

Ellipses Pharma presents 'encouraging' data on next generation selective RET inhibitor EP0031 at ASCO 2023 annual conference

Data of the Phase 1 Study of KL590586 (EP0031/A400), presented at ASCO, reported preliminary efficacy and safety for a total of 109 patients. EP0031/A400 is a potent next generation specific RET inhibitor with broad activity against common RET fusions and mutations, including solvent front resistance mutations. Therefore, EP0031/A400 may have the potential to overcome resistance to first generation RET inhibitors.

Safety: A400/EP0031 was generally well tolerated with most treatment-related adverse events grade 1-2.

KL590586 (A400/EP0031)

safety profile

All doses (10-120mg) and patients, N=109		
TRAEs (≥25% overall)	Any grade, n (%)	Grade 3*, n (%)
Overall	103 (94.5)	26 (23.9)
AST	56 (51.4)	2 (1.8)
ALT	53 (48.6)	2 (1.8)
Constipation	34 (31.2)	0
Creatinine	33 (30.3)	1 (0.9)
Headache	33 (30.3)	1 (0.9)
Anemia	31 (28.4)	3 (2.8)
Bilirubin	31 (28.4)	1 (0.9)
Dose interruptions	40 (36.7)	→
Dose reductions	7 (6.4)	
Dose discontinuations	3 (2.8)	→

- No dose-limiting toxicities (DLT) were observed
- 103 (94.5%) patients had a TRAE - most were grade 1-2
- Low frequency of hyponatremia (any grade 7.3%, ≥3 grade 0.9%); and hypertension (any grade 4.6%), lymphopenia (any grade 4.6%), and prolonged QTc (any grade 2.8%) all with no grade ≥3
- The only grade 3 TRAE with frequency ≥ 2% was anemia
- Median time to 1st dose interruption = 1.9 mo
 - Average duration = 1.8 weeks
- Low frequency of dose reductions/discontinuations

Presented by: Qing Zhou, Prof

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Efficacy: In the overall RET-altered tumor population, patients who received A400/EP0031 at doses between 40 and 120mg once a day had an objective response rate of 60% with a disease control rate of 90%.

Clinical activity of KL590586 (A400/EP0031)

in RET-altered cancers

CHANGE IN TUMOR SIZE FOR PATIENTS ADMINISTERED KL590586 40-120MG QD

- Across all tumor types and doses (40-120 mg QD) confirmed ORR was 60% (54/90), DCR was 94% (85/90)
- For the 90mg dose, ORR was 63% (35/56) and DCR was 95% (53/56)

