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CLINICAL TRIAL PROTOCOL

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A Phase III study of perioperative dostarlimab in patients with dMMR/MSI-H resectable colon cancer: AZUR-2 study design

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ABSTRACT

The role of perioperative immunotherapy as a chemotherapy-free option for patients with resectable mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) colon cancer is evolving, with early-phase neoadjuvant studies reporting favorable long-term outcomes. AZUR-2 is an ongoing global, Phase III, open-label, randomized study evaluating the efficacy of perioperative dostarlimab monotherapy compared with standard of care (SoC) (adjuvant chemotherapy or surveillance) in adult patients with previously untreated, pathologically confirmed, radiologically evaluable T4N0 or Stage III resectable dMMR/MSIH colon adenocarcinoma. Patients will be randomized 2:1 to receive neoadjuvant dostarlimab 500 mg every 3 weeks (4 cycles), followed by surgery, then adjuvant dostarlimab 1000 mg every 6 weeks (6 cycles), or to receive immediate surgery followed by SoC. The primary endpoint is event-free survival assessed by blinded independent central review. The key secondary endpoint is overall survival; additional secondary endpoints include pathological response assessed by residual viable tumor determined by local assessment, safety, and tolerability.

Clinical trial registration: NCT05855200 (www.clinicaltrials.gov).

PLAIN LANGUAGE SUMMARY

What is the purpose of the study?

Researchers are trying to find better ways of treating colon cancers that have spread beyond the colon to nearby tissues (also known as "advanced" colon cancer). There are different kinds of colon cancer and one type is called mismatch repair deficient, or dMMR for short. This means that the cancer cells have a faulty gene repair system.

Immunotherapy works by helping the immune system to recognize and kill cancer cells. Immunotherapy is more effective than chemotherapy in patients with advanced dMMR colon and rectal cancer that is not suitable for surgery. Researchers would like to know whether immunotherapy will also deliver better outcomes than chemotherapy for patients with dMMR colon cancer undergoing surgery.

What will the study look at?

AZUR-2 is an ongoing clinical study in adults with previously untreated advanced dMMR colon cancer that is suitable for surgery. The study will divide approximately 711 patients into two groups. One group will be treated with an immunotherapy drug called dostarlimab, then undergo surgery, then continue with dostarlimab.

The other group will be treated using the typical approach used in clinical practice: surgery, then either chemotherapy or careful monitoring. The study will compare the findings for the two groups to see whether dostarlimab given before and after surgery is better at controlling colon cancer than the current method of surgery followed by chemotherapy or monitoring. The study will also determine how safe this new treatment approach is.

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AZUR-2; colon cancer; dostarlimab; immune checkpoint inhibitors; perioperative immunotherapy; resectable; dMMR; MSI-H

1. Introduction

Colon and rectal cancer combined is the third leading cancer type in the United States and worldwide [1,2]. In the United States, there were an estimated 106,590 new cases of colon cancer in 2024 [1]. While 91% of patients with localized colon cancer at diagnosis survive for 5 years or more, this rate drops to 73% for patients with regional disease (spread to nearby lymph nodes) at diagnosis and to 13% for those with metastatic disease [3].

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Article highlights

Background and rationale:
- Colon and rectal cancer combined is the third leading cancer type in the United States and worldwide.
- Neoadjuvant therapy is not an established treatment option in the management of patients with colon cancer and current guideline-recommended options for high-risk Stage II (tumor node [TN] stage T4N0) or Stage III colon cancer focus on surgery with adjuvant chemotherapy.
- A subgroup of patients with mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) colon cancer derive limited benefit from adjuvant chemotherapy
- Recent studies suggest that neoadjuvant immunotherapy could provide a new treatment option for patients with early-stage dMMR/MSI-H colon cancer.
- AZUR-2 is designed to evaluate the safety and efficacy of perioperative dostarlimab compared with standard of care (SoC) in patients with dMMR/MSI-H, high-risk Stage II or Stage III colon cancer.

