Dear Ms. McClure,

On behalf of Pfizer Oncology, I am submitting the following to the NCCN Genitourinary Guidelines Panel requesting the Panel's consideration for inclusion in the NCCN Compendia listing.

- **Request for NCCN Guidelines Panel to review data for a specific indication**
  - INLYTA (axitinib) as 1st line therapy for predominantly clear cell advanced renal cell carcinoma.

- **Specific changes recommended within the NCCN Guidelines (one sentence)**
  - For selected patients with relapsed or medically unresectable predominantly clear cell stage IV renal carcinoma

- **Statement of whether the submitted use is or is not FDA approved for that indication**
  - The submitted use is not approved by the FDA for this indication.

- **Rationale for recommended change (one sentence)**
  - Axitinib was shown to have clinical activity with an acceptable safety profile in treatment-naïve patients with metastatic renal cell carcinoma in a phase 3 trial vs sorafenib (mPFS of 10.1 months vs 6.5) and a phase 2 trial evaluating dose titration of axitinib (mPFS = 14.6 months).

- **Citation of literature support and complete articles supporting recommended change:**

A multicenter, randomized phase 3 trial compared axitinib versus sorafenib in patients with treatment-naive, measurable, clear cell metastatic renal cell carcinoma. The patients (n=288) were stratified by ECOG performance status and randomly assigned in a 2:1 ratio to receive axitinib (n=192) or sorafenib (n=96). The primary endpoint of progression-free survival (PFS), as assessed by independent review, was not statistically significant. Median PFS was 10.1 months with axitinib compared to 6.5 months with sorafenib (hazard ratio 0.77; 95% CI 0.56–1.05; one-sided p=0.038). Response rates, by independent assessment, were 32% and 15%, respectively. Adverse events more common (≥10% difference) with axitinib were diarrhea, hypertension, weight decrease, decreased appetite, dysphonia, hypothyroidism, and upper abdominal pain; those more common with sorafenib included palmar-plantar erythrodysesthesia, rash, alopecia, and erythema.

In addition, a second multicenter clinical trial was conducted in the 1st line RCC setting. In this randomized phase 2 study of axitinib dose titration in previously untreated patients, the median PFS, per investigator assessment, was 14.6 months (95% CI 11.5-17.3) in all patients (n=213), and the objective...
response rate was 48% (95% CI 42–55). The most frequently reported adverse events were hypertension, diarrhea, and fatigue.

Both these randomized trials were recently published by Hutson et al and Rini et al in Lancet Oncology.

We appreciate the Panel’s thorough consideration of the data for axitinib (INLYTA) for use in 1st line therapy for predominantly clear cell advanced renal cell carcinoma.

Sincere regards,

Laura Cisar

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