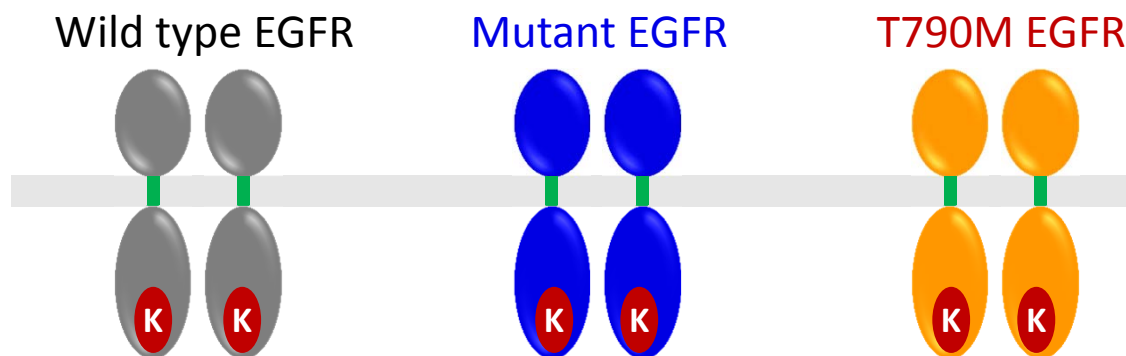


# **HM61713, an EGFR-mutant Selective Inhibitor**

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**Seoul, Korea**

# Development of 3<sup>rd</sup> generation EGFR TKIs in NSCLC



## 1<sup>st</sup> Generation TKI

Gefitinib, Erlotinib

### Activity Range

- Skin Rash/Diarrhea due to WT inhibition
- Inactive for T790M

## 2<sup>nd</sup> Generation TKI

pan-HER inhibitors

### Activity Range

- Severe Skin Rash/Diarrhea
- Inadequate drug concentration for T790M inhibition

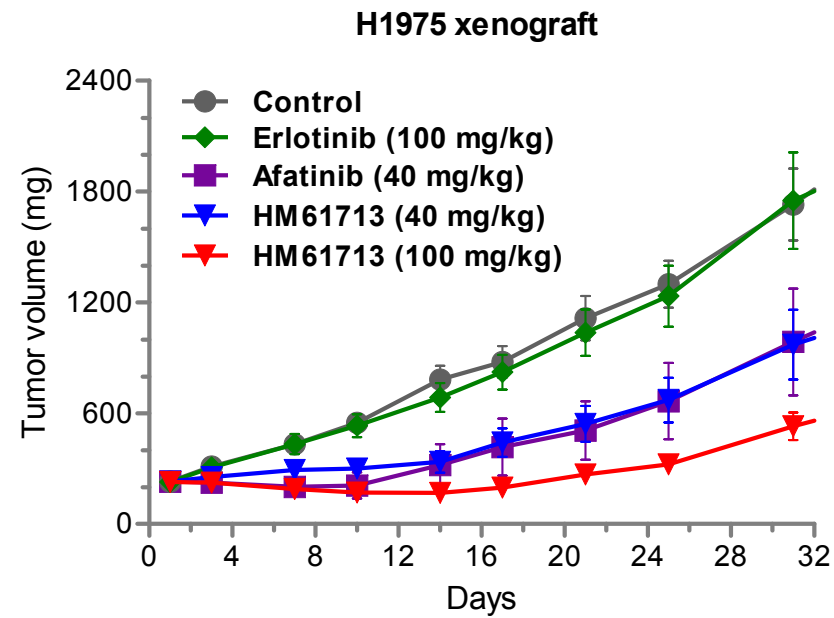
## 3<sup>rd</sup> Generation TKI

EGFR mutant selective inhibitor

### Activity Range

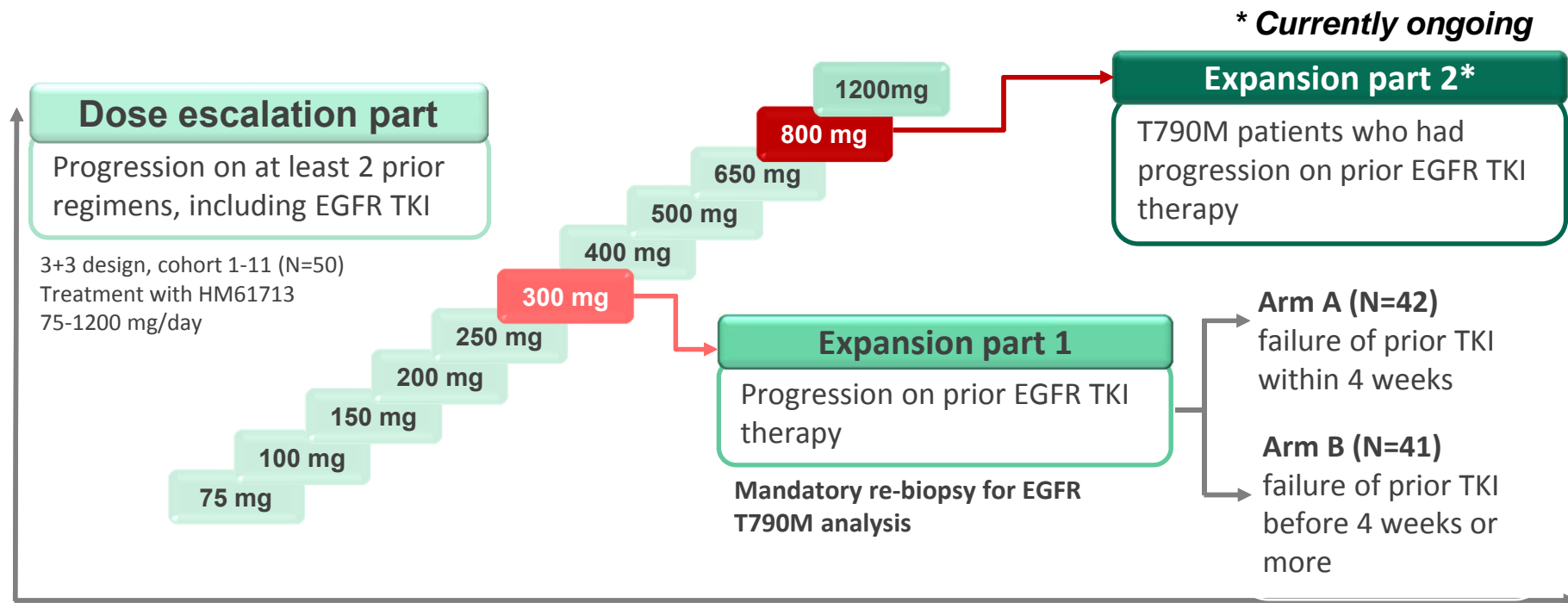
- Reduced Skin Rash/Diarrhea
- Sufficient drug concentration for T790M inhibition

## HM61713, *in vivo* efficacy in H1975 (L858R/T790M)



# Phase I/II Study to assess the safety, tolerability and pharmacokinetics and anti-tumor activity of HM61713 in NSCLC patients with EGFR mutation (NCT01588145)

- Open-label study conducted at 16 centers in Korea
