

LIBRETTO-531: A Phase III Study of Selpercatinib vs Investigator Choice of Cabozantinib or Vandetanib in Patients with Multikinase Inhibitor-Naïve Advanced or Metastatic *RET*-Mutant Medullary Thyroid Cancer

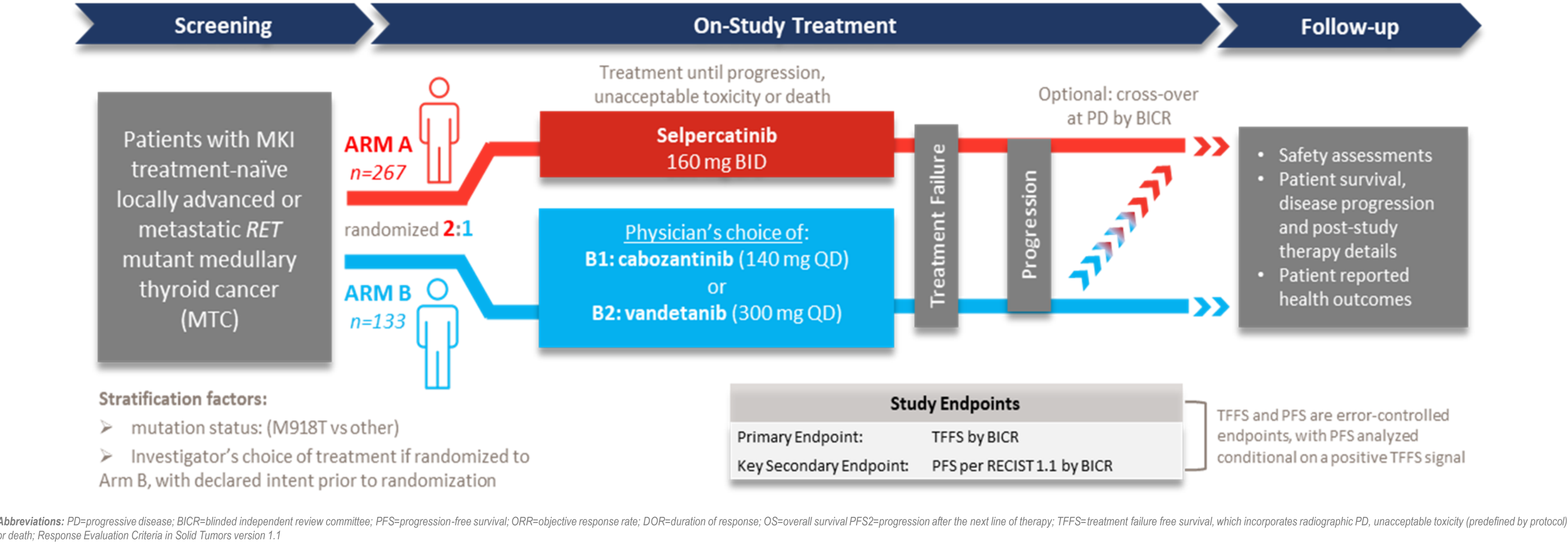
Marcia S. Brose,¹ Jaume Capdevila,² Rossella Elisei,³ Lori J. Wirth,⁴ Sophie Leboulleux,⁵ Andreas Sashegyi,⁶ Boris K. Lin,⁶ Victoria Soldatenkova,⁶ Jennifer Wright,⁶ Bruce Robinson,⁷ Makoto Tahara,⁸ Ana O. Hoff,⁹ Mimi Hu,¹⁰ Eric J. Sherman¹¹

¹University of Pennsylvania, Pennsylvania, PA, USA; ²Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; ³University of Pisa, Pisa, Italy; ⁴Massachusetts General Hospital, Boston, MA, USA; ⁵Gustave Roussy, Villejuif, France; ⁶Eli Lilly and Company, Indianapolis, IN, USA; ⁷Royal North Shore Hospital, St Leonards, Australia; ⁸National Cancer Center Hospital East, Kashiwa, Japan; ⁹Instituto de Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; ¹⁰The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ¹¹Memorial Sloan Kettering Cancer Center, Manhattan, NY, USA

