Beta Pharma
Better Medicine Better Life

BPI-7711
Presentation and Discussion
in
NACLC 2019

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BPI-7711 Phase I study results presented by Dr. Yuankai Shi

IASLC

2019 North America Conference on Lung Cancer

A Phase I Study of BPI-7711 in EGFR/T790M Mutation NSCLC

Yuankai Shi, MD, PhD

National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College
Beijing, China

Yuankai Shi[1], Jian Fang[2], Yongqian Shu[3], Donglin Wang[4], Huiqing Yu[4], Yanqiu Zhao[5], Liangming Zhang[6], Bo Zhu[7], Xingya Li[8], Gongyan Chen[9], Jianhua Shi[10], Rongsheng Zheng[11], Jian'an Huang[12], Sheng Yang[1], Jieran Long[2], Wen Gao[3], Michael Greco[13], Guoqiang Hu[14], Xiao Li[14]

[1] Cancer Hospital, Chinese Academy of Medical, Beijing/China. [2]Beijing Cancer Hospital, Beijing/China. [3]Jiangsu Province Hospital, Nanjing/China. [4]Chongqing Cancer Hospital, Chongqing/China. [5]Henan Cancer Hospital, Zhengzhou/China. [6]Yantai Yuhuangding Hospital, Yantai/China. [7]The Second Affiliated Hospital of Army Medical University, PLA, Chongqing/China. [8]The First Affiliated Hospital of Zhengzhou University, Zhengzhou/China. [9]Harbin Medical University Cancer Hospital, Harbin/China. [10]Shandong Linyi Tumor Hospital, Linyi/China. [11]The First Affiliated Hospital of Bengbu Medical College, Bengbu/China. [12]The First Affiliated Hospital of Soochow University, Suzhou/China. [13]Beta Pharma, Princeton, NJ/USA. [14]Beta Pharma, Shanghai/China.

DISCLOSURES

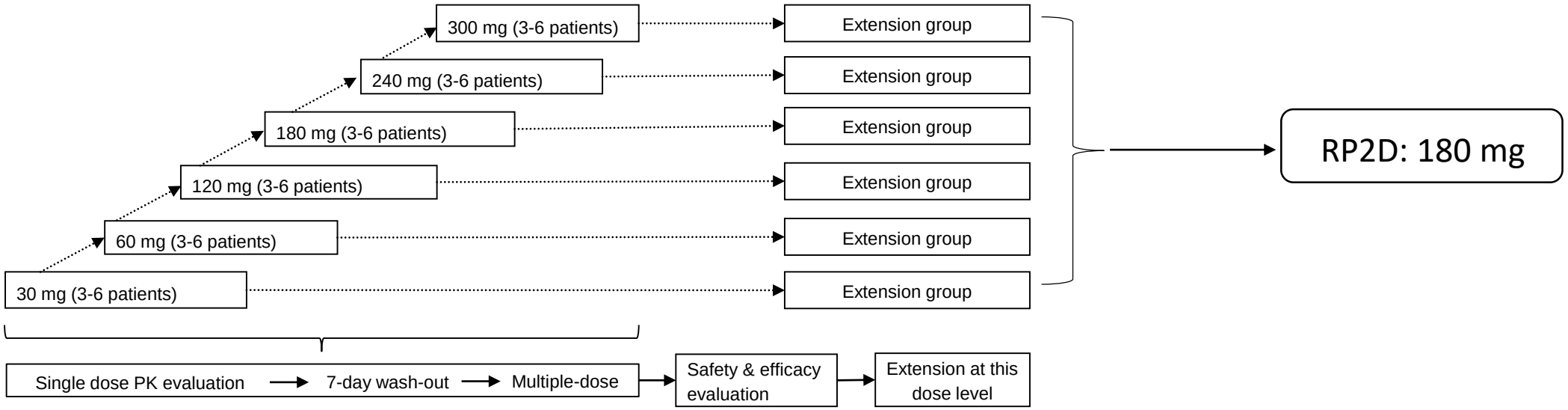
Commercial Interest	Relationship(s)
Beta Pharma	Principle Investigator

Background

- **BPI-7711 is a 3rd generation irreversible EGFR-TKI.**
- **This phase I study was conducted to determine the safety and efficacy of BPI-7711 in NSCLC patients with advanced or recurrent EGFR/T790M mutation progressed after 1st/2nd generation EGFR-TKI treatment (NCT03386955).**

Study Design

- Dose escalation + dose expansion design.
- BPI-7711 was orally administered at doses of 30 to 300 mg once daily.
- Treatment efficacy was evaluated every 6 weeks.
- First patient was dosed in September 11, 2017.



Demographic

- **As of July 15, 2019, 162 patients were enrolled. 43.8% of patients had brain metastasis at enrollment.**
- **All patients had prior exposure to first-generation EGFR-TKIs.**

	30 mg (N= 11)	60 mg (N= 6)	120 mg (N= 26)	180 mg (N= 83)	240 mg (N= 33)	300 mg (N= 3)	Total (N= 162)
Age (Years)							
Mean (SD)	51.7 (10.72)	56.0 (10.20)	54.3 (9.08)	58.2 (9.18)	58.2 (9.61)	55.7 (2.89)	57.0 (9.42)
Median	54	52.5	51	59	60	54	57
Min - Max	34.0 - 68.0	47.0 - 73.0	34.0 - 73.0	39.0 - 75.0	37.0 - 75.0	54.0 - 59.0	34.0 - 75.0
Sex, n (%)							
Male	4(36.4)	1(16.7)	10(38.5)	21(25.3)	15(45.5)	1(33.3)	52(32.1)
Female	7(63.6)	5(83.3)	16(61.5)	62(74.7)	18(54.5)	2(66.7)	110(67.9)
Prior EGFR-TKIs Regimen, n (%)							
Gefitinib	6(54.5)	2(33.3)	12(46.2)	43(51.8)	14(42.4)	1(33.3)	78(48.1)
Erlotinib	2(18.2)	0	2(7.7)	12(14.5)	9(27.3)	0	25(15.4)
Icotinib	3(27.3)	4(66.7)	12(46.2)	32(38.6)	12(36.4)	2(66.7)	65(40.1)
Brain metastasis, n (%)	5(45.5)	2(33.3)	12(46.2)	35(42.2)	16(48.5)	1(33.3)	71(43.8)
Bone metastasis, n (%)	4(36.4)	5(83.3)	9(34.6)	30(36.1)	17(51.5)	1(33.3)	66(40.7)

Efficacy (Independent Radiological Review Committee Review)