- Objectives
  - Primary: safety and tolerability
  - Secondary: preliminary efficacy, pharmacokinetics of HM61713 and metabolites
  - Exploratory: biomarker study



# Patient Characteristics (1)

	Escalation N=35	Expansion		
		Arm A (N=42)	Arm B (N=41)	Total (N=83)
Median age, (range)	58 (35-81)	61 (38-80)	56 (38-79)	59 (38-80)
Gender, N (%)				
Male	8 (22.9)	18 (42.9)	13 (31.7)	31 (37.3)
Female	27 (77.1)	24 (57.1)	28 (68.3)	52 (62.7)
ECOG, N (%)				
0-1/ 2	33 (94.3) / 2 (5.7)	39 (92.9) / 3 (7.1)	37 (90.2) / 4 (9.8)	76 (91.6) / 7 (8.43)
Prior lines of chemotherapy				
Median (range)	3 (2-7)	2 (1-7)	3 (1-7)	2 (1-7)
1 regimen	-	16 (38.1)	4 (9.8)	20 (24.0)
2 regimens	11 (31.4)	19 (45.2)	14 (34.2)	33 (39.8)
≥ 3 regimens	24 (68.6)	7 (16.7)	23 (56.1)	30 (36.1)
T790M status, N (%)				
Positive	1 ( 2.9)	27 (64.3)	21 (51.2)	48 (57.8)
Negative	2 ( 5.7)	15 (35.7)	19 (46.3)	34 (41.0)
Unknown	32 (91.4)	0 ( 0.0)	1 ( 2.4)	1 ( 1.2)

