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Expanded Access Program (EAP) Use of Pralsetinib in advanced NSCLC with RET rearrangement

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Introduction

- Rearranged during transfection (RET) gene rearrangement
  - ✓ Well-known driver event in non-small cell lung cancer (NSCLC)
  - ✓ Lead to the generation of oncogenic intracellular RET fusion proteins capable of ligand-independent activation
  - ✓ RET fusions are present in 1–2% of NSCLCs and are an important therapeutic target
- Multikinase inhibitors with anti-RET activity
  - ✓ Such as cabozantinib, vandetanib, and Lenvatinib have been investigated in early clinical trials of RET-positive NSCLCs
  - ✓ Showed modest clinical activity with high rates of treatment-related toxicity
- Pralsetinib
  - ✓ Potent and selective inhibitor of RET kinase
  - ✓ Has shown its efficacy in oncogenic RET altered tumors

Objective & endpoints

- Objective
  - ✓ Evaluate the efficacy and safety of EAP use of pralsetinib in pretreated, advanced NSCLC patients with RET-rearrangement in single medical center
- Endpoints
  - ✓ Primary endpoint: investigator-assessed overall response rate (ORR) per RECIST version 1.1.
  - ✓ Secondary endpoints: duration of response (DOR), progression-free survival (PFS), overall survival (OS) and safety profiles.

Study design & evaluation

- Study design
  - ✓ Retrospective, non-randomized, open label, single-arm, single center, phase II study
- Evaluation
  - ✓ Patients with advanced NSCLC received pralsetinib 400 mg once daily as part of the EAP at Samsung Medical Center, South Korea
  - ✓ Baseline characteristics, treatment history, efficacy and safety outcomes were evaluated through retrospective chart review

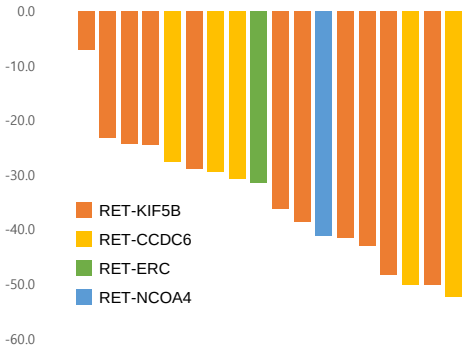
Results

- Between April 2020 to September 2021, 27 patients with NSCLC received pralsetinib
- Seven patients who died within three months and 1 patient who arbitrarily refrained after 7 days were excluded from this analysis

Baseline characteristics

		N	% (range)
Age	Median (range)	51	
	≥65	2	10.5
	<65	17	89.5
Sex	Male	6	31.6
	Female	13	68.4
Smoking	Never smoker	16	84.2
	Ex-smoker	2	10.5
	Current smoker	1	5.3
Histology	Adenocarcinoma	16	84.2
	Adenosquamous carcinoma	2	10.5
	Undifferentiated malignant tumor	1	5.3
EGFR	No	19	100
ALK	No	19	100
ROS1	No	13	68.4
	Unknown	6	31.6
PD-L1 (22C3) CDx	Median	0.5	(0-90)
PD-L1 (SP263)	Median	0.5	(0-40)
Surgery	No	17	89.5
	Yes	2	10.5
Prior palliative chemotherapy lines	Median	2	(1-8)
Distant metastasis at chemotherapy start	Liver	2	10.5
	Brain	6	31.6
Follow up duration	Median	14	10.7-17.3
Dose reduction	No	10	52.6
	Yes	9	47.4
Dose interuption	No	12	63.2
	Yes	7	36.8

Waterfall plot



Overall response

	N	%
Overall response rate	11	57.9
Partial response	11	57.9
Stable disease	8	42.1
Progression	0	0

Hematologic adverse events

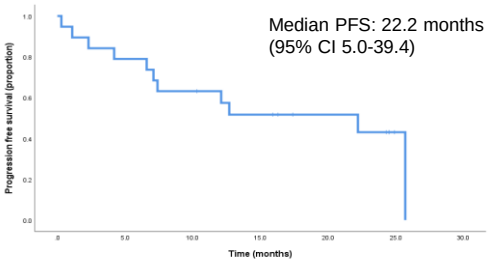
	Any	Grade 1-2	Grade 3-4
Leukopenia	12 (63.2%)	10 (52.6%)	2 (10.5%)
Anemia	17 (89.5%)	11 (57.9%)	6 (31.6%)
Thrombocytopenia	13 (68.4%)	11 (57.9%)	2 (10.5%)
Neutropenia	13 (68.4%)	10 (52.6%)	3 (15.8%)
Elevated AST	18 (94.7%)	16 (84.2%)	2 (10.5%)
Elevated ALT	17 (89.5%)	14 (73.7%)	3 (15.8%)
Elevated ALP	8 (42.1%)	6 (31.6%)	2 (10.5%)
Bilirubinemia	4 (21.1%)	4 (21.1%)	0 (0.0%)
Elevated Creatinine	8 (42.1%)	8 (42.1%)	0 (0.0%)
Elevated CK	3 (37.5%)	3 (37.5%)	0 (0.0%)
Hyponatremia	10 (52.6%)	9 (56.2%)	1 (6.3%)

Non-hematologic adverse events

	N	%
Edema	8	42.1
Pneumonitis	7	36.8
General weakness	3	15.8
Hypertension	3	15.8
Diarrhea	2	10.5
Fever	2	10.5
PTE	2	10.5
Extrapulmonary tuberculosis	2	10.5
Stomatitis	1	5.3
Constipation	1	5.3
QT prolongation	1	5.3

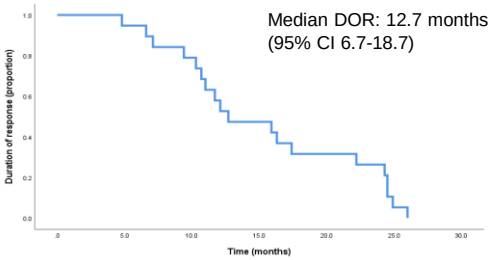
Progression free survival

Median PFS: 22.2 months
(95% CI 5.0-39.4)



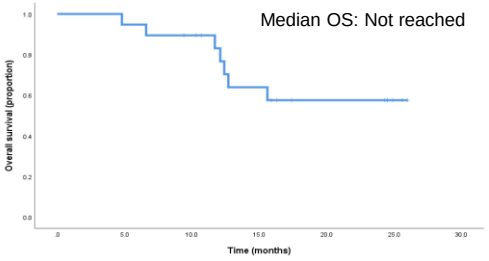
Duration of response

Median DOR: 12.7 months
(95% CI 6.7-18.7)



Overall survival

Median OS: Not reached



Conclusion

- Pralsetinib was found to have clinical benefit which is consistent with a pivotal study, when used in EAP in RET-rearranged NSCLC patients

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