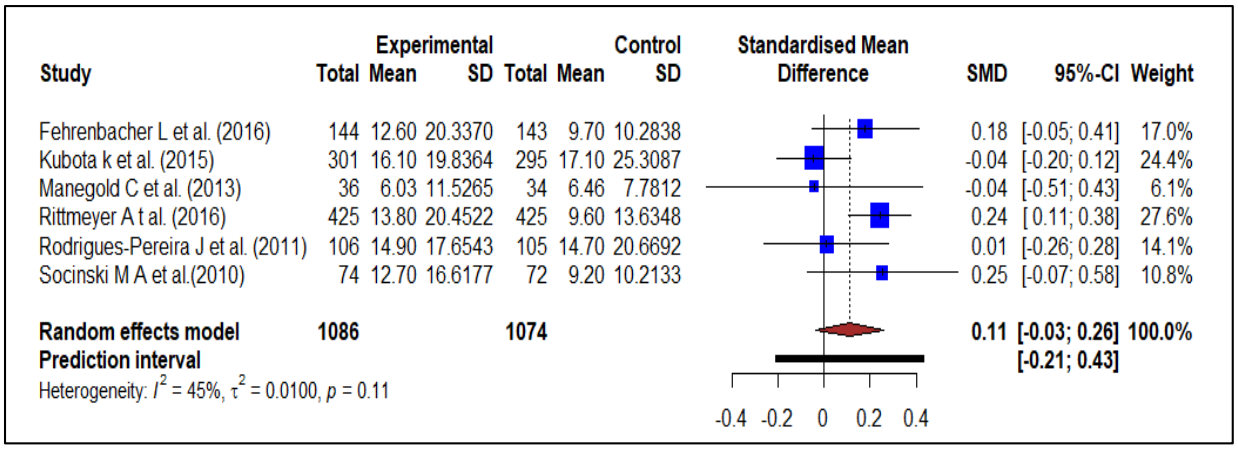

Figure 2: Forest plot representing the overall survival of docetaxel- versus antineoplastic agents- treatment; the Hedge's corrected standardized Mean difference (SMD) is 0.11 and Higgin's and Thompson's I^2 statistic is 45%.

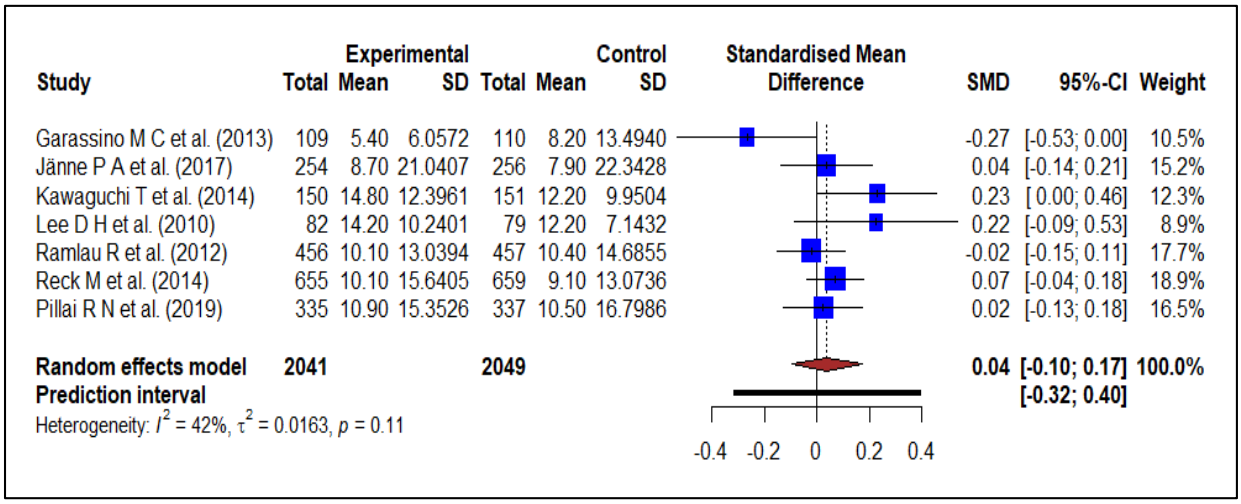

Figure 3: Forest plot representing the overall survival of docetaxel- versus kinase inhibitors-treatment; the Hedge's corrected standardized mean difference (SMD) is 0.04 and Higgin's and Thompson's I^2 statistic is 42%.

