

Phase 2/3 trial of pumitamig (PD-L1 × VEGF-A bsAb) plus chemotherapy versus bevacizumab plus chemotherapy in previously untreated, unresectable, or metastatic colorectal cancer (ROSETTA CRC-203)

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Background

- Non-microsatellite instability high/mismatch repair-deficient metastatic colorectal cancer (non-MSI-H/dMMR mCRC) has limited benefit from immune checkpoint inhibition and is treated with first-line standard chemotherapy with/without biologic agents, such as anti-VEGF or anti-EGFR therapy¹⁻⁴
- Pumitamig (BNT327/BMS986545) is an investigational bispecific antibody engineered to simultaneously target both PD-L1 and VEGF-A within the tumor and tumor microenvironment, a dual mechanism intended to enhance anti-tumor immunity and inhibit angiogenesis (**Figure 1**)^{5,6}
- Pumitamig plus chemotherapy has shown encouraging efficacy and manageable safety in patients with solid tumors^{7,8}
- Pumitamig is currently being evaluated in first-line non-MSI-H/dMMR mCRC in the phase 2/3 ROSETTA CRC-203 trial (ClinicalTrials.gov ID: NCT07221357) and in a phase 2 trial (NCT07133750) in combination with chemotherapy (**Table 1**)

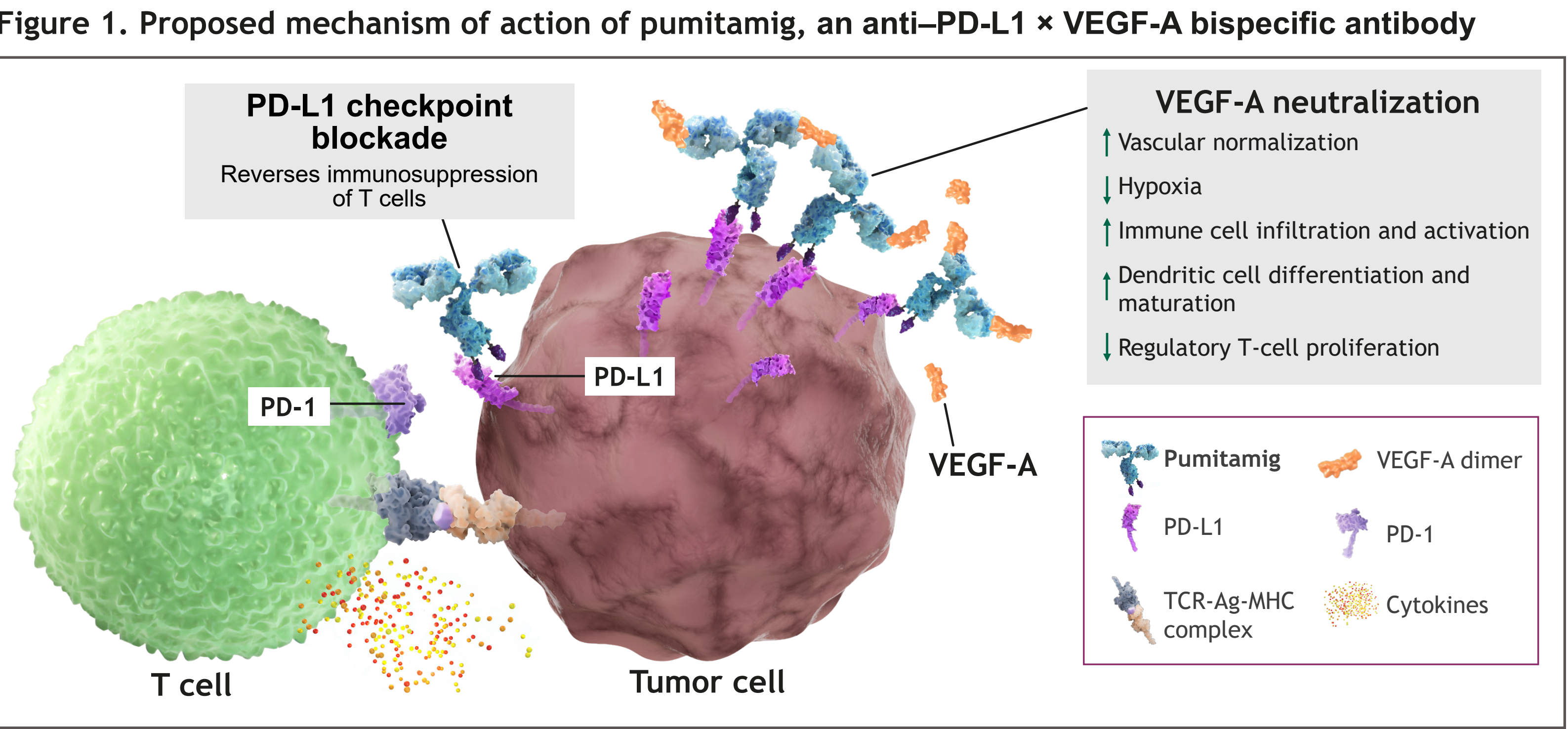


Table 1. Pumitamig trials in patients with mCRC

Line	Population	Combination regimen	Comparator	Phase	NCT ID/Study name
1	non-MSI-H/dMMR, <i>BRAF</i> WT	Pumitamig + chemotherapy (FOLFOX/FOLFIRI/CAPOX)	Bevacizumab + chemotherapy (FOLFOX/FOLFIRI/CAPOX)	2/3	NCT07221357/ROSETTA CRC-203
1	MSS or MSI-L/pMMR mCRC	Pumitamig + chemotherapy	None	2	NCT07133750/PM8002-B018C-CRC-R

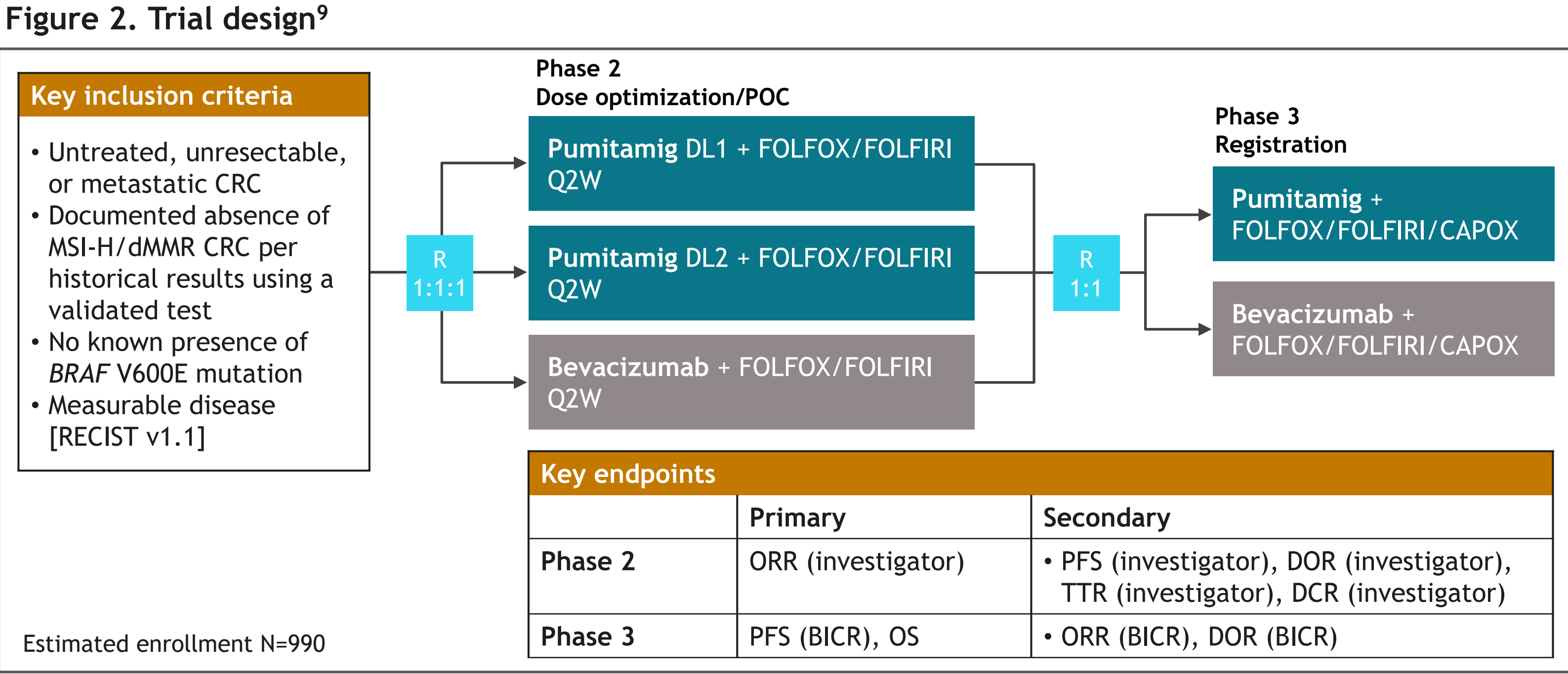
Pumitamig (BNT327/BMS986545) is jointly developed by BioNTech and Bristol Myers Squibb.