Study design:
- This study is an ongoing global, Phase III, open-label, randomized study designed to evaluate the effect of perioperative dostarlimab monotherapy versus SoC (surgery and either watchful waiting or adjuvant chemotherapy, as appropriate) in patients with previously untreated T4N0 or Stage III dMMR/MSI-H resectable colon cancer.
- Approximately 711 patients will be randomized 2:1 to receive either neoadjuvant dostarlimab 500 mg intravenous (IV) every 3 weeks for 4 cycles, followed by surgery, then adjuvant dostarlimab 1000 mg IV every 6 weeks for 6 cycles, or to receive immediate surgery followed by SoC adjuvant chemotherapy (adjuvant folinic acid plus fluorouracil plus oxaliplatin or capecitabine plus oxaliplatin for 12–24 weeks) or surveillance, selected by the physician.
- Patients will be stratified according to radiological TN staging established at screening, with at least 50% of patients having high-risk Stage III (T4 or N2) disease.

Outcome measures/endpoints:
- The primary endpoint is event-free survival (EFS), where an event is defined as disease recurrence based on radiological assessment by blinded independent central review or local pathological assessment, disease progression precluding surgery, treatment-related toxicity precluding surgery, or death.
- The key secondary endpoint is overall survival (OS) (from date of randomization to date of death by any cause). Additional secondary endpoints include pathological response assessed by residual viable tumor (RVT), EFS with recurrence assessed by local radiological assessment, safety and tolerability, pharmacokinetics, and immunogenicity.
- Exploratory endpoints include: the association between circulating tumor DNA dynamics and clinical activity; time to second subsequent therapy after recurrence or death due to any cause; antitumor activity in the neoadjuvant period per Response Evaluation Criteria in Solid Tumors version 1.1; dostarlimab-associated pharmacodynamic changes; and patient-reported outcomes.

Conclusion:
- This study will provide the first randomized data evaluating the safety and efficacy of perioperative dostarlimab compared with SoC in patients with previously untreated T4N0 or Stage III resectable dMMR/MSI-H colon cancer.

Current treatment recommendations for colon cancer are largely guided by disease stage and mismatch repair (MMR)/microsatellite instability (MSI) status [4–8]. Guidelines recommend universal testing for MMR status in patients with colon cancer to inform treatment and prognosis. MMR deficiency (dMMR) has been associated with improved prognosis for Stage II disease but poor prognosis for Stages III and IV [9]. The immune checkpoint inhibitors nivolumab (with or without ipilimumab) and pembrolizumab have demonstrated superiority to chemotherapy in dMMR/MSI-high (MSI-H) unresectable (pembrolizumab only) or metastatic colon and rectal cancer, and are now approved globally [10–15]. For high-risk Stage II (tumor node [TN] stage T4N0) or Stage III colon cancer, guidelines generally recommend surgery with adjuvant chemotherapy [4,5]. However, patients with dMMR/MSI-H tumors derive limited benefit from adjuvant chemotherapy compared with those with mismatch repair-proficient/microsatellite stable disease [4,16,17].

Given the clinical benefit of immunotherapy in the unresectable/metastatic setting, studies are exploring a potential role for neoadjuvant and adjuvant treatment with immune checkpoint inhibitors in patients with resectable dMMR/MSI-H colon cancer [18–21]. Neoadjuvant immunotherapy has demonstrated promising efficacy in the treatment of early-stage dMMR colon cancer [18,19]. In colorectal cancer studies, efficacy of immunotherapy is typically evaluated based on pathological response rates, with the optimal outcome being that of pathological complete response. This measure is clinically relevant as patients who attain a pathological complete response achieve improved survival outcomes and a lower likelihood of tumor recurrence compared with patients showing a lesser degree of response in colorectal cancer [19,22,23]. The exploratory NICHE study in patients with non-metastatic colon cancer, investigating the safety and efficacy of neoadjuvant immunotherapy (ipilimumab and nivolumab with or without celecoxib), showed that the subgroup of patients with dMMR tumors had a high rate of pathological responses [18]. The NICHE-2 expansion cohort study in patients with localized dMMR colon cancers confirmed the high rates of response, with a major pathological response seen in 98% (n = 109/111) of patients, including 95% (n = 105/111) with a major pathological response and 68% (n = 75/111) with a pathological complete response (pCR) [19]. There were no safety concerns and no significant delays to surgery [19]. In the Phase II RESET-2 trial in patients with resectable Stage I – III dMMR colon cancer, neoadjuvant treatment with pembrolizumab achieved a pCR rate of 44% (n = 37/84). A significantly higher pCR rate was seen in patients with Stage I – II (n = 20/33) versus Stage III disease (n = 17/51) (61% vs 33%; $p = 0.02$) [20]. While the treatment duration of neoadjuvant immunotherapy in patients with dMMR colon and rectal cancer has varied across studies, a recent systematic review suggests that a longer duration of neoadjuvant immunotherapy for locally advanced dMMR colon and rectal cancer may increase the complete response rate, with treatment courses ranging from 1 to 7 months [24].