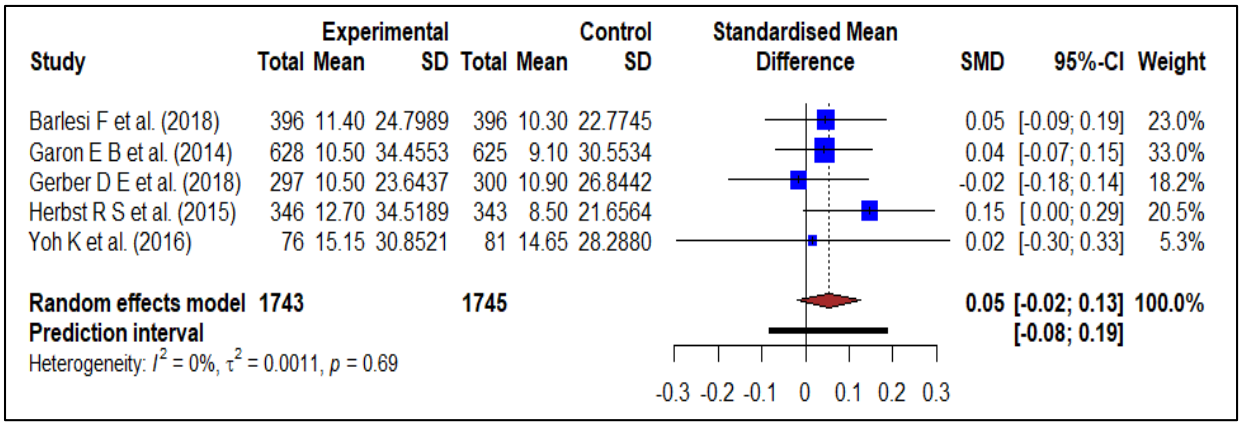

Figure 4: Forest plot representing the overall survival of docetaxel- versus monoclonal antibodies- treatment; the Hedge's corrected standardized mean difference (SMD) is 0.05 and Higgin's and Thompson's I^2 statistic is 0%.

Evidence of publication bias can be seen in the funnel plot. The publication bias is determined using Egger's test. Egger's test yielded a p-value of 0.9479 in this study, indicating that there was no publication bias.

