January 12, 2017

Submission Request
National Comprehensive Cancer Network

Re: Clinical Evidence in Support of Sunitinib, As A Treatment Option, for the Adjuvant Treatment of Adult Patients at High Risk of Recurrent Renal Cell Carcinoma (RCC) Following Nephrectomy

Name:	Andrew G. Clair, Ph.D.
Company:	Pfizer Inc, Pfizer Oncology
Address:	235 East 42nd Street, NY, NY 10017
	Office: 219/7/98; Mail Stop: 219/7/02
Phone:	212-733-5991
Email:	andrew.clair@pfizer.com
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NCCN Guidelines Panel: Kidney Cancer

On behalf of Pfizer Inc, I respectfully request that the NCCN Kidney Cancer Guidelines Panel review the enclosed data for inclusion in the kidney cancer guidelines.

Specific Changes: We recommend the use of SUTENT® (sunitinib malate), as a treatment option, for the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy.

FDA Clearance: SUTENT® (sunitinib malate) capsules, oral, is approved for the treatment of advanced renal cell carcinoma (RCC). The approved dose for this indication is 50 mg once daily, with or without food, 4 weeks on treatment followed by 2 weeks off.

Note this request is specific to the approved indication of advanced RCC only and is not requested for the two other currently approved indications for SUTENT®; Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate or progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease.

Supporting data: Results from an international, randomized, double-blind phase 3 trial which examined sunitinib versus placebo in 615 patients with loco-regional renal cell carcinoma at high risk of tumor recurrence post-nephrectomy demonstrated that sunitinib met its primary endpoint of prolonged disease-free survival (DFS) by blinded-independent central review [1,2]. Patients taking sunitinib experienced a significantly prolonged median DFS of 6.8 years (95% CI, 5.8 to not reached) compared with 5.6 years for placebo (3.8 years-6.6 years) (HR, 0.761; 95% CI, 0.594-0.975; P=0.030), resulting in an overall reduction in risk of recurrence of 24 percent. Overall survival data were immature at data cut-off. Median overall survival was not reached in either arm (HR, 1.014; 95% CI, 0.716-1.435; P=0.938). While there was a similar incidence of serious adverse events in the two arms (21.9% for sunitinib versus 17.1% for placebo), no deaths were attributed to toxic effects and the safety profile of adjuvant sunitinib was consistent with the experience in treating metastatic RCC. Treatment related adverse events were more frequent in the sunitinib arm (98.4%) versus placebo (75.7%); discontinuations from treatment due to adverse events (drug related or not) occurred in 28.1% of sunitinib patients versus 5.9% in the placebo arm. Health-related quality of life, a secondary endpoint, using the self-administered QLQ-C30 and EQ-5D questionnaire confirmed that only appetite loss and diarrhea reached clinical significance

versus placebo while fatigue, social functioning and EQ5D, a generic health status scale, all did not reach clinical significance.

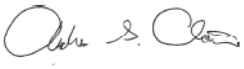
Rationale for the request: With a recurrence free rate at 5 years of about 40%, reducing risk of relapse through adjuvant therapy is a very important goal in patients with RCC at high-risk. S-TRAC is a positive well designed randomized clinical trial demonstrating a positive risk-benefit ratio for patients at high risk of recurrence, and provides a treatment option for these patients with a high unmet medical need. Disease-free survival (DFS) is an important and accepted endpoint in the adjuvant setting across multiple tumor types. DFS (or RFS) has been the primary basis of approval for numerous adjuvant treatments in oncology including colon cancer, breast cancer, melanoma, and GIST. In S-TRAC, the relative reduction in risk of recurrence was 24% which falls into the range of 12-60% observed for these indications. Furthermore, the effect of one-year adjuvant sunitinib treatment was maintained over time with a higher proportion of patients who received sunitinib being disease-free at 3 and 5 years (5.4% and 8.0%, respectively), despite treatment discontinuations.

In summary, SUTENT® in the S-TRAC trial met the fundamental principles of adjuvant therapy and conforms to an emerging consensus on clinical benefit from anti-cancer treatments[3]. SUTENT®, as a treatment option, for the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy provides an important treatment option in cancer care.

Literature Support

1. Ravaud A, Motzer RJ, Pandha HS, et al. Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy [published online October 10, 2016]. *N Engl J Med.* DOI: 10.1056/NEJMoa1611406.
2. Ravaud A, Motzer RJ, Pandha HS, et al. Phase III trial of sunitinib (SU) vs placebo (PBO) as adjuvant treatment for high-risk renal cell carcinoma (RCC) after nephrectomy (S-TRAC). Presented at: 2016 ESMO Congress; October 7-11, 2016; Copenhagen, Denmark. Abstract for LBA11.
3. N. I. Cherny, R. Sullivan, U. Dafni, et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). Annals of Oncology 26: 1547–1573, 2015 doi:10.1093/annonc/mdv249. Published online 30 May 2015.

Sincerely,



Andrew G. Clair, Ph.D.
Senior Director
US Medical Affairs, Pfizer Oncology
Tel: 212-733-5991
Mobile: 718-755-1194
andrew.clair@pfizer.com