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High dose osimertinib in patients with advanced stage EGFR exon 20 mutation-positive NSCLC: results from a phase 2 multicenter study, POSITION20

Abstract 1214P

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INTRODUCTION

- Non-small cell lung cancer (NSCLC) patients with an EGFR exon 20 mutation (EGFRex20+) are lacking clinical benefit to epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKI's)
- High dose of the EGFR TKI osimertinib shows promising antitumor activity to EGFRex20+ in vitro (Hirano, Yasuda et al. 2015)
- The safety and efficacy results from a multicenter single arm phase 2 study investigating osimertinib in EGFRex20+ NSCLC patients are reported here.

METHODS

KEY ELIGIBILITY

Advanced NSCLC
EGFRex20+ (mutation, deletion and/or insertion)
T790M negative
Pre-treatment chemotherapy allowed
Asymptomatic brain metastasis
WHO PS 0-2

TREATMENT REGIMEN

Osimertinib 160mg daily
Till progression or unacceptable toxicity

ENDPOINTS

1st: Objective response rate (ORR, RECIST 1.1)
2nd: Safety, duration of response (DoR), progression free survival (PFS) and overall survival OS)

STATISTICAL DESIGN

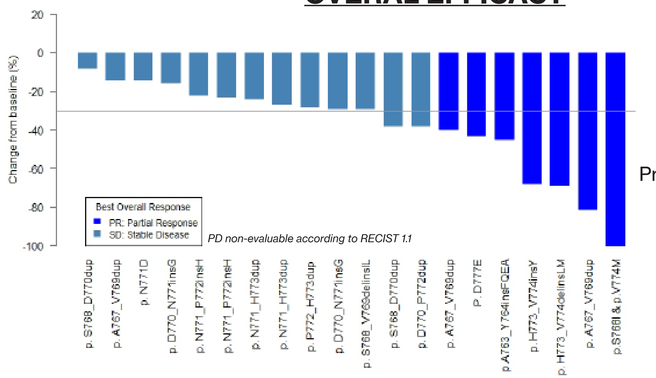
Simon's two stage, single arm, phase II trial

15 pts → (> 1 PR) → 25 pts

Target ORR (PR/CR): 30%
(alpha = 0.10; power = 0.80)

RESULTS

OVERAL EFFICACY



Confirmed ORR:
7 / 25, **28%**

Partial (n = 7) 28%
Stable (n = 13) 52%
Progressive (n = 5) 20%

DoR = 4.2 months

mPFS = 6.8 months

mOS = 15.2 months

Table 2. Treatment-related adverse events

Toxicity (N=25)	Gr 1 N (%)	Gr 2 N (%)	Gr 3 N (%)	Gr 4 N (%)	Total N (%)
Diarrhea	14 (56)	3 (12)	1 (4)	0	18 (72)
Dry skin*	10 (40)	1 (4)	0	0	11 (44)
Fatigue	10 (40)	1 (4)	0	0	11 (44)
Rash or acne*	8 (32)	2 (8)	0	0	10 (40)
Dyspnoea	8 (32)	1 (4)	0	0	9 (36)
Paronychia	9 (36)	0	0	0	9 (36)
Anaemia	6 (24)	1 (4)	1 (4)	0	8 (32)
Coughing	7 (28)	0	0	0	7 (28)
Myalgia	4 (16)	2 (8)	1 (4)	0	7 (28)
Anorexia	3 (12)	3 (12)	0	0	6 (24)
CPK increased	3 (12)	1 (4)	2 (8)	0	6 (24)
Back pain	4 (16)	1 (4)	0	0	5 (20)
Dry eyes	5 (20)	0	0	0	5 (20)
Mucositis oral	4 (16)	1 (4)	0	0	5 (20)
Nausea	5 (20)	0	0	0	5 (20)
Platelets decreased	4 (16)	1 (4)	0	0	5 (20)
Constipation	2 (8)	1 (4)	0	0	3 (12)
Dry mouth	3 (12)	0	0	0	3 (12)
Pruritus	0	3 (12)	0	0	3 (12)
Fissures	3 (12)	0	0	0	3 (12)

Treatment related toxicities observed >10% of pts are shown.

* This category is a grouped term

Treatment discontinuation due to grade 3 TRAE: 8% (n=2)
Including pneumonitis [n=1] and left ventricular systolic dysfunction [n=1]
Dose reduction from 160mg to 80mg: 21% (n=5)
Including grade 3 TRAE (diarrhea [n=1] and hepatotoxicity [n=1]) grade 2 TRAE (QTc prolongation [n=1], nausea [n=1] and increased CPK in combination with myalgia [n=1])

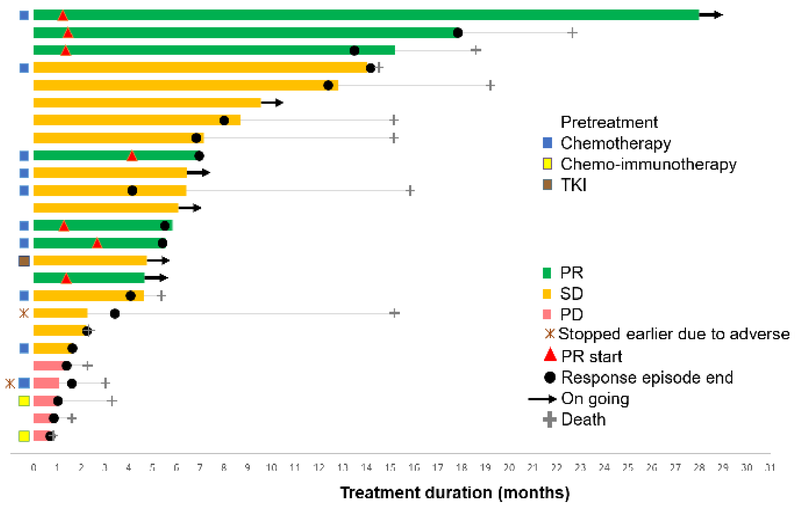
CONCLUSION

Osimertinib 160mg daily shows antitumor activity in EGFRex20+ NSCLC patients, with an ORR of 28%

TRAEs are consistent with other reports

Table 1. Patient and tumor characteristics

Characteristic	N = 25 (%)
Age (years)	68 (46 – 87)
Sex	7 (28%) male | 18 (72%) female
ECOG performance status 0 | 1 | 2	9 (36%) | 15 (60%) | 1 (4%)
Baseline brain metastases (asymptomatic)	4 (16%)
Medium # prior therapies (range)	1 (1, 3)
EGFR exon20 mutation subtype (most common >1 are listed)	p. A767_V769dup (12%) p. N771_H773dup (12%) p. S768_D770dup (8%) p. D770_N771insG (8%) p. N771_P772insH (8%) p. P772_H773dup (8%)



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