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NCCN Guidelines Panel: Soft Tissue Sarcoma

Attention: NCCN Guideline Panel for Soft Tissue Sarcoma
Update to May 18 Submissions
for Ripretinib (4th Line and 2nd/3rd Line GIST)

On behalf of Deciphera, I would like to thank the NCCN Soft Tissue Sarcoma Panel for including ripretinib as the preferred 4th line treatment option in patients with advanced gastrointestinal stromal tumor (GIST). We are pleased to share that since the release of the revised guidelines on May 28, there have been several publication updates that we would like to request the Panel take into consideration for a future update.[1-3]

Subsequent to the approval of ripretinib by the FDA on May 15, additional information has been released publicly that support our two initial submissions.

- We are pleased to inform the NCCN Panel that the pivotal Phase 3 clinical study (INVICTUS) has been published by *Lancet Oncology*.[1]
- Additionally, two posters were presented at the ASCO Annual Virtual Meeting 2020 that further support both the Quality of Life benefit and Safety Profile of ripretinib in GIST.[2,3]
- The ripretinib Phase 1 clinical study manuscript has been accepted for publication in a peer-reviewed oncology journal. The article will be available shortly and supports inclusion of ripretinib as a 2nd and 3rd line GIST treatment, and supports ripretinib as a Category 1 therapy in 4th line GIST.

We believe that these publications support the requests made in our two submissions dated May 18th. As a summary of these requests, we respectfully ask that the Panel consider:

1. Updating ripretinib to **Category 1** in 4th line GIST. The publication of two separate clinical studies demonstrating consistent safety and efficacy results of ripretinib in advanced GIST patients (a total of 168 patients who had received three or more prior therapies) supports this request.

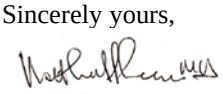
2. Including ripretinib as a **Category 2A** therapy in 2nd and 3rd line GIST.

3. Updating both GIST-5 and GIST D to reflect these proposed updates. As GIST-D is a new addition to the guidelines, we have attached a schematic for the Panel's convenience (Attachment A) that reflects the changes requested in our two May 18th submissions.

4. Removing **footnote "aa"** (GIST-5) as ripretinib has been shown to be effective after 3 to 7 prior therapies in the pivotal Phase 3 study

In summary, ripretinib provides an effective, well-tolerated, FDA-approved treatment for advanced GIST patients with clinically meaningful improvements in both PFS and OS. Thank you for your consideration.

Sincerely yours,



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References:

1. Blay J-Y, Serrano C, Heinrich MC, et al. Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*. Published online: June 5, 2020. DOI: https://doi.org/10.1016/S1470-2045(20)30168-6
2. Heinrich MC, George S, Zalcberg J, et al. Quality of life (QoL) and self-reported function with ripretinib in ≥4th line therapy for patients with gastrointestinal stromal tumors (GIST): analyses from INVICTUS. Poster presented at the 2020 ASCO Annual Virtual Meeting; May 29-31, 2020. Poster # 423
3. George S, Heinrich MC, Zalcberg J, et al. Safety profile of ripretinib, including impact of alopecia and palmar-plantar erythrodysesthesia syndrome (PPES) on patient reported outcomes (PROs), in ≥4th line advanced gastrointestinal stromal tumors (GIST): analyses from INVICTUS. Poster presented at the 2020 ASCO Annual Virtual Meeting; May 29-31, 2020. Poster # 427

Attachment A

Requested changes to GIST-D 1 of 2, SYSTEMIC THERAPY AGENTS AND REGIMENS for GIST

Red reflects changes requested in Submission Letter 1

Blue reflects changes requested in Submission Letter 2

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
First-line therapy for unresectable recurrent or metastatic disease	• **Imatinib[a] (category 1)** • **Avapritinib[a,b] (for GIST with *PDGFRA* exon 18 mutation, including *PDGFRA* D842V mutations)**		
Second-line therapy for unresectable or metastatic disease (progressive disease or intolerance to imatinib)	• **Sunitinib[a] (category 1)**	• **Ripretinib**	
Third-line therapy for unresectable or metastatic disease (progressive disease or intolerance to imatinib and sunitinib)	• **Regorafenib[a] (category 1)**	• **Ripretinib**	
Fourth-line therapy for unresectable or metastatic disease (progressive disease or intolerance to imatinib, sunitinib, and regorafenib)	• **Ripretinib[a,d] (category 1)**		
Fifth-line therapy for unresectable or metastatic disease (progressive disease or intolerance to imatinib, sunitinib, regorafenib, and ripretinib)			• **Sorafenib** • **Nilotinib** • **Dasatinib (for patients with *PDGFRA* D842V mutation)** • **Pazopanib** • **Everolimus + TKI[c]** • **Avapritinib[a,b]**

[a]FDA-approved TKIs for the treatment of GIST.
[b]Indicated for GIST with *PDGFRA* exon 18 mutation, including *PDGFRA* D842V mutations.
[c]TKIs to be considered for use in combination with everolimus include imatinib, sunitinib, or regorafenib.
[d]Ripretinib is indicated for use in patients who have received prior treatments with 3 or more kinase inhibitors, including imatinib.