For all efficacy-evaluable patients (N=128):

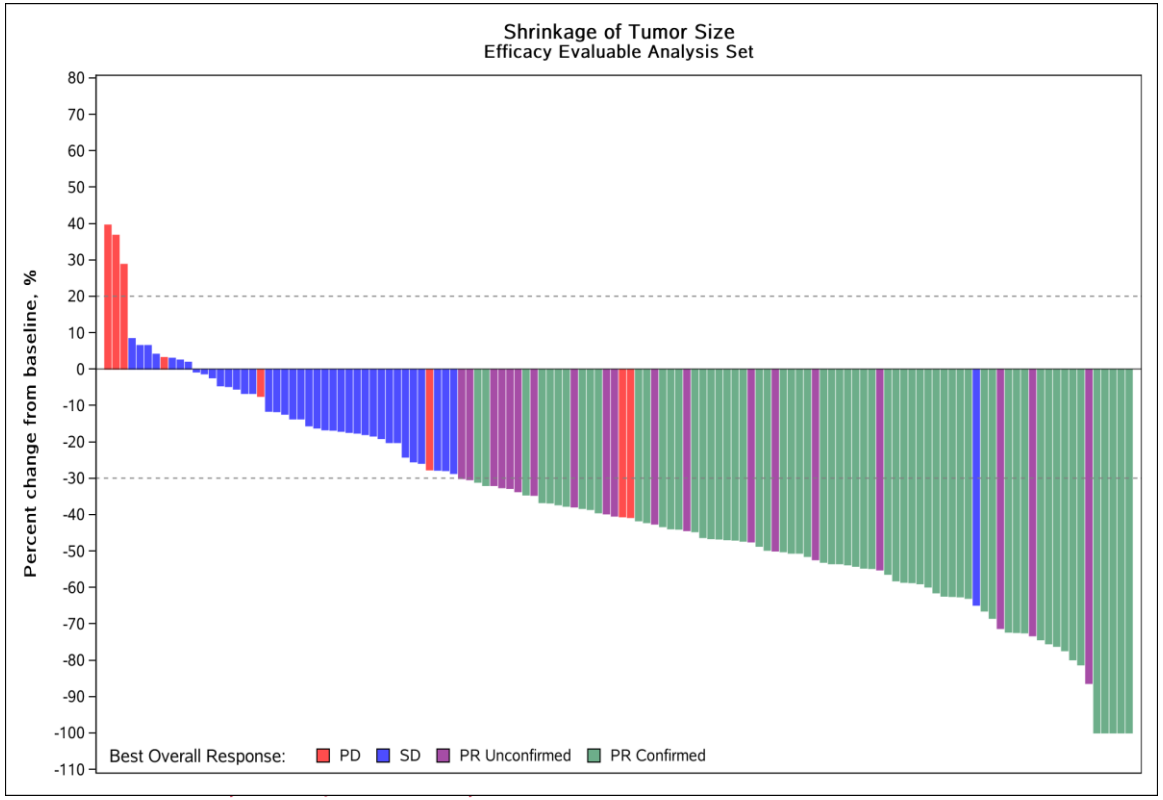
- **The ORR of all doses was 63.3%, DCR was 93.8%.**
- **For patients in 180 mg (RP2D) cohort, ORR was 73.1%, DCR was 96.2%.**

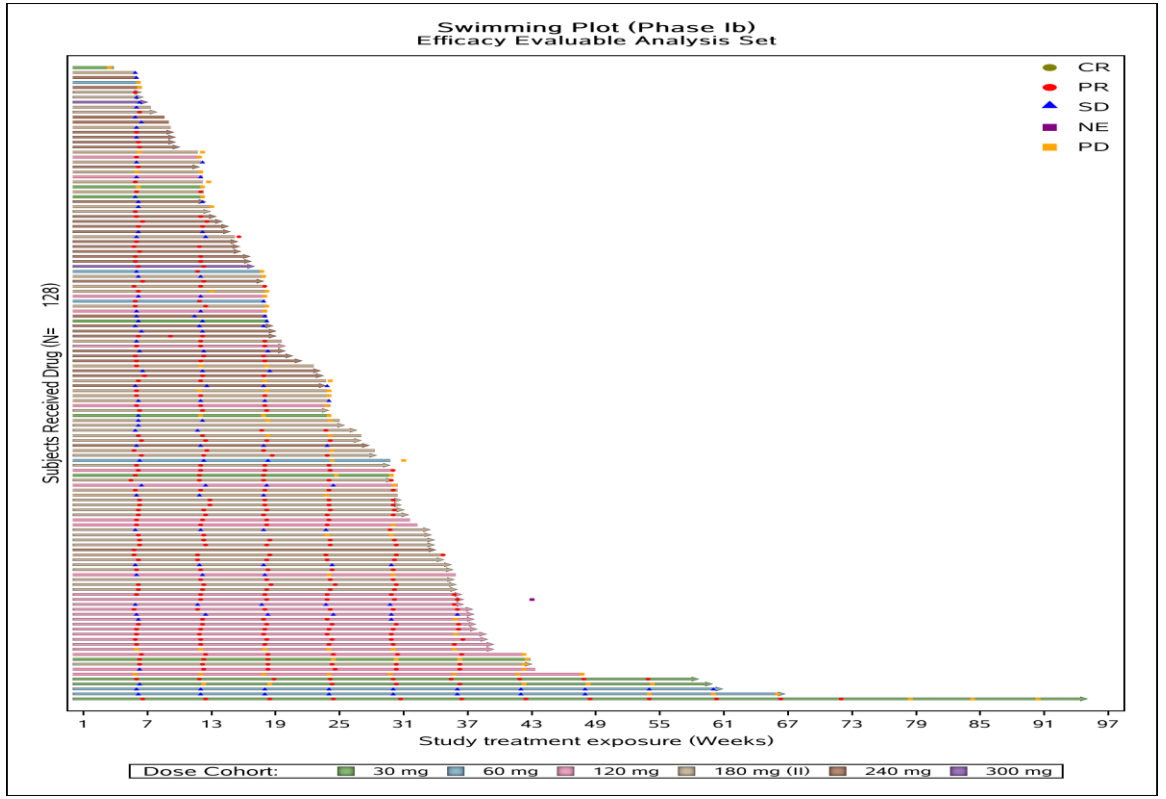
	30 mg (N= 10)	60 mg (N= 6)	120 mg (N= 26)	180 mg (N= 52)	240 mg (N= 32)	300 mg (N= 2)	Total (N= 128)
Best Overall Response, n (%)							
CR Confirmed	0	0	0	0	0	0	0
CR Unconfirmed	0	0	0	0	0	0	0
PR Confirmed	4(40.0)	1(16.7)	16(61.5)	29(55.8)	11(34.4)	1(50.0)	62(48.4)
PR Unconfirmed	0	1(16.7)	2(7.7)	9(17.3)	7(21.9)	0	19(14.8)
SD	4(40.0)	3(50.0)	6(23.1)	12(23.1)	13(40.6)	1(50.0)	39(30.5)
NE	0	0	0	0	0	0	0
PD	2(20.0)	1(16.7)	2(7.7)	2(3.8)	1(3.1)	0	8(6.3)
ORR, n (%)	4(40.0)	2(33.3)	18(69.2)	38(73.1)	18(56.3)	1(50.0)	81(63.3)
Confirmed ORR, n (%)	4(40.0)	1(16.7)	16(61.5)	29(55.8)	11(34.4)	1(50.0)	62(48.4)
DCR, n (%)	8(80.0)	5(83.3)	24(92.3)	50(96.2)	31(96.9)	2(100)	120(93.8)

