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FURLONG: Furmonertinib versus gefitinib in treatment-naïve *EGFR* mutated non-small cell lung cancer: a randomized, double-blind, multi-center, phase III study

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Disclosure information

I have nothing to disclose.

FURLONG Study Design

A randomized, double-blind, multi-center phase III study conducted in 55 hospitals in mainland China

Key inclusion criteria:
- age≥18
- ECOG PS 0/1
- Locally advanced or metastatic adenocarcinoma
- *EGFR* mutation positive detected with tissue by central lab
- No prior anti-tumor therapy
- Asymptomatic CNS metastases allowed

Randomized 1:1

N=358

Furmonertinib 80mg QD (n=178)

Gefitinib 250mg QD (n=180)

Treatment until:
- Disease progression
- Intolerable toxicity
- Initiation of new therapy
- Withdrawal of consent

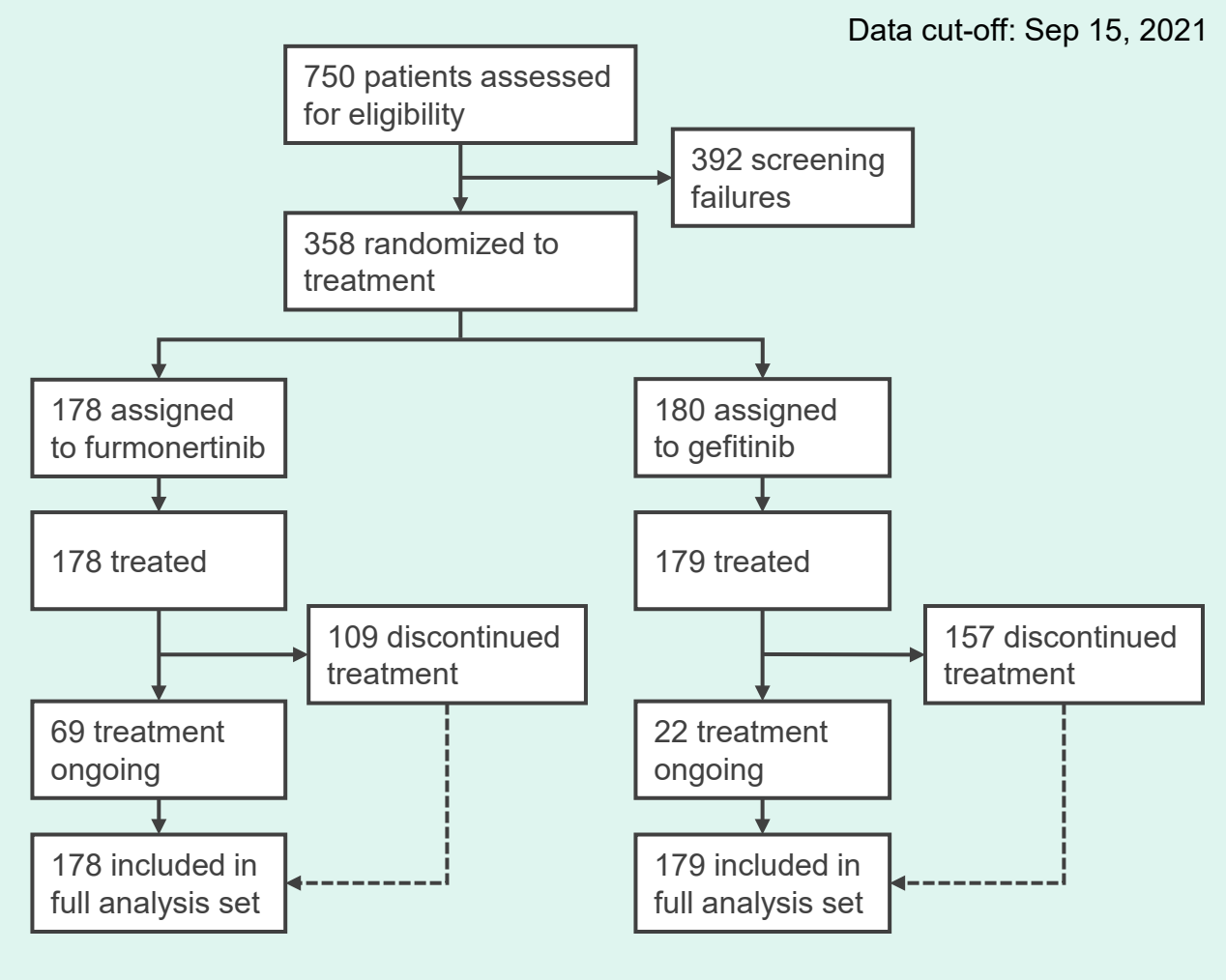
Stratification factors: *EGFR* mutations（Ex19Del vs L858R）, CNS metastases（yes vs no）