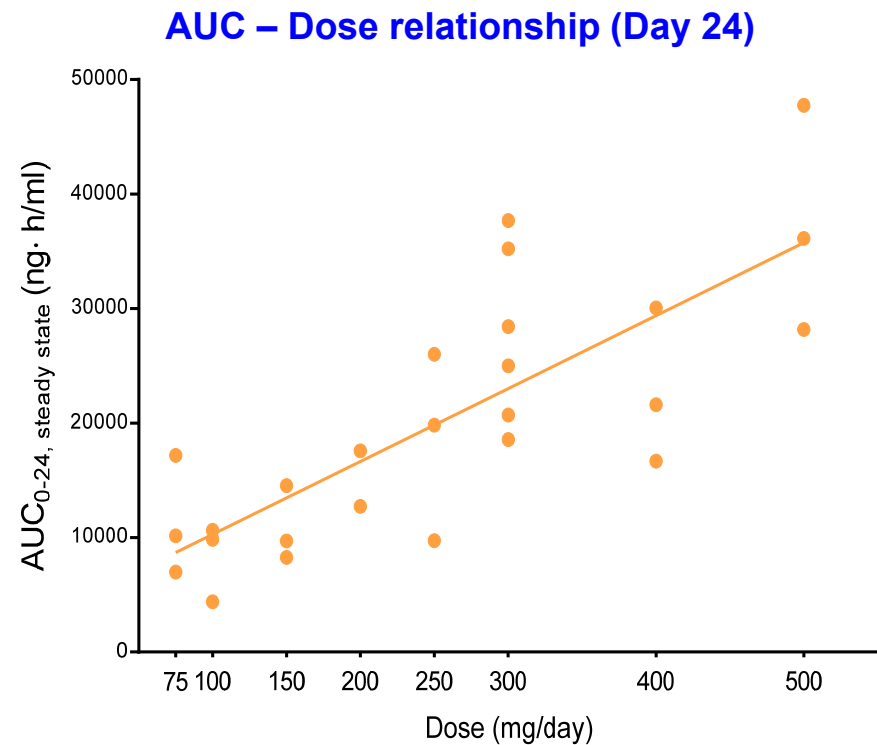
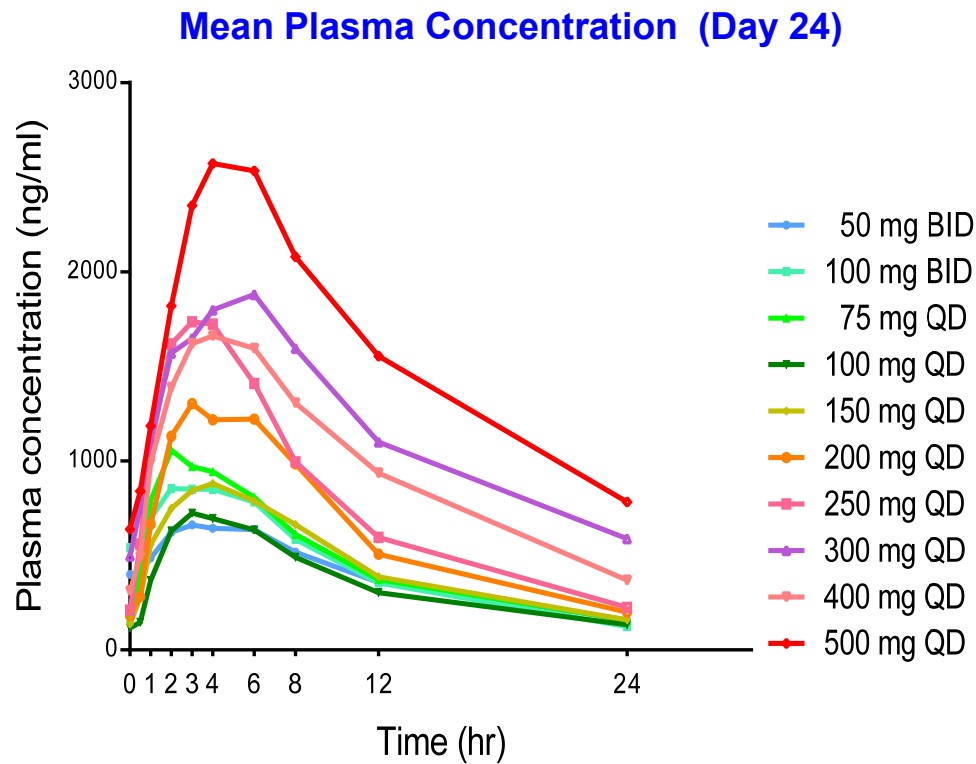
# Patient Characteristics (2)

	Escalation	Expansion		
	N=35	Arm A (N=42)	Arm B (N=41)	Total (N=83)
Prior TKI				
Gefitinib	26 (74.3)	28 (66.7)	31 (75.6)	59 (71.1)
Erlotinib	5 (14.3)	12 (28.6)	11 (26.9)	23 (27.7)
Afatinib	4 (11.4)	-	1 ( 2.4)	1 ( 1.2)
Dacomitinib	-	2 ( 4.8)	-	2 ( 2.4)
Histology, N (%)				
Adenocarcinoma	34 (97.2)	41 (97.6)	41 (100)	82 (98.8)
Squamous cell carcinoma	-	1 ( 2.4)	-	1 ( 1.2)
Others	1 ( 2.8)	-	-	-
EGFR mutation				
Exon 19 deletion	1 ( 2.9)	23 (54.8)	21 (51.2)	44 (53.0)
L858R	1 ( 2.9)	16 (38.1)	14 (34.1)	30 (36.1)
Others*	-	1 ( 2.4)	1 ( 2.4)	2 ( 2.4)

\* G719X or Ins. 3 dup.

