1349P - Continuing Osimertinib in combination with Chemotherapy after Osimertinib Failure reduces CNS progression in patients with EGFR-mutated NSCLC and CNS metastases

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Background

- Central nervous system (CNS) metastases are common among patients with advanced EGFR mutation positive NSCLC.
- Osimertinib exhibits high CNS activity. CNS objective response rate was 91% with osimertinib in the FLAURA study.
- Chemotherapy is the standard treatment for advanced EGFR mutation positive NSCLC patients failing osimertinib but has limited CNS activity.
- The role of continuing osimertinib concurrently with chemotherapy after osimertinib failure for CNS control is uncertain.

Methods

- All patients with metastatic EGFR mutation positive NSCLC who progressed on osimertinib and received chemotherapy from 01 Nov 2017 to 17 March 2023 in a tertiary institution were retrospectively reviewed.
- The primary endpoint was comparison of time to CNS progression between patients treated with osimertinib plus chemotherapy versus chemotherapy alone after osimertinib failure.
- Time to CNS progression was defined from the starting date of chemotherapy to radiological or clinical progression of CNS metastases.
- Hazard ratios and 95% confidence intervals were estimated by Cox regression.

Patients

Baseline Characteristics*		Total Population (n=180)			Patients with CNS metastases (n=82)		
		Osim+ChT (n=33)	ChT alone (n=147)	P value	Osim+ChT (n=30)	ChT alone (n=52)	P value
Age (%)	<=60	17 (51)	64 (43)	0.41	15 (50)	27 (52)	0.87
	>60	16 (49)	83 (57)		15 (50)	25 (48)	
Gender (%)	Female	22 (67)	89 (61)	0.56	21 (70)	35 (67)	1.00
	Male	11 (33)	58 (39)		9 (30)	17 (33)	
Performance status (%)	0-1	27 (82)	130 (88)	0.38	25 (83)	44 (85)	1.00
	2	6 (18)	17 (12)		5 (17)	8 (15)	
EGFR mutation (%)	Ex19del	16 (49)	87 (59)	0.31	15 (50)	31 (60)	0.49
	L858R	16 (49)	59 (40)		15 (50)	21 (40)	
	Others*	1 (2)	1 (1)		-	-	
Line of Osimertinib (%)	1	12 (36)	16 (11)	**0.001**	9 (30)	3 (6)	**0.007**
	2	21 (64)	131 (89)		21 (70)	49 (94)	
CNS metastases (%)	No	3 (9)	95 (65)	**<0.001**			
	Yes	30 (91)	52 (35)				
Prior WBRT (%)	No	25 (76)	120 (82)	0.47	22 (73)	25 (48)	**0.037**
	Yes	8 (24)	27 (18)		8 (27)	27 (52)	

*Baseline characteristics were documented at the time of chemotherapy initiation and not at the time of cancer diagnosis. ChT, chemotherapy; CNS, central nervous system; EGFR, epidermal growth factor receptor; Osim, osimertinib; WBRT, whole brain radiotherapy

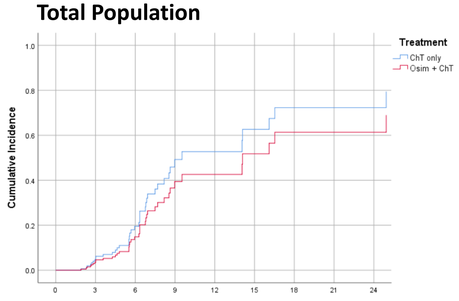
Results

Total Population	OSIM+ChT (n=33)	ChT alone (n=147)	Hazard Ratio (95% CI)	P value
Median PFS – months (95% CI)*	6.2 (5.5-6.8)	4.8 (4.2-5.4)	0.72 (0.48-1.09)	0.12
CNS progression – no. (%)	**7 (21)**	**33 (22)**	**0.74 (0.33-1.68)**	**0.88**
Patients with CNS metastases	**(n=30)**	**(n=52)**		
Median PFS – months (95% CI)*	6.2 (5.6-6.7)	4.8 (4.1-5.5)	0.62 (0.38-1.00)	0.05
CNS progression – no. (%)	**6 (20)**	**24 (46)**	**0.32 (0.13-0.81)**	**0.02****
Salvage WBRT – no (%)	**2 (7)**	**11 (21)**	**0.24 (0.05-1.08)**	**0.06**

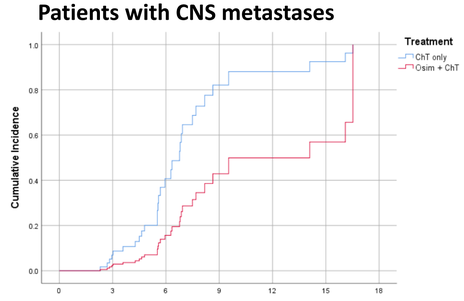
*Systemic/CNS progression or death.
**Results remained significant after adjustment for Line of Osimertinib and Prior WBRT . P value after adjustment=0.016
ChT, chemotherapy; CNS, central nervous system; Osim, osimertinib; PFS, progression free survival; WBRT, whole brain radiotherapy

Risk of CNS Progression

Total Population



Patients with CNS metastases



Conclusion

Continuing osimertinib concurrently with chemotherapy after osimertinib may reduce CNS progression in patients with known CNS metastases, and the risk of being subjected to whole brain radiotherapy. Future prospective study is warranted to address this issue.

References

1. Reungwetwattana et al. J Clin Oncol 36, no. 33 (November 20, 2018) 3290-3297

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