Mortality Among EGFR-mutated Advanced NSCLC Patients After Starting First-line Osimertinib Treatment: A Real-world, US Attrition Analysis

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INTRODUCTION

- The recommended first-line therapy for patients with epidermal growth factor receptor–mutated (EGFRm) advanced non-small cell lung cancer (NSCLC) is osimertinib, a 3rd-generation irreversible EGFR tyrosine kinase inhibitor (TKI)[1]
  - Although osimertinib demonstrated efficacy versus other EGFR TKIs in the phase 3 FLAURA trial,[2,3] most patients receiving first-line osimertinib will eventually develop resistance[4]
- A retrospective real-world analysis of patients with EGFRm NSCLC estimated 28% of first-line patients treated with a 1st/2nd-generation EGFR TKI (ie, erlotinib, afatinib, and gefitinib) died before receiving a 2nd line of therapy (LOT; eg, osimertinib)[5]
- Analyses of mortality of US patients who received osimertinib as a first-line therapy in the real-world setting have not yet been published

OBJECTIVE

- This real-world analysis estimated all-cause mortality of patients with EGFRm NSCLC after starting first-line osimertinib monotherapy and before receiving a 2nd LOT to determine if the risk of death prior to starting the 2nd LOT was similar to that seen with 1st/2nd generation EGFR TKIs

METHODS

- Data from the ConcertAI (Cambridge, MA) Patient360 NSCLC database (>100 geographically dispersed US community oncology practices) and the Flatiron Health (New York, NY) Advanced Non-small Cell Lung Cancer (aNSCLC) Enhanced Data Mart (EDM; >800 sites of care within the United States) were analyzed separately
  - A previous analysis had shown a 20% to 30% overlap in patients with EGFR exon 20 insertion mutations between these data sources[6]
- Included patients were diagnosed with advanced NSCLC after January 1, 2018 and were eligible if they:
  - Had confirmed EGFR exon 19 deletions (ex19del) or exon 21 L858R mutations
  - Received osimertinib as first-line monotherapy
- The following were assessed:
  - The proportion of patients who died after receiving first-line osimertinib monotherapy and prior to starting a 2nd LOT was calculated
  - Demographics, baseline disease characteristics, and risk factors were summarized for patients treated with first-line osimertinib monotherapy
  - Analyses were stratified by key known prognostic factors in NSCLC: age and Eastern Cooperative Oncology Group performance status (ECOG PS)

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RESULTS

Patient Mortality

- In the ConcertAI Patient360 NSCLC database, among the first-line osimertinib population (n=518), 128 (25%) died before receiving a 2nd LOT (**Figure 1A**)
- In the Flatiron aNSCLC EDM database, among the first-line osimertinib population (n=1,633), 369 (23%) died before receiving a 2nd LOT (**Figure 1B**)

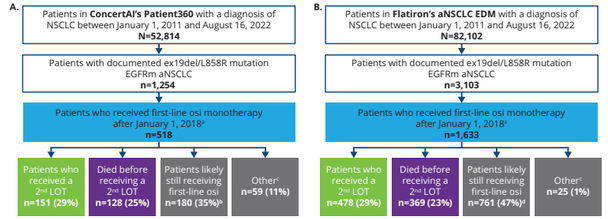
Risk Factor Analysis

- In both databases, patients who died prior to receiving a 2nd LOT were older, had a higher mean Charlson comorbidity score, and had a poorer performance status than those who did not die before starting the 2nd LOT (**Table 1**)

Survival Times

- The survival times stratified by age and ECOG PS are shown in **Figure 2**
  - **ConcertAI:** median time to death was 277 days for patients with an ECOG PS of 0 or 1 and 100 days for patients with an ECOG PS of 2 or 3
  - **Flatiron:** median time to death was 314 days for patients with an ECOG PS of 0 or 1 and 169 days for patients with an ECOG PS of 2 or 3