Subgroup Analysis by Mutation Type	180 mg			Total		
	Ex19del (N= 34)	L858R (N= 17)	Others (N= 1)	Ex19del (N= 86)	L858R (N= 40)	Others (N= 2)
ORR, n (%)	28(82.4%)	10(58.8%)	0	63(73.3%)	18(45.0%)	0

Efficacy (Independent Radiological Review Committee Review)

- **Most patients achieved significant tumor shrinkage.**
- **The median time to response was 6.1 weeks.**
- **64.8% of the patients were still under treatment.**





Efficacy for Brain Metastases

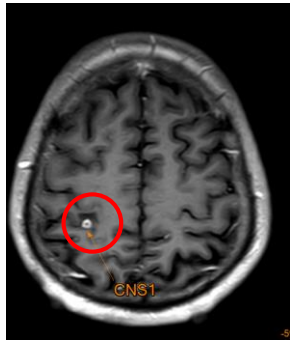
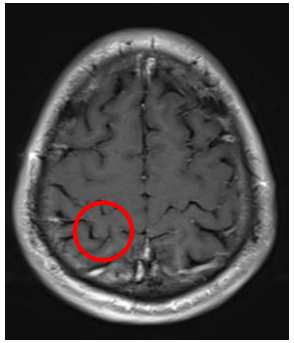
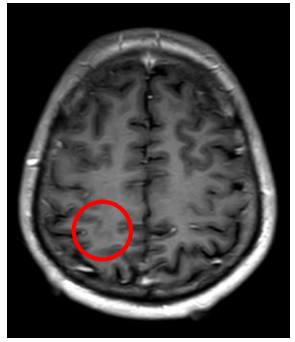
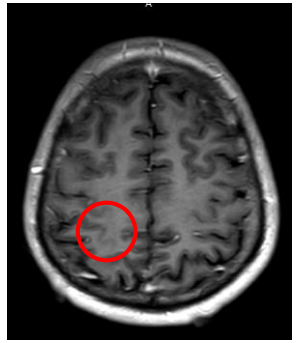
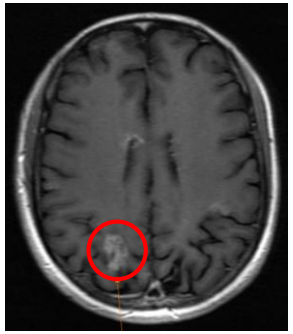
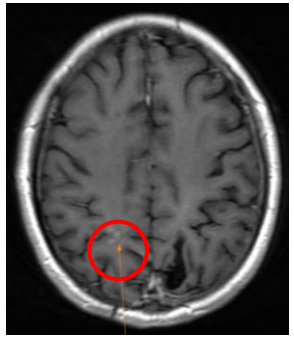
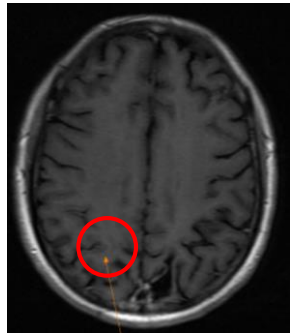
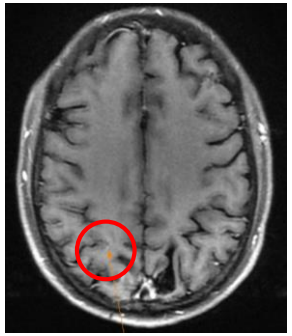
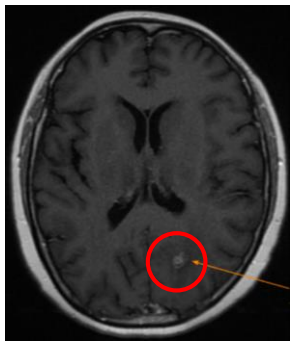
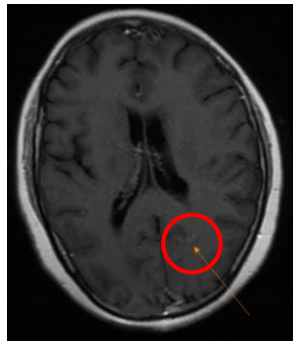
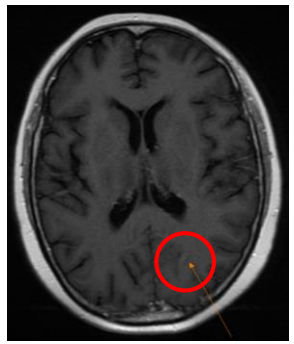
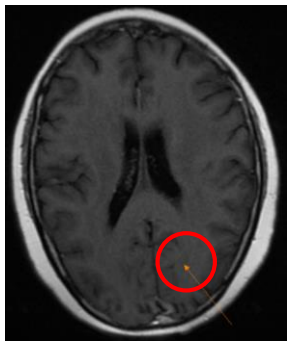
For 51 patients with Brain Metastases:

- **The Brain Metastases ORR of all doses was 35.3% and DCR was 96.1%.**
- **In 180 mg (RP2D) cohort, Brain Metastases ORR was 44% and DCR was 100%.**