Biological responses to surgery (and psychological stress induced by preparing for, undergoing, and recovering from surgery) activate numerous signaling pathways that can in turn lead to immune suppression and stimulation of undetected residual tumor cells and the tumor microenvironment, promoting local recurrence and metastasis [25]. The immediate perioperative period, spanning around 3 weeks before surgery to 3 weeks after, is considered a critical window for impacting cancer treatment outcomes [25]. In colorectal cancer, perioperative treatment combines neoadjuvant and adjuvant strategies, aiming to target both the tumor and its microenvironment. This approach seeks to promote tumor downstaging prior to surgery and mitigate surgery-related immunosuppression, thereby decreasing the risk of local recurrence and metastasis [25,26].

Perioperative immunotherapy approaches have been shown to improve survival outcomes beyond those observed with neoadjuvant or adjuvant immunotherapy in solid tumors, including melanoma and lung cancer [27,28], but data are limited in colon cancer [29]. While the role of neoadjuvant immunotherapy in early-stage colon cancer is still evolving, taken together, data support evaluating perioperative immunotherapy approaches in patients with early-stage dMMR/MSI-H colon cancer.

Dostarlimab, a programmed cell death receptor 1 (PD-1) inhibitor, is approved in the United States for the treatment of adult patients with dMMR advanced or recurrent solid tumors that have progressed on or following prior treatment, including those with colon cancer [30]. Dostarlimab monotherapy achieved an objective response rate of 43.5% in the subgroup of patients with dMMR and MSI-H/POLE-altered advanced colon and rectal cancer in the Phase I GARNET trial (n = 115) [31]. Additionally, an ongoing Phase II study in patients with locally advanced dMMR rectal cancer receiving a 6-month course of dostarlimab reported a clinical complete response (cCR) rate of 100% in 49 patients who completed treatment; cCRs were observed as early as 3 months into treatment and were durable, with a 96% recurrence-free survival at 2 years without the need for chemotherapy, radiation, or surgery [32].

The Phase III AZUR-2 study (NCT05855200) will evaluate the efficacy and safety of perioperative dostarlimab compared with standard of care (SoC) in patients with previously untreated T4N0 or Stage III resectable dMMR/MSI-H colon cancer. To our knowledge, this study will provide the first randomized data in this important treatment setting. Given the efficacy of immune checkpoint inhibitors in dMMR colon and rectal cancer, we hypothesize that patients will have improved outcomes with perioperative dostarlimab compared with SoC.

2. Methods

2.1. Study design

AZUR-2 is an ongoing global, Phase III, open-label, randomized study designed to evaluate the effect of perioperative dostarlimab monotherapy versus SoC in patients with previously untreated T4N0 or Stage III dMMR/MSI-H resectable colon cancer (Figure 1). Patient input on the study design was obtained to minimize patient burden associated with study participation and to provide input on the study outcomes considered most important to patients. An independent data monitoring committee will periodically review results and assess for continued benefit-risk ratio for enrolled patients. Content is based on Protocol Amendment 4 (approved 22 August 2024).

2.2. Eligibility criteria

Eligible patients are aged ≥18 years with untreated, pathologically confirmed, radiologically evaluable resectable colon adenocarcinoma that is clinically staged as T4N0 or III. Radiological assessment of clinical staging is used for enrollment due to the perioperative approach. Eligible patients have dMMR (determined locally or by the central reference laboratory) or MSI-H (determined locally) tumor status and must be Eastern Cooperative Oncology Group performance status (ECOG PS) 0 or 1.