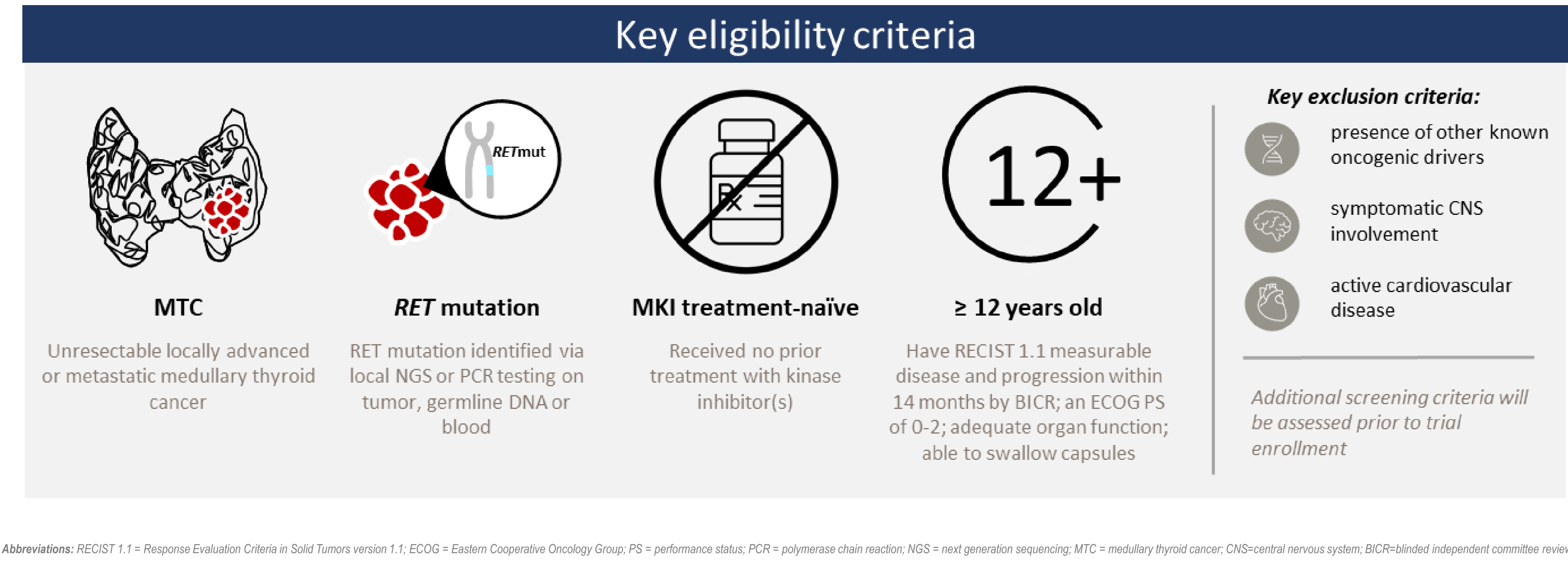
ABOUT THE LIBRETTO-531 TRIAL

- LIBRETTO-531 (also referred to as J2G-MC-JZJB [JZJB]) is a multicenter, open-label, randomized, controlled, Phase III trial comparing selpercatinib to cabozantinib or vandetanib in patients with advanced/metastatic *RET*-mutant MTC (NCT04211337).
- This study is active and recruiting participants, with planned enrollment of 400 patients at approximately 150 sites in 21 countries.

