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A Randomized, Multi-Center, Double-Blind Phase II Study of Fruquintinib in Patients with Advanced Non-Small Cell Lung Cancer (NCT02590965)

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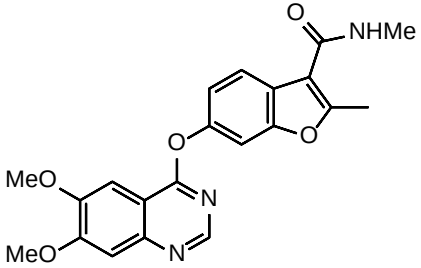
Disclosure

- Leading principal investigator (PI) of fruquintinib phase II clinical trial in lung cancer sponsored by Hutchison MediPharma (NCT02590965);
- Received research support from AstraZeneca, Boehringer Ingelheim, Hutchison MediPharma and Roche;
- Received speaker fees from AstraZeneca, Eli Lilly, Roche, and Sanofi;
- An advisor of AstraZeneca, Boehringer Ingelheim, Hutchison MediPharma, and Roche.

Background

- Lung cancer is the leading cause of cancer-related deaths globally with a poor survival rate.[1]
- Few targeted therapies are available for patients who fail two lines of standard chemotherapy.
- Fruquintinib is a potent and highly selective oral VEGFR inhibitor and demonstrated good anti-tumor activity against NSCLC.[2]
- In Phase I clinical studies, fruquintinib demonstrated encouraging anti-tumor activity including NSCLC. The RP2D was determined to be 5 mg once daily for 3 weeks on and 1 week off.[3]



Molecular formula: $C_{21}H_{19}N_3O_5$

Molecular weight: 393.40

NSCLC: non-small cell lung cancer; RP2D: recommended Phase 2 dose; VEGFR: vascular endothelial growth factor receptor

1. Torre, LA, et al., Global cancer statistics, 2012; 2. Sun Q, et al., Cancer Biol. & Therapy, 15:12, 1635-1645, 2014; Cao J, et al., Cancer Chemther Pharmacol., 78:259-269, 2016

Study Design

- Stage IIIB/IV histologically or cytologically confirmed non-squamous NSCLC
- Failed 2 prior chemotherapy regimens
- Age 18-75
- ECOG PS 0-1

N=91

→ R 2:1

→ Fruquintinib + BSC (5 mg QD po) 3 weeks on/1 week off N=61 → PD

→ Placebo + BSC 3 weeks on/1 week off N=30 → PD

Primary Endpoint

- PFS

Secondary Endpoints

- ORR
- DCR
- OS
- Safety

Stratification by EGFR status: mutant vs. wild type vs. unknow

Tumor assessment: 4 week, 8 week, then every 8 weeks thereafter

BSC (best support care); DCR (Disease control rate); EGFR (epidermal growth factor receptor)
ORR (Objective response rate); OS (overall survival); PD (progressive disease); PFS (progression free survival)