Exclusion criteria include patients with distant metastatic disease; receipt of prior therapy (including chemotherapy, immunotherapy, biologic therapy, targeted therapy, or radiotherapy) or surgery for the current diagnosis of colon cancer for which they are being considered for the trial; known additional malignancy that progressed or required active treatment within the past 2 years; and immunocompromised patients or those with active autoimmune disease that required systemic treatment within the past 2 years. Patients with symptomatic bowel obstruction (determined per Investigator assessment) are also excluded, but patients with a bowel obstruction could become eligible after the obstruction is relieved by a diverting stoma (defunctioning ileostomy or colostomy); the latter exclusion criterion was added after study start by a protocol amendment on 22 August 2024. Patients are not eligible if an obstruction, in the

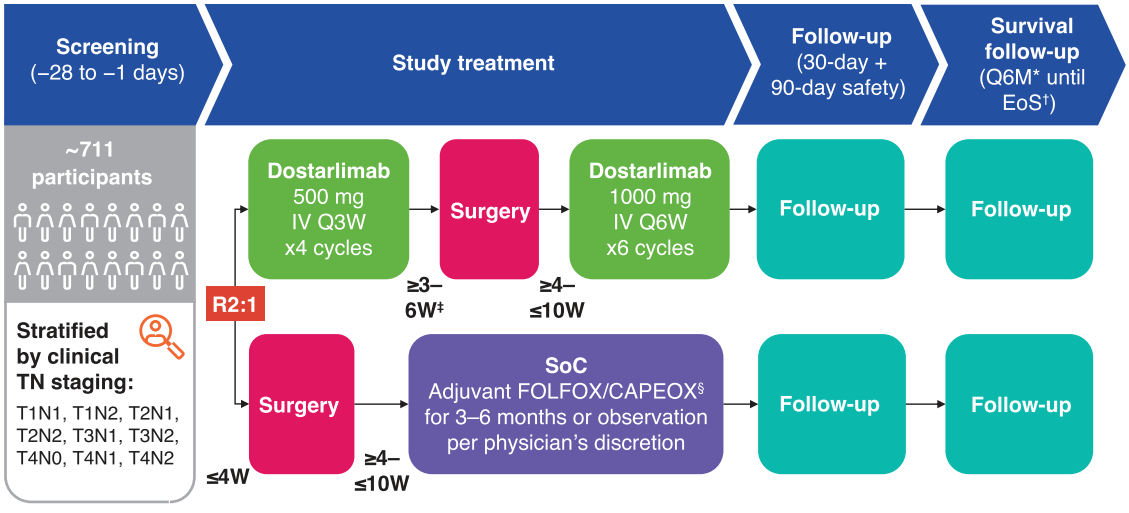

Figure 1. Study Schema.

*From end of safety follow-up; †when the last patient in the study has completed 5 years of follow-up; ‡from last dostarlimab dose; §DPD testing in advance of FOLFOX/CAPEOX treatment is mandatory in European countries and has been implemented in all countries participating in the study.

Abbreviations: CAPEOX, capecitabine plus oxaliplatin; DPD, dihydropyrimidine dehydrogenase; EoS, end of study; FOLFOX, folinic acid plus fluorouracil plus oxaliplatin; IV, intravenous; N, node; R, randomized; QxM; every × months; QxW, every × weeks; SoC, standard of care; T, tumor; TN, tumor, node; W, week.

context of the current colon cancer diagnosis, is treated with colonic stents.

2.3. Interventions

Approximately 711 patients will be randomized 2:1 to receive either neoadjuvant dostarlimab 500 mg intravenous (IV) every 3 weeks (Q3W) for 4 cycles, followed by surgery, then adjuvant dostarlimab 1000 mg IV every 6 weeks (Q6W) for 6 cycles, or to receive immediate surgery followed by SoC (adjuvant chemotherapy: folinic acid plus fluorouracil plus oxaliplatin [FOLFOX] or capecitabine plus oxaliplatin [CAPEOX] for 12–24 weeks) or surveillance (watch and wait), selected by the physician. SoC will be determined based upon the patient's pathologic stage and their investigator's opinion. For patients with Stage III tumors, management will include adjuvant chemotherapy unless the patient is found to have a contraindication to chemotherapy. For patients with T4N0 tumors, management may include either adjuvant chemotherapy or surveillance if adjuvant treatment is not indicated per the investigator's opinion.

Study participation will continue until disease progression, unacceptable toxicity, withdrawal of consent, or at the Investigator's discretion. For randomization, patients will be stratified into nine strata groups according to local radiological TN staging established at screening as follows: T1N1, T1N2, T2N1, T2N2, T3N1, T3N2, T4N0, T4N1, or T4N2. At least 50% of patients enrolled in the study will have high-risk Stage III disease (T4 or N2: T4N1, T4N2, T3N2, T2N2, or T1N2).