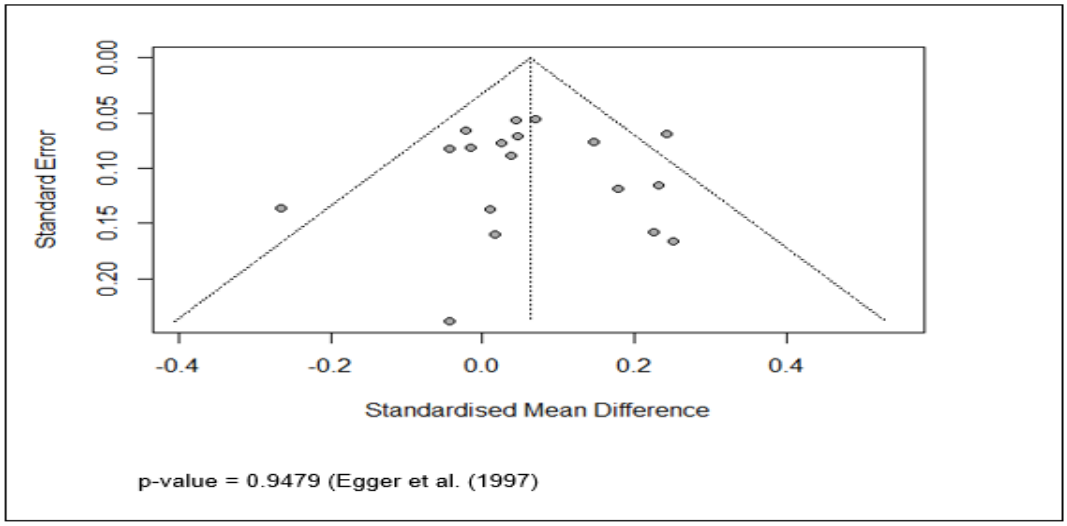

Figure 6: Funnel plot showing publication bias

DISCUSSION

NSCLC is one of the most often diagnosed cancer and the major cause of cancer-related mortality worldwide. First-line treatment is the treatment used to treat a cancer when it has been diagnosed. Second-line treatment refers to treatment when the first-line treatment has failed, stopped working, or has intolerable adverse effects. This meta-analysis includes 18 RCTs[13-29] of 9738 patients with stage III-IV NSCLC. The experimental group received docetaxel-based chemotherapy, whereas the control group received antineoplastic agents, kinase inhibitors, and monoclonal antibodies-based chemotherapy. These studies are examined in order to determine whether or not patients' overall survival has improved. Platinum-based dual-drug combination chemotherapy has been the standard of treatment for patients with advanced NSCLC.[21,23] The primary goal was to compare the two chemotherapy regimens' OS in individuals with advanced NSCLC. Docetaxel was the only approved chemotherapy for the second-line treatment of advanced NSCLC, with evidence of improved survival and quality of life.[21]

Six trails were added (Fehrenbacher L et al. (2016), Rittmeyer A t al. (2016), Kubota k et al. (2015), Manegold C et al. (2013), Rodrigues-Pereira J et al. (2011), Socinski M A et al. (2010) with 2160 cases to compare docetaxel with antineoplastic agents. Kubota k et al. (2015) compare the S-1 plus cisplatin versus docetaxel plus cisplatin. Manegold C et al. (2013) compares the improvement of OS between docetaxel and cilengitide. Rodrigues-Pereira J et al. (2011) evaluated survival without toxicity in patients with advanced, nonsquamous NSCLC treated with pemetrexed/carboplatin vs docetaxel/carboplatin as a first-line treatment. Fehrenbacher L et al. (2016) and Rittmeyer A t al. (2016) compare the safety and effectiveness

of atezolizumab versus docetaxel in second-and third-line NSCLC. The permuted randomisation method is used to receive either oral S-1 80 mg/m^2/day plus cisplatin 60 mg/m^2, cilengitide 600 mg/m^2, Pemetrexed 500mg/m^2/3W + Carboplatin 5mg/ml/min, atezolizumab 1200mg or 60mg/m^2 docetaxel plus cisplatin, 75mg/m^2 docetaxel, Docetaxel 75mg/m^2/3W + Carboplatin 5mg/ml/min.[14,21,23,25-27] The OS is the primary endpoint of all six studies. The increase in PD-L1 expression was related to improving OS rate. In individuals with previously treated NSCLC, Oral S-1 plus cisplatin is not inferior to docetaxel plus cisplatin with HR=1.013 (96.4% CI, 0.837-1.227).[21] In the Pemetrexed/Carboplatin versus the Docetaxel/Carboplatin group the OS is similar with hazard ratio 0.93 [95% confidence interval: 0.66 –1.32]).[26] Atezolizumab increased survival significantly with hazard ratio [HR] 0.73 [95% CI 0.53–0.99]; p=004 compared to docetaxel.[14,21,23,25] For patients with advanced NSCLC and good performance status, current studies support platinum-based cytotoxic drug combinations as the first-line treatment. Although cisplatin may have a modest advantage in terms of survival or response, carboplatin is favored for combination chemotherapy in certain patients due to its good tolerability and convenience of administration.[26]