Primary endpoint: PFS (assessed by IRC)

Secondary endpoints: ORR, DCR, DOR, OS, DepOR, TTP, safety, PROs

ECOG: Eastern Cooperative Oncology Group; PS: performance status; EGFR: epidermal growth factor receptor; CNS: central nervous system; IRC: independent review committee; PFS: progression-free survival; ORR: objective response rate; DCR: disease control rate; DOR: duration of response; OS: overall survival; DepOR: depth of response; TTP: time to progression; PRO: patient-reported outcome.

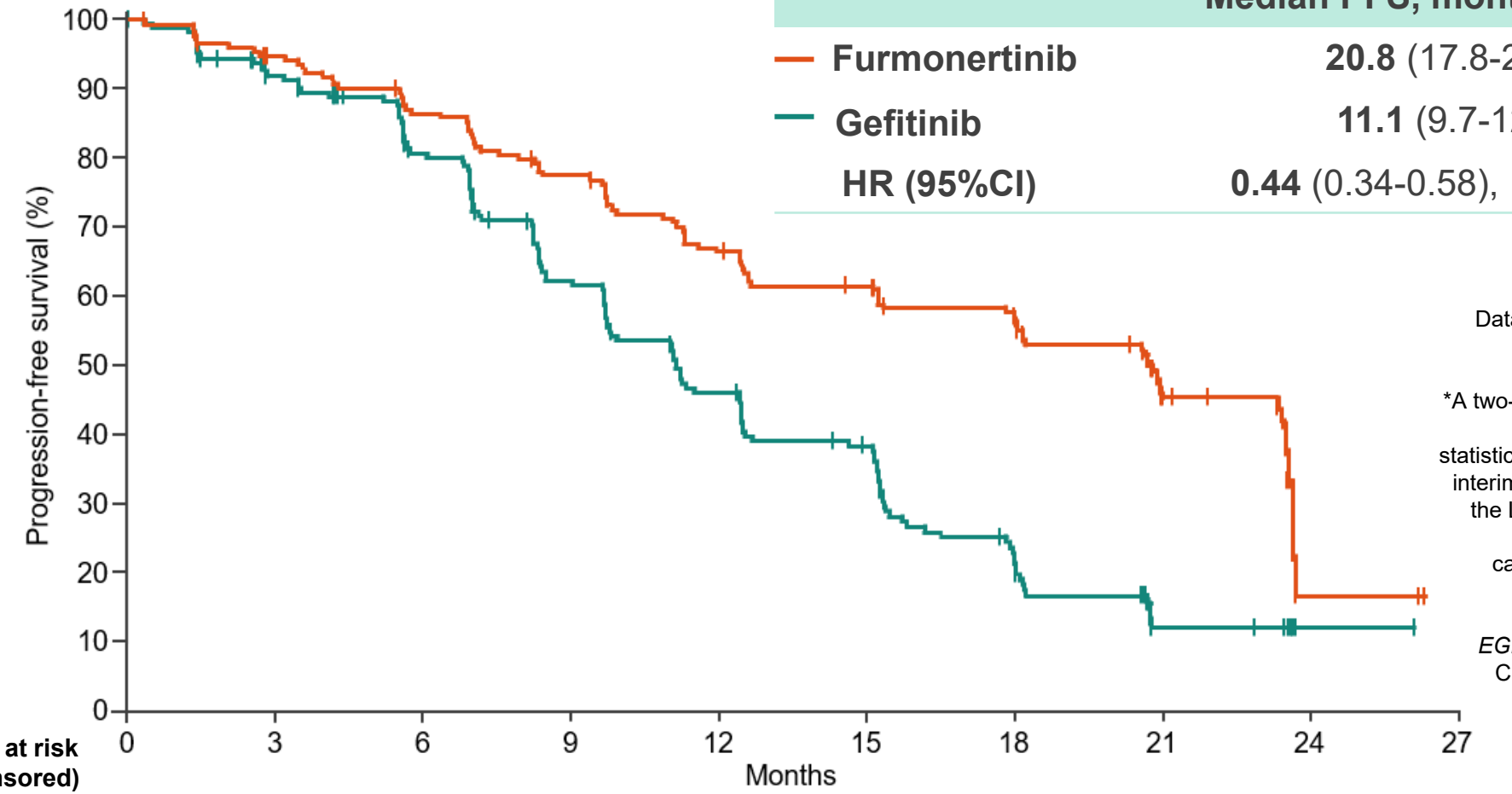
Trial profile & baseline characteristics