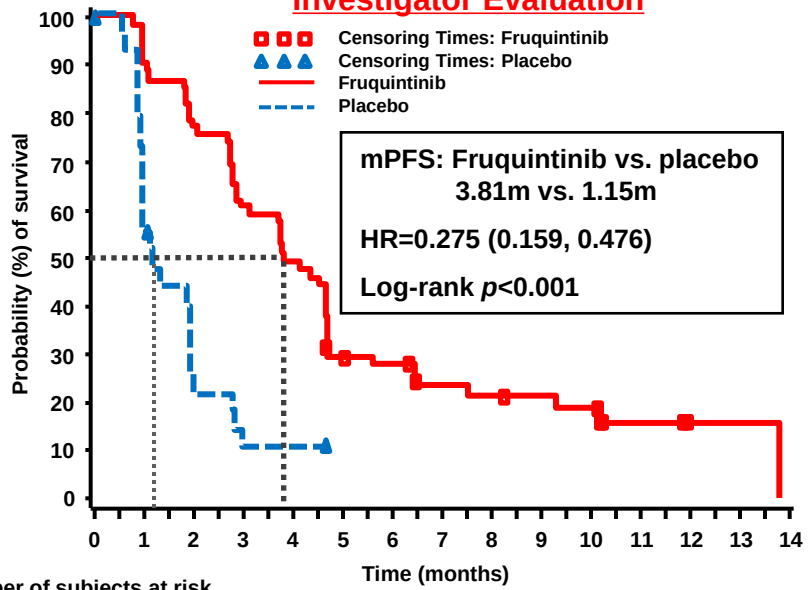
Patient Baseline Characteristics

Baseline Characteristics (ITT, N=91)		Fruquintinib (N=61) n (%)	Placebo (N=30) n (%)
Age in years, median (range)		55 (36,68)	56.5 (34,73)
Age	<65 years ≥65 years	54 (88.5) 7 (11.5)	24 (80.0) 6 (20.0)
Gender	Male Female	34 (55.7) 27 (44.3)	12 (40.0) 18 (60.0)
ECOG PS	0 1	4 (6.6) 57 (93.4)	1 (3.3) 29 (96.7)
EGFR status	Mutant Wild type Unknown	30 (49.2) 27 (44.3) 4 (6.6)	15 (50.0) 13 (43.3) 2 (6.7)
Prior EGFR inhibitor treatment	Yes No	23 (37.7) 38 (62.3)	13 (43.3) 17 (56.7)

ITT (intent to treat)

Progression Free Survival

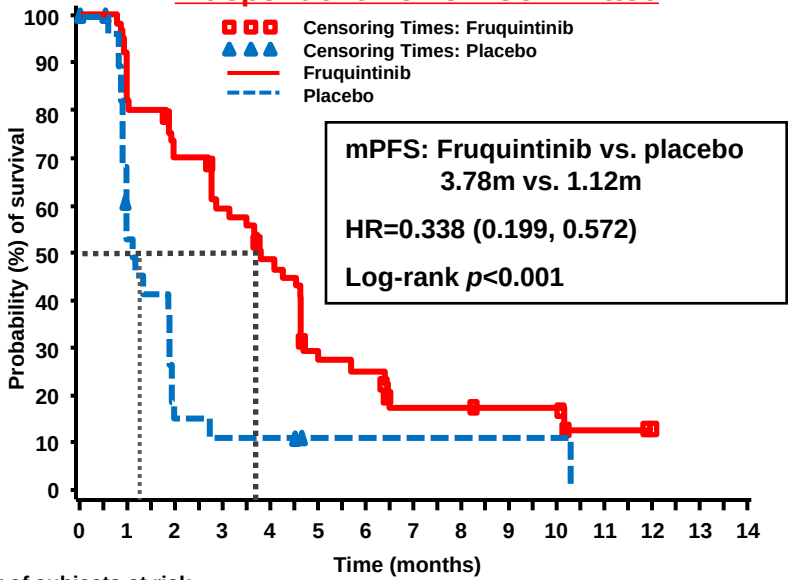
Investigator Evaluation



Number of subjects at risk

Fruquintinib	61	55	47	37	30	17	15	10	9	8	7	3	1	1	0
Placebo	30	16	6	3	3	0	0	0	0	0	0	0	0	0	0