In patients with metastatic NSCLC, antibodies targeting the immune checkpoint molecules PD-1 or PD-L1 improve OS when compared to standard-of-care treatment.[13] Five studies are undertaken (Barlesi F et al. (2018), Garon E B et al. (2014), Gerber D E et al. (2018), Herbst R S et al. (2015), Yoh K et al. (2016) to compare the docetaxel-based therapy with monoclonal antibodies-based therapy. The meta-analysis of a phase 3 trial of avelumab against docetaxel in patients with advanced NSCLC and disease progression after platinum-based chemotherapy is explained by Barlesi F et al. Garon E B et al. (2014) compared the efficacy and safety of docetaxel with ramucirumab or placebo as second-line treatment for patients with stage IV NSCLC post-platinum-based therapy. The efficacy of bavituximab coupled with docetaxel in patients with previously treated advanced NSCLC is investigated by Gerber D E et al. (2018). Herbst R S et al. (2015) explains the efficacy and safety of Pembrolizumab compared with docetaxel. Yoh K et al. (2016) explains phase II, double-blind, randomized, placebo-controlled research in Japanese patients with NSCLC investigated the efficacy and safety of second-line ramucirumab-docetaxel. The patients were randomised to receive either avelumab 10 mg/kg, ramucirumab (10 mg/kg), docetaxel plus bavituximab 3 mg/kg, pembrolizumab 10 mg/kg or docetaxel 75 mg/m^2, docetaxel plus placebo, docetaxel 60 mg/m.[13,16-18,28] OS was the main outcome in all the five studies which was assessed when several deaths in the PD-L1-positive sample had occurred. As compared to docetaxel the median OS of avelumab showed a favorable safety profile but did not enhance in the patients with platinum-treated PD-L1-

positive NSCLC with an HR of 0.90 [96% CI 072–112][13]; Ramucirumab plus docetaxel increases survival in patients with stage IV NSCLC as a second-line treatment with hazard ratio 0·86 (95% CI 0·75−0·98; p=0·023).[16] In previously treated advanced NSCLC patients, the combination of bavituximab and docetaxel did not increase OS with HR 1.06 (95% CI, 0.88-1.29; P=0.533). OS was significantly greater for pembrolizumab 2 mg/kg versus docetaxel with hazard ratio [HR] 0·71 (95% CI 0·58–0·88; p=0·0008).[18] In patients with previously treated, PD-L1-positive, advanced NSCLC, pembrolizumab improves OS and has a favorable benefit-to-risk profile.[28]

For a majority of patients who acquire the unresectable disease, palliative chemotherapy is the initial treatment approach.[24] In few patients, agents directing epidermal growth factor receptor (EGFR; cetuximab), vascular endothelial growth factor (VEGF; bevacizumab), or the EGFR tyrosine kinase pathway (erlotinib, gefitinib), heat shock protein 90 (HSP 90) may improve OS in addition to chemotherapy (bevacizumab, cetuximab) or administer as single agents, stabilizes oncogenic client proteins necessary for the survival, growth and invasive potential of cancer [24]. 7 clinical studies are considered (Lee D H et al. (2010), Garassino M C et al. (2013), Ramlau R et al. (2012), Kawaguchi T et al. (2014), Reck M et al. (2014), Jänne P A et al. (2017), Pillai R N et al. (2019)) to compare the docetaxel with a kinase inhibitor. TKIs that target the EGFR tyrosine kinase are effective against NSCLC that has been previously treated. Lee D H et al compared gefitinib to docetaxel in patients with advanced or metastatic NSCLC who had previously received platinum-based chemotherapy. Garassino M C et al. (2013) compared the efficacy of erlotinib to that of docetaxel, a common second-line treatment. In platinum pre-treated patients with advanced or metastatic non-squamous NSCLC, Ramlau R et al. (2012) analyzed the efficacy of aflibercept (Ziv-aflibercept), a recombinant human fusion protein targeting the VEGF pathway, with or without docetaxel. Kawaguchi T et al. (2014) compared the efficacy of erlotinib with docetaxel in previously treated patients with advanced NSCLC. Reck M et al. (2014) evaluated the safety and efficacy of docetaxel with nintedanib as second-line therapy for NSCLC. For advanced *KRAS*-mutant NSCLC, Jänne P A et al. (2017) investigated the efficacy of the mitogen-activated protein kinase kinase (MEK) inhibitor, selumetinib and docetaxel with docetaxel alone as second-line therapy. Pillai R N et al. (2019) assessed the amalgamation of ganetespib and docetaxel for second-line therapy of patients with advanced lung adenocarcinoma. A randomised clinical method is used to receive either Gefitinib (250 mg/d), erlotinib orally 150mg/day, (Ziv-)aflibercept 6 mg/kg intravenous plus docetaxel 75 mg/m^2, erlotinib 150 mg/D, nintedanib 200 mg orally, selumetinib 75mg/0.5D + docetaxel 75mg/m^2/3W, ganetespib 150 mg/m or docetaxel (75