As the study includes multimodal treatment in molecularly selected and imaging-staged patients, enrollment involves a multidisciplinary team of healthcare professionals; implementation of the study design as well as patient monitoring involves close communication across the full team, including oncologists, endoscopic or gastrointestinal specialists, surgeons, pathologists, radiologists, research coordinators, nursing staff, and other ancillary staff. Recommendations for determining TN stage by radiological imaging are being provided to investigators to facilitate enrollment [29].

2.4. Outcome measures/endpoints

The primary endpoint is event-free survival (EFS) with recurrence assessed by blinded independent central review (BICR), where an event is defined as disease recurrence (based on radiological assessment by BICR or local pathological assessment of new lesions), disease progression precluding surgery (based on local assessment), treatment-related toxicity precluding surgery, or death. The key secondary endpoint is overall survival (OS; the time from date of randomization to the date of death by any cause). Pathological response (assessed by residual viable tumor [RVT] and defined as no more than 50% RVT, with complete pathological response defined as no RVT in primary tumor or lymph nodes) will also be included as a secondary endpoint and will be determined by local assessment (Figure 2). Other secondary endpoints will include EFS with recurrence assessed by local radiological assessment; safety and tolerability including frequency and severity of adverse events; pharmacokinetic profile; and immunogenicity.

Exploratory endpoints include: the association between circulating tumor DNA dynamics and clinical activity; time to second subsequent therapy after recurrence, or death due to any cause; antitumor activity in the neoadjuvant period per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) by local assessment; proportion of R0 (complete resection), R1 (microscopic residual tumor), and R2 (macroscopic residual tumor) resections as assessed at primary surgery; assessment of dostarlimab-associated pharmacodynamic changes by tumor proteomics and immunophenotyping; and patient-reported outcomes (PROs). Exploratory investigation of blood and tissue biomarkers of response will include assessment of programmed death ligand 1 expression and other immune markers by immunohistochemistry; tumor mutational analysis; molecular subtyping; and expression of immune signatures.

2.5. Study procedures

Patient demographics, disease characteristics, medical history, and additional baseline assessments will be collected during the screening period. Clinical TN staging will be established with radiological assessment ahead of study entry and, when not already known, dMMR/MSI-H status will be determined during prescreening by local pathological testing where available, or central testing.

For patients within the experimental arm, antitumor activity will be assessed radiologically in the neoadjuvant period, by comparison of the screening (baseline) versus pre-surgery scans (assessment by Investigator per RECIST v1.1). For all patients, efficacy will be assessed radiologically (assessment by BICR and Investigator per RECIST v1.1) every 6 months for 3 years and then per standard practice for years 4 and 5.

Survival follow-up will continue until the end of study, defined as patient death, loss to follow-up, withdrawal of consent, completion of all study follow-up, or investigator's decision to be discontinued from study.

Pathological staging per American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) tumor node metastasis (TNM) of the surgical specimen will be determined for all patients in both treatment arms. For patients within the experimental arm at sites participating in determining RVT, pathological assessment of response on the surgical specimen will be performed to determine the primary lesion response (including lymph nodes and regression bed of all foci removed as part of surgery) to neoadjuvant therapy. RVT is the visual quantification of viable invasive tumor and tumor-regression microscopic findings (Figure 2) [30,31].

Safety will be evaluated throughout the study at patient visits at screening, throughout treatment, and at 30 and 90 days after last dose of adjuvant therapy or surgery (whichever occurs last). Serious adverse events that have been assessed as related to the study treatment will be recorded until the end of the survival follow-up period.

Tissue, blood, and plasma samples will be collected throughout the study for biomarkers, pharmacokinetic, and immunogenicity assessments.