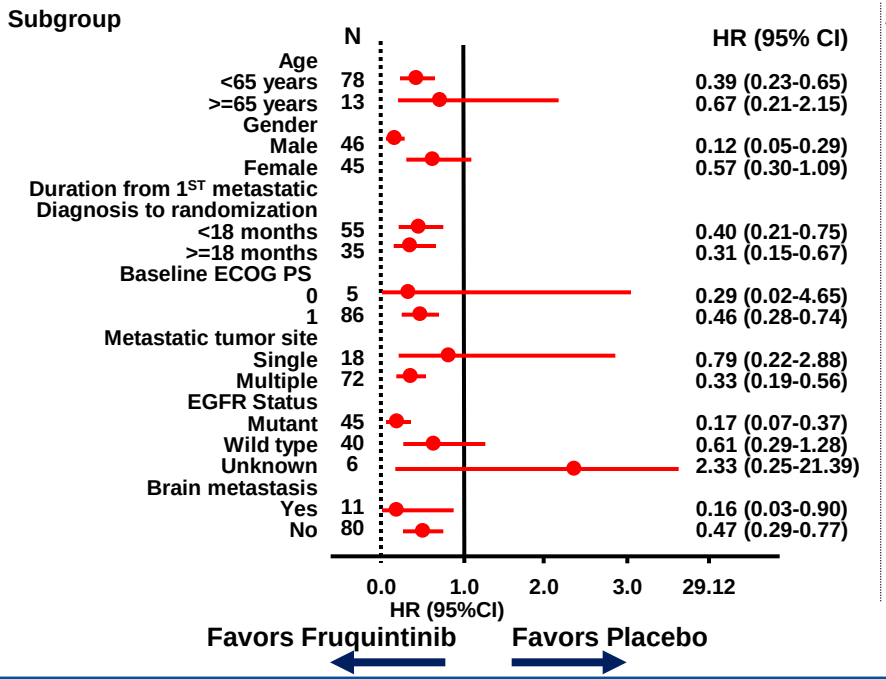
Independent Review Committee

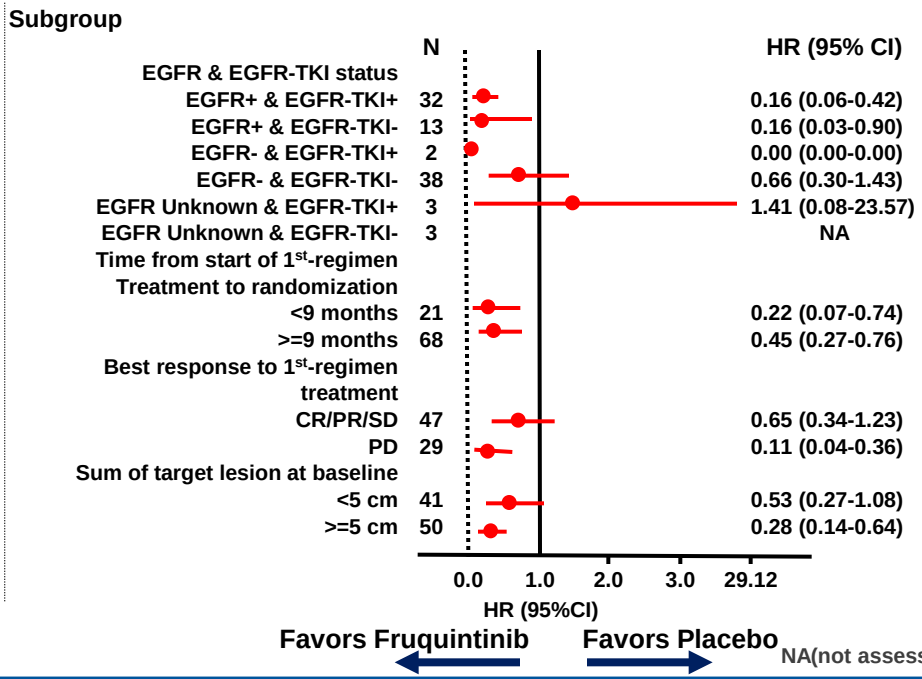


Number of subjects at risk

Fruquintinib	61	55	42	33	26	12	11	6	6	5	5	2	0	0	0
Placebo	30	14	4	3	3	1	1	1	1	1	1	0	0	0	0

PFS Subgroup Analysis



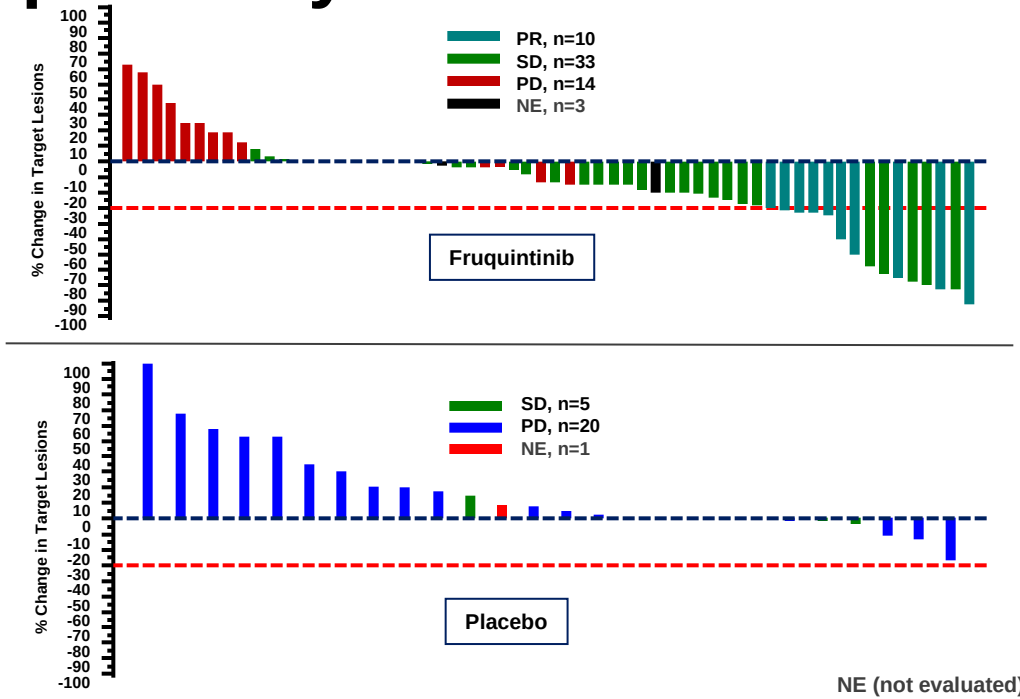


NA(not assessable)

