SWOG CANCER RESEARCH NETWORK

INVESTIGATOR LETTER

Date: January 22, 2019

To: **S1500** Participating Investigators

From: Sumanta K. Pal, M.D. – S1500 Study Chair
Primo N. Lara, Jr., M.D. – S1500 Study Co-Chair
Ian M. Thompson, Jr., M.D. – SWOG Genitourinary Committee Chair

RE: Interim analysis of **S1500**: "A Randomized, Phase II Efficacy Assessment of Multiple MET Kinase Inhibitors (Cabozantinib [NSC #761968], Crizotinib [NSC #749005], Savolitinib [NSC #785348], and Sunitinib [NSC #736511]) in Metastatic Papillary Renal Carcinoma (PAPMET)"

S1500 Arm 3 (crizotinib) and Arm 4 (savolitinib) were permanently closed to accrual on December 5, 2018, following the results of a planned futility interim analysis. The interim analysis was conducted to compare the efficacy of the experimental arms (crizotinib and savolitinib) to the efficacy of the standard of care arm (sunitinib) in terms of progression-free survival. The interim analysis of cabozantinib has not been conducted yet. It will be performed when the required number of progression-free survival events have occurred on that arm.

Patients who have received treatment on **S1500** must be notified that the study team reviewed patient data to date and found that patients on treatment with crizotinib or savolitinib in this study were noted to have less favorable outcomes than those treated with sunitinib by the timelines noted below. The manner by which this notification should take place is at the discretion of the local Institutional Review Board (IRB). At a minimum, patients currently receiving the experimental therapy (crizotinib or savolitinib) must be notified of the results of the interim analysis. The attached "Patient Information Letter" may be used if desired. Documentation that this information has been provided must be retained in the patient's research record on site and will be subject to verification at the time of a Quality Assurance audit.

If there is evidence of radiographic or clinical progression, then (as per the study guidelines) patients should be removed from protocol-based therapy. Enrollment to the study will be closed until a forthcoming amendment is issued.

Patients currently receiving treatment on **S1500** Arm 3, may continue treatment with crizotinib at the discretion of the treating physician if the patient is deriving clinical benefit, agrees to continue treatment, and if their physician feels that it is in the patient's best interest to continue treatment at this time. No additional consent is required for patients who will continue crizotinib treatment.

Patients currently receiving treatment on **S1500** Arm 4, may continue treatment with savolitinib at the discretion of the treating physician if the patient is deriving clinical benefit, agrees to continue treatment, and if their physician feels that it is in the patient's best interest to continue treatment at this time. No additional consent is required for patients who will continue savolitinib treatment.

Patients on Arms 3 and 4 who are currently receiving protocol treatment must be notified at their next study visit or within 30 days of distribution of this notice to make the determination of whether to continue treatment.

Patients on Arms 3 and 4 who have completed or been removed from protocol treatment must be notified within 90 days of distribution of this notice.

Patients on Arms 1 and 2 must be notified within 90 days of distribution of this notice.

Sites are expected to continue the protocol-specified data submission requirements in Section 14.0 for all patients.

Continued follow-up and reporting of adverse events, progression and survival is important to all subsequent analyses of this trial. Therefore, sites are expected to continue to submit follow-up forms on this trial. We also request that any outstanding forms be completed and submitted as soon as possible.

Please direct questions to:
Eligibility/Data Submissions: **S1500**Question@swog.org
Protocol/Regulatory: vgarcia@swog.org
S1500 Treatment-related/Medical: **S1500**Question@swog.org

Thank you for your continued participation in the **S1500** trial.

*[Patient Letter: For all patients registered to **S1500**]*

PATIENT INFORMATION LETTER

S1500, ""A Randomized, Phase II Efficacy Assessment of Multiple MET Kinase Inhibitors (Cabozantinib [NSC #761968], Crizotinib [NSC #749005], Savolitinib [NSC #785348], and Sunitinib [NSC #736511]) in Metastatic Papillary Renal Carcinoma (PAPMET)" Study Chairs:

Treatment Arms: Arm 3 (crizotinib) and Arm 4 (savolitinib)

You are participating in the S1500 trial, a SWOG research study for papillary renal carcinoma. It was stated in your Consent Form that you would be given any new information that might affect your health and/or your willingness to continue in the study. We, the SWOG study investigators, have new information regarding the effectiveness of crizotinib (Arm 3) and savolitinib (Arm 4) for patients in the study. The Data and Safety Monitoring Committee (DSMC), reviewed the patient data to date based on a prespecified plan and found that neither crizotinib nor savolitinib on average, did a better job lengthening the time that the patient's cancer did not progress compared to those patients receiving sunitinib. The study team also reviewed these data and agreed with the DSMC assessment. Based on this review, Arms 3 and 4 will be closed to future patient enrollment.

If you are currently receiving crizotinib or savolitinib, you may continue to receive the drug if you and your physician feel that you are receiving clinical benefit and it is in your best interest to continue the treatment. All patients will continue to be followed as described in your Consent Form, whether you decide to continue or discontinue study treatment. If your cancer gets worse, you should stop receiving the treatment.

Should you and your physician decide to stop the treatment, you will continue to be followed off study treatment and further treatment options will be discussed by your treating physician.

We have greatly appreciated your participation in the trial. The results from this research study will contribute to the knowledge of how best to treat patients with metastatic papillary renal carcinoma. You should discuss any questions you have about this "Patient Information Letter" with your study doctor.

Thank you very much for your participation.

Sincerely,

Sumanta K. Pal, M.D.
Primo N. Lara, Jr., M.D.
Ian M. Thompson, Jr., M.D.