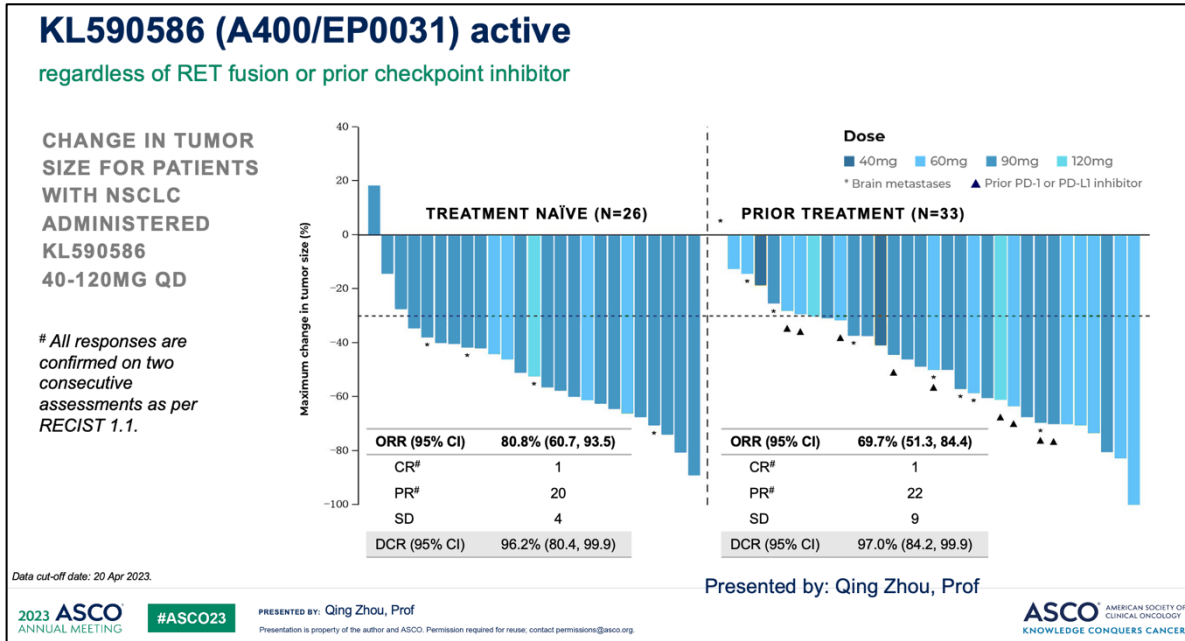
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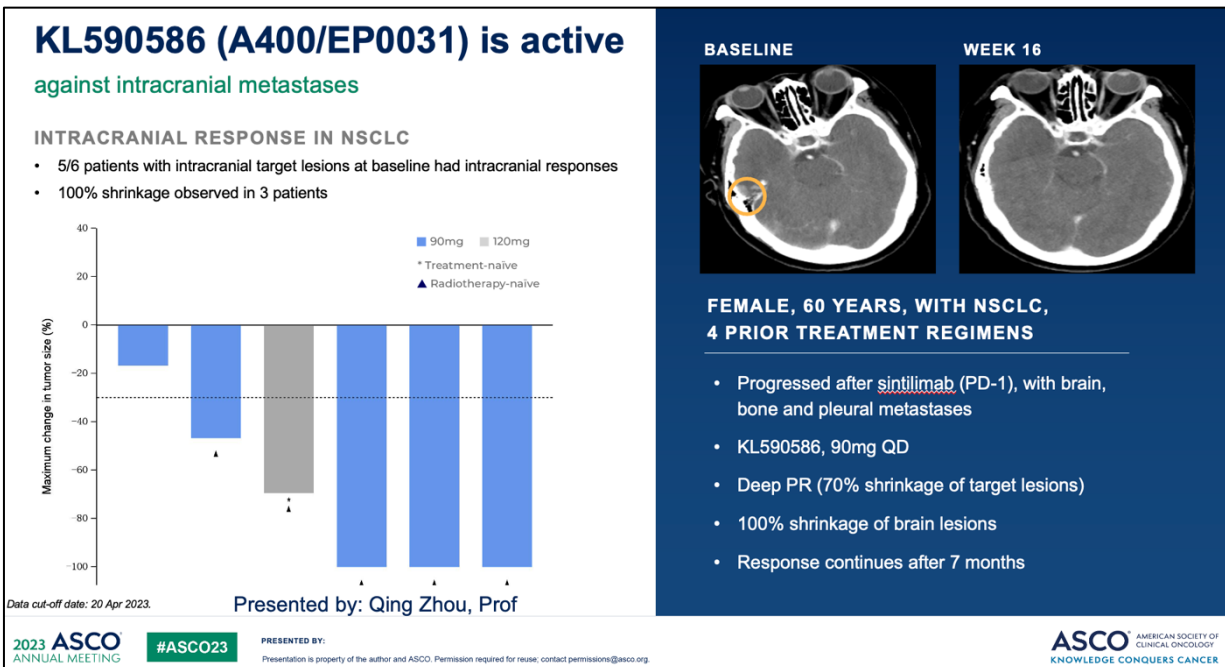
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Two specific treatment cohorts were highlighted:

- Patients, with previously untreated RET-fusion positive advanced NSCLC with an objective response rate of 80.8% (21/26 patients).
- Patients with RET-fusion positive NSCLC who had received prior systemic treatment, including chemo-immunotherapy, with an objective response rate of 69.7% (23/33 patients). Disease control rates of >96% were reported for each cohort.



Importantly, evidence of clinical activity was also reported in cohorts of patients with brain metastases as well as patients that had received prior 1st generation SRI.



EP0031/A400 is the subject of a global, modular Phase 1/2 trial to evaluate safety, tolerability and efficacy in patients with advanced RET-altered tumors. The study is open in multiple sites across the US ([NCT05443126](https://clinicaltrials.gov/ct2/show/study/NCT05443126)) <https://happylungsproject.org/current-clinical-trials/>.

CLINICAL STUDY FOR PATIENTS WITH RET+ SOLID TUMOURS

EP0031 is a novel experimental drug which has the potential to overcome resistance that some cancers can develop to first generation selective RET inhibitors, it's being investigated in a Phase 1/2 study in the US and EU

DOSE FINDING MODULE

ENROLLING NOW

Patients will receive different doses of the study drug to find out which is best to give to adult patients with RET-altered solid tumours

1. All patients with RET altered solid tumours
2. Patients may be enrolled regardless of whether they have been previously treated with an SRI
3. Patients with spinal cord compression, stable brain metastasis or those living with HIV may be enrolled

CLINIC VISITS

1. Cycle 1: Five visits to clinic
2. Subsequent cycles: Two visits to clinic
3. Each cycle is 28 days long
4. Patient expenses will be reimbursed

Study has planned expansion cohorts

Active Site	Contact
Site 1: UCLA (USA)	agianoukakis@lundquist.org
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New sites are being recruited
please scan QR for updates