	30 mg (N= 5)	60 mg (N= 2)	120 mg (N= 13)	180 mg (N= 25)	240 mg (N= 6)	Total (N= 51)
Best Overall Response, n (%)						
CR Confirmed	1(20.0)	1(50.0)	0	1(4.0)	0	3(5.9)
CR Unconfirmed	0	0	0	0	0	0
PR Confirmed	0	0	4(30.8)	7(28.0)	0	11(21.6)
PR Unconfirmed	0	0	0	3(12.0)	1(16.7)	4(7.8)
SD	2(40.0)	1(50.0)	9(69.2)	14(56.0)	5(83.3)	31(60.8)
NE	1(20.0)	0	0	0	0	1(2.0)
PD	1(20.0)	0	0	0	0	1(2.0)
ORR, n (%)	1(20.0)	1(50.0)	4(30.8)	11(44.0)	1(16.7)	18(35.3)
Confirmed ORR, n (%)	1(20.0)	1(50.0)	4(30.8)	8(32.0)	0	14(27.5)
DCR, n (%)	3(60.0)	2(100)	13(100)	25(100)	6(100)	49(96.1)

 # This analysis was based on radiographical response criteria of RANO-BM .

Durable Response of Brain Metastases

	Baseline	6-week	12-week	18-week
A 49yr male in 180 mg • 6-week: BM CR • 12-week: BM CR • 18-week: BM CR				
A 46yr female in 180 mg • 6-week: BM PR • 12-week: BM PR • 18-week: BM PR				
A 52yr female in 120 mg • 6-week: BM SD • 12-week: BM PR • 18-week: BM PR				

Safety (CTCAE 4.03)

- **No dose-limiting toxicity was observed and maximum tolerated dose was not reached.**
- **Grade ≥ 3 TEAEs were occurred in 17.3% of patients. 8.0% were treatment-related.**
- **SAEs were reported in 8.6% of patients. 1.2% were treatment-related.**

n (%)	30 mg (N= 11)	60 mg (N= 6)	120 mg (N= 26)	180 mg (N= 83)	240 mg (N= 33)	300 mg (N= 3)	Total (N= 162)
TEAE	11(100)	6(100)	22(84.6)	66(79.5)	30(90.9)	3(100)	138(85.2)
TEAE with Grade ≥ 3	2(18.2)	2(33.3)	5(19.2)	13(15.7)	6(18.2)	0	28(17.3)
Serious TEAE	1(9.1)	1(16.7)	2(7.7)	6(7.2)	3(9.1)	1(33.3)	14(8.6)
TEAE Leading to Dose Reduction	0	0	0	1(1.2)	0	0	1(0.6)
TEAE Leading to Dose Interruption	1(9.1)	0	2(7.7)	10(12.0)	3(9.1)	1(33.3)	17(10.5)
TEAE Leading to Dose Discontinuation	1(9.1)	0	0	2(2.4)	1(3.0)	0	4(2.5)
TEAE Leading to Death	1(9.1)	0	0	1(1.2)	0	0	2(1.2)
Drug Related TEAE	9(81.8)	4(66.7)	17(65.4)	49(59.0)	23(69.7)	2(66.7)	104(64.2)
Drug Related TEAE with Grade ≥ 3	0	1(16.7)	2(7.7)	7(8.4)	3(9.1)	0	13(8.0)
Drug Related Serious TEAE	0	0	1(3.8)	1(1.2)	0	0	2(1.2)
Drug Related TEAE Leading to Dose Reduction	0	0	0	1(1.2)	0	0	1(0.6)
Drug Related TEAE Leading to Dose Interruption	0	0	2(7.7)	6(7.2)	2(6.1)	0	10(6.2)
Drug Related TEAE Leading to Dose Discontinuation	0	0	0	1(1.2)	1(3.0)	0	2(1.2)
Drug Related TEAE Leading to Death	0	0	0	0	0	0	0

Safety (CTCAE 4.03)

- **Most TEAEs were grade 1 or 2. Most common TEAEs (≥ 10%) were decreased WBC, ANC, and platelet.**
- **Rash occurred in 8.6% patients, and diarrhea in 3.7% patients.**
- **ECG QT prolongation was observed in 3 patients, and all of them were grade 1 or 2.**
- **There were no interstitial lung disease reported.**

Related TEAE (≥5%)	30 mg (N= 11)		60 mg (N= 6)		120 mg (N= 26)		180 mg (N= 83)		240 mg (N= 33)		300 mg (N= 3)		Total (N= 162)	
Preferred Term, n (%)	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3
White blood cell count decreased[1]	2(18.2)	0	1(16.7)	0	11(42.3)	1(3.8)	23(27.7)	0	14(42.4)	0	0	0	51(31.5)	1(0.6)
Neutrophil count decreased[2]	1(9.1)	0	2(33.3)	0	11(42.3)	0	18(21.7)	1(1.2)	11(33.3)	2(6.1)	0	0	43(26.5)	3(1.9)
Platelet count decreased[3]	0	0	0	0	5(19.2)	1(3.8)	16(19.3)	0	10(30.3)	0	0	0	31(19.1)	1(0.6)
Anemia	1(9.1)	0	0	0	2(7.7)	0	8(9.6)	1(1.2)	3(9.1)	0	0	0	14(8.6)	1(0.6)
Rash[4]	2(18.2)	0	1(16.7)	0	1(3.8)	0	4(4.8)	3(3.6)	5(15.2)	0	1(33.3)	0	14(8.6)	3(1.9)
Alanine aminotransferase increased	2(18.2)	0	1(16.7)	0	3(11.5)	0	2(2.4)	0	1(3.0)	0	0	0	9(5.6)	0
Aspartate aminotransferase increased	1(9.1)	0	1(16.7)	0	2(7.7)	0	3(3.6)	0	2(6.1)	0	0	0	9(5.6)	0
Lymphocyte count decreased	0	0	0	0	2(7.7)	0	5(6.0)	0	2(6.1)	0	0	0	9(5.6)	0

AE of Interest	30 mg (N= 11)		60 mg (N= 6)		120 mg (N= 26)		180 mg (N= 83)		240 mg (N= 33)		300 mg (N= 3)		Total (N=162)	
Preferred Term, n (%)	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3	Any Grade	Grade >=3
Rash[4]	2(18.2)	0	1(16.7)	0	1(3.8)	0	4(4.8)	3(3.6)	5(15.2)	0	1(33.3)	0	14(8.6)	3(1.9)
Diarrhea	2(18.2)	0	0	0	1(3.8)	0	3(3.6)	0	0	0	0	0	6(3.7)	0
Electrocardiogram QT prolonged	1(9.1)	0	0	0	0	0	1(1.2)	0	1(3.0)	0	0	0	3(1.9)	0
Interstitial lung disease	0	0	0	0	0	0	0	0	0	0	0	0	0	0

