Updated Network Meta-Analysis of First-Line *EGFR*-Targeted Tyrosine Kinase Inhibitor Treatments for Locally Advanced or Metastatic Non-Small Cell Lung Cancer With *EGFR*-Activating Mutations

Kelly A. Larkin-Kaiser,[1] Tayler Scory,[1] Megan Farris,[1] Keith Wilner,[2] Jasmina Ivanova[3]

[1]Medlior Health Outcomes Research Ltd., Calgary, AB, Canada; [2]Pfizer Inc., La Jolla, CA, USA; [3]Pfizer Inc., New York, NY, USA

Objective

To conduct a network meta-analysis (NMA) utilizing updated/mature randomized controlled trial (RCT) results for overall survival (OS) to examine the efficacy of first-line epidermal growth factor receptor-tyrosine kinase inhibitor (*EGFR*-TKI) comparators for the treatment of *EGFR* mutation positive (*EGFR*+) advanced non-small cell lung cancer (NSCLC).

Conclusion

Dacomitinib showed a numerical improvement of OS compared with other *EGFR*-TKIs and had the highest probability of being ranked first in the network. Therefore, dacomitinib should be considered as one of the standard first-line treatment options for patients diagnosed with advanced *EGFR*+ NSCLC.

Background

- Lung cancer is one of the most common cancers, with 2.1 million new lung cancer cases reported globally in 2018.[1]
- NSCLC represents 85 % of lung cancers with >50 % being diagnosed with advanced disease.[2]
- In patients with *EGFR*+ advanced NSCLC, *EGFR*-TKIs are recommended for first-line treatment.[3,4]
- This study uses updated/mature RCT results for OS to update a previously published NMA of *EGFR*-TKIs.[5]

Methods

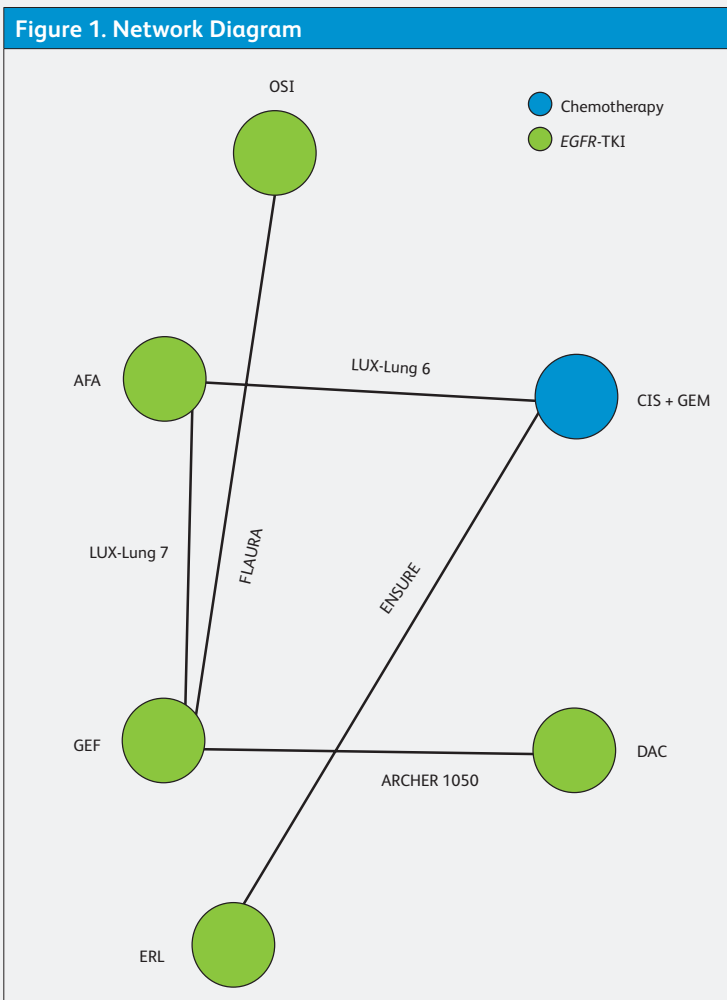
SYSTEMATIC REVIEW

- An initial search included 11 databases and identified RCTs that measured OS published between January 2004 – August 2018.[5]
- In an update, a manual search included new articles affiliated with the ARCHER 1050[6] and FLAURA trials[7] up to November 2019.

STATISTICAL METHODS

- Bayesian NMA compared OS among *EGFR*-TKIs in overall *EGFR*+ advanced NSCLC population (**Figure 1**), and in Asian/non-Asian and EGFR exon 19 deletion/exon 21 L858R substitution mutation subgroups.

Figure 1. Network Diagram



Abbreviations: AFA, afatinib; CIS + GEM, cisplatin plus gemcitabine; DAC, dacomitinib; ERL, erlotinib; GEF, gefitinib; OSI, osimertinib.

NMA Results

OVERALL POPULATION

- Five RCTs were included in the NMA.
- Dacomitinib demonstrated a significant improvement of OS vs gefitinib and a numerical improvement of OS vs afatinib, erlotinib, and osimertinib (**Table 1** and **Figure 2**).
- Dacomitinib had the highest probability of being ranked first in the network (50.1 %), followed by osimertinib (24.6 %), erlotinib (15.4 %), and afatinib (9.1 %).

