K073338

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SECTION 3

510(K) SUMMARY

VERIDEX LLC
a Johnson & Johnson company

1001 US Highway 202
Raritan, NJ 08869

510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is

807.92 (a)(1):

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807.92 (a)(2): Device Name – trade name and common name, and classification

Trade name: CellSearch™ Circulating Tumor Cell Kit

Common name: CellSearch™ Circulating Tumor Cell Kit

Classification: Immunomagnetic Circulating Cancer Cell Selection and Enumeration System, Class II, 21 CFR 866.6020, Product Code NQI, Immunology Devices- 82

807.92 (a)(3): Identification of the legally marketed predicate device
CellSearch™ Circulating Tumor Cell Kit, K071729

807.92 (a)(4): Device Description
The CellSearch™ Circulating Tumor Cell Kit contains a ferrofluid-based capture reagent and immunofluorescent reagents. The ferrofluid reagent consists of nanoparticles with a magnetic core surrounded by a polymeric layer coated with antibodies targeting the EpCAM antigen for capturing CTC. After immunomagnetic capture and enrichment, fluorescent reagents are added for identification and enumeration of CTC. The fluorescent reagents include the following: anti-CK-Phycoerythrin (PE) specific for the intracellular protein cytokeratin (characteristic of epithelial cells), DAPI which stains the cell nucleus, and anti-CD45-Allophycocyanin (APC) specific for leukocytes.

The reagent/sample mixture is dispensed by the CellTracks® AutoPrep® System into a cartridge that is inserted into a MagNest® cell presentation device. The strong magnetic field of the MagNest® device attracts the magnetically labeled epithelial cells to the surface of the cartridge. The CellTracks® Analyzer II or CellSpotter® Analyzer automatically scans the entire surface of the cartridge, acquires images and displays any event to the user where CK-PE and DAPI fluorescence are co-located. Images are presented to the user in a gallery format for final classification. An event is classified as a tumor cell when its morphological features are consistent with that of a tumor cell and it exhibits the phenotype EpCAM+, CK+, DAPI+ and CD45-.

807.92 (a)(5): Intended use

The CellSearch™ Circulating Tumor Cell Kit is intended for the enumeration of circulating tumor cells (CTC) of epithelial origin (CD45-, EpCAM+, and cytokeratins 8, 18+, and/or 19+) in whole blood.

The presence of CTC 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 breast, colorectal or prostate* cancer. The test is to be used as an aid in the monitoring of patients with metastatic breast, colorectal or prostate cancer. Serial testing for CTC should be used in conjunction with other clinical methods for monitoring metastatic breast, colorectal and prostate cancer. Evaluation of CTC at any time during the course of disease allows assessment of patient prognosis and is predictive of progression free survival and overall survival.

*Metastatic prostate cancer patients in this study were defined as having two consecutive increases in the serum marker PSA above a reference level, despite standard hormonal management. These patients are commonly described as having androgen-independent, hormone-resistant, or castration-resistant prostate cancer

807.92 (a)(6): Technological Similarities and Differences to Predicate

There have been no material changes to the CellSearch™ Circulating Tumor Cell Kit; this 510(k) is being submitted for an expanded indication for use.

807.92 (b)(1): Brief Description of Non-clinical data

Recovery

Blood samples from a single healthy donor were pooled and five of six 7.5 mL aliquots were spiked with approximately 1300, 325, 81, 20, and 5 cultured breast cancer cells (SK-BR-3). The sixth tube was unspiked pooled blood and served as a zero point. These samples were processed on the CellTracks® AutoPrep® System with the CellSearch™ Circulating Tumor Cell Kit and CTC counts were determined on the CellTracks® Analyzer II. The experiment was repeated for four additional donors. The observed cell counts were plotted against the results of the expected cell count. The results are summarized in **Table 1**.

Table 1: Percent Detection Estimates.

