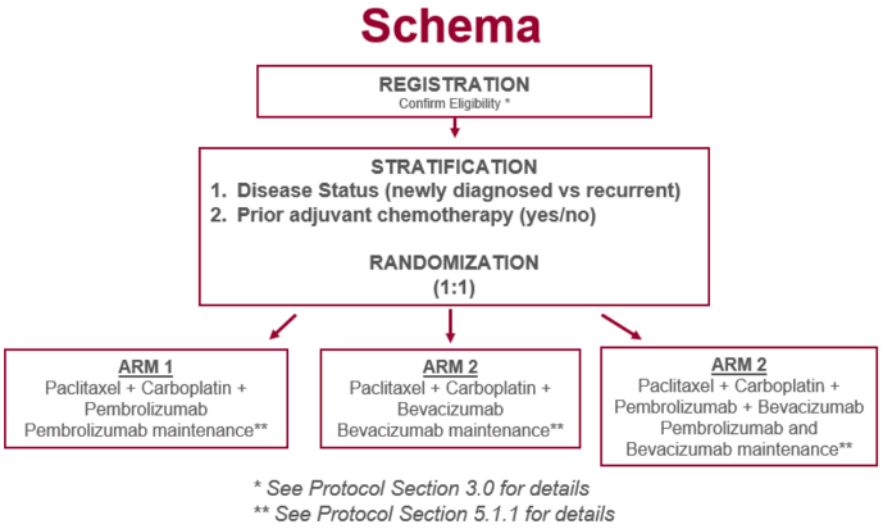
Dear Investigators,

We are writing to solicit your participation in NRG-GY035, "**A Randomized Phase III Trial of Carboplatin, Paclitaxel, Pembrolizumab versus Carboplatin, Paclitaxel, Bevacizumab versus Carboplatin, Paclitaxel, Pembrolizumab, Bevacizumab in the Treatment of pMMR, *TP53* Mutated Advanced or Recurrent Endometrial Cancer**". This trial builds upon the Phase III NRG GY018 study, which examined the survival benefit of adding checkpoint inhibitor therapy (pembrolizumab) to carboplatin and paclitaxel in patients with both mismatch repair deficient (dMMR) and mismatch repair proficient (pMMR), advanced or recurrent endometrial cancer. While the greatest progression-free survival (PFS) benefit in NRG-GY018 was observed in those with dMMR tumors, a modest, statistically significant PFS benefit was also noted in those with pMMR tumors. As most patients with advanced or recurrent endometrial cancer have pMMR tumors, there remains a critical need to identify strategies that further—and sustainably--improve outcomes for patients with pMMR disease.

There is significant scientific rationale for combining either VEFG inhibition with chemotherapy or VEGF inhibition with checkpoint inhibition and chemotherapy in patients with advanced-stage or recurrent, pMMR and TP53 mutated tumors. Your participation in this trial will be critical for successfully establishing a standard therapeutic approach for this patient population in the frontline setting. Below are the trial study schema, objectives, and key eligibility criteria.



Primary Objective:

- To demonstrate that bevacizumab in combination with carboplatin, paclitaxel, and pembrolizumab is superior to carboplatin, paclitaxel, and pembrolizumab (the control arm) or carboplatin, paclitaxel, and bevacizumab in prolonging PFS in patients with pMMR, TP53 mutated advanced stage (III or IV) or recurrent endometrial cancer.

Secondary Objectives:

- To demonstrate that bevacizumab in combination with carboplatin, paclitaxel, and pembrolizumab is superior to carboplatin, paclitaxel, and pembrolizumab or carboplatin, paclitaxel, and

bevacizumab in prolonging OS in patients with pMMR, TP53 mutated advanced stage (III or IV) or recurrent endometrial cancer.
- To examine the impact of the addition of bevacizumab in combination with carboplatin, paclitaxel, and pembrolizumab on PFS and OS based on type of p53 IHC aberrancy (over expression/cytoplasmic expression versus null [complete absence of staining]) and mutation type.
- To evaluate toxicity on treatment with bevacizumab when combined with carboplatin, paclitaxel, and/or pembrolizumab as assessed by CTCAE v.5.0.
- To explore the anti-tumor activity in each treatment arm as assessed by objective response rate in the subset of patients with measurable disease by RECIST 1.1.

Key Inclusion Criteria:

- Stage III and Stage IVA RECIST-evaluable disease; Stage IVB (with or without measurable disease), or recurrent (with or without measurable disease) endometrial cancer.
- Tumoral mismatch repair proficient (pMMR) disease as assessed by immunohistochemistry (IHC), AND
- P53 IHC with aberrant staining pattern (aberrant p53 expression is consistent with mutant *TP53*). *TP53* mutation by next-generation sequencing will also be accepted.
- No prior chemotherapy for treatment of endometrial cancer OR Prior adjuvant chemotherapy provided it was completed ≥ 12 months prior to registration.
- No prior pembrolizumab or bevacizumab.

Important Patient Safety Consideration: Finally, investigators may omit bevacizumab in Cycle 1 based on clinical judgment and patient safety considerations. While this flexibility is not explicitly stated in the current protocol, NRG Oncology will permit this approach effective immediately. This is consistent with existing protocol language allowing treatment modifications in accordance with institutional standards of care. An upcoming trial amendment will more explicitly address this clinical trial guidance.

We would appreciate your help to identify potential participants and would be happy to discuss a patient with you to review suitability for this study. The study can be found on ClinicalTrials.gov. Thank you for your consideration of enrolling patients on **NRG-GY035.**

Yours Sincerely,

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