

Schema

EA3231 Version Date: November 7, 2024

Eligibility:

- Advanced RAIR DTC with BRAFV600E mutation
- Measurable disease by RECIST
- Documented radiographic PD (RECIST 1.1) over any time interval on or after first line multi kinase inhibitor
- Patients with 2 cm growth in single lesion within 3 months prior to randomization are excluded
- 1-2 prior multi kinase inhibitors, including lenvatinib and/or sorafenib
- ECOG Performance Status 0-2

R Arm A: Dabrafenib 150 mg PO Α BID Ν D Trametinib 2 mg PO Treatment will continue QD 0 until disease progression **Stratification Factors:** or intolerable toxicity. Μ Baseline tumor burden (sum of all target Crossover is allowed at Ζ lesions) < or 4 cm. time of RECIST progression. Α Т Arm B: Cabozantinib 60 mg PO QD 0 Ν

N=240 Randomization 1:1

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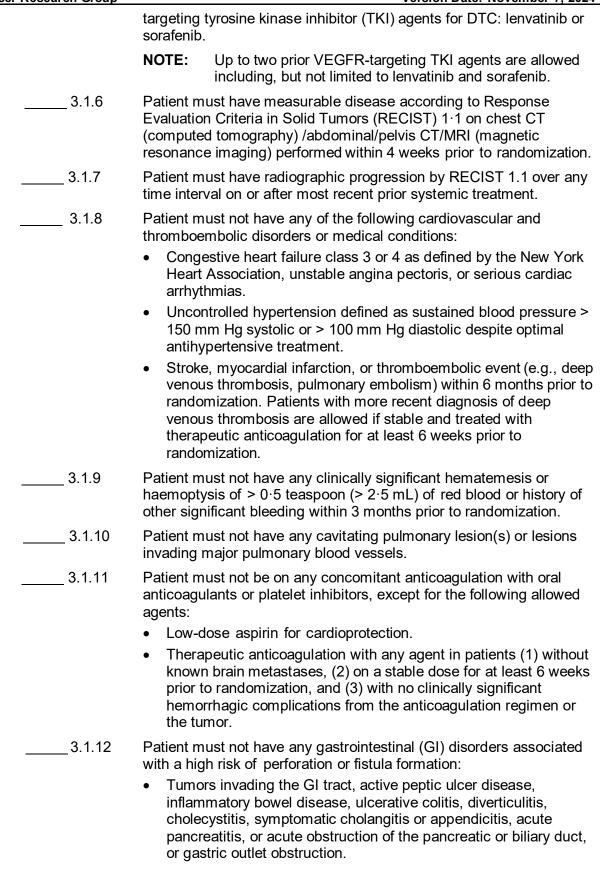
3. Selection of Patients

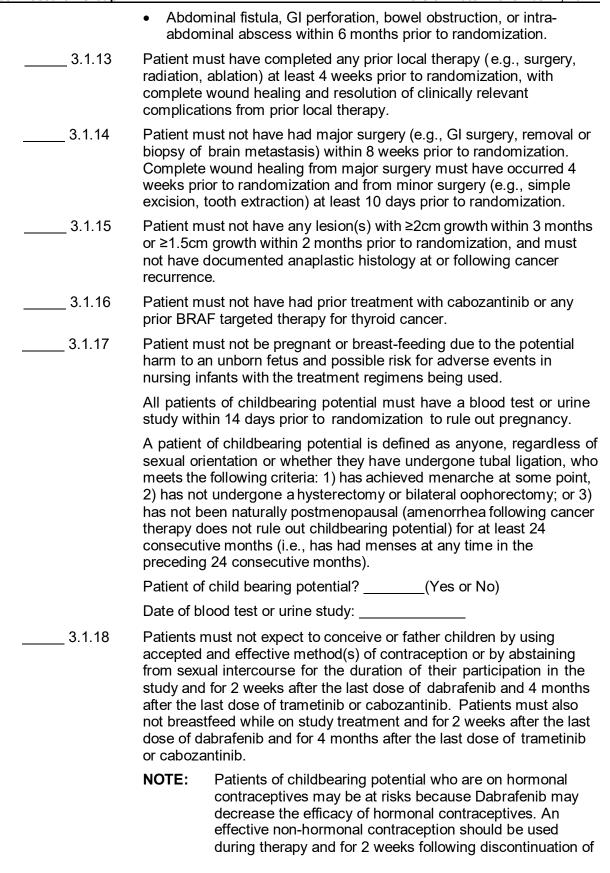
Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday four weeks later would be considered Day 28.

ECOG-ACRIN Patient No.

Patient's I	nitials (L, F, M)		
Physician	Signature and Date		
NOTE:	CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit, and require reporting to the IRB of record as non-compliance.		
	All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (<u>EA.ExecOfficer@ecog-acrin.org</u>) or the Group's Regulatory Officer (<u>EA.ExecOfficer@ecog-acrin.org</u>).		
NOTE:	Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to randomization by the treating physician.		
3.1 <u>Eli</u>	Eligibility Criteria		
3.1	.1 Patient must be ≥ 18 years of age.		
3.1	Patient must have an ECOG Performance Status 0-2.		
3.^	 Patient must have differentiated thyroid cancer (DTC) with BRAF V600E mutation as determined by local testing, including the following subtypes (Note: results of a previous biopsy will be accepted): Papillary thyroid carcinoma including histological variants of PTC such as follicular variant, tall cell, columnar cell, cribriform-morular, solid, oxyphil, Warthin-like, trabecular, tumor with nodular fasciitis-like stroma, Hürthle cell variant of papillary carcinoma, poorly differentiated. Follicular thyroid carcinoma including histological variants of FTC 		
	such as Hürthle cell, clear cell, insular, and poorly differentiated.		
3.′	1.4 Patient must have been previously treated with or deemed ineligible for treatment with Iodine-131 for DTC, and must be receiving thyroxine suppression therapy.		
3.´	Patient must have had prior treatment with at least one of the following vascular endothelial growth factor receptors (VEGFR)-		





dabrafenib and at least 4 months following the last dose of trametinib and cabozantinib.

3.1.19	Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-
	making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible.
3.1.20	Patient must have adequate organ and marrow function as defined below (these labs must be obtained ≤ 28 days prior to protocol randomization):
	_ Hgb ≥ 8 g/dL
	Hgb:Date of Test:
	_ Leukocytes ≥ 3,000/mcL
	Leukocytes:Date of Test:
	_ Absolute neutrophil count (ANC) ≥ 1,500/mcL
	ANC:Date of Test:
	_ Platelets ≥ 100,000/mcL
	Platelets:Date of Test:
	_ Total Bilirubin ≤ 2.0 x institutional upper limit of normal (ULN)
	Total Bilirubin:Institutional ULN:
	Date of Test:
	_ AST(SGOT)/ALT(SGPT) \leq 3.0 × institutional ULN or < 5.0 x ULN with the presence of hepatic metastasis
	AST:Institutional ULN:
	Date of Test:
	ALT:Institutional ULN:
	Hepatic metastases?(Yes or No)
	_ Estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m²
	eGFRDate of Test:
	Urine protein/creatinine (UPC) ratio ≥1
	Urine protein:Date of Test:
	Urine protein/creatinine ratio: Date of Test:
3.1.21	Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of randomization are eligible for this trial.
3.1.22	For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

OPTIONAL: TI

This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.