[1]including white blood cell count decreased and leukopenia; [2]including neutrophil count decreased and neutropenia;
[3]including platelet count decreased and thrombocytopenia; [4]including rash, drug eruption, rash maculo-popular and rash pruritic;

Conclusions

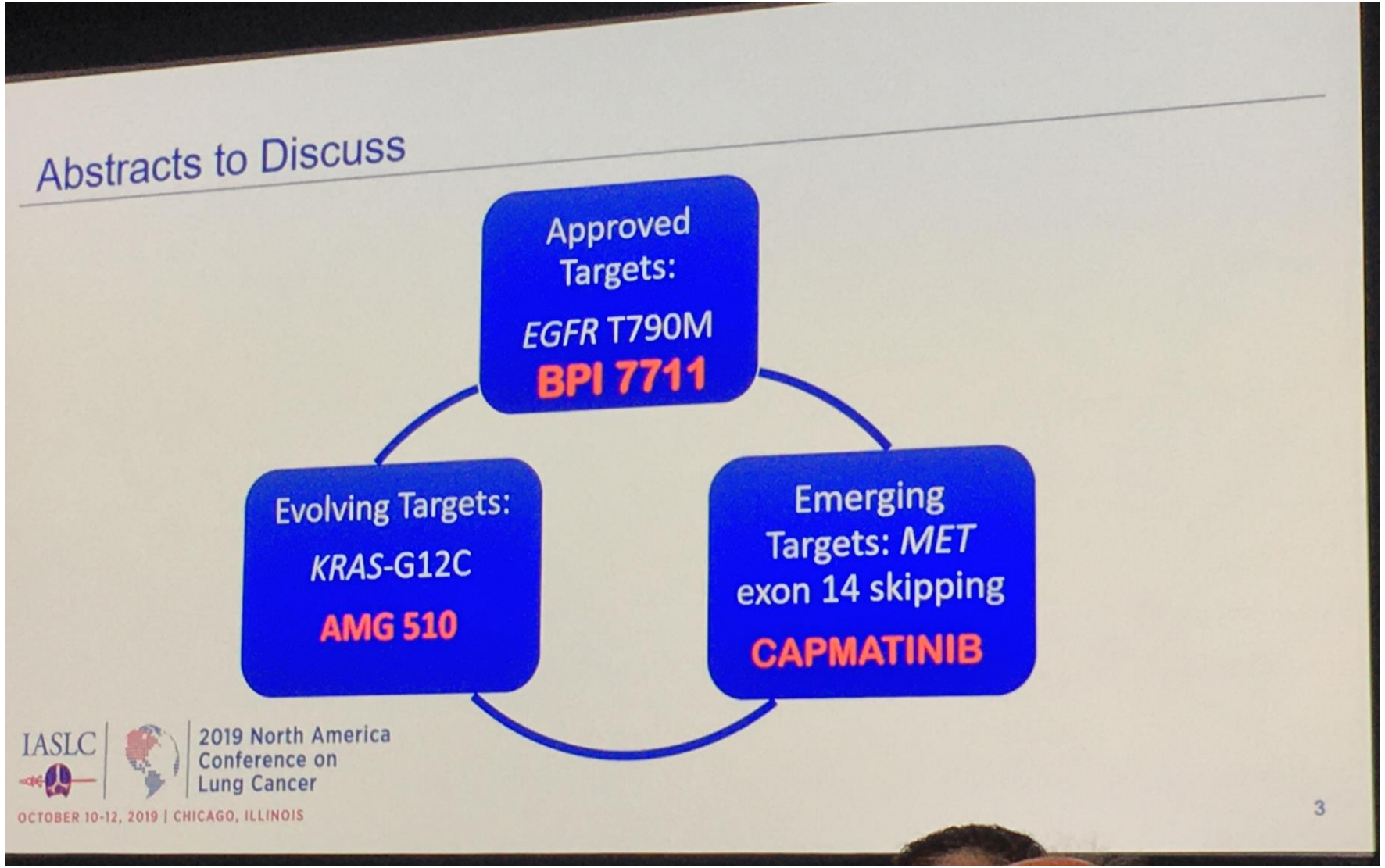
- **BPI-7711 was well tolerated and highly effective in NSCLC patients with advanced or recurrent EGFR/T790M mutation progressed after 1st generation EGFR-TKI treatment.**
- **BPI-7711 demonstrated a promising efficacy on brain metastases.**
- **Pivotal phase II clinical trial is ongoing and phase III clinical study already started.**

Acknowledgements

We would like to thank:

- **the participating patients and their families**
- **all investigators and their study teams**

Discussion on BPI-7711 Phase I study results presented by Professor Jyoti D. Patel


