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Results from the registrational phase 1/2 ARROW trial of pralsetinib (BLU-667) in patients with advanced *RET* mutation-positive medullary thyroid cancer

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Disclosures

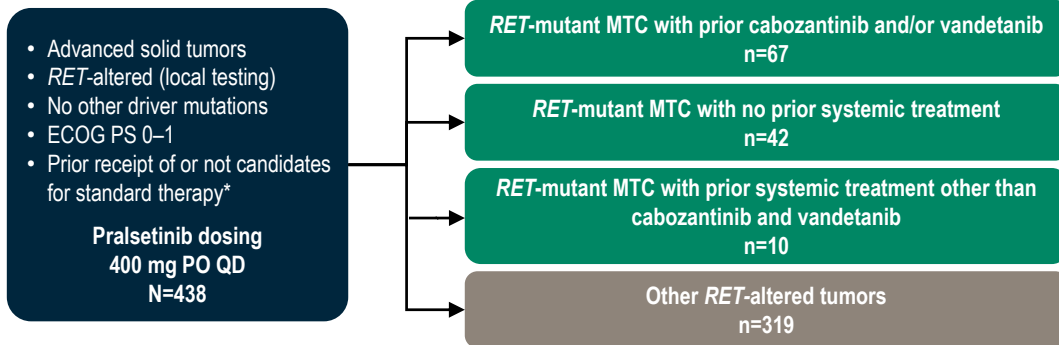
Mimi Hu has participated in advisory boards for Blueprint Medicines Corporation, Eli Lilly and Company, and Loxo Oncology, and has served as a consultant for Veracyte.

Pralsetinib is approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with metastatic *RET* fusion-positive NSCLC. Pralsetinib has not been approved for the treatment of any other indication in the USA by the FDA or for any indication in any other jurisdiction by any other health authority.

RET mutations are oncogenic drivers in MTC

- MTC accounts for **1–5%** of all thyroid cancers¹
- *RET* mutations are present in **50–90%** of sporadic MTC and nearly **100%** of germline MTC cases as part of MEN2 syndrome^{1,2}
- The MKIs cabozantinib and vandetanib are approved treatment options for advanced MTC, but have high rates of dose reductions and treatment discontinuations due to AEs^{3,4}
- Pralsetinib is highly potent and selective inhibitor of wild-type *RET* and *RET* with oncogenic alterations, including V804M/L gatekeeper mutations⁵

Registrational phase 1/2 study of pralsetinib in patients with solid tumors (ARROW)



Key endpoints

- **Blinded, independent central review**
ORR and DOR per RECIST v1.1
- **Safety**

ARROW (NCT03037385) is an ongoing, international multicenter phase 1/2 study across 84 sites in 11 countries

*Until protocol amended in July 2019 to allow enrollment of treatment-naïve, standard therapy-eligible patients. Data cutoff February 13, 2020.

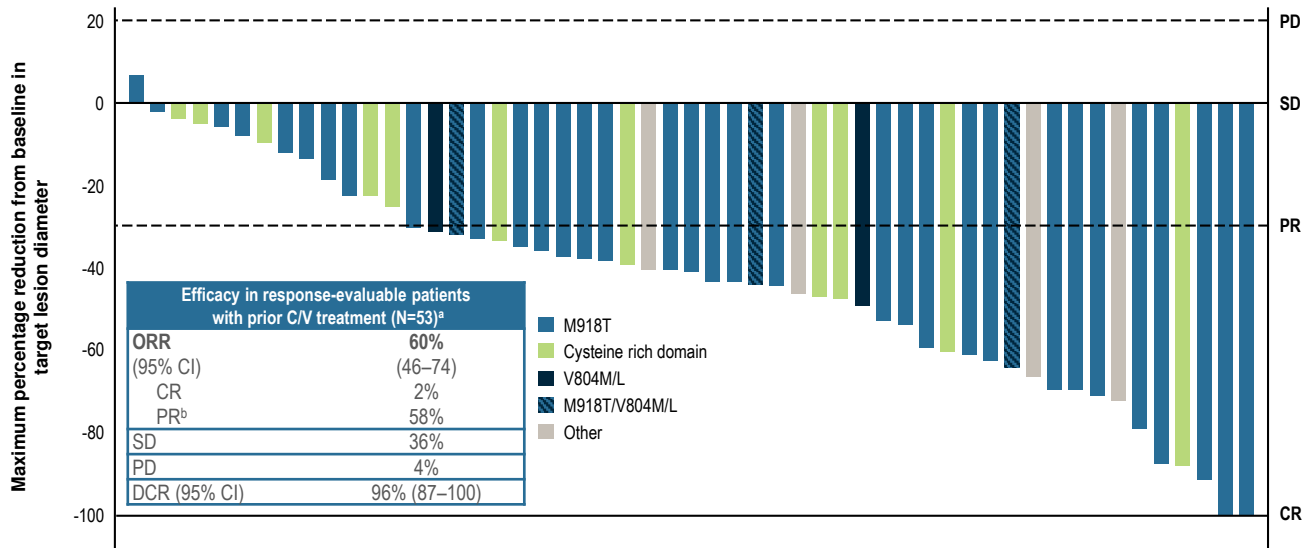
ECOG PS, Eastern Cooperative Oncology Group performance score; DOR, duration of response; NSCLC, non-small cell lung cancer; ORR, overall response; PO, orally; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Baseline demographics and disease characteristics in *RET*-mutant MTC population