# Pharmacokinetics

- Pharmacokinetics were dose linear over the dose range (75–500 mg/day)



# Adverse Event ( $\geq 10\%$ of patients)

- As of cut-off date, 118 patients have been administered with maximum 380 days

N (%)	Grade 1	Grade 2	$\geq$ Grade 3	Total (N=118)
Nausea	30 (25.4)	8 ( 6.8)	-	38 (32.2)
Skin exfoliation	28 (23.7)	3 ( 2.5)	-	31 (26.3)
Headache	21 (17.8)	7 ( 5.9)	1 ( 0.8)	29 (24.6)
Rash	22 (18.6)	6 ( 5.1)	-	28 (23.7)
Decreased appetite	18 (15.3)	6 ( 5.1)	1 ( 0.8)	25 (21.2)
Diarrhea	21 (17.8)	4 ( 3.4)	-	25 (21.2)
Pruritus	11 ( 9.3)	8 ( 6.8)	-	19 (16.1)
Constipation	11 ( 9.3)	7 ( 5.9)	-	18 (15.3)
Dry skin	12 (10.2)	3 ( 2.5)	-	15 (12.7)
Vomiting	10 ( 8.5)	5 ( 4.2)	-	15 (12.7)
Productive cough	8 ( 6.8)	6 ( 5.1)	-	14 (11.9)
Abdominal pain upper	8 ( 6.8)	5 ( 4.2)	-	13 (11.0)
Cough	7 ( 5.9)	6 ( 5.1)	-	13 (11.0)
Dyspepsia	10 ( 8.5)	2 ( 1.7)	-	12 (10.2)
Dyspnea	5 ( 4.2)	4 ( 3.4)	3 ( 2.5)	12 (10.2)



# Lab Abnormality ( $\geq 3\%$ of patients)

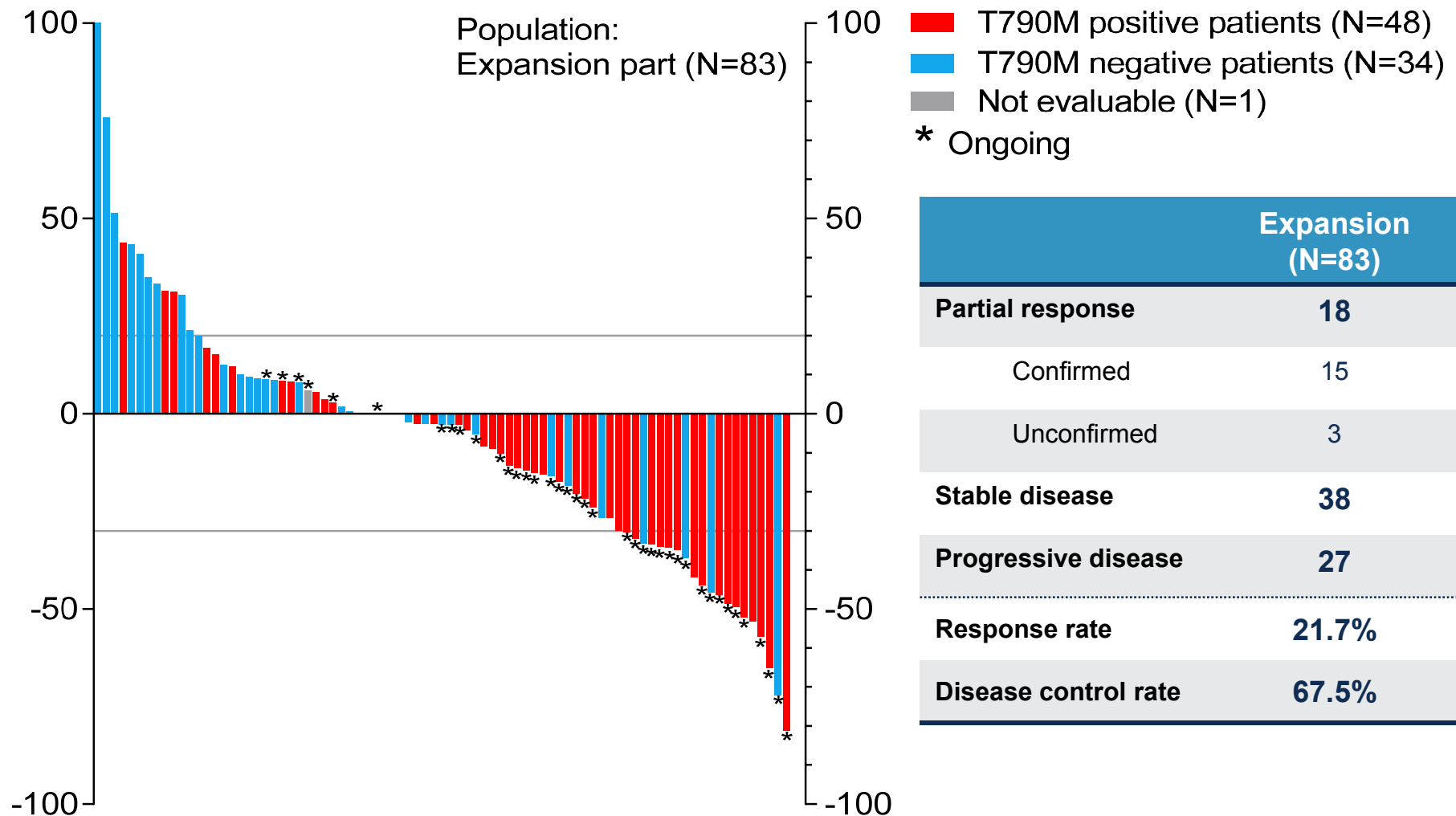
- Most laboratory abnormalities were Gr1/2