Abstracts to Discuss
Approved Targets:
EGFR T790M
BPI 7711
Evolving Targets:
KRAS-G12C
AMG 510
Emerging Targets: MET exon 14 skipping
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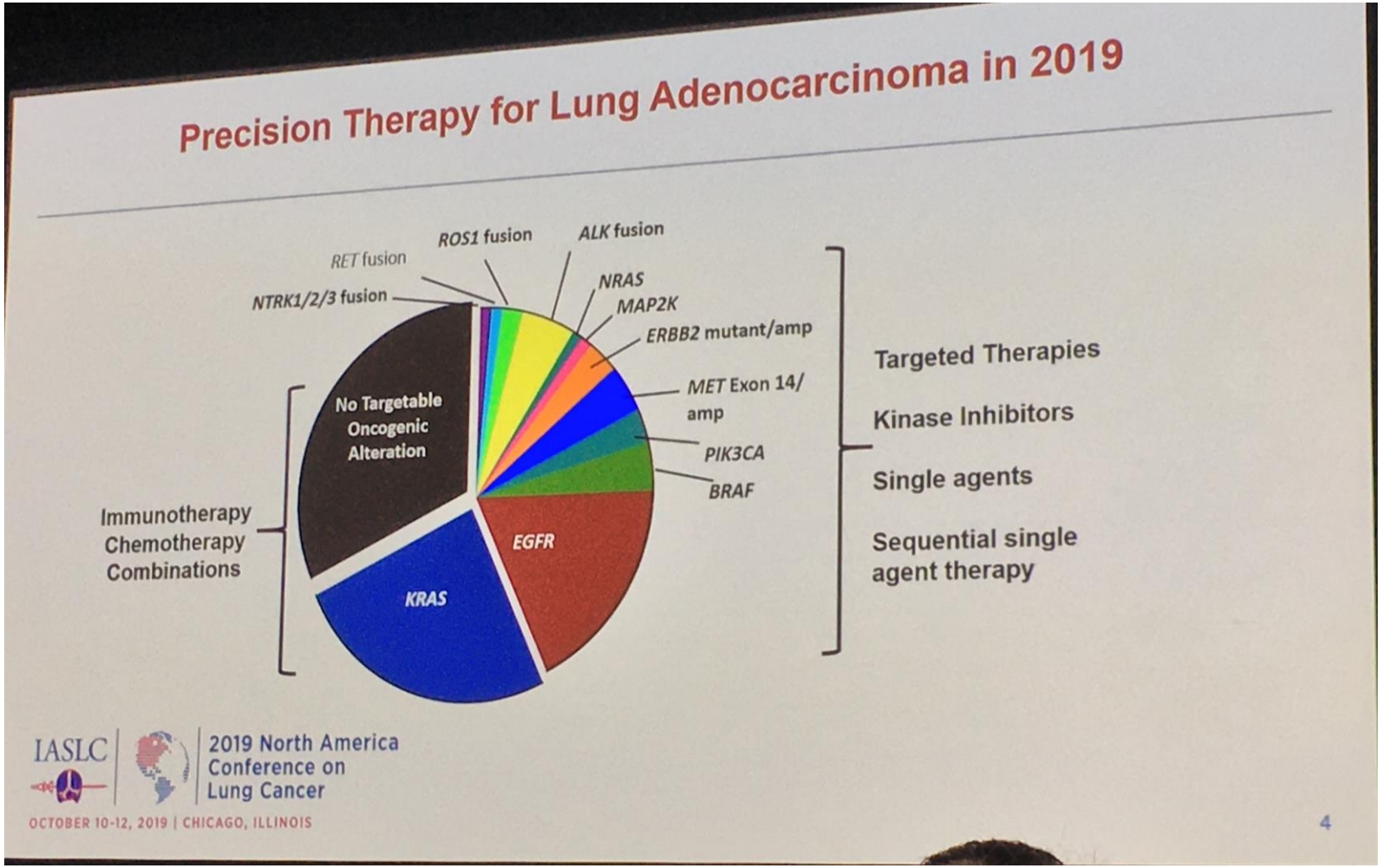
Precision Therapy for Lung Adenocarcinoma in 2019
RET fusion
ROS1 fusion
ALK fusion
NTRK1/2/3 fusion
NRAS
MAP2K
ERBB2 mutant/amp
MET Exon 14/ amp
PIK3CA
BRAF
No Targetable Oncogenic Alteration
EGFR
KRAS
Immunotherapy Chemotherapy Combinations
Targeted Therapies
Kinase Inhibitors
Single agents
Sequential single agent therapy
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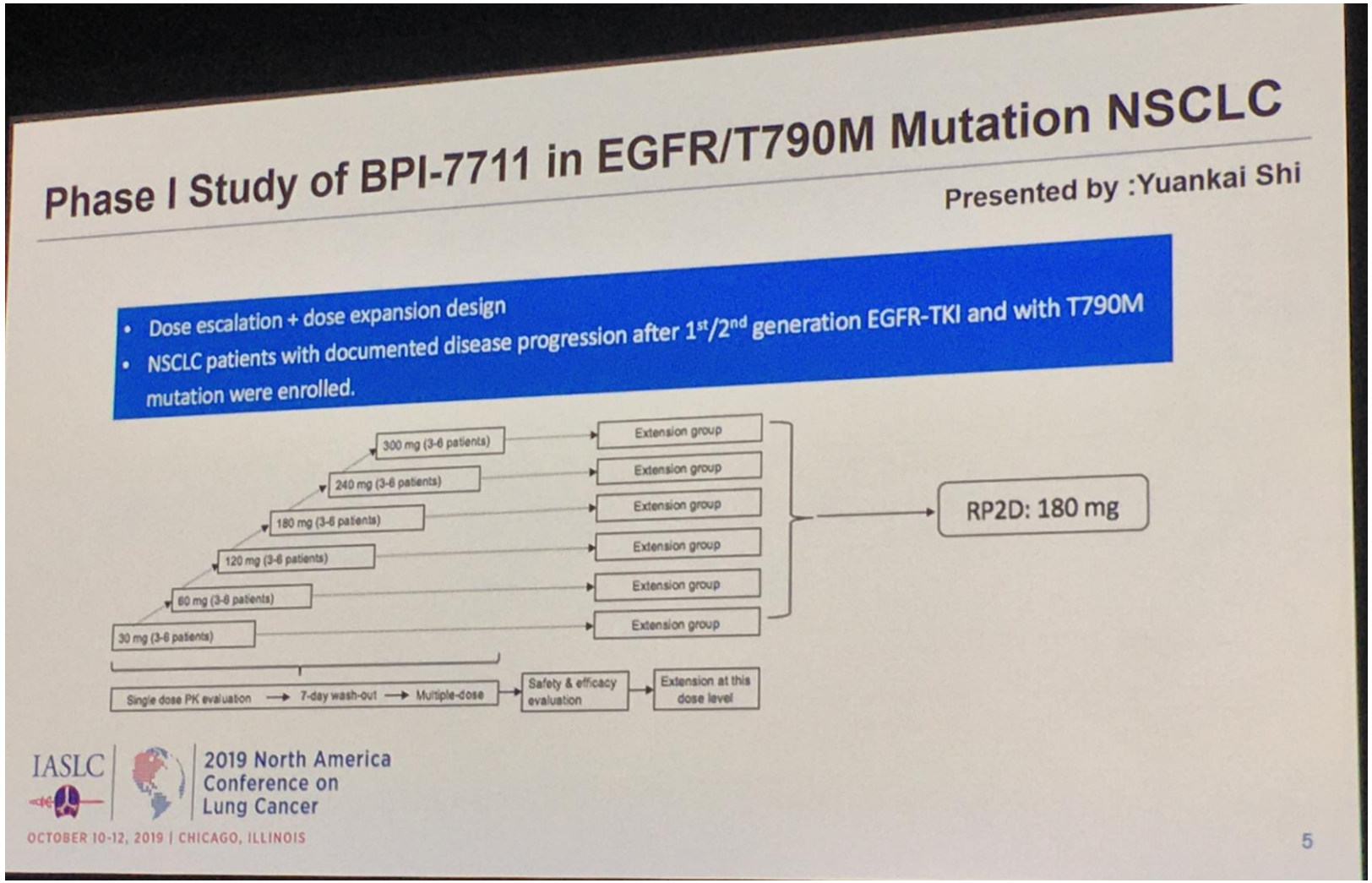
Phase I Study of BPI-7711 in EGFR/T790M Mutation NSCLC
Presented by :Yuankai Shi
Dose escalation + dose expansion design
NSCLC patients with documented disease progression after 1st/2nd generation EGFR-TKI and with T790M mutation were enrolled.
300 mg (3-6 patients)
240 mg (3-6 patients)
180 mg (3-6 patients)
120 mg (3-6 patients)
60 mg (3-6 patients)
30 mg (3-6 patients)
Extension group
Extension group
Extension group
Extension group
Extension group
Extension group
RP2D: 180 mg
Single dose PK evaluation
7-day wash-out
Multiple-dose
Safety & efficacy evaluation
Extension at this dose level
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BPI-7711 in EGFR/T790M Mutation NSCLC

Demographics

- The data cut-off date for this analysis was 15 Jul 2019.
- 162 patients were dosed into 6 dose escalation and expansion cohorts (30~300mg).
- The study is still ongoing.