Expected Tumor Cell Count	Mean Observed Tumor Cell Count	Range of Percent Recovery
1300	1215	91 to 95%
325	308	82 to 101%
81	85	80 to 136%
20	22	95 to 140%
5	7	120 to 200%

To determine the overall, or least squares fit, for the comparison of the observed and expected cell counts across all the data, linear regression analysis was performed. The regression equation for these 30 samples was $Y=0.93x + 3.87$ with an $R^2=0.999$ ($R=0.999$). The results of this study indicate that on average, over the tested CTC range, the recovery, as derived from regression analysis, is 93%.

Given the linear response of the tumor cell counts, one would expect the slope of the observed versus expected plot to be 1.0. However, the slope was 0.93. This is because the CellTracks® AutoPrep® System with CellSearch™ CTC Kit involves the capture and fluorescent labeling of cells followed by their detection and enumeration by the CellTracks® Analyzer II. The loss of cells could therefore be attributed to one of the following possibilities; 1) the recovery of only 93% of the tumor cells spiked into 7.5mL of blood by the CellTracks® AutoPrep® System, 2) the detection of only 93% of the tumor cells present in the sample chamber by the CellTracks® Analyzer II or 3) a combination of both of these sources of error.

Linearity / Reportable Range

Another way to examine the previous data is to analyze it as a dilution series to evaluate test linearity. We removed the confounding variable of percent recovery by using the observed value of the initial sample in the dilution series (i.e. the first tube) divided by the dilution factors to determine the expected values for the dilution series for each patient sample. Regression of all of these numbers of observed tumor cells versus the numbers of expected tumor cells yielded a slope of 1.007, an intercept of 3.0, and an $R^2 = 0.990$ ($R = 0.995$). Therefore, once the percent recovery (cell loss) was factored out of the CTC values of each of the initial samples, the analysis of the data demonstrated that the detection of CTC was linear over the reportable range of 0 to 1238 tumor cells.

Limits of Detection

One CTC per 7.5 mL can be detected by the CellTracks® Analyzer II resulting in a limit of detection of 1 CTC in a cartridge. Linear regression shows that on average, 93% of CTC present in a 7.5 mL blood sample are recovered using the CellTracks® AutoPrep® System (see **Recovery** section). The loss of approximately 7% of the CTC in the sample is not sufficient to reduce the limit of detection of 1 CTC.

Reproducibility:

a. System Reproducibility with CellSearch™ Circulating Tumor Cell Control

Three separate CellSearch™ Circulating Tumor Cell Control samples were prepared and processed each day for over 30 days, per the long run method of NCCLS guideline EP5-A[2]. Each single-use sample bottle contains a low and a high concentration of cells from a fixed cell line that have been pre-stained with two different fluorochromes. Summary statistics for the high and low control cells is presented below.

Table 2. Summary of Precision Analyses

	Low	High
N	99	99
Mean cell count	48	969
Total Precision Standard Deviation (S_T) % CV	18%	5%

b. System Reproducibility with Patient Samples
Metastatic Breast Cancer (MBC)

A total of 163 duplicate blood samples were collected from 47 metastatic breast cancer patients over the course of the clinical study. These samples were processed at multiple sites to determine the reproducibility of CTC measurements. The regression equation for the comparison of these 163 duplicate samples was $Y=0.98x + 0.67$, $R^2=0.99$. **Figure 1** shows a scatter plot of the duplicate CTC results in blood from MBC patients plotted on a logarithmic scale, with the threshold of 5 CTC indicated by the dashed lines.

Figure 1: Reproducibility of CTC Counts in Duplicate MBC Samples (n=163) with Average of <5 or ≥5 CTC per 7.5 mL of blood.