Characteristic	All 400 mg pralsetinib (N=92) ^a	Prior cabozantinib and/or vandetanib treatment (n=61)	No prior systemic treatment (n=22)
Median age (range), years	59 (19–83)	58 (25–83)	60 (19–81)
Male, n (%)	63 (68)	41 (67)	16 (73)
ECOG PS, n (%)			
0	37 (40)	17 (28)	15 (68)
1–2 ^b	55 (60)	44 (72)	7 (32)
History of CNS/brain metastases, n (%)	9 (10)	5 (8)	3 (14)
<i>RET</i> mutation	92 (100)	61 (100)	22 (100)
M918T	56 (61)	41 (67) ^c	8 (36)
Cysteine rich domain ^d	27 (29)	14 (23)	11 (50)
V804M/L	3 (3)	2 (3)	1 (5)
Other ^e	6 (7)	4 (7)	2 (9)

^aIncludes patients enrolled by July 11, 2019, data cutoff February 13, 2020. Patients enrolled by this date either received standard therapy or were not candidates for standard therapy; 9 patients received prior systemic therapy other than cabozantinib or vandetanib. ^bECOG PS of 2 was allowed prior to a protocol amendment. ^cThree patients classified with M918T as the primary mutation also had a V804L or V804M mutation. ^dCysteine rich domain includes: C609, C611, C618, C620, C630 and/or C634. ^eOther includes: D898_E901del (1), L790F (1), A883F (2), K666E (1) and R844W (1). CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance score.

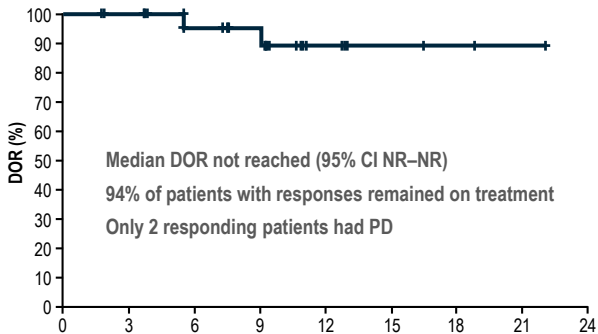
Clinical response to pralsetinib in patients with prior cabozantinib and/or vandetanib treatment



^aBlinded independent central review of tumor response; response-evaluable patients enrolled by July 11, 2019, as of a data cut-off February 13, 2020. Six patients without measurable disease at baseline on central review, and 2 patients without a post-baseline tumor response assessment were not response evaluable. ^b1 PR pending confirmation. C/V, cabozantinib and/or vandetanib; CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

DOR and PFS with pralsetinib in patients with prior cabozantinib and/or vandetanib treatment