Best Tumor Response by Treatment

Response Rate	Fruquintinib (N=61) n (%)	Placebo (N=30) n (%)
Complete response (CR)	0	0
Partial response (PR)	10 (16.4)	0
Stable disease (SD)	33 (54.1)	5 (16.7)
Progressive disease (PD)	14 (23.0)	20 (66.7)
Overall response rate (ORR)*	10 (16.4)	0
Disease control rate (DCR)**	43 (70.5)	5 (16.7)

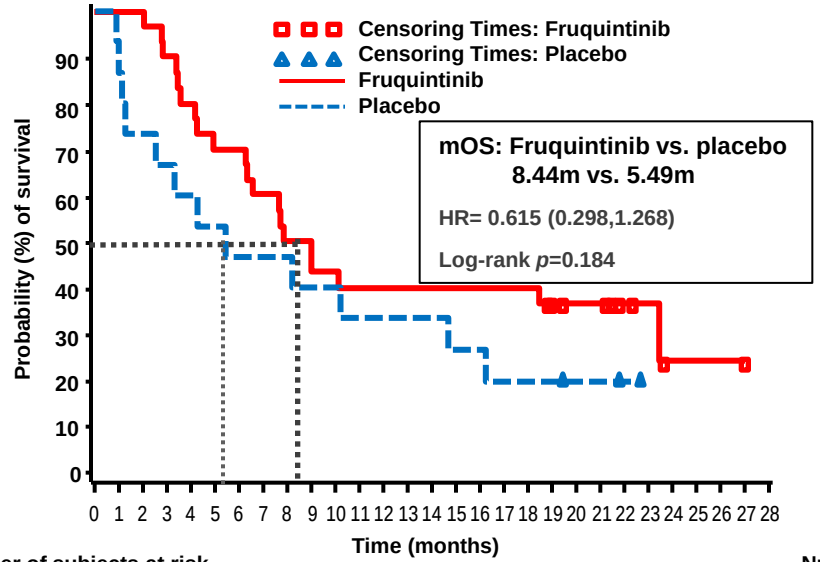
* p=0.021; **p<0.001.



NE (not evaluated)

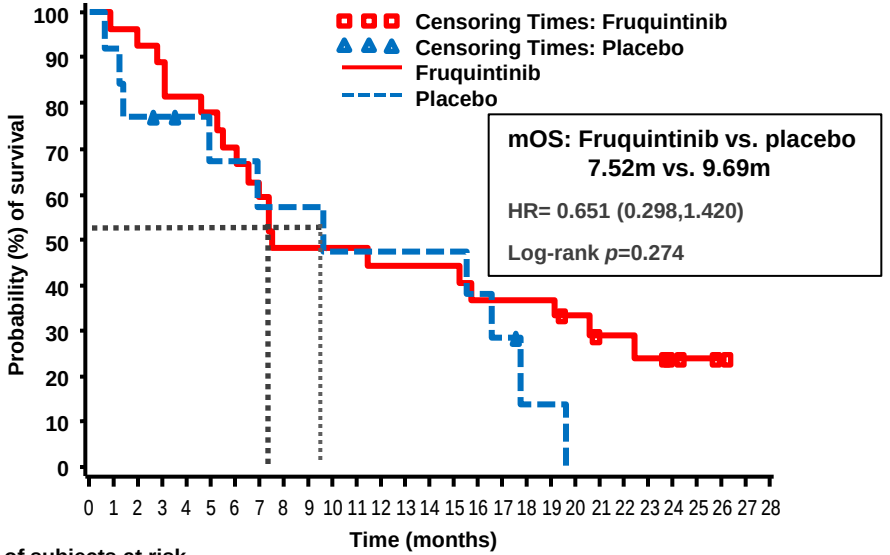
Overall Survival

EGFR Mutant (N=45)