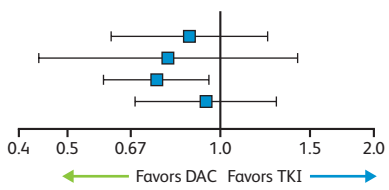
Table 1. Relative Efficacy HRs and 95% CrIs for all *EGFR*-TKI Comparisons for OS

	Treatment HR (95% CrI)				
Treatment	**Afatinib**	**Dacomitinib**	**Erlotinib**	**Gefitinib**	**Osimertinib**
Afatinib		0.87 (0.61–1.24)	1.10 (0.69–1.74)	1.16 (0.89–1.52)	0.93 (0.66–1.31)
Dacomitinib	1.15 (0.81–1.64)		1.26 (0.70–2.25)	1.34 (1.06–1.69)	1.07 (0.77–1.47)
Erlotinib	0.91 (0.57–1.45)	0.79 (0.44–1.42)		1.06 (0.62–1.81)	0.85 (0.48–1.51)
Gefitinib	0.86 (0.66–1.12)	0.75 (0.59–0.95)	0.94 (0.55–1.60)		0.80 (0.64–1.00)
Osimertinib	1.08 (0.76–1.52)	0.94 (0.68–1.29)	1.18 (0.66–2.10)	1.25 (1.00–1.56)	

Note: cells correspond to relative effects of column treatments vs row treatments (HR < 1.0 indicates benefit in favor of the column treatment).
Abbreviations: CrI, credible interval; *EGFR*-TKI, epidermal growth factor receptor – tyrosine kinase inhibitor; HR, hazard ratio; OS, overall survival.

Figure 2. Forest Plots of HRs and 95% CrIs for Dacomitinib vs *EGFR*-TKI Comparisons for OS

TKI comparison	HR (95% CrI)
Afatinib	0.87 (0.61, 1.24)
Erlotinib	0.79 (0.44, 1.42)
Gefitinib	0.75 (0.59, 0.95)
Osimertinib	0.94 (0.68, 1.29)



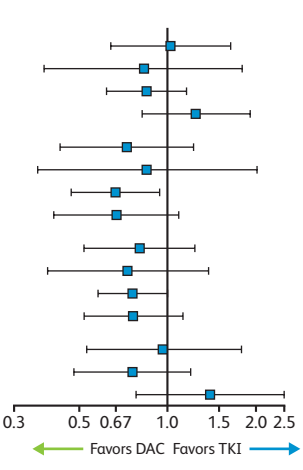
Note: x-axis not on a linear scale.
Abbreviations: CrI, credible interval; DAC, dacomitinib; *EGFR*-TKI, epidermal growth factor receptor – tyrosine kinase inhibitor; HR, hazard ratio; OS, overall survival.

SUBGROUP ANALYSES

- Results of exon 21 L858R substitution mutation and Asian subgroup analyses were consistent with those in the overall population (**Figure 3**).
- In the exon 19 deletion mutation subgroup, afatinib and osimertinib demonstrated a numerical improvement of OS relative to dacomitinib.
- In the non-Asian subgroup, osimertinib demonstrated a numerical improvement of OS relative to the other *EGFR*-TKIs; however, the network for non-Asian subgroup included only 3 RCTs with small sample sizes of non-Asian patients in each trial.

Figure 3. Forest Plot of HRs and 95% CrIs for Dacomitinib vs *EGFR*-TKI Comparisons for OS in all Subgroups

Subgroup	TKI comparison	HR (95% CrI)
Exon 19 deletion	AFA	1.02 (0.64, 1.64)
	ERL	0.83 (0.38, 1.80)
	GEF	0.85 (0.62, 1.16)
	OSI	1.25 (0.82, 1.91)
Exon 21 L858R substitution mutation	AFA	0.73 (0.43, 1.23)
	ERL	0.85 (0.36, 2.02)
	GEF	0.67 (0.47, 0.94)
	OSI	0.67 (0.41, 1.09)
Asian	AFA	0.80 (0.52, 1.24)
	ERL	0.73 (0.39, 1.38)
	GEF	0.76 (0.58, 1.00)
	OSI	0.76 (0.52, 1.13)
Non-Asian	AFA	0.97 (0.53, 1.79)
	GEF	0.76 (0.48, 1.20)
	OSI	1.40 (0.78, 2.50)



Note: x-axis not on a linear scale.
Abbreviations: AFA, afatinib; CrI, credible interval; DAC, dacomitinib; *EGFR*-TKI, epidermal growth factor receptor – tyrosine kinase inhibitor; ERL, erlotinib; GEF, gefitinib; HR, hazard ratio; OS, overall survival;OSI, osimertinib.

Electronic Poster

An electronic version of this poster may be obtained by scanning this QR code with your smartphone app. Copies of this poster obtained through the QR code are for personal use only and may not be reproduced without permission from ISPOR® and the authors of this poster. To request permission or to ask questions about the poster please contact Jasmina.Ivanova@pfizer.com

References: 1. Bray et al., 2018; **2.** Cancer Research UK, 2016; **3.** Planchard et al., 2018; **4.** Wood et al., 2015; **5.** Franek et al., 2019; **6.** Mok et al., 2019; **7.** Ramalingam et al., 2020.

Funding sources: This work was sponsored by Pfizer Inc. Larkin-Kaiser KA, Scory T, & Farris M are employed by Medlior Health Outcomes Research Ltd, who were paid consultants to Pfizer Inc. Ivanova J & Wilner K are employed by Pfizer and own stock. Medlior was responsible for collection, analysis, and reporting of data, for which it received funding from Pfizer.

Prepared for the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Virtual Meeting · May 18–20, 2020