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VIRTUAL CONGRESS

SAFETY, TOLERABILITY AND PRELIMINARY EFFICACY OF POZIOTINIB WITH TWICE DAILY DOSING STRATEGY IN EGFR/HER2 EXON 20 MUTANT NON-SMALL CELL LUNG CANCER

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Poziotinib is an investigational drug not approved for marketing

DECLARATION OF INTERESTS

Adrian Sacher, MD

Research Support (Institutional): AstraZeneca, Amgen, Genentech, Merck, Lilly, Pfizer, Bayer, BMS, Spectrum, GSK, Iovance, CRISPR Therapeutics, RAIN Therapeutics

Advisory Board Member & Honoraria: Amgen, AstraZeneca, Merck, Genentech-Roche, Bayer, BMS, Pfizer, Tesaro, KisoJi

Steering Committee: Iovance, Galvanize Therapeutics

ZENITH20: A 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)
- **Secondary**
  - Disease Control Rate (DCR)
  - Duration of Response (DOR)
  - Safety & Tolerability
- ORR based on Central independent imaging review

Cohort 3: Primary endpoint criteria: ORR 95% lower bound >20%

Cohort 5: Dosing exploration

Enrolling

Cohort 4
First-line NSCLC with **HER2** exon 20 insertions (16mg QD; 8mg BID)

Cohort 5
Previously Treated or First-line NSCLC with EGFR or **HER2** exon 20 insertions (6mg, 8mg BID; 10mg, 12mg, 16mg QD)

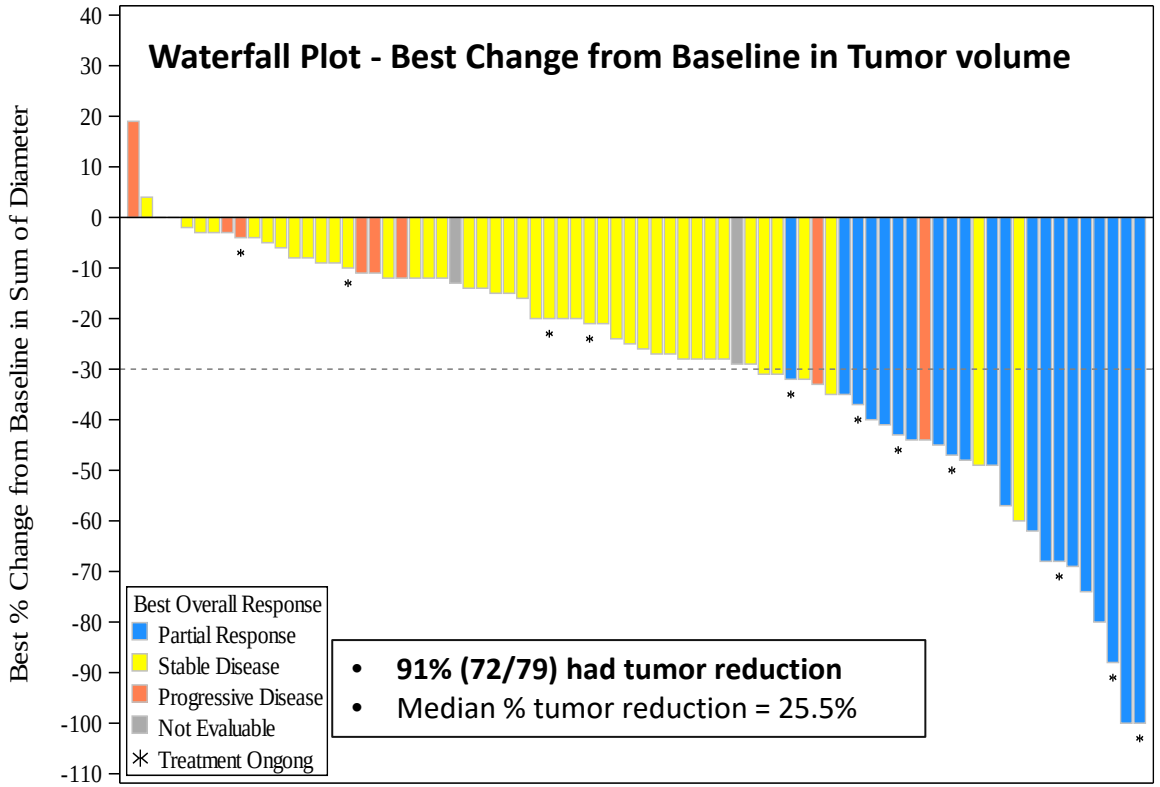
Cohort 6
EGFR Osimertinib Failures (8mg BID)