FIGURE 1: Patient Attrition Among First-line Osimertinib Monotherapy



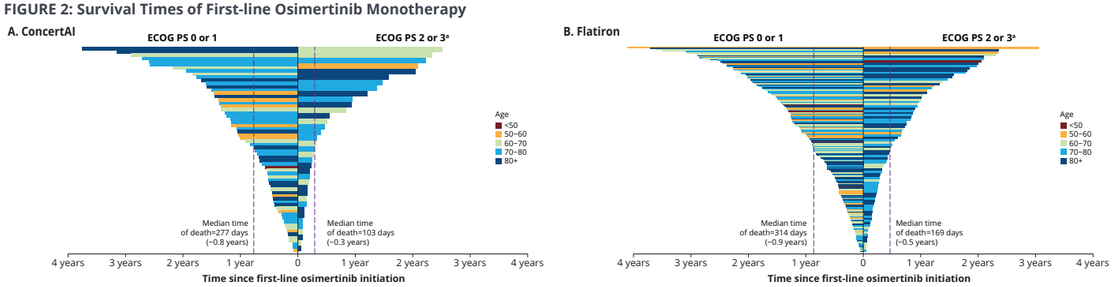
aNSCLC, advanced non-small cell lung cancer; EDM, Enhanced Data Mart; EGFRm, epidermal growth factor receptor-mutated; ex19del, exon 19 deletion; LOT, line of therapy; NSCLC, non-small cell lung cancer; osi, osimertinib. aLOT1 start – LOT1 end] >2; median follow-up from first-line osimertinib initiation was 545 days (1.5 years) for ConcertAI and 429 days (1.2 years) for Flatiron. bBased on their last clinical activity (most recent entry in the database was an order of osimertinib; n=91), medication order of osimertinib within 90 days of last clinical activity (n=75), or data curation indicating ongoing use of osimertinib (n=14). cIncluding possible loss to follow up, inactivity in dataset, treatment discontinuation; dBased on an order or administration of osimertinib within 90 days prior to, or any time after, last confirmed activity.

TABLE 1: Demographic and Baseline Disease Characteristics Risk Factor Analysis

	ConcertAI			Flatiron		
Characteristic, n (%)	Died before starting 2nd LOT (n=128)	Did not die before starting 2nd LOT (n=390)	*P* value	Died before starting 2nd LOT (n=369)	Did not die before starting 2nd LOT (n=1,264)	*P* value
Age, median (range), years	74.3 (47.5–88.0)	68.9 (36.5–88.8)	<0.01	74.8 (38.3–85.4)	69.0 (32.9–85.7)	<0.01
Female	84 (66)	273 (70)	0.41	240 (65)	863 (68)	0.27
Race			0.24			0.34
White	91 (71)	243 (62)		209 (57)	679 (54)	
Asian	19 (15)	64 (16)		40 (11)	180 (14)	
Black or African American	6 (5)	40 (10)		22 (6)	83 (7)	
Other	12 (9)	43 (11)		48 (13)	137 (11)	
Not recorded	–	–		50 (14)	185 (15)	
Modified Charlson score,[a] mean (SD)	0.77 (0.98)	0.37 (0.69)	<0.01	0.47 (0.85)	0.35 (0.79)	0.011
0	63 (49)	282 (72)		251 (68)	949 (75)	
1-2	54 (42)	101 (26)		97 (26)	260 (21)	
3+	11 (9)	6 (2)		14 (4)	30 (2)	
Not recorded	0	1 (<1)		7 (2)	25 (2)	
Baseline ECOG PS[b]			<0.01			<0.01
0	21 (16)	121 (31)		77 (21)	404 (32)	
1	45 (35)	144 (37)		129 (35)	465 (37)	
2+	41 (32)	35 (9)		94 (25)	140 (11)	
NA	21 (16)	90 (23)		69 (19)	255 (20)	
EGFR subtype			0.39			0.32
Ex19del	65 (51)	217 (56)		195 (53)	718 (57)	
L858R	63 (49)	173 (44)		171 (46)	540 (43)	
Both	0	0		3 (1)	6 (<1)	
Baseline brain metastases	62 (48)	140 (36)	0.016	NA	NA	NA

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletions; LOT, line of therapy; NA, not available; SD, standard deviation. [a]Excluding cancer-specific categories; values any time prior to first-line initiation. [b]Value closest to first-line initiation and 1 year prior to first-line initiation.

FIGURE 2: Survival Times of First-line Osimertinib Monotherapy



ECOG PS, Eastern Cooperative Oncology Group performance status.
[a]Patients with ECOG PS=4 (1 in ConcertAI and 3 in Flatiron) are not shown in the swimplots.

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KEY TAKEAWAY

Further optimization of first-line therapy for patients with EGFRm NSCLC is needed to improve long-term outcomes, especially for those who are older, or have comorbidities or poorer performance status

CONCLUSIONS

- Approximately one-quarter of the patients with EGFRm NSCLC receiving first-line osimertinib died prior to receiving a 2nd LOT; this was at a similar rate to that seen with 1st/2nd-generation EGFR TKIs[5]
- Patients who died before receiving a 2nd LOT tended to be older, had a higher Charlson comorbidity score, or had a poorer performance status

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