N (%)	Grade 1	Grade 2	$\geq$ Grade 3	Total (N=118)
ALT increased	7 ( 5.9)	-	1 ( 0.8)	8 ( 6.8)
Platelet count decreased	6 ( 5.1)	1 ( 0.8)	-	7 ( 5.9)
AST increased	5 ( 4.2)	-	1 ( 0.8)	6 ( 5.1)
Neutrophil count decreased	-	3 ( 2.5)	2 ( 1.7)	5 ( 4.2)
ECG QT prolonged	1 ( 0.8)	1 ( 0.8)	2 ( 1.7)	4 ( 3.4)

ALT: alanine aminotransferase

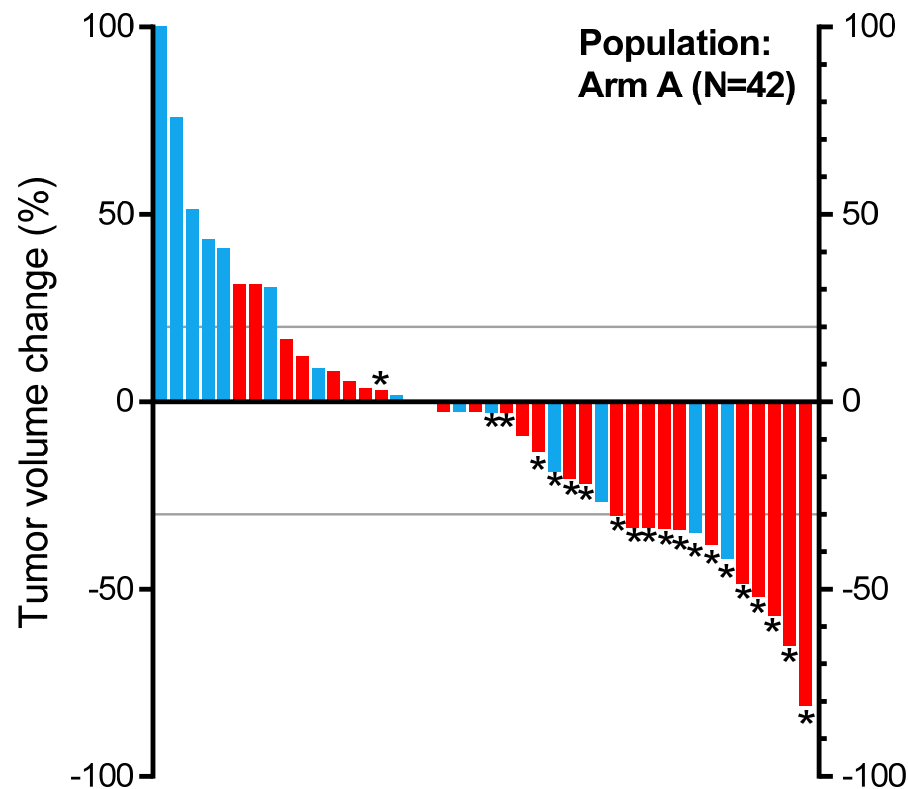
