

Patient Name: John Doe	Requesting Physician: David A. Smith, M.D.	Collected: 03/13/2009
Sex: Male	Client/Group Facility: Oncology Associates, PA	Received: 03/20/2009
Date of Birth (Age): 10/10/1958 (50 years)	Additional Recipient: Mark Howard, M.D.	Reported: 03/23/2009
SSN: 212-22-2234	Submitting Pathologist: Tim Jackson, M.D.	Case #: C09-123445
Patient ID: 23445921	Specimen ID: 232323233	Req #:

CellSearch™ Circulating Tumor Cell

CLINICAL HISTORY

Metastatic prostate cancer.

RESULTS

Circulating Tumor Cells (CTCs): 7 **(UNFAVORABLE)**

INTERPRETATION

Results are reported as the number of circulating tumor cells (CTCs) per 7.5 ml of blood. A CTC count of 5 or more per 7.5 ml of blood at any time during the course of the disease is associated with a poor prognosis and is predictive of shorter progression-free survival and overall survival.

REFERENCE RANGE

Favorable: < 5 CTCs
Unfavorable: ≥ 5 CTCs

INTENDED USE

The CellSearch™ Circulating Tumor Cell Kit is intended for the enumeration of circulating tumor cells (CTCs) of epithelial origin (CD45-, EpCAM+, and cytokeratins 8, 18+, and/or 19+) in whole blood. The presence of CTCs in the peripheral blood, as detected by the CellSearch™ Circulating Tumor Cell Kit, is associated with decreased progression free-survival and decreased overall survival in patients treated for metastatic prostate, colorectal or breast cancer. The test is to be used as an aid in the monitoring of patients with metastatic prostate, colorectal or breast cancer. Serial testing for CTCs should be used in conjunction with other clinical methods for monitoring metastatic prostate, colorectal and breast cancer.

Evaluation of CTCs at any time during the course of disease allows assessment of patient prognosis and is predictive of progression-free survival and overall survival.

CLINICAL NOTES

Clinical Trial Design (Metastatic Prostate Cancer)

A prospective, multi-institutional clinical trial was conducted to determine whether the number of CTCs predicted disease progression and survival in patients undergoing treatment for metastatic prostate cancer. Metastatic prostate cancer patients in this study were defined as having two consecutive increases in the serum marker prostate-specific antigen (PSA) above a reference level, despite standard hormonal management. A total of 231 metastatic prostate cancer patients with evidence of PSA progression despite standard hormonal therapy and starting a new line or type of chemotherapy were enrolled. Clinical data were analyzed on an intent-to-treat basis.

Baseline CTC count was determined prior to initiation of a new line of chemotherapy, 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy. For the baseline analyses, progression-free survival (PFS) was determined from the time of the baseline blood draw to the determination of progression or death, and overall survival (OS) was determined from the time of the baseline blood draw to the date of death or the date of last contact with the patient. For the follow-up analyses, PFS was determined from the time of the follow-up blood draw to diagnosis of progression or death, and OS was determined from the time of the follow-up blood draw to the date of death or the date of last contact with the patient.

For this study, disease progression was determined using PSA, imaging, and/or clinical signs and symptoms. The CTC results obtained from the baseline and follow-up blood draws at 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy were classified as being Favorable (<5 CTCs) or Unfavorable (≥5 CTCs).

Progression-Free Survival (PFS) and Overall Survival (OS) Analysis

At baseline, patients undergoing treatment for metastatic prostate cancer with ≥5 CTCs per 7.5 ml whole blood had shorter median PFS (4.2 months vs. 5.8 months) and shorter OS (11.5 months vs. 21.7 months) than patients having <5 CTCs per 7.5 ml blood.

Similarly, MPC patients with elevated CTCs (≥5 CTCs) at any of the various follow-up blood draw time points had a much higher likelihood of rapid progression and dying sooner than did those with <5 CTCs. The median PFS and OS times for those patients with <5 CTCs ranged from 4.1 to 6.5 months and 19.6 to 21.7 months, respectively and were substantially longer than the median PFS and OS times for those

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CellSearch™ Circulating Tumor Cell

patients with ≥ 5 CTCs, which ranged from 1.2 to 4.2 months and 6.7 to 11.5 months, respectively.

Reduction or Increase of CTC Predicts Improved or Decreased PFS and OS

Metastatic prostate cancer patients with ≥ 5 CTCs at all time points had the shortest median PFS (2.5 months vs. 6.5 months) and shortest median OS (6.8 months vs. > 26 months) compared to the patients with <5 CTCs at all time points.

The difference in the median PFS (7.3 months vs. 4.2 months) and median OS (21.3 months vs. 9.3 months) between those patients who showed a CTC reduction after the initiation of therapy was significantly longer compared to those patients who showed a CTC increase.

Comparison of Median OS between Favorable and Unfavorable CTC and PSA Reduction Groups

The difference in overall survival between patients with Unfavorable (≥ 5 CTCs) CTCs and Favorable (<5 CTCs) CTCs were highly significant at all time points tested, whereas Unfavorable (<30% or <50% PSA reduction from baseline) and Favorable ($\geq 30\%$ or $\geq 50\%$ PSA reduction from baseline) PSA evaluations were not significant until 6-8 weeks after the initiation of therapy. Although the differences in median OS between the Unfavorable and Favorable PSA reduction groups were significant, the separation between the Favorable and Unfavorable CTC groups appeared greater and was significant at all time points after the initiation of therapy.

LIMITATIONS

CellSearch™ results should be used in conjunction with all clinical information derived from diagnostic tests (i.e., imaging, laboratory tests), physical examination and complete medical history in accordance with appropriate patient management procedures.

This prognostic study does not demonstrate that any current line of therapy is any more or less effective than any other or no therapy.

CellSearch™ results and imaging results are not equivalent in assessing the transition of patients between non-progressive disease and progressive disease.

REFERENCES

1. CellSearch™ Circulating Tumor Cell Kit Instructions for Use — Metastatic Prostate Cancer (MPC) Patient Clinical Data.
2. de Bono, J., Scher, H., Montgomery, R., et al.: Circulating Tumor Cells Predict Survival Benefit from Treatment in Metastatic Castration-Resistant Prostate Cancer. Clin Cancer Res., 14(19): 6302-9, 2008.

If you have any questions on this report please do not hesitate to contact the BioVantra client support center at (866) 627-8221.

Peter A. Tsivis, M.D.

Pathologist Electronic Signature

03/23/2009

Date