Characteristics, data are median (range) or n (%)		Furmonertinib (n=178)	Gefitinib (n=179)
Age	**Median**	59 (31-81)	60 (32-83)
Sex	**Female**	116 (65%)	111 (62%)
	Male	62 (35%)	68 (38%)
ECOG PS	**0**	39 (22%)	28 (16%)
	1	138 (76%)	151 (84%)
	2	1 (1%)	0
***EGFR* mutation**	**Ex19Del**	91 (51%)	92 (51%)
	L858R	87 (49%)	87 (49%)
Smoking history	**Yes**	41 (23%)	44 (25%)
	No	137 (77%)	135 (75%)
Disease stage	**III**	10 (6%)	7 (4%)
	IV	168 (94%)	172 (96%)
CNS metastases	**Yes**	63 (35%)	58 (32%)
	No	115 (65%)	121 (68%)

ECOG: Eastern Cooperative Oncology Group; PS: performance status; EGFR: epidermal growth factor receptor; CNS: central nervous system

Primary endpoint: Progression-free survival



	Median PFS, months (95%CI)
Furmonertinib	**20.8** (17.8-23.5)
Gefitinib	**11.1** (9.7-12.5)
HR (95%CI)	**0.44** (0.34-0.58), **p<0.0001***

Data cut-off: Sep 15, 2021
Maturity: 62%

*A two-sided p-value of 0.049 was considered to be statistically significant after an interim analysis according to the Lan-DeMets approach. HR and 95% CIs were calculated using the Cox proportional hazards model, stratified with *EGFR* mutation types and CNS metastases status.

Number at risk (number censored)	0	3	6	9	12	15	18	21	24	27
Furmonertinib	178 (0)	160 (9)	144 (11)	128 (12)	109 (13)	99 (15)	87 (20)	30 (63)	2 (82)	0 (84)
Gefitinib	179 (0)	151 (14)	125 (22)	93 (26)	67 (28)	53 (31)	28 (33)	7 (44)	1 (50)	0 (51)

PFS subgroup analysis

		Furmonertinib n/N	Gefitinib n/N	HR (95%CI)	p value
Age (years)	<65	60/118	89/114	0.36 (0.26, 0.51)	<0.0001
	≥65	34/60	39/65	0.68 (0.43, 1.09)	0.1088
Sex	Male	33/62	56/68	0.39 (0.25, 0.61)	<0.0001
	Female	61/116	72/111	0.49 (0.35, 0.70)	<0.0001
ECOG PS	0	16/39	23/28	0.33 (0.17, 0.63)	0.0005
	1	78/138	105/151	0.49 (0.36, 0.66)	<0.0001
	2	0/1	0/0	NE (NE, NE)	NE
Smoking history	Yes	24/41	33/44	0.53 (0.30, 0.92)	0.0232
	No	70/127	95/135	0.42 (0.31, 0.58)	<0.0001
EGFR mutation	Ex19del	38/91	60/92	0.35 (0.23, 0.53)	<0.0001
	L858R	56/87	68/87	0.54 (0.37, 0.77)	0.0006
CNS Metastases*	Yes	36/63	42/58	0.50 (0.32, 0.80)	0.0028
	No	56/115	86/121	0.42 (0.30, 0.59)	<0.0001
Overall		94/178	128/179	0.45 (0.34, 0.59)	<0.0001

Data cut-off: Sep 15, 2021

*CNS metastases were determined from baseline data for the CNS lesion site, medical history, surgery, or radiotherapy, all reported by investigators.
HRs and p values were estimated with unstratified Cox proportional hazards model and unstratified log-rank test.