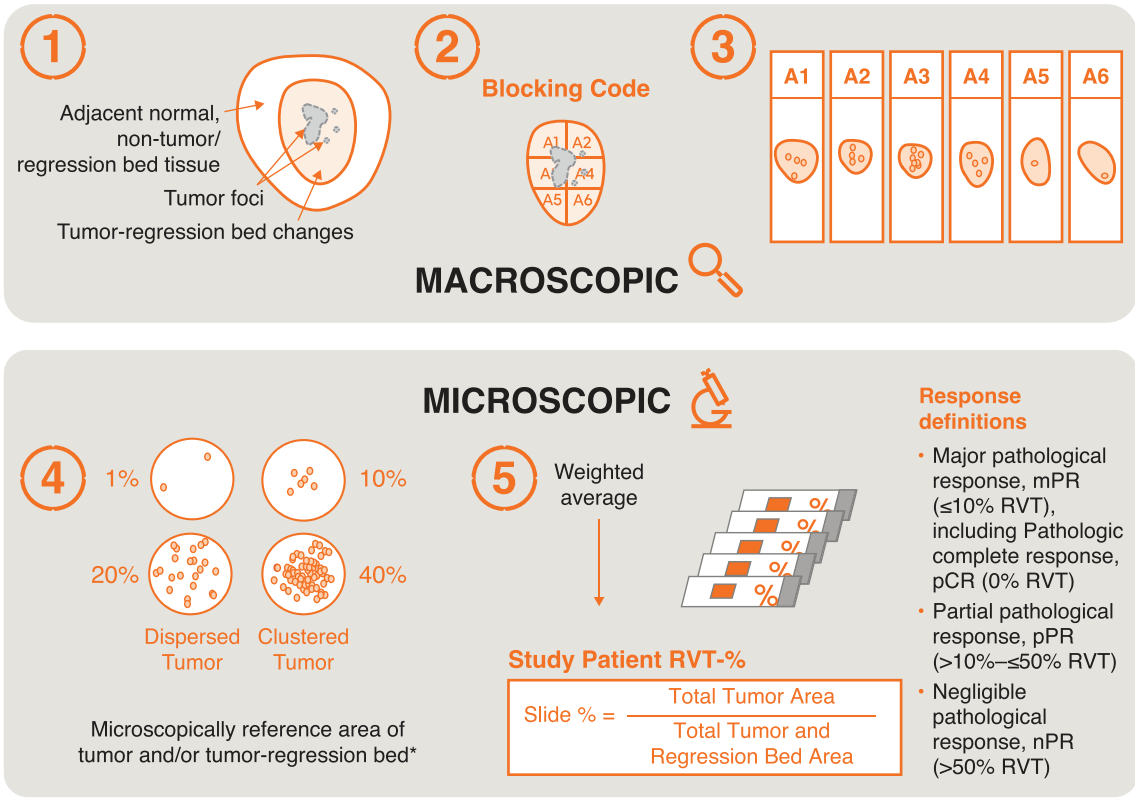

Figure 2. RVT methodology.

*Invasive tumor only; excludes in situ or premalignant epithelial proliferation, such as adenoma. Macroscopic examination of the specimen includes the entire regression bed and residual tumor in the entire specimen (not shown) to enable AJCC/UICC TNM and RVT staging. Pathologist examination (#1) and informed selections for paraffin-embedded tissue block processing (#2) and slide preparation (#3) are performed. Microscopic review (#4) approximates the viable tumor within slides containing regression bed changes. The average of individual slide % scores determine the subject-level RVT score (#5). Study response buckets include pCR, mPR, pPR, and nPR.

Abbreviations: AJCC, American Joint Committee on Cancer; mPR, major pathologic response; nPR, negligible pathologic response; pCR, pathologic complete response; pPR, partial pathologic response; RVT, residual viable tumor; TNM, tumor node metastasis; UICC, Union for International Cancer Control.

PROs will be collected throughout the study using multiple instruments to assess disease and treatment-related symptoms, and impact on health-related quality of life.

2.6. Sample size

Approximately 711 patients will be randomized 2:1 to receive either perioperative dostarlimab followed by surgery followed by dostarlimab, or to receive immediate surgery followed by SoC adjuvant chemotherapy or surveillance. Sample size determination was based on an assumed 3-year EFS for SoC of 78% and a true EFS difference of 10%. Under these assumptions, the log-rank test will have 90% power to detect a difference in the EFS survival curve at the interim analysis assuming 94 events and 95% power at the primary analysis, assuming 110 events using 1-sided 2.5% level of significance.

2.7. Recruitment

AZUR-2 is currently recruiting in Argentina, Australia, Belgium, Brazil, Canada, China, Czech Republic, Estonia, Finland, France, Germany, Hungary, Italy, Japan, Mexico, the Netherlands, Norway, Panama, Poland, Portugal, Republic of Korea, Spain, Sweden, Taiwan, Turkey, United Kingdom, and the United States (Figure 3). Activation is pending in India. The planned primary analysis completion date is December 2028, and the planned study completion date is December 2030.

