REAL WORLD COMPARISON OF GEFITINIB, AFATINIB, ERLOTINIB, AND OSIMERTINIB IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS: A MULTICENTER RETROSPECTIVE COHORT STUDY

Peragine C[1], Bedi D[2], Kolko T[2], Thawer A[1], Cheng S[3], Doherty M[3], Menjak I[3], Liu G[4], DeAngelis C[1,2,5]

[1] Department of Pharmacy, Odette Cancer Centre and Sunnybrook Health Sciences Centre, Toronto, Ontario; [2] Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario ; [3] Division of Medical Oncology, Odette Cancer Centre and Sunnybrook Health Sciences Centre, Toronto, Ontario; [4] Princess Margaret Cancer Centre, Toronto, Ontario; [5] Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, Ontario

BACKGROUND

Our single-centre study at Sunnybrook Health Sciences' Odette Cancer Centre (OCC) found that exposure to oral anticancer medication (OAM) clinical pharmacy services (CPS) increased the likelihood of early treatment interruption (dose reduction/hold/discontinuation in first 2 months) in non-small cell lung cancer (NSCLC) patients, but the effect was confounded by OAM prescribed. OAM-CPS consists of proactive pharmacist follow-up via telephone, utilizing a standardized algorithm developed at OCC. The algorithm provides guidance on timing of follow-up, grading of toxicity, and recommended toxicity management.

OBJECTIVE

To evaluate OAM agent, treatment centre, and OAM-dedicated CPS exposure as predictors of early OAM modification, disease progression, and survival in a multicenter retrospective cohort of advanced NSCLC patients.

METHODS

Electronic medical records were reviewed for OAM-naïve NSCLC patients from OCC and Princess Margaret Cancer Centre (PMCC) prescribed gefitinib, afatinib, erlotinib and osimertinib between January 2012 and December 2018. Odds of early OAM modification (temporary hold, dose reduction, or discontinuation within two months of starting therapy), disease progression at 36 months, and mortality at 36 months were assessed using multivariable logistic regression and cox-proportional hazards models. Covariates included OAM agent (gefitinib as referent), treatment centre (OCC as referent), and CPS exposure (no OAM-CPS as referent).

RESULTS

Patient demographics are summarized in Table 1. Table 2 and Table 3 show the rates and odds, respectively, of early OAM modification, progression and death at 12 months, and progression and death at 36 months.

Of note, afatinib (OR 4.9, 95% CI 2.6-9.2, p<0.01) and erlotinib (OR 2.1, 95% CI 1.1-3.9, p=0.03) use increased odds of OAM modification. Erlotinib use increased odds of death (OR 2.1, 95% CI 1.5-2.9, p<0.01) and disease progression (OR 1.7, 95% CI 1.3-2.2, p<0.01). Afatinib use reduced odds of mortality at 36 months (OR 0.5, 95% CI 0.3-0.7, p<0.01).

CONCLUSION

Afatinib increased the odds of early OAM modification but reduced odds of mortality at 36-months. Erlotinib was inferior to gefitinib for all outcomes, consistent with its use in the second line setting. Treatment centre and OAM-CPS exposure did not affect odds of early OAM modification, disease progression, or mortality.

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Table 1. Patient demographic and treatment characteristics

Female	313	62%
Age (median, range)	66	(28-95)
East Asian/South Asian	296	59%
Caucasian	98	19%
Black	18	4%
Other/Unknown	93	18%
Ex/Ever Smoker	161	32%
Never Smoker	328	65%
Current smoker	16	3%
Histology		
Adenocarcinoma	464	92%
Adenosquamous	8	2%
Squamous	26	5%
Unknown/Other	7	1%
Stage 2	2	0%
Stage 3	23	5%
Stage 4	467	92%
Unknown stage	13	3%
Metastases	397	79%
Brain metastases	170	34%
Start year 2012-2014	181	36%
Start year 2015-2016	164	32%
Start year 2017-2018	160	32%
Gefitinib	336	67%
Erlotinib	66	13%
Afatinib	64	13%
Osimertinib	39	8%
OCC site	269	53%
PMH site	236	47%
OAM-CPS	147	29%

Table 2. Rates of early OAM modification, progression and death at 12 months, and progression and death at 36 months

		Early OAM modification		Progression at 12 months		Death at 12 months		Progression at 36 months		Death at 36 months	
	N	n	%	n	%	n	%	n	%	n	%
All	505	124	25%	300	59%	104	21%	413	82%	240	48%
Gefitinib	336	60	18%	192	57%	55	16%	282	84%	166	49%
Afatinib	64	37	58%	37	58%	9	14%	49	77%	16	25%
Erlotinib	66	23	35%	47	71%	30	45%	54	82%	40	61%
Osimertinib	39	4	10%	24	62%	10	26%	28	72%	18	46%
OCC	269	57	21%	174	65%	68	25%	223	83%	125	46%
PMH	236	31	13%	126	53%	36	15%	190	81%	115	49%
OAM-CPS	147	38	26%	94	64%	35	24%	119	81%	58	39%
No OAM-CPS	358	50	14%	206	58%	69	19%	294	82%	182	51%

Table 3. Odds of early OAM modification, progression and death at 12 months, and progression and death at 36 months as determined by multivariable logistic and cox regression with gefitinib, OCC, and no OAM-CPS referents

	Early OAM modification			Progression at 12 months			Death at 12 months			Progression at 36 months			Death at 36 months		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Afatinib[a]	**4.9**	**(2.6-9.2)**	**<0.01**	**0.5**	**(0.4-0.8)**	**<0.01**	**0.5**	**(0.3-0.9)**	**0.02**	0.9	(0.7-1.1)	0.21	**0.5**	**(0.3-0.7)**	**<0.01**
Erlotinib[a]	**2.2**	**(1.1-3.9)**	**0.03**	**2.2**	**(1.6-3.0)**	**<0.01**	**2.9**	**(1.9-4.4)**	**<0.01**	**1.7**	**(1.3-2.2)**	**<0.01**	**2.1**	**(1.5-2.9)**	**<0.01**
Osimertinib[a]	0.4	(0.1-1.1)	0.08	0.9	(0.6-1.4)	0.60	0.9	(0.5-1.5)	0.69	**0.7**	**(0.5-1.0)**	**0.03**	1.2	(0.8-1.9)	0.32
PMH[b]	0.7	(0.4-1.3)	0.24	1.0	(0.8-1.1)	0.57	0.9	(0.7-1.1)	0.26	1.0	(0.8-1.1)	0.42	0.9	(0.8-1.1)	0.27
OAM-CPS	0.8	(0.4-1.4)	0.40	1.0	(0.8-1.2)	0.90	0.9	(0.7-1.2)	0.54	0.9	(0.8-1.0)	0.11	1.1	(0.9-1.3)	0.53

[a] as compared to gefitinib, [b] as compared to OCC, [c] as compared to no OAM-CPS

DISCLOSURES

Authors have the following to disclose concerning possible personal or financial relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

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