AST: aspartate aminotransferase

# Best Change from Baseline in Target Lesions : Expansion part

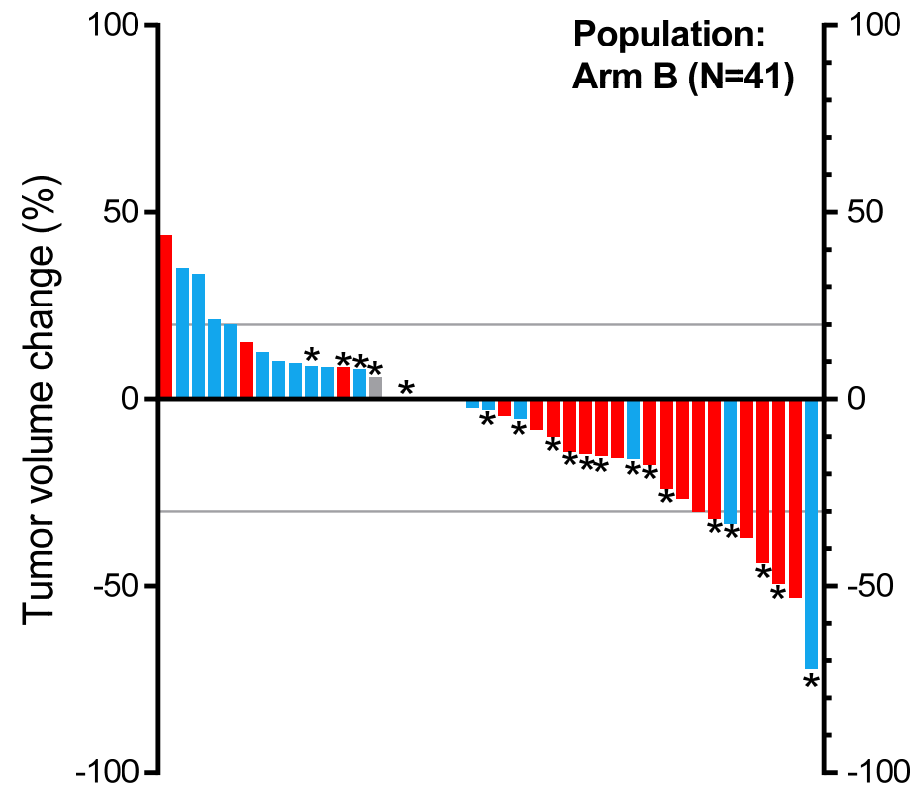


# Best Change from Baseline in Target Lesions : Arm A versus Arm B

■ T790M positive patients  
■ T790M negative patients  
 \* Ongoing    ■ Not evaluable



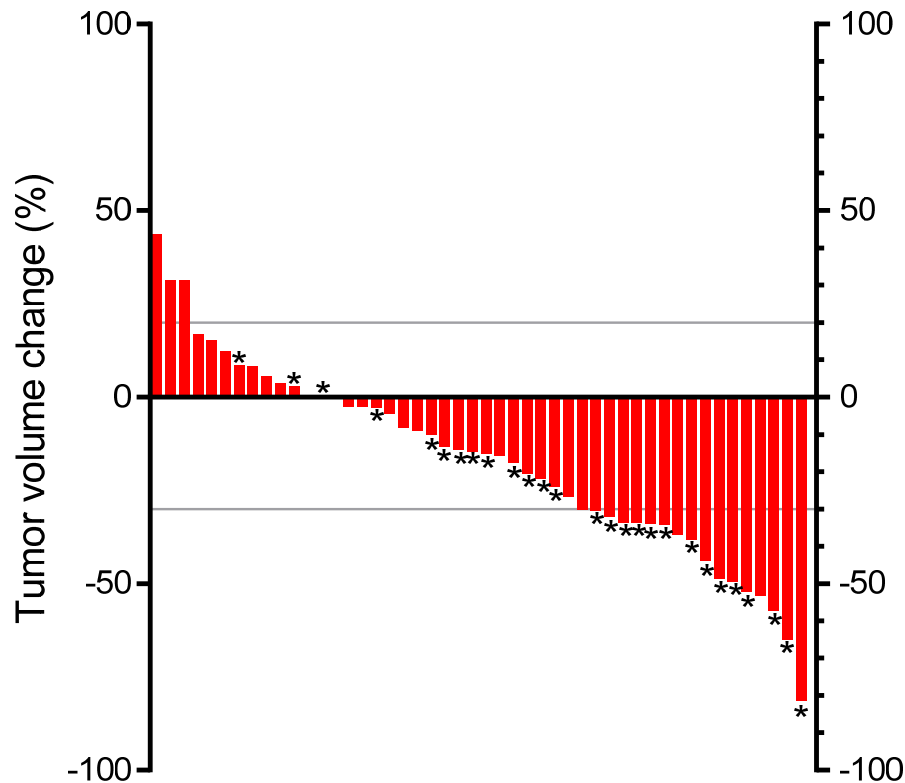
Response rate	23.8%
Disease control rate	61.9%