	30 mg (N= 11)	60 mg (N= 6)	120 mg (N= 26)	180 mg (N= 83)	240 mg (N= 33)	300 mg (N= 3)	Total (N= 162)
Age (Years)							
Mean (SD)	51.7 (10.72)	56.0 (10.20)	54.3 (9.08)	58.2 (9.18)	58.2 (9.61)	55.7 (2.89)	57.0 (9.42)
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Gefitinib	6(54.5)	2(33.3)	12(46.2)	43(51.8)	14(42.4)	1(33.3)	78(48.1)
Erlotinib	2(18.2)	0	2(7.7)	12(14.5)	9(27.3)	0	25(15.4)
Icotinib	3(27.3)	4(66.7)	12(46.2)	32(38.6)	12(36.4)	2(66.7)	65(40.1)
Brain metastasis, n (%)	5(45.5)	2(33.3)	12(46.2)	35(42.2)	16(48.5)	1(33.3)	71(43.8)
Bone metastasis, n (%)	4(36.4)	5(83.3)	9(34.6)	30(36.1)	17(51.5)	1(33.3)	66(40.7)

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BPI-7711 in EGFR/T790M Mutation NSCLC

Demographics

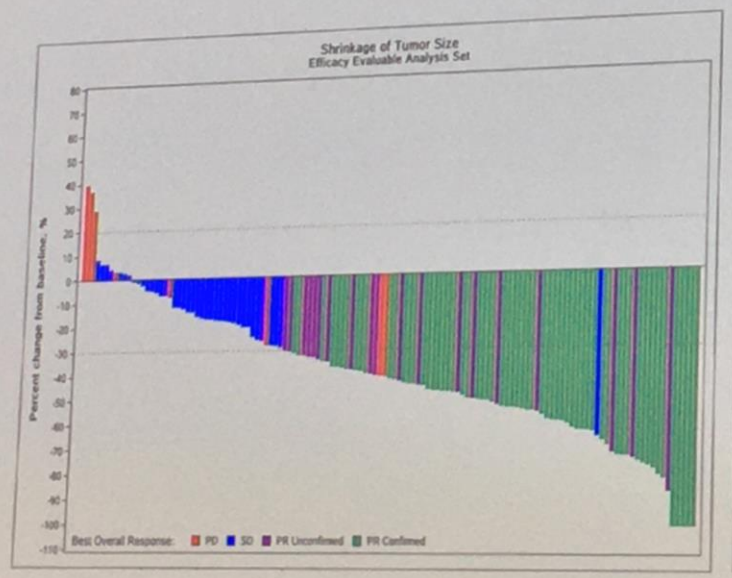
- The data cut-off date for this analysis was 15 Jul 2019.
- 162 patients were dosed into 6 dose escalation and expansion cohorts (30~300mg).
- The study is still ongoing.

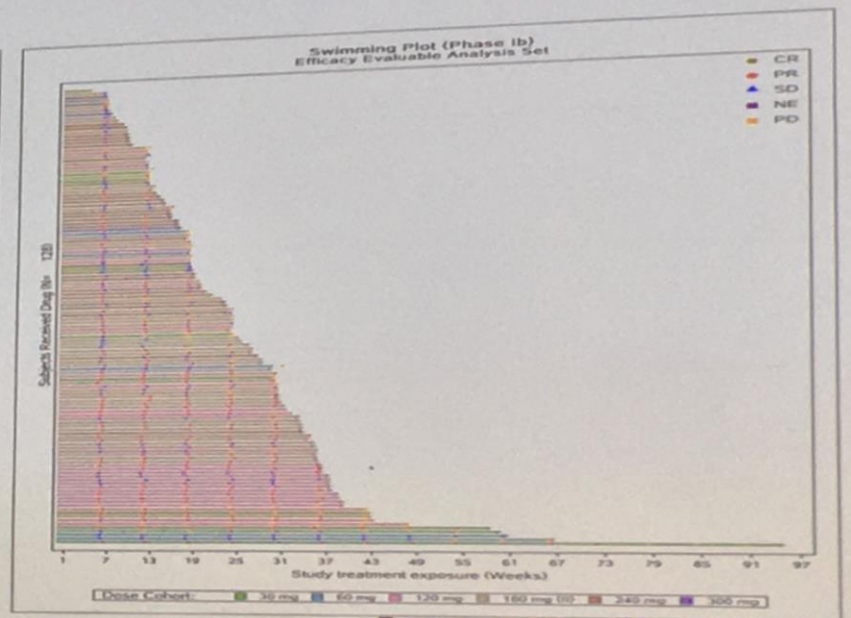
	30 mg (N= 11)	60 mg (N= 6)	120 mg (N= 26)	180 mg (N= 83)	240 mg (N= 33)	300 mg (N= 3)	Total (N= 162)
Age (Years)							
Mean (SD)	51.7 (10.72)	56.0 (10.20)	54.3 (9.08)	58.2 (9.18)	58.2 (9.61)	55.7 (2.89)	57.0 (9.42)
Median	54	52.5	51	59	60	54	57
Min - Max	34.0 - 68.0	47.0 - 73.0	34.0 - 73.0	39.0 - 75.0	37.0 - 75.0	54.0 - 59.0	34.0 - 75.0
Sex, n (%)							
Male	4(36.4)	1(16.7)	10(38.5)	21(25.3)	15(45.5)	1(33.3)	52(32.1)
Female	7(63.6)	5(83.3)	16(61.5)	62(74.7)	18(54.5)	2(66.7)	110(67.9)
Prior EGFR-TKIs Regimen, n (%)							
Gefitinib	6(54.5)	2(33.3)	12(46.2)	43(51.8)	14(42.4)	1(33.3)	78(48.1)
Erlotinib	2(18.2)	0	2(7.7)	12(14.5)	9(27.3)	0	25(15.4)
Icotinib	3(27.3)	4(66.7)	12(46.2)	32(38.6)	12(36.4)	2(66.7)	65(40.1)
Brain metastasis, n (%)	5(45.5)	2(33.3)	12(46.2)	35(42.2)	16(48.5)	1(33.3)	71(43.8)
Bone metastasis, n (%)	4(36.4)	5(83.3)	9(34.6)	30(36.1)	17(51.5)	1(33.3)	66(40.7)

BPI-7711 in EGFR/T790M Mutation NSCLC

Efficacy (Independent Radiological Review Committee Review)

- Significant improvement in the tumor size of most of the patients
- The median time to response was 6.1 weeks.
- 64.8% of the patients were still under treatment.