2.8. Statistical analyses

Primary analysis of the study will occur when approximately 110 events have been observed, expected to be after all patients have completed approximately 3 years of follow-up, with an interim analysis conducted approximately 12 months earlier. A stratified log-rank test will be used to assess the primary endpoint of EFS.

2.9. Ethics and dissemination

This study will be conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences international ethical guidelines, applicable International Council for Harmonisation (ICH) for Good Clinical Practice guidelines, and applicable laws and regulations. The protocol, protocol amendments, informed consent form, investigator's brochure, and other relevant documents will be approved by the

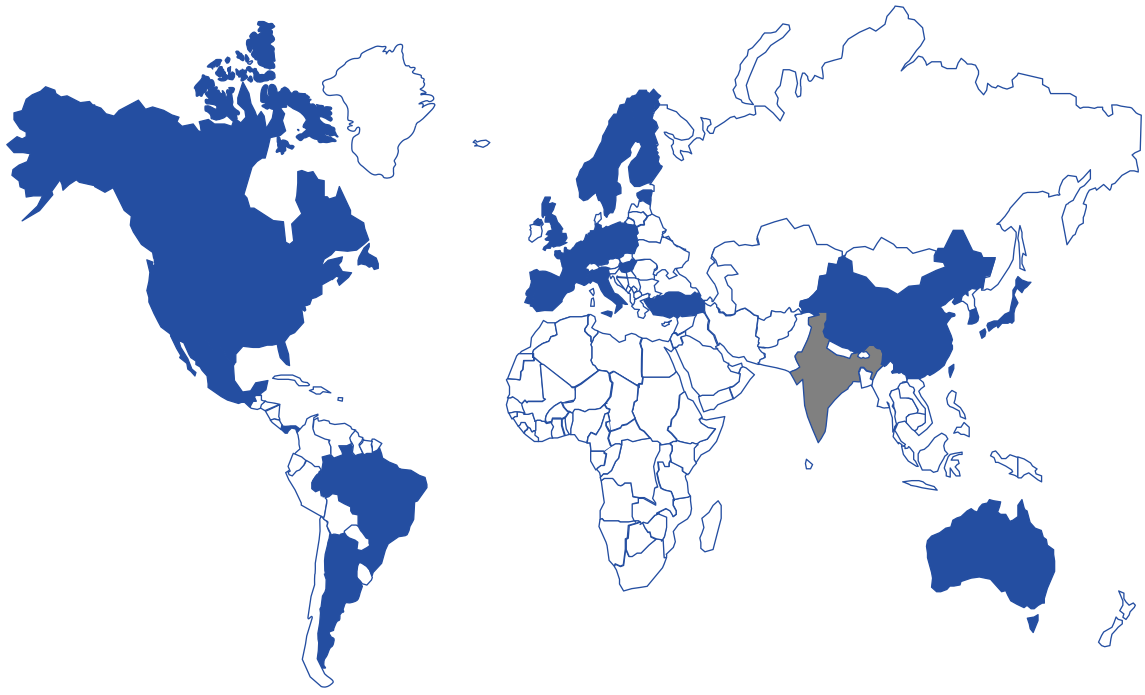

Figure 3. Recruiting countries.
Currently recruiting countries are shown in blue; countries where recruitment is pending are shown in gray.

institutional review board or ethics committee (IRB/IEC) of participating centers before study initiation. The investigator or the investigator's representative will communicate to potential patients that their participation is voluntary and obtain a signed written statement of informed consent that meets the requirements of Title 21 of the US Code of Federal Regulations part 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, privacy and data protection requirements, where applicable, and the IRB/IEC or study center.

The findings of this study will be presented at relevant congresses and published in peer-reviewed journals.

3. Conclusions

AZUR-2 is an ongoing global, Phase III, open-label, randomized study designed to evaluate the efficacy and safety of perioperative dostarlimab monotherapy versus SoC (surgery with adjuvant chemotherapy or surveillance as appropriate) in patients with previously untreated T4N0 or Stage III dMMR/MSI-H resectable colon cancer. There is a high unmet need to develop novel perioperative therapies in this patient population to improve disease control and long-term outcomes as current adjuvant chemotherapy options have shown limited benefit.