mg/m^2), IV placebo plus docetaxel (75 mg/m^2), placebo + docetaxel 75mg/m^2/3W until unacceptable side effects or progression of disease based on histology, ECOG performance status, earlier bevacizumab treatment, and presence of brain metastases.[8,15,19,20,22,24,29] The OS is estimated as a primary and secondary endpoint in these studies. Overall survival has longer improvement in Gefitinib than docetaxel with HR 0.870 (95% confidence interval, 0.613-1.236; two-sided P = 0.4370).[15] The addition of (Ziv-)aflibercept to conventional docetaxel therapy has HR 1.01 (95% CI:0.87- 1.17) did not improve OS.[24] Erlotinib was unsuccessful in showing an improvement in OS when compared to docetaxel in an EGFR with HR= 0.91 (95% CI, 0.68 -1.22; *P* =0.53).[22] Nintedanib in combination with docetaxel improves the OS compared to docetaxel plus placebo with HR 0·75 [95% CI 0·60–0·92], p=0·0073). Addition of selumetinib to docetaxel with an HR 1.05 [95% CI, 0.85-1.30]; *P* = .64) did not improve OS compared to docetaxel.[19] The addition of ganetespib to docetaxel did not increase survival in patients with advanced-stage lung adenocarcinoma receiving salvage therapy.[29]

Our analysis included limitations that must be addressed while evaluating the data. Firstly, the different treatment schedules contribute to increased clinical heterogeneity in the meta-analysis, making meta-analysis interpretation more difficult. In three trials, docetaxel was used in conjunction with other medicines, either cisplatin or carboplatin, in the control arm. The quality of results was affected by the quality of results of each of the individual studies. Finally, because the studies in this analysis were conducted in the West, the findings must be confirmed in Asia. Since overall survival was widely used, we could conclude that this meta-analysis supports the docetaxel-based second-line therapy for the patients who have advanced NSCLC. From the results, it was concluded that docetaxel was more efficient than antineoplastic agents, kinase inhibitors and monoclonal antibodies for the second-line treatment of advanced NSCLC. Along with the parameters used in the study, biological behaviour subgroups such as those entirely refractory, those with partial and incomplete responses, and those with short and extended disease-free intervals will be examined in future meta-analysis investigations.

CONCLUSION

In a total of 9738 patients from 18 studies, it was indicated that overall survival was dramatically improved in patients who received docetaxel-based therapy than those who received antineoplastic agents, kinase inhibitors, and monoclonal antibodies-based treatment. In the overall meta-analysis, patients in the standard treatment arm had a slightly better OS than those in the experimental treatment arm. It is a meta-analysis for trials before the era of

Immunotherapy and targeted therapy. We may infer that docetaxel-based second-line therapy for patients with advanced NSCLC is supported by this meta-analysis. As per the results, docetaxel was more effective in the second-line treatment of advanced NSCLC than antineoplastic agents, monoclonal antibodies and kinase inhibitors.

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