Summary of secondary endpoints

Endpoint	Furmonertinib n=178	Gefitinib n=179	OR / HR	p-value
ORR (95%CI)	89% (83-93)	84% (78-89)	1.50 (0.80-2.83)	0.2078
DCR (95%CI)	96% (91-98)	93% (89-97)	1.56 (0.61-3.98)	0.3551
DOR, median (95%CI)	19.7 months (16.8-22.1)	10.5 months (8.5-11.3)	0.39 (0.29-0.52)	**<0.0001**
DepOR, median (range)	61.1% (-61.1, 91.4)	55.9% (-56.0, 100)	-	0.0852
TTP, median (95%CI)	20.9 months (18.0-23.5)	11.2 months (9.7-12.5)	0.41 (0.31-0.55)	**<0.0001**
OS*, median (95%CI)	NR	NR	0.94 (0.65-1.36)	0.7446

*In the gefitinib group, 43% patients had received third-generation EGFR-TKIs after progression. All the endpoints above were assessed by IRC (independent review center) excluding OS. Maturity of OS was 32%. ORR: objective response rate; DCR: disease control rate; DOR: duration of response; OS: overall survival; DepOR: depth of response; TTP: time to progression; NR: not reached; HR: hazard ratio. OR: odds ratio.

Safety summary

Median duration of exposure: 18.3 months with furmonertinib and 11.2 months with gefitinib

Treatment-emergent adverse events (TEAEs)

	Furmonertinib (n=178)	Gefitinib (n=179)
Any AE	178 (100%)	177 (99%)
Grade ≥3 AE	62 (35%)	60 (34%)
SAE	44 (25%)	29 (16%)
Dose interruption	27 (15%)	34 (19%)
Dose reduction	5 (3%)	6 (3%)
Discontinuation	11 (6%)	7 (4%)
AE with outcome of death	10 (6%)	3 (2%)

Treatment-related adverse events (TRAEs)

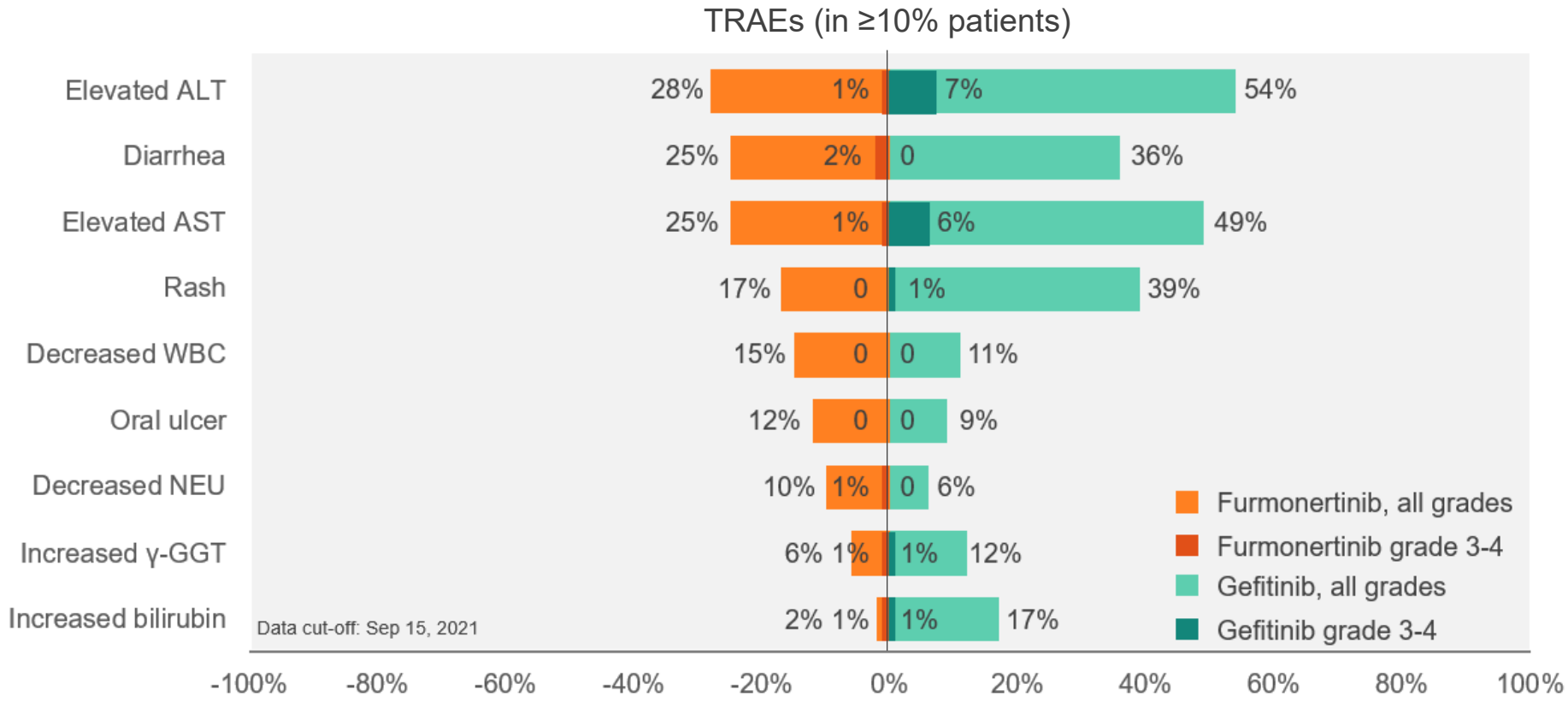
	Furmonertinib (n=178)	Gefitinib (n=179)
Any TRAE	160 (90%)	170 (95%)
Grade ≥3 TRAE	**20 (11%)**	**32 (18%)**
TRSAE	10 (6%)	11 (6%)
Dose interruption	24 (13%)	28 (16%)
Dose reduction	5 (3%)	NA*
Discontinuation	6 (3%)	4 (2%)
TRAE with outcome of death	0	0