STUDY DESIGN

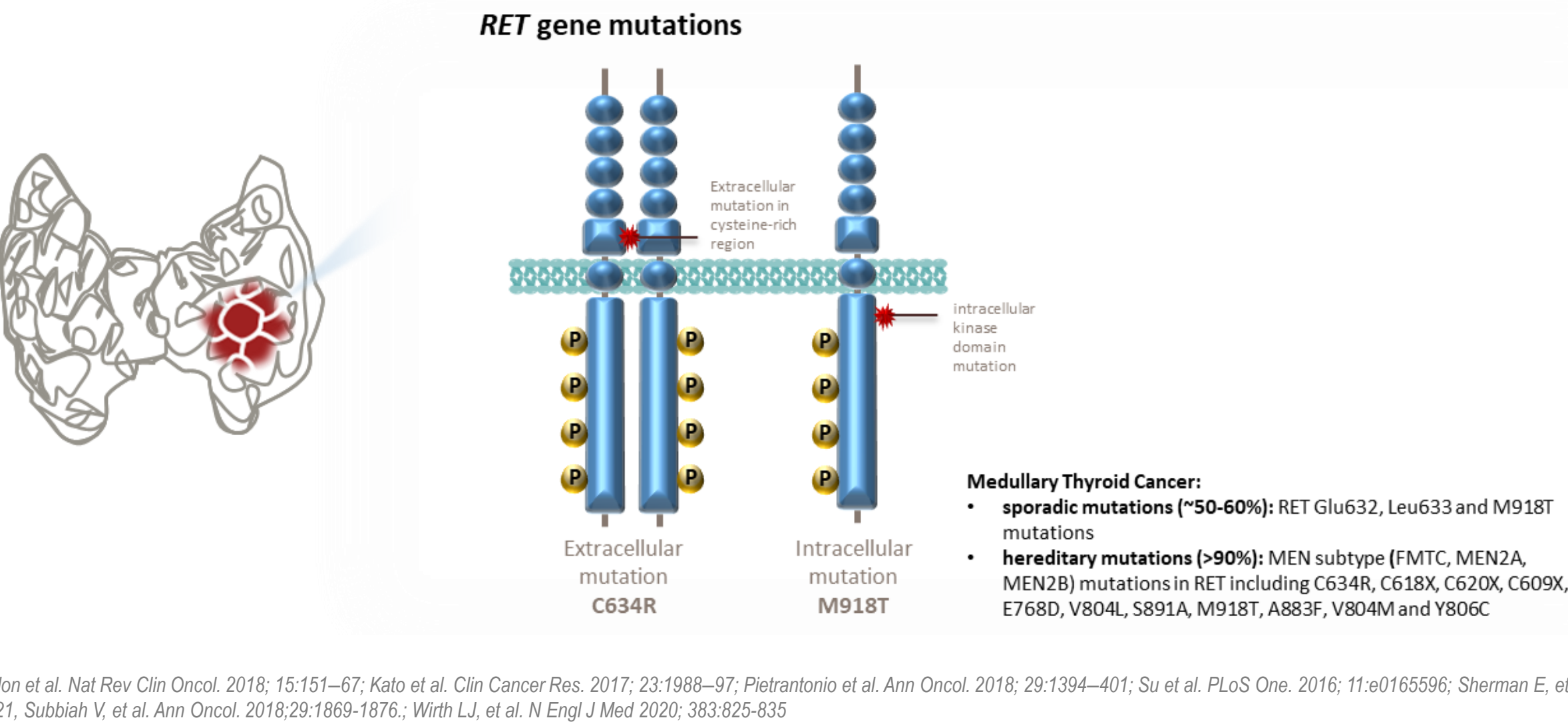


KEY ELIGIBILITY CRITERIA



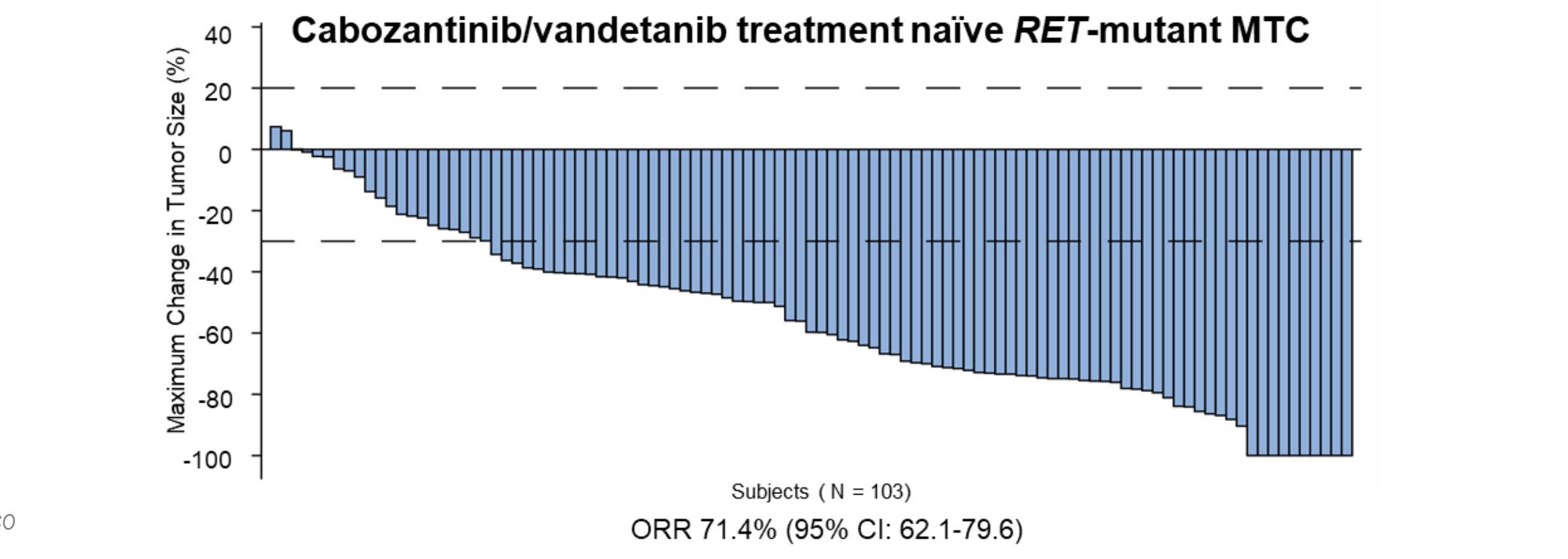
Activating *RET* Alterations are Actionable Oncogenic Drivers

- Activating *RET* gene alterations are common in medullary thyroid cancer (MTC), yet many patients with *RET*-mutant MTC are treated with multi-kinase inhibitors instead of *RET* targeted therapy
- Multikinase inhibitors with anti-*RET* activity have limited efficacy due to incomplete inhibition and significant toxicity
- Selpercatinib is a first-in-class, highly selective and potent, CNS active *RET* kinase inhibitor



Efficacy of Selpercatinib in *RET*-Altered Thyroid Cancers

- Selpercatinib has nanomolar potency against wild type *RET* and *RET* alterations including M918T, MKI resistance-associated V804M, and others
- Selpercatinib is efficacious in adults with *RET*-mutant MTC and *RET* fusion-positive thyroid cancer
- The manageable toxicity profile and durable anti-tumor activity demonstrated in the LIBRETTO-001 phase 1/2 trial led to approval of selpercatinib in multiple countries including the United States and Europe



Study Objectives

Primary Endpoint
To compare treatment failure free survival (TFFS), which incorporates radiographic PD, unacceptable toxicity (predefined by protocol) or death, of patients with progressive, advanced, kinase inhibitor naïve, <i>RET</i> -mutant MTC treated with selpercatinib versus cabozantinib or vandetanib