- This phase 2/3 trial (NCT07221357) evaluates the safety and efficacy of pumitamig versus bevacizumab (both in combination with chemotherapy) in patients with previously untreated, unresectable, or metastatic CRC

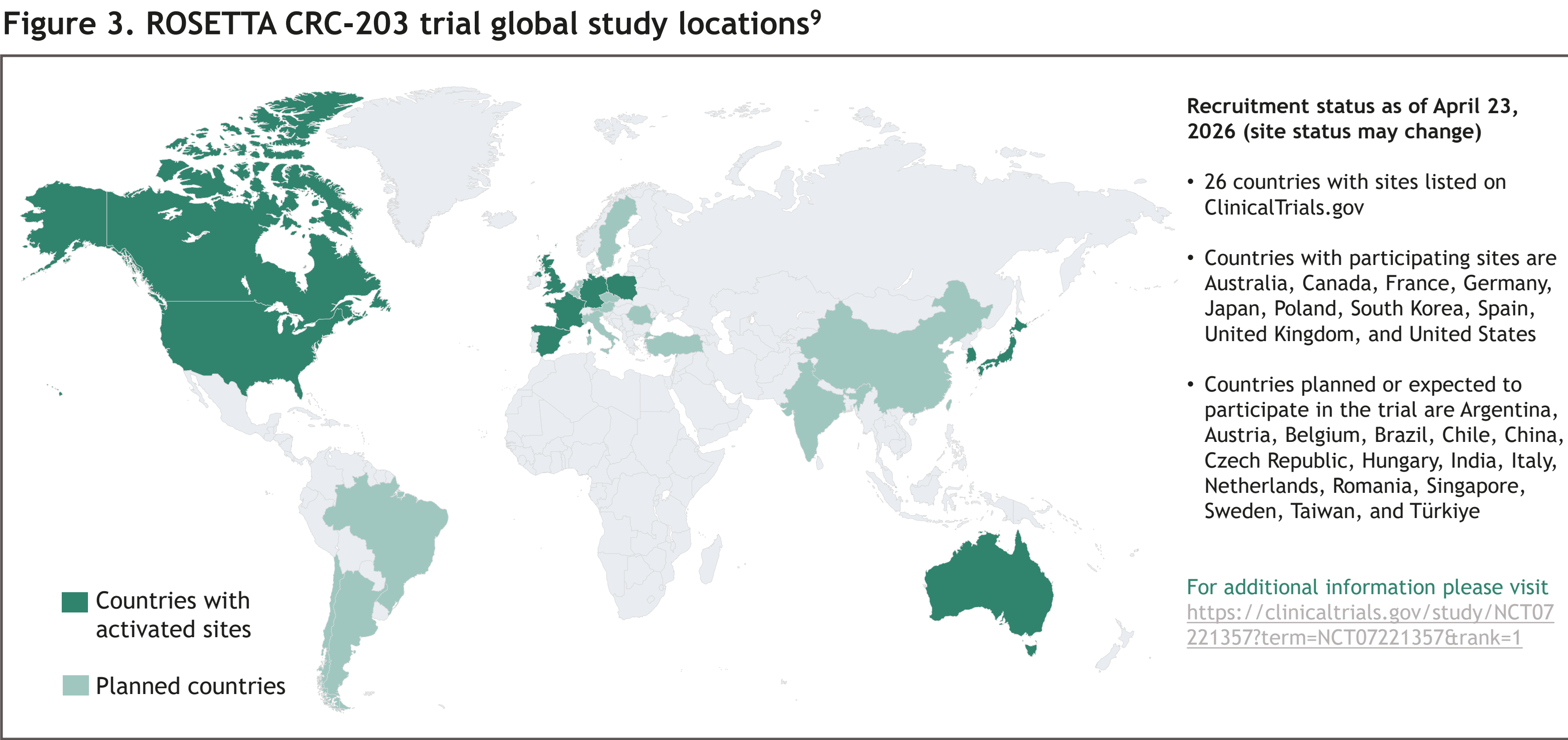
Methods

Trial design

- ROSETTA CRC-203 is a global, randomized, blinded phase 2/3 trial evaluating pumitamig plus chemotherapy versus bevacizumab plus chemotherapy in patients with mCRC (**Figure 2**)
- Eligible patients are aged ≥18 years with untreated, histologically confirmed recurrent or metastatic colorectal adenocarcinoma that is not amenable to curative surgery; measurable disease (per RECIST v1.1); documented absence of MSI-H/dMMR or mismatch repair-deficient mCRC; and no known presence of a gene encoding the BRAF protein V600E mutation (per local testing)
- Key exclusion criteria include untreated central nervous system metastases, significant cardiovascular disease, recent or active malignancy, and prior systemic therapy with checkpoint inhibitors
- In the phase 2 dose optimization part of this trial, patients will be randomized 1:1:1 to receive pumitamig (low or high dose) plus FOLFOX or FOLFIRI, or bevacizumab plus FOLFOX or FOLFIRI. The primary endpoint is ORR; secondary endpoints include PFS (investigator), DOR (investigator), TTR (investigator) and DCR (investigator)
