996P - Activity of OsimeRTInib in NSCLC with UNcommon EGFR Mutations: Retrospective Observational Multicenter Study (ARTICUNO)

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Background

Osimertinib is a third-generation TKI representing the standard of care for treatment of metastatic non-small cell lung cancer (NSCLC) harboring classical *EGFR* mutations. In 10-20% of cases, *EGFR* presents an assorted group of uncommon mutations which confer variable sensitivity to first- and second-generation EGFR TKIs, with overall lower therapeutic activity. Data of Osimertinib in this heterogenous group of mutations are limited and strongly warranted.

Methods

This is a retrospective multicenter study of patients with advanced NSCLC with any uncommon alteration of *EGFR* and treated with Osimertinib since August 2017. Investigators collected response in terms of overall response rate (ORR) and disease control rate (DCR) by RECIST 1.1 criteria. Progression free survival (PFS), duration of response (DOR) and overall survival (OS) were estimated by Kaplan-Meier method.

Results

Table 1. Patient clinical characteristics.

Characteristics	N= 65 (%)
Median age (range) – yr	68 (31 – 87)
Sex	
Female	40 (62)
Male	25 (38)
ECOG performance status	
PS 0-1	56 (86)
PS ≥ 2	9 (14)
Smoking history	
Yes	41 (63)
No	24 (37)
Ethnicity	
Caucasian	60 (92)
Other	5 (8)
Brain metastases at baseline	19 (29)
Line of therapy	
1° line	52 (80)
2° line	10 (15)
≥ 3° line	3 (5)
TKI naïve	
Yes	57 (88)
No	8 (12)

Table 2. Distribution of uncommon *EGFR* mutations in the study population and outcome with Osimertinib. Patients with at least one major uncommon mutations (G719X, L861X or S768I) are regrouped in each cluster.

Major uncommon mutation +/- other mut.	38 (58%)	Outcome (95% CI)
G719X	**19 (29)**	**ORR**: 50% (26-74), **DCR**: 89% (65-99), **mPFS**: 11 months (5-15)
G719A/X	7 (11)	
G719A+aqT790M	1 (2)	
G719X+I706T+aqT790M	1 (2)	
G719S+dnT790M	2 (3)	
G719X/A/S/C+S768I	5 (8)	
G719A+L861Q	2 (3)	
G719S+A289V	1 (2)	
L861X	**15 (23)**	**ORR**: 50% (23-77), **DCR**: 86% (57-98), **mPFS**: 9 months (5-14)
L861Q/R	10 (15)	
L861Q+aqT790M	2 (3)	
L861Q+G719A	2 (3)	
L861Q+V834L	1 (2)	
S768I	**11 (17)**	**ORR**: 55% (23-83), **DCR**: 91% (59-100), **mPFS**: 17 months (7-24)
S768I	1 (2)	
S768I+aqT790M	1 (2)	
S768I+L858R	4 (6)	
S768I+G719X/A/S/C	5 (8)	

OTHERS (minor mutations or Ins20)	27 (42%)	Best Response
L858R+dnT790M (N=2), L833V+L858R, Del19+L747Q, I740_K745dup, V738_I744ins, EGFR-KDD, D770_N771insSVD	8 (12)	**CR/PR**
V738_A743del, Del19+A750P, Del19+S751V, Del19+L858R, Del19+P753S+aqT790M, V769_D770insASV, A767_V769dup	7 (11)	**SD**
Y801C, R831C, A702S, V765M, D770_N771insSVD, G709T, A767_V769dup, A702_K728del, E709_T710delinsD (N=2)	10 (15)	**PD**
V769_D770insASV, E868Q	2 (3)	**NE**

Keys: aq=acquired, dn=*de novo*, CR=complete response, PR= partial response; SD=stable disease, NE=not evaluable

As of April 2022, 65 patients were identified in 18 institutions in Italy. Main clinical and biological characteristics of the study population are detailed in Table 1. Major uncommon mutations were the most frequent, largely occurring as compound. More than one third of cases presented heterogeneous minor uncommon mutations (Table 2).

Median time of follow up was 13 months. ORR and DCR were 45% (CI 95%, 32-58) and 78% (CI 95%, 66-88) in the overall evaluable population (N=60), and 49% (CI 95%, 34-64) and 78% (CI 95%, 66-88) in TKI-naïve (excluded ins20) cohort, respectively. Median PFS and DOR in TKI-naïve were 11 months (CI 95%, 7-18) and not reached (CI 95%, 5+), respectively.

Conclusion

➢ This is the widest known dataset of patients with uncommon *EGFR* mutations treated with Osimertinib. Major uncommon mutations were the most frequent, widely occurring as compound. A large group presented heterogeneous minor uncommon mutations. Osimertinib showed relevant activity, overall, numerically comparable with data from Osimertinib in a Korean trial and from Afatinib.

Ref: JH Cho et al., *JCO* 2020; JCH Yang et al. *JTO* 2020

ARTICUNO study is still ongoing and more data will be presented

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Conflict of interest: nothing to declare