Cohort 7
Atypical EGFR or HER2 mutations (8mg BID)

ZENITH20 COHORT 3 EFFICACY

	Treated N=79
Treatment ongoing, n (%)	12 (15)
Age, median (range)	60 (32-81)
Female / Male, n	44 / 35
Time of follow up in months, median (range)	9.2 (0.8 – 19.8)
Objective Response Rate, n (%) 95% CI	22 (27.8) 18.4 – 39.1
Disease Control Rate, n (%) 95% CI	68 (86.1) 76.5 – 92.8
Duration of response in months, median (range)	6.5 (1.1 – 16.1+)
Progression-free-survival in months, median (range)	7.2 (0.8 – 19.8+)

Efficacy data based on central review using RECIST 1.1



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ZENITH20-COHORT 5: BID DOSING EXPOSURE AND SAFETY

Preliminary data (enrolling)	16mg QD	8mg BID	12mg QD	6mg BID
Enrolled	22	16	23	16
Drug interruption, n (%) Median Days to first interruption	18 (82) 13	10 (63) 14	20 (87) 19	8 (50) 28
Dose reduction Median Days to first reduction	13 (59) 30	8 (50) 18	13 (57) 35	6 (38) 58
Treatment related AE ≥Grade 3	10 (45)	5 (31)	9 (39)	3 (19)
≥Grade 3 AEs of special interest Diarrhea Rash Stomatitis Pneumonitis	8 (36) 2 (9) 2 (9) 5 (23) 0	3 (19) 1 (6) 1 (6) 2 (13) 0	8 (35) 3 (13) 5 (22) 1 (4) 0	3 (19) 0 2 (13) 1 (6) 0

ZENITH20-COHORT 5 PRELIMINARY DATA: BID DOSING EFFICACY

Preliminary data (enrolling)	Cohort 1 16mg QD N=10 (%)	Cohort 5a 16mg QD N=10 (%)	Cohort 5d 8mg BID N=10 (%)
Best overall response			
PR - Partial Response	2 (20)	2 (20)	3 (30)
SD - Stable Disease	5 (50)	4 (40)	2 (20)
PD - Progressive Disease	2 (20)	0	1 (10)
NE- Not Evaluable (withdrawn)	1 (10)	4 (40)	2 (20)
NA – Too Early to Assess	0	0	2 (20)

SUMMARY AND CONCLUSIONS

- ZENITH20-Cohort 3: Clinically meaningful activity shown in treatment-naïve mNSCLC patients with EGFR exon 20 mutations at 16mg QD dosing
    - ORR of 27.8% and Median PFS of 7.2 months and tumor reduction in 91% patients
- ZENITH20-Cohort 5: Preliminary data demonstrate improved tolerability with BID dosing
    - Reduced dose interruption from QD to BID by:
        - 23% in 16mg dose level
        - 43% in 12mg dose level
    - BID dosing reduced treatment emergent ≥Grade 3 AEs and treatment-related AEs in both dose levels
- Preliminary data suggests potentially improved anti-tumor activity with BID dosing
- ZENITH20 data is maturing and actively enrolling to further evaluate impact of dosing variation

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