While the study data will be subject to potential subjective bias from investigators or patients that is inherent in open-label studies, assessing the primary endpoint of EFS through BICR will serve to limit bias on this particular endpoint. As with all clinical studies, patient selection will affect the generalizability of the results of AZUR-2, and real-world studies will be needed in the future to confirm the results. A detailed discussion of all potential study limitations will be included in the publication of the primary findings upon completion of the study.

In terms of strengths of this study, there are important elements that will inform future trials. The novel treatment sequencing, particularly regarding the timing of surgery for patients randomized to the experimental arm, requires close communication across a multidisciplinary team during both patient enrollment and throughout the study treatment. By investigating this perioperative approach with radiological and RVT assessment, AZUR-2 will improve our understanding of the treatment effect of neoadjuvant immunotherapy. To our knowledge, this is the first global study using local RVT scoring to determine pathological response.

Recent favorable data with dostarlimab for advanced/recurrent dMMR colon and rectal cancer and locally advanced dMMR/MSI-H rectal cancer suggests that dostarlimab could provide significant benefit for patients with early-stage dMMR/MSI-H colon cancer [31,33]. Furthermore, studies have demonstrated high rates of response to neoadjuvant immunotherapy in patients with early-stage dMMR/MSI-H colon cancer [18,19]. The AZUR-2 study has been designed to assess the safety and efficacy of perioperative dostarlimab compared with SoC. By exploring novel perioperative treatment regimens, AZUR-2 aims to establish a foundation for a novel treatment approach of perioperative dostarlimab as an alternative to chemotherapy to reduce the risk of recurrence and improve long-term outcomes in patients with previously untreated T4N0 or Stage III resectable dMMR/MSI-H colon cancer. By incorporating exploratory biomarker endpoints, the study also seeks to personalize treatment strategies to identify markers of treatment response as well as patients most likely to benefit from perioperative immunotherapy.

Taken together, the findings of AZUR-2 have the potential to influence future research, inform treatment guidelines and reshape clinical practice by providing a viable alternative to adjuvant chemotherapy, which has limited benefit in resectable dMMR/MSI-H colon cancer, thereby improving patients' quality of life.

Acknowledgments

This protocol was presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium, January 18–20 2024, San Francisco, USA (Starling N., et al. *J Clin Oncol*. 2024 Jan; 42(3_suppl):TPS240).

Author contributions

NStarling, DC, KE, NStjepanovic, and JFS contributed to study concept or design; NStarling, EE, JHS, AB, EO, GM, RF, YLL, and AK contributed to data acquisition; MT, NC, DC, KE, and NStjepanovic contributed to data analysis; NStarling, DC, KE, NStjepanovic, and JFS contributed to data interpretation.

Disclosure statement

NStarling had paid consulting/advisory roles for AstraZeneca, Pfizer, MSD, MSD Oncology, Novartis UK, Servier, GSK, Gilead Sciences, Seagen, and Janssen; received travel/accommodation/expenses from MSD Oncology, Guardant Health, Servier, and GSK; received honoraria from Lilly, Merck Serono, Servier, GSK, Amgen, Pierre Fabre, Lilly, Novartis, MSD Oncology, Seagen, Merck, Bristol Myers Squibb, and AstraZeneca; received research funding from AstraZeneca, Pfizer/EMD Serono, Bristol Myers Squibb, Guardant Health, and Merck Serono; participated in an unpaid advisory board for Guardant Health.

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YLL had paid consulting/advisory roles for Pfizer, AstraZeneca, Roche/Genentech, Novartis, Merck, Asofarma, Bristol Myers Squibb; received travel/accommodation/expenses from Roche/Genentech, Merck, Bristol Myers Squibb, Asofarma.

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MT is an employee of GSK and holds financial equities in GSK.

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Ethical declaration

This study will be conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences international ethical guidelines, applicable International Council for Harmonisation (ICH) for Good Clinical Practice guidelines, and applicable laws and regulations. The protocol, protocol amendments,

informed consent form, investigator's brochure, and other relevant documents will be approved by the institutional review board or ethics committee (IRB/IEC) of participating centers before study initiation. The investigator or the investigator's representative will communicate to potential patients that their participation is voluntary and obtain a signed written statement of informed consent that meets the requirements of Title 21 of the US Code of Federal Regulations part 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, privacy and data protection requirements, where applicable, and the IRB/IEC or study center.

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