

Name: Jorge Villacian
Company/Organization: Janssen Diagnostics, LLC
Address: 700 Highway 202 South, Raritan, NJ, 08869
Phone: 1-908-927-5869
Email: jvillaci@its.jnj.com
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NCCN Guidelines™ Panel: Prostate Cancer

On behalf of Janssen Diagnostics LLC, I respectfully request the NCCN Guidelines™- Prostate Cancer Panel to review the enclosed data for inclusion of the CELLSEARCH® Circulating Tumor Cell Test as an aid in disease monitoring in metastatic prostate cancer patients.

Specific Change:

Recommend the use of the CELLSEARCH® Circulating Tumor Cell Test in patients with metastatic prostate cancer as an early and sensitive indicator of progression in the assessment of response to Docetaxel.

FDA Clearance:

The CELLSEARCH® CTC test is FDA-cleared for the monitoring of patients with metastatic breast, colorectal and prostate cancer.¹

Rationale:

Inclusion of this test in the treatment decision algorithm for patients with metastatic prostate cancer treated with Docetaxel will offer an earlier (after only one cycle) and more sensitive indicator of progressive disease compared to current objective response criteria that will lead to a more informed, individualized discussion and treatment decision for the patient with benefit of avoiding exposure to unnecessary toxicity of ineffective treatment.

In support of the proposed change we would like to refer to the following recent published data:

- A Phase 3, prospective, randomized clinical study, of Docetaxel With or Without Atrasentan for Metastatic Castration-Resistant Prostate Cancer (SWOG S0421). This study demonstrated that an early rise (cycle one) in CTCs as measured by the CELLSEARCH® CTC test in the face of therapy initiation reflects primary treatment resistance and is highly prognostic of poor outcome (HR, 6.47)². The authors stated that *“on the basis of these findings, an early (cycle one) rise in CTC count in a man receiving docetaxel would likely herald poor outcome. Given the potential toxicities of docetaxel and the recent emergence of alternative (eg, hormonal) therapies in this disease state, a rise in CTC count after docetaxel initiation perhaps could trigger a change in management strategy”*. It was

concluded that the S0421 trial offers strong validation in support of incorporating CTC enumeration into the standard management of men initiating first-line docetaxel for the treatment of mCRPC. Additionally, it mentioned that perhaps more importantly, even an early rise in CTC is highly prognostic of poor OS and may constitute a clinical indication to forego further docetaxel and switch therapy.

- A recent prospective longitudinal analysis of CTCs by Thalgott et al. investigated the predictive value of the CELLSEARCH® CTC test in peripheral blood of 122 mCRPC patients undergoing first-line chemotherapy with 3-weekly docetaxel³. This study confirmed that early post-treatment CTC counts after one cycle of docetaxel have a significant predictive accuracy for survival as early as 9–12 weeks before the first radiologic response assessment. The authors concluded that these data indicate that categorical CTC counts should be incorporated into diagnostics and treatment guidance as an earlier and more sensitive prognostic parameter for survival compared to current objective response criteria.

The following publications are submitted with the Full Package Insert. We would like to acknowledge the contributions of the NCCN panel members who are also co-authors of some of these publications.

1. CellSearch™ Circulating Tumor Kit, INSTRUCTIONS FOR USE, Distributed by Janssen Diagnostics, LLC. Raritan, NJ. June 2014.
2. Goldkorn, A., et al. (2014) Circulating Tumor Cell Counts Are Prognostic of Overall Survival in SWOG S0421: A Phase III Trial of Docetaxel With or Without Atrasentan for Metastatic Castration-Resistant Prostate Cancer. J Clin Oncol 32, 1136-42.
3. Thalgott, M., et al. (2015). Circulating tumor cells versus objective response assessment predicting survival in metastatic castration-resistant prostate cancer patients treated with docetaxel chemotherapy. J Cancer Res Clin Oncol, published ahead of print, March 2015.

Sincerely,

Jorge Villacian
Chief Medical Officer
Janssen Diagnostics, LLC
Office Phone: 1-908-927-5869
jvillaci@its.jnj.com