Number of subjects at risk																											
Fruquintinib	30	30	30	27	24	21	21	18	15	15	13	12	12	12	12	12	12	12	10	8	8	4	3	1	1	1	1	0
Placebo	15	14	11	10	9	8	7	7	7	6	6	5	5	5	4	4	3	3	3	2	2	1	0	0	0	0	0	0

EGFR Wild Type (N=40)



Number of subjects at risk																											
Fruquintinib	27	26	25	24	22	21	19	16	13	13	13	13	12	12	12	12	10	10	10	8	6	6	5	3	2	1	0	0
Placebo	13	12	10	9	8	7	7	6	6	6	5	5	5	5	5	5	4	3	1	1	0	0	0	0	0	0	0	0

Treatment-Emergent Adverse Event Summary

Overview of TEAE	Fruquintinib (N=61) n (%)	Placebo (N=30) n (%)
at least one TEAE	61 (100)	27 (90.0)
at least one SAE	8 (13.1)	4 (13.3)
at least one Grade3 TEAE	23 (37.7)	6 (20.0)
at least one Grade4 TEAE	4 (6.6)	2 (6.7)
at least one Grade5 TEAE	3 (4.9)	2 (6.7)
at least one related TEAE	59 (96.7)	22 (73.3)
at least one TEAE leading to dose interruption	9 (14.8)	0
at least one TEAE leading to dose reduction	8 (13.1)	0
at least one TEAE leading to treatment discontinuation	6 (9.8)	1 (3.3)

Treatment-Emergent Adverse Event

TEAEs (overall rate > 10%)	Fruquintinib (N=61) n (%)			Placebo (N=30) n (%)		
	Grade 1-2	Grade 3-4	Total *	Grade 1-2	Grade 3-4	Total*
At least one TEAE	38 (62.3)	20 (32.8)	61 (100)	19 (63.3)	6 (20.0)	27 (90.0)
Palmar-plantar erythrodysaesthesia syndrome	26 (42.6)	3 (4.9)	29 (47.5)	0	0	0
Proteinuria	19 (31.1)	1 (1.6)	20 (32.8)	5 (16.7)	0	5 (16.7)
Hypertension	9 (14.8)	5 (8.2)	14 (23.0)	0	1 (3.3)	1 (3.3)
Blood pressure increased	4 (6.6)	2 (3.3)	6 (9.8)	0	0	0
Fatigue	11 (18.0)	2 (3.3)	13 (21.3)	5 (16.7)	0	5 (16.7)
Blood thyroid stimulating hormone increased	17 (27.9)	0	17 (27.9)	0	0	0
Vomiting	8 (13.1)	0	8 (13.1)	8 (26.7)	0	8 (26.7)
Dysphonia	15 (24.6)	0	15 (24.6)	1 (3.3)	0	1 (3.3)
Cough	11 (18.0)	1 (1.6)	12 (19.7)	4 (13.3)	0	4 (13.3)
Nausea	10 (16.4)	0	10 (16.4)	5 (16.7)	0	5 (16.7)
Diarrhoea	13 (21.3)	1 (1.6)	14 (23.0)	1 (3.3)	0	1 (3.3)
Constipation	9 (14.8)	0	9 (14.8)	5 (16.7)	0	5 (16.7)
Mouth ulceration	12 (19.7)	1 (1.6)	13 (21.3)	0	0	0
Aspartate aminotransferase increased	12 (19.7)	0	12 (19.7)	1 (3.3)	0	1 (3.3)
Decreased appetite	7 (11.5)	0	7 (11.5)	5 (16.7)	0	5 (16.7)
Weight decreased	9 (14.8)	1 (1.6)	10 (16.4)	2 (6.7)	0	2 (6.7)
Back pain	8 (13.1)	0	8 (13.1)	2 (6.7)	0	2 (6.7)

*Grade 5 TEAEs: 3 in Fruquintinib and 2 in placebo.

Conclusion

- Fruquintinib met the primary endpoint and significantly improved progression free survival compared with placebo in 3rd line advanced non-squamous NSCLC.
- Fruquintinib demonstrated a favorable trend in improving overall survival in this study.
- Fruquintinib was well tolerated with an acceptable safety profile in this study
- A Phase III study is ongoing to confirm the survival benefit in 3rd line advanced non-squamous NSCLC.

Acknowledgment

- We would like to thank all patients and their families who participated in this trial.
- We would like to thank all investigators, study coordinators and the entire project team.
- We would like to acknowledge the sponsor for this trial: Hutchison MediPharma Limited.