Response rate	19.5%
Disease control rate	73.2%

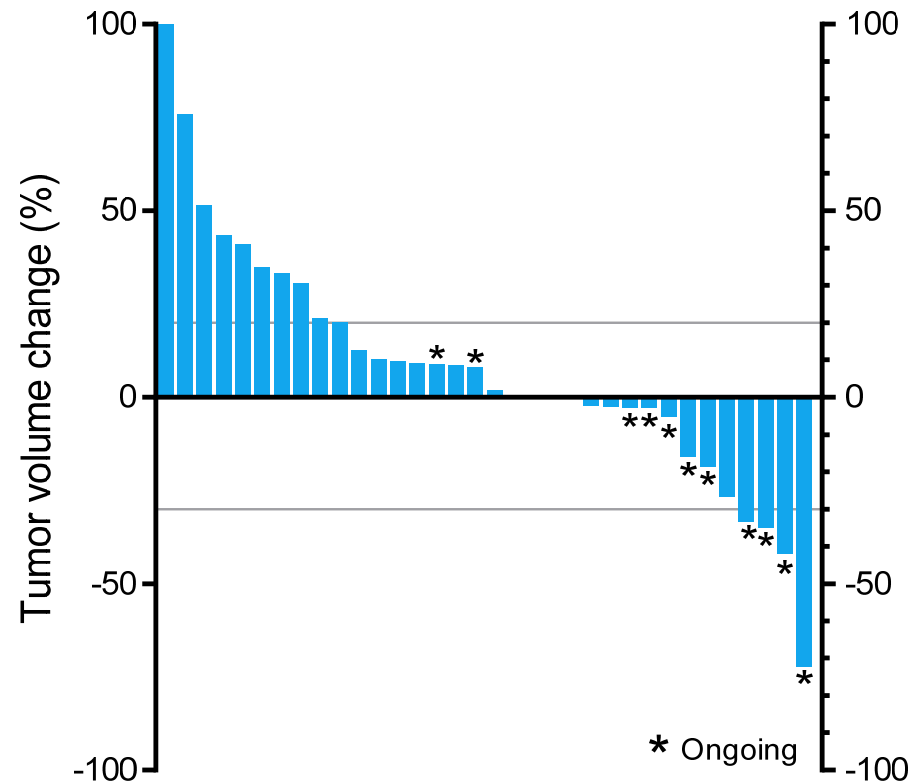
# Best Change from Baseline in Target Lesions : T790M+ versus T790M-

**Population:  
T790M positive patients (N=48)**



Response rate	29.2%
Disease control rate	75.0%

**Population:  
T790M negative patients (N=34)**



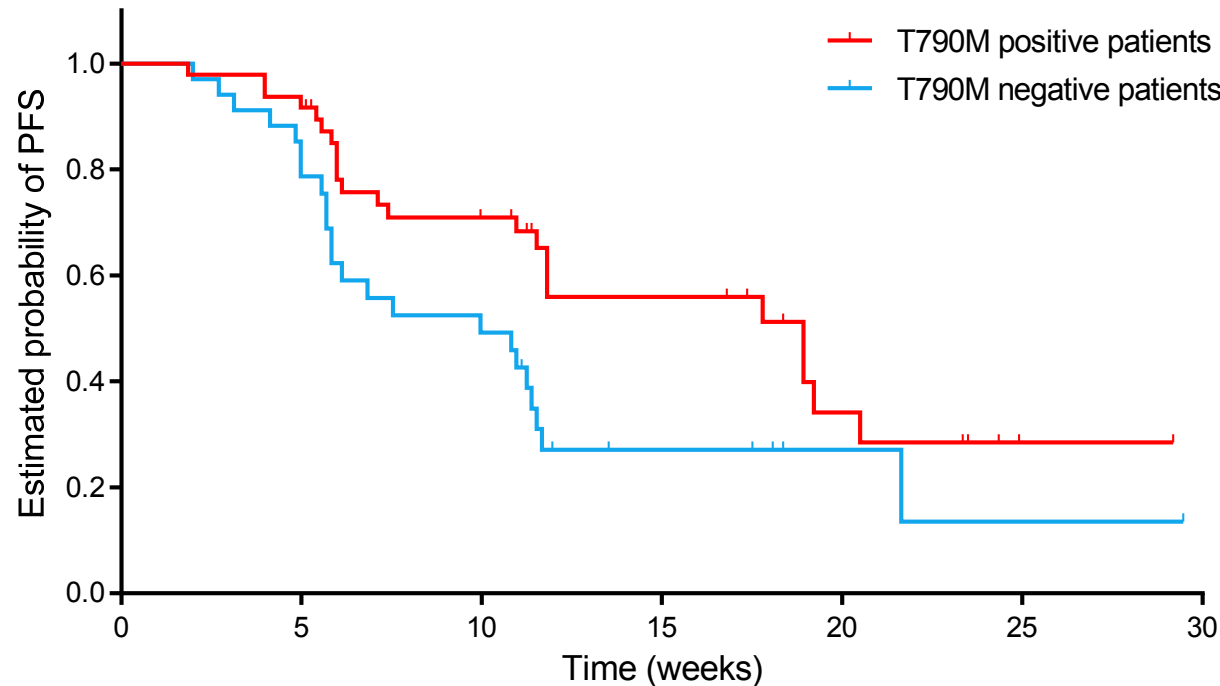
Response rate	11.8%
Disease control rate	55.9%