- In phase 3, eligible patients will be randomized 1:1 to receive pumitamig at the recommended phase 3 dose plus FOLFOX (Q2W), FOLFIRI (Q2W), or CAPOX (Q3W), or bevacizumab plus the same choices of chemotherapy. The primary endpoints are PFS by BICR and OS; key secondary endpoints include ORR (BICR) and DOR (BICR)



- Recruitment status
- The global recruitment status and study locations for the ROSETTA CRC-203 trial shown in **Figure 3** reflect activated and planned sites according to ClinicalTrials.gov as of April 16, 2026



Abbreviations:

Ag, antigen; BICR, blinded independent central review; *BRAF*, B-raf proto-oncogene; *BRAF* WT, *BRAF* V600 wild type; bsAb, bispecific antibody; CAPOX, capecitabine + oxaliplatin; CRC, colorectal cancer; DCR, disease control rate; DL, dose level; DOR, duration of response; EGFR, epidermal growth factor receptor; FOLFIRI, folinic acid + fluorouracil + irinotecan; FOLFOX, folinic acid + fluorouracil + oxaliplatin; mCRC, metastatic colorectal cancer; MHC, major histocompatibility complex; MSI-H, microsatellite instability-high; MSI-L, microsatellite instability-low; MSS, microsatellite stable; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; POC, proof of concept; pMMR, mismatch repair-proficient; Q2W, every 2 weeks; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TCR, T-cell receptor; TTR, time to response; VEGF, vascular endothelial growth factor; VEGF-A, vascular endothelial growth factor A.

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