Presented by :Yuankai Shi

Pretreated EGFR T790M+ Efficacy Comparison?

	BPI-7711	Osimertinib		
Trial	Ph I (Shi et al)	AURA (phase II)	AURA 2 (phase II)	AURA 3 (phase III)
N	162 (100% Asian)	201 (57% Asian)	210 (63% Asian)	279 (64% Asian)
ORR (%)	63.6	66		71
DCR (%)	93.8	91		93
Intracranial RR (%)	35.3	54		70
mPFS	NR	9.9 mo.		10.1 mo.

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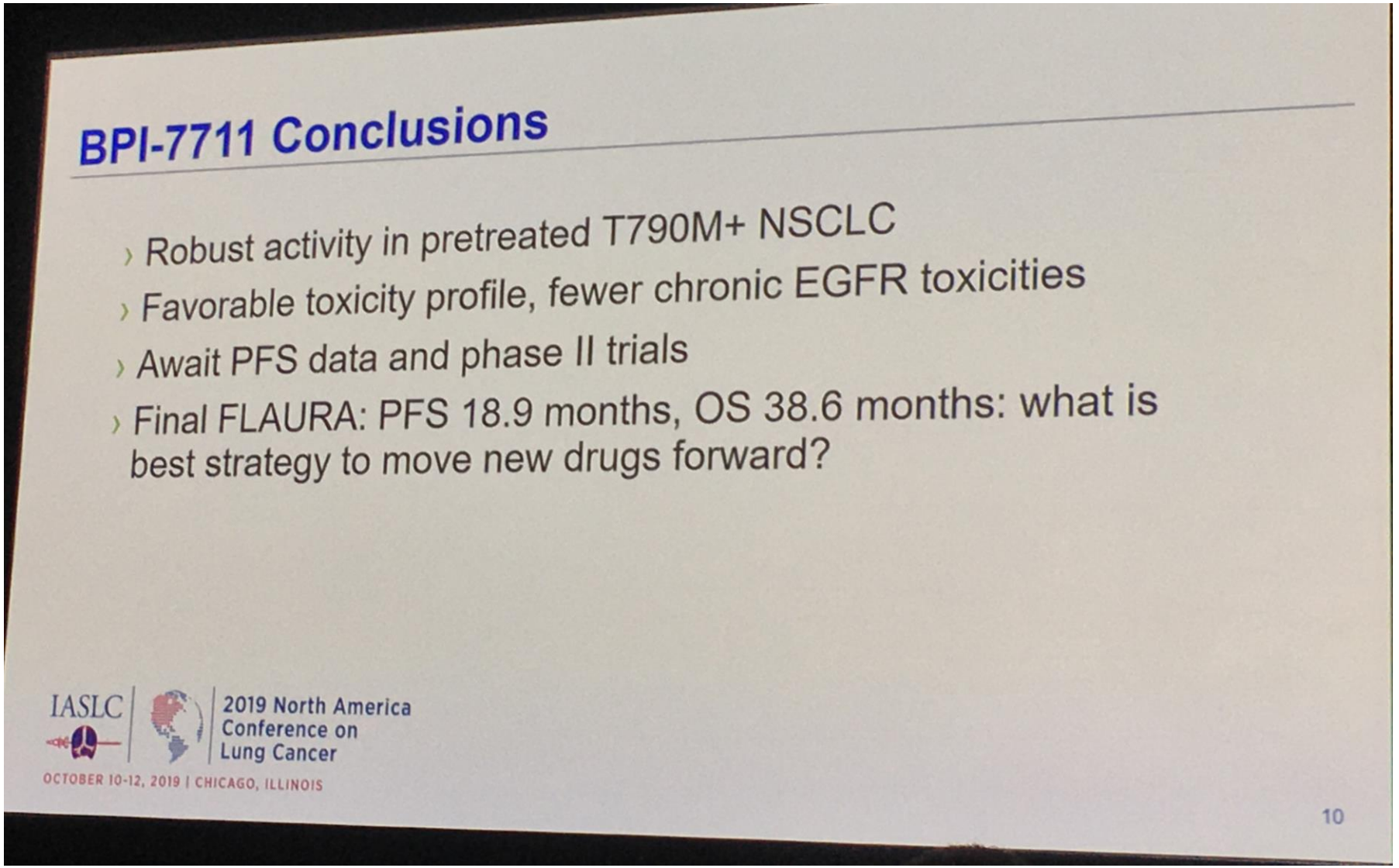
Yang et al. JCO 2017
Goss et al. Lancet Oncol 2016
Mok et al. NEJM 2017

Pretreated EGFR T790M+ Toxicity Comparison?

	BPI-7711	Osimertinib
Rash	Any Gr 8.6% ≥ Gr 3 1.9%	Any Gr 41% ≥ Gr 3 0.5%
Diarrhea	Any Gr 3.7% ≥ Gr 3 0%	Any Gr 42% ≥ Gr 3 1%
QT prolongation	Any Gr 1.9 ≥ Gr 3 0%	Any Gr 2.7% ≥ Gr 3 0.2%
Interstitial Lung Disease	0%	1-3%
White Bld Cell count decreased	Any Gr 31.5% ≥ Gr 3 0.6%	Any Gr 63% ≥ Gr 3 3.3%
Neutrophil count decreased	Any Gr 26.5% ≥ Gr 3 1.9 %	Any Gr 33% ≥ Gr 3 3.4%

Package insert


BPI-7711 Conclusions
› Robust activity in pretreated T790M+ NSCLC
› Favorable toxicity profile, fewer chronic EGFR toxicities
› Await PFS data and phase II trials
› Final FLAURA: PFS 18.9 months, OS 38.6 months: what is best strategy to move new drugs forward?
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