## Best Overall Response: Expansion Part

	T790M (+) patients			T790M (-) patients		
	Arm A (N=27)	Arm B (N=21)	Total (N=48)	Arm A (N=15)	Arm B (N=19)	Total (N=34)
<b>Partial response</b>	<b>8</b>	<b>6</b>	<b>14</b>	<b>2</b>	<b>2</b>	<b>4</b>
<b>Confirmed</b>	7	5	12	1	2	3
<b>Unconfirmed</b>	1	1	2	1		1
<b>Stable disease</b>	10	12	22	6	9	15
<b>Progressive disease</b>	9	3	12	7	8	15
<b>Response rate</b>	<b>29.6%</b>	<b>28.6%</b>	<b>29.2%</b>	<b>13.3%</b>	<b>10.5%</b>	<b>11.8%</b>
<b>Disease control rate</b>	66.7%	85.7%	75.0%	53.3%	57.9%	55.9%

# Progression-Free Survival

## : Expansion part (T790M+ versus T790M-)



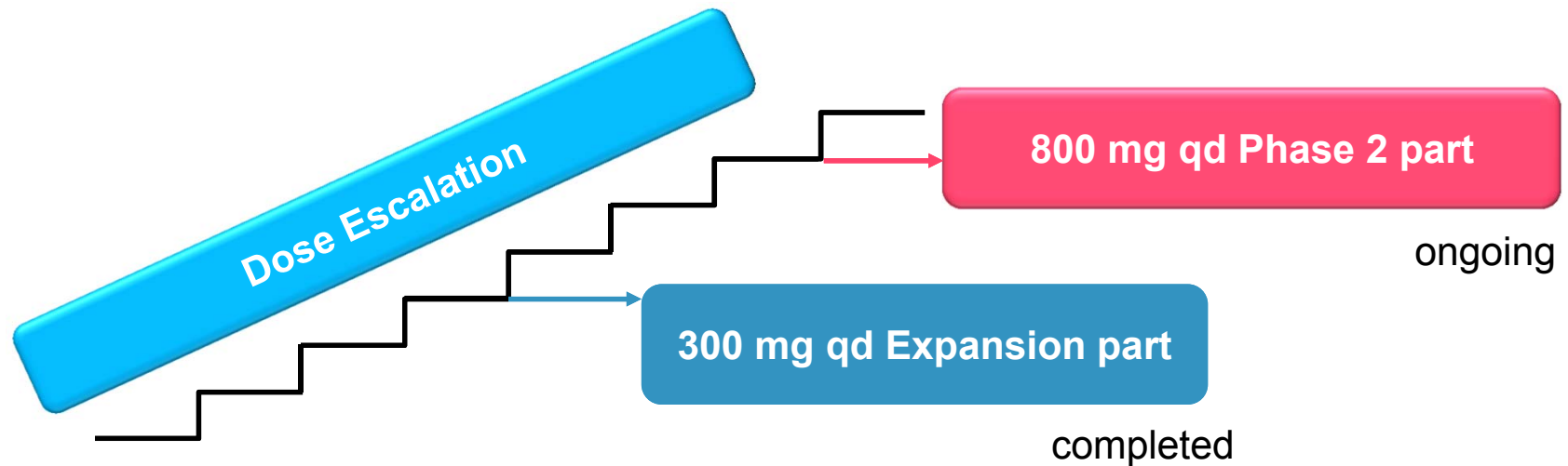
	T790M status	
	Positive (N=48)	Negative (N=34)
Number of events, n (%)	23 (47.9)	23 (67.7)
Median PFS, weeks, [95% CI]	<b>18.9</b> (11.5, 20.5)	<b>10.0</b> (5.7, 11.5)

# Conclusions

- HM61713 is well tolerated in advanced NSCLC patients with EGFR mutations who had received EGFR TKIs
- Promising efficacy was observed in patients who had progressed on prior EGFR TKIs within 4 weeks (arm A) or before 4 weeks or more (arm B) in the 300 mg expansion cohort
- The efficacy was more prominent in T790M positive tumors (ORR 29.2%, DCR 75.0%) than in T790M negative (ORR 11.8%, DCR 55.9%)

# Current Clinical Development

- The phase 2 part is ongoing at the dose of 800 mg qd





**Thank you for your attention !**