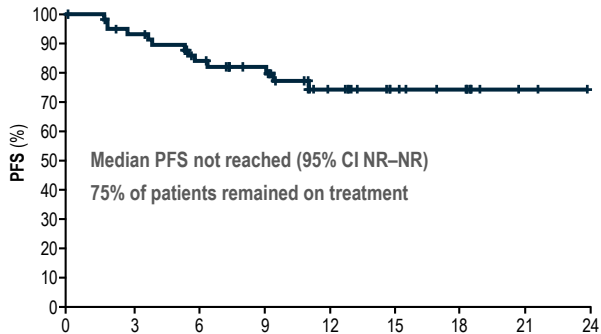
DOR



Numbers at risk

31 28 20 17 7 3 2 1 0

PFS

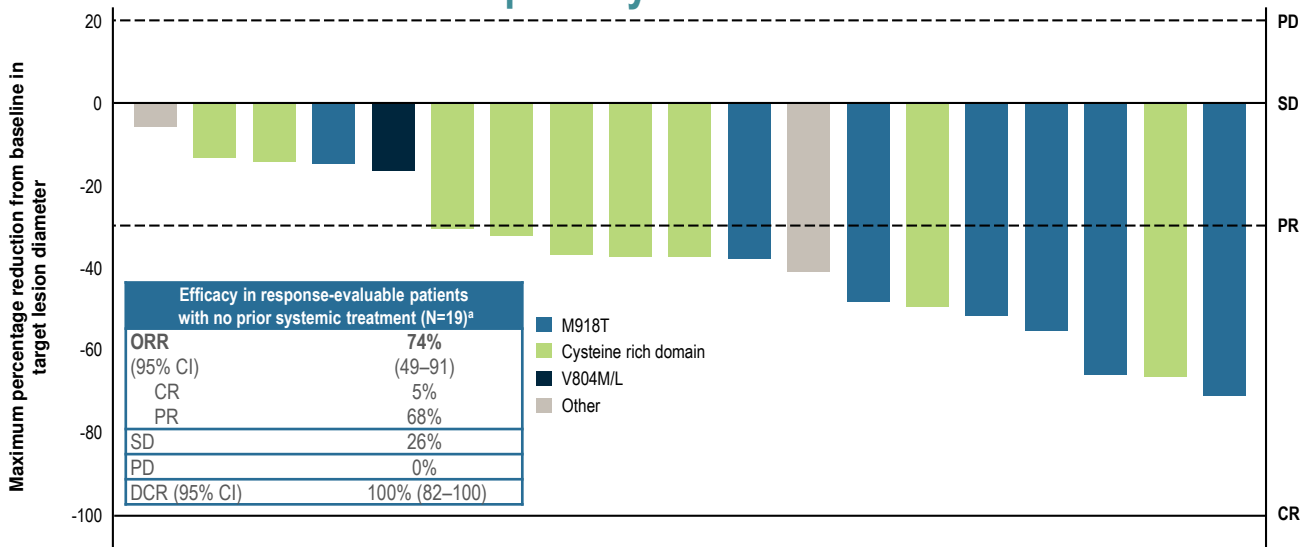


Numbers at risk

61 53 43 36 22 11 8 2 0

Blinded independent central review of tumor response; Patients enrolled by July 11, 2019, as of a data cut-off February 13, 2020. DOR presented for response-evaluable population and includes confirmed responses only; PFS presented for efficacy population.
 DOR, duration of response; NR, not reached; PFS, progression-free survival.

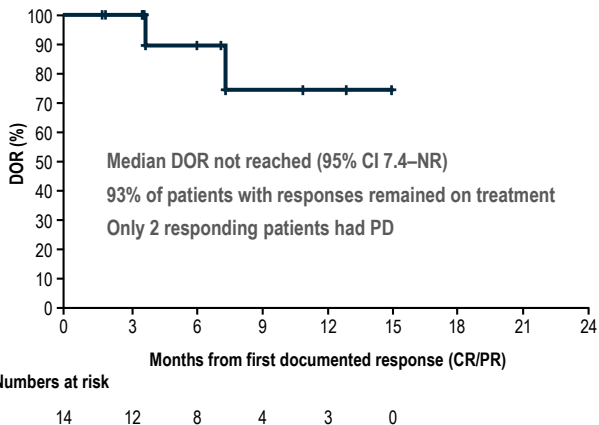
Clinical response to pralsetinib in patients with no prior systemic treatment



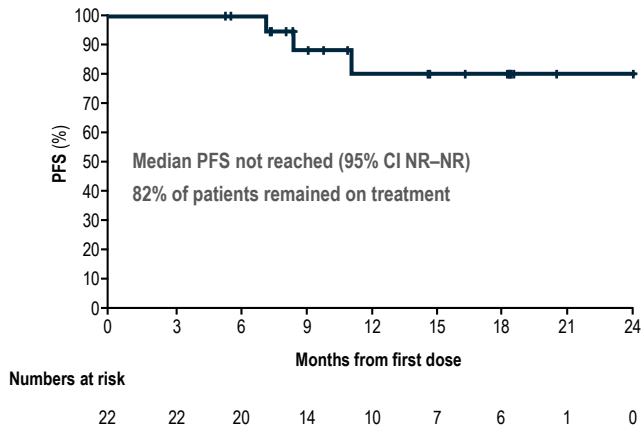
^aBlinded independent central review of tumor response; response-evaluable patients enrolled by July 11, 2019, as of a data cut-off February 13, 2020. Two patients without measurable disease at baseline on central review and 1 patient who experienced major protocol violation were not response evaluable.

DOR and PFS with pralsetinib in patients with no prior systemic treatment

DOR



PFS



Pralsetinib safety profile (all tumor types)

TRAEs in ≥15% of patients	Pralsetinib 400 mg QD (N=438)	
	All grades	Grade ≥3
Aspartate aminotransferase increased	34%	2%
Anemia	24%	8%
Alanine aminotransferase increased	23%	2%
Constipation	23%	1%
Hypertension	22%	11%
White blood cell count decreased	18%	3%
Neutropenia	18%	10%
Neutrophil count decreased	16%	6%
Hyperphosphatemia	15%	1%

- Pralsetinib was well tolerated
- TRAEs were primarily Grade 1–2 and reversible
- 4% of patients discontinued due to TRAEs
- Median dose intensity was 92% (range 18–100)

Summary

- Pralsetinib demonstrated potent and durable clinical activity in *RET*-mutant advanced MTC regardless of line of therapy
 - 60% ORR and 96% DCR in patients with prior C/V treatment
 - 74% ORR and 100% DCR in systemic treatment-naïve patients who were not candidates for standard therapies
- Responses were observed regardless of *RET* mutation genotype, including 5 of 6 (83%) patients with V804X gatekeeper mutation
- Pralsetinib was well tolerated at 400 mg QD; only 4% of patients discontinued due to TRAEs
- US NDA under review

Acknowledgments

- Participating patients and families
- Pralsetinib investigators and research coordinators
- Colleagues at Blueprint Medicines Corporation