2021 ASCO® ANNUAL MEETING

CNS ACTIVITY OF POZIOTINIB IN NSCLC WITH EXON 20 INSERTION MUTATIONS

Xiuning Le[1], Marina C Garassino[2], Robin Cornelissen[3], Mark A Socinski[4], Nishan Tchekmedyian[5], Julian R Molina[6], Christina S Baik[7], Arsela Prelaj[8], Chul Kim[9], Sharon Leu[10], Lyndah K Dreiling[10], Francois Lebel[10], Jeffrey M Clarke[11]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]University of Chicago Medical Center, Chicago, IL; [3]Erasmus Medical Center, Rotterdam, Netherlands; [4]AdventHealth Cancer Institute, Orlando, FL; [5]Pacific Shores Medical Group, Huntington Beach, CA; [6]Mayo Clinic, Rochester, MN; [7]Seattle Cancer Care Alliance, Seattle, WA; [8]Istituto Nazionale Tumori of Milan, Italy; [9] Georgetown University, Washington DC; [10]Spectrum Pharmaceuticals, Irvine, CA; [11]Duke University Medical Center, Durham, NC

Poziotinib is an investigational drug not approved by the FDA

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Disclosures

Xiuning Le, receives consulting/advisory fees from EMD Serono (Merck KGaA), AstraZeneca, Spectrum Pharmaceuticals, Inc., Eli Lilly, Boehringer Ingelheim, Bristol-Myers Squibb and Celgene, and Research Funding from Eli Lilly, and Boehringer Ingelheim.

Introduction

- Metastatic NSCLC harboring EGFR or HER2 exon 20 insertion mutations is a uniformly fatal disease and represents an unmet medical need
- Brain metastasis in NSCLC is frequent, occurs in up to 25% of patients and is associated with short survival (mOS of 2-5 months following WBRT[1])
- Poziotinib is a potent, irreversible TKI that targets exon 20 insertion mutations
- Two previous case reports in exon 20 mutated brain metastases suggest poziotinib CNS penetration[2, 3]
- Here we present poziotinib CNS activity in NSCLC with EGFR or HER2 exon 20 insertion mutations in the ongoing ZENITH20 Study

[1]Langer CJ, Mehta MP. et al. J Clin Oncol. 2005
[2]Pandey A et al, Clin Breast Cancer, 2018
[3]Tchekmedyian N, et al. JTO Clin and Res Reports, 2020

Figure 1. ZENITH20 Phase 2 Multi-cohort International Trial

Fully Enrolled

- **Cohort 1**
  Previously treated NSCLC with EGFR exon 20 insertions (16mg QD)
- **Cohort 2**
  Previously treated NSCLC with HER2 exon 20 insertions (16mg QD)
- **Cohort 3**
  First-line NSCLC with EGFR exon 20 insertions (16mg QD)

Objectives

- **Primary**
  - Objective Response Rate (ORR)
    - **Based on Central Independent Review**
- **Secondary**
  - Duration of Response (DOR)
  - Safety & Tolerability

- **Baseline CNS assessment required only in symptomatic patients**
- **Stable CNS metastasis allowed if:**
  - Asymptomatic, without requirement for high-dose steroids or anti-convulsant therapy
  - After recent RT, sequential post-txt MRI ≥ 4 wks showing stable disease
  - Intracranial assessment based modified RECIST by central review

Enrolling

- **Cohort 4**
  First-line NSCLC with HER2 exon 20 insertions (16mg QD; 8mg BID)
- **Cohort 5**
  NSCLC with EGFR or HER2 exon 20 mut (6mg, 8mg BID; 10mg, 12mg, 16mg QD)
- **Cohort 6**
  EGFR Osimertinib Failures (8mg BID)
- **Cohort 7**
  Atypical EGFR or HER2 mutations (8mg BID)

Table 1. Demographics and Patient Disposition

	CNS Subgroup N=36	Non-CNS Subgroup N=248	All Patients N=284
Median age, yrs (range)	58.5 (30, 75)	61 (25, 86)	60.5 (25, 86)
Gender: female / male	25 / 11	154 / 94	179 / 105
ECOG Status: 0 / 1	13 / 23	108 / 140	12 / 163
n (%)			
EGFR	22 (61)	172 (69)	194 (68)
HER2	14 (39)	76 (31)	90 (32)
Length of Follow-up (months)			
Median (Min, Max)	5.5 (0.9, 11.1)	9.2 (0.03, 26.0)	9.2 (0.03, 26.0)

Pooled analysis ZENITH20 cohorts 1-3

Poziotinib Activity in Patients with Brain Metastases at Baseline (N=36)

Table 2. Overall Response (ORR)

	Cohort 1 - EGFR (previously-treated) (N=12)	Cohort 2 - HER2 (previously-treated) (N=14)	Cohort 3 - EGFR (treatment naive) (N=10)	Total (N=36)
In pts with CNS disease (n=36)	1 (8.3%)	4 (28.6%)	3 (30.0%)	8 (22.2%)
In all patients (N=284)	14.8%	27.8%	27.8%	64 (22.5%)