Major Secondary Endpoints
To compare PFS, based on RECIST 1.1 criteria, of selpercatinib versus cabozantinib or vandetanib
To compare the tolerability of selpercatinib versus cabozantinib or vandetanib
Other Secondary Endpoints
To compare other efficacy outcomes, based on RECIST 1.1 criteria, observed in patients with progressive, advanced, kinase inhibitor naïve, <i>RET</i> -mutant MTC treated with selpercatinib versus cabozantinib or vandetanib

Abbreviations: RECIST 1.1 = Response Evaluation Criteria in Solid Tumors version 1.1; PD = progressive disease; PFS = progression-free survival; MTC = medullary thyroid cancer

Doses and Dosing Schedule

	Arm A (Selpercatinib)	Arm B (Investigator's Discretion of B1: Cabozantinib or B2: Vandetanib)	
Intervention	Selpercatinib	Cabozantinib	Vandetanib ^a
Dose	160 mg	140 mg	300 mg
Schedule	BID continuously in 28-day cycles	QD continuously in 28-day cycles	QD continuously in 28-day cycles
Route	Oral	Oral	Oral

^a Starting dose of vandetanib for patients with creatinine clearance <50mL/min is 200mg QD
Specific dosing for adolescents is provided in the protocol
Abbreviations: BID = twice daily; QD = once daily

Participating Countries / Planned Enrollment



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