*6 patients (3%) had dose reduction in the gefitinib group, but only furmonertinib placebo was reduced because dose reduction of gefitinib was not allowed according to the prescribing information of gefitinib. TRAE: treatment-related adverse event; TEAE: treatment-emergent adverse event; AE: adverse event. TRSAE: treatment-related serious adverse event. Treatment-related adverse events were judged by investigators.

Data cut-off: Sep 15, 2021

The most frequent treatment-related adverse events

Median duration of exposure: 18.3 months with furmonertinib and 11.2 months with gefitinib



AEs of interest:

- interstitial lung disease (ILD) was recorded in 1 patient in each group (grade 1 in furmonertinib group, grade 2 in gefitinib group)
- QT prolongation was recorded in 9% and 7% patients in furmonertinib group and gefitinib group, respectively.

Treatment-related adverse events were judged by investigators. Treatment-related adverse events of ≥10% in either group are listed. ALT: alanine aminotransferase; AST: aspartate aminotransferase; WBC: white blood cell count; NEU: neutrophil count; GGT: glutamyltransferase. TRAE: treatment-related adverse events/.

Conclusions

- In this randomized, double-blind, phase III FURLONG study, furmonertinib was associated with a significant longer PFS compared with gefitinib in untreated *EGFR* mutated NSCLC (20.8 vs 11.1 months, HR 0.44). This benefit is consistent across prespecified subgroups.

- Despite a longer duration of exposure, furmonertinib showed an overall favorable safety profile versus gefitinib, with relatively lower frequency of grade ≥3 TRAEs (11% vs 18%), diarrhea, rash and liver abnormalities.

- These results suggest that furmonertinib is a potential preferred first-line therapy in *EGFR* mutated Chinese NSCLC patients compared with gefitinib.

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	Beijing Chest Hospital	Taihe Hospital	The First People's Hospital of Changzhou
Harbin Medical University Cancer Hospital	Affiliated Hospital of Hebei University	The First Affiliated Hospital Of Guangzhou Medical University	The First Affiliated Hospital of Zhengzhou University
Hunan Cancer Hospital	The First Hospital of Jilin University	Army Medical Center of PLA	PLA Cancer Centre of Nanjing Bayi Hospital
Xuzhou Central Hospital	Affiliated Hospital of Nantong University	Weifang People's Hospital	Zhejiang Cancer Hospital
The First Hospital of China Medical University	Tianjin Medical University Cancer Institute & Hospital	Zhongshan Hospital	Beijing Cancer Hospital (ZW)
The People's Hospital of Guangxi Zhuang Autonomous Region	The First Affiliated Hospital of Xinxiang Medical University	Henan Province People's Hospital	Beijing Cancer Hospital (JF)
Cancer Hospital of Xinjiang Medical University	Shanxi Province People’s Hospital	Nanjing First Hospital	Affiliated Hospital of Guilin Medical University
The Affiliated Hospital of Xuzhou Medical College	The Second People’s Hospital of Neijiang	The Affiliated Hospital of Inner Mongolia Medical University	The Second Affiliated Hospital Zhejiang University School of Medicine
Nantong Cancer Hospital	General Hospital of Ningxia Medical University	Lishui City People's Hospital	Sir Run Run Shaw Hospital Zhejiang University School of Medicine
The First Affiliated Hospital of Wenzhou Medical University	Henan Cancer Hospital	The Second Affiliated Hospital of Nanchang University	People's Hospital of Xinjiang Uygur Autonomous Region
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