Table 3. CNS and Correlating ORR

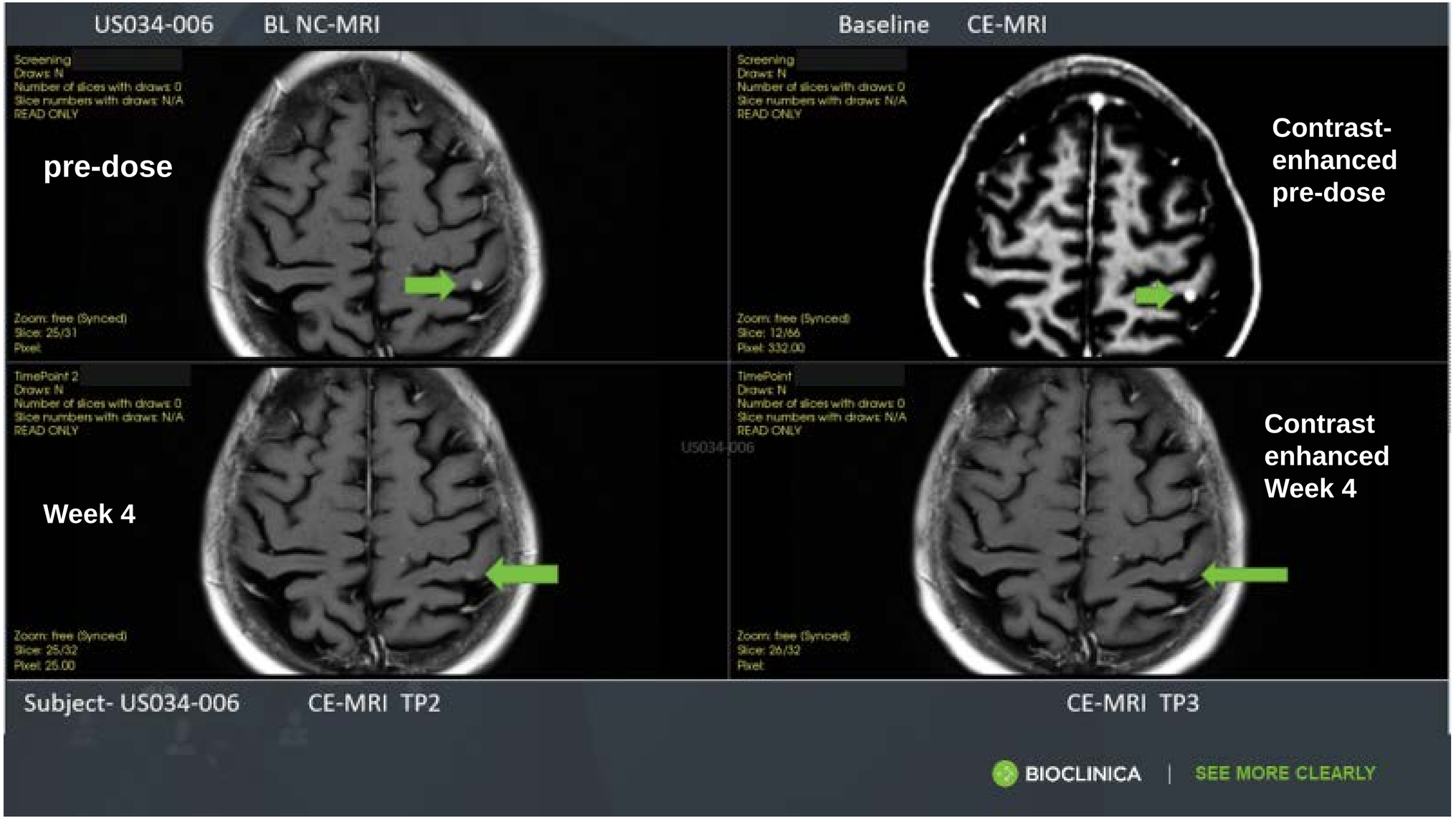
Best CNS Response	N (%)	Prior WBRT[a] N	Best Overall Response			
			PR	SD	PD	NE
Total	36 (100)	12	8	17	7	4
Complete Response[b]	3 (8.3)	1	2	0	1	0
Stable Disease[c]	24 (66.7)	8	5	13	4	2
Progressive Disease	2 (5.6)	0	0	0	2	0
Not Evaluable	7 (19.4)	3	1	4	0	2

[a] WBRT completed within ~12 weeks of study entry, excludes WBRT> 12 wks from enrollment, and Stereotactic Radiosurgery

[b] 2 consecutive MRI/CT scans with absence of non-target lesions

[c] At least 1 MRI/CT scan performed ≥28 days post first treatment showed no progression and no new lesion before first PD

Figure 2. CNS Activity in a Treated Patient from Independent Review



PT US0034-006 had CR at WK4 and confirmed at Wk8 by MRI

Summary and Conclusions

- In ZENITH20 cohort 1-3, a total of 36 patients (12.7%) had baseline CNS metastasis upon enrollment

- In this subgroup of patients with CNS metastasis:
  - Systemic ORR was 22%, similar to the patients who had no CNS metastasis, demonstrating intracranial activity correlating with extracranial activities
  - 3 (8%) patients achieved intracranial complete responses and 24 (67%) patients had stable disease

- Clinically meaningful CNS activity was seen in poziotinib treated patients with CNS metastasis.