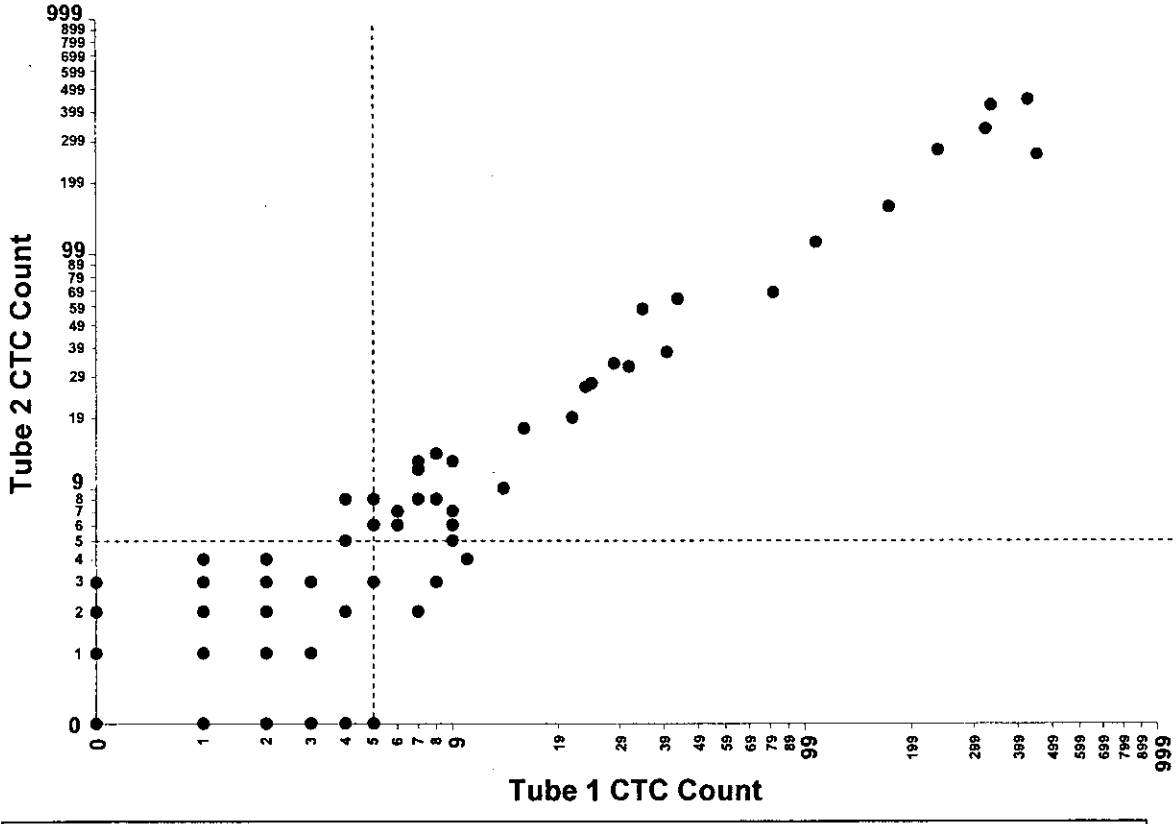


Figure 1 Note: There may be more than one point superimposed over another. For example, on this plot, there are 50 instances (31%) where both tubes had 0 CTC, 18 instances (11%) where Tube 1 had 0 CTC and Tube 2 had 1 CTC, and another 18 instances (11%) where Tube 1 had 1 CTC and Tube 2 had 0 CTC.

Metastatic Colorectal Cancer (MCRC)

A total 1,627 duplicate blood samples were collected from 430 MCRC patients over the course of the clinical study. These samples were processed at multiple sites to determine the reproducibility of CTC measurements. The regression equation for the comparison of these 1,627 duplicate samples was $Y=0.98x + 0.18$, $R^2=0.96$. **Figure 2** shows a scatter plot of the duplicate CTC results in blood from MCRC patients plotted on a logarithmic scale, with the threshold of 3 CTC indicated by the dashed lines.

Figure 2: Reproducibility of CTC Counts in Duplicate MCRC Samples (n=1627) with Average of <3 or ≥3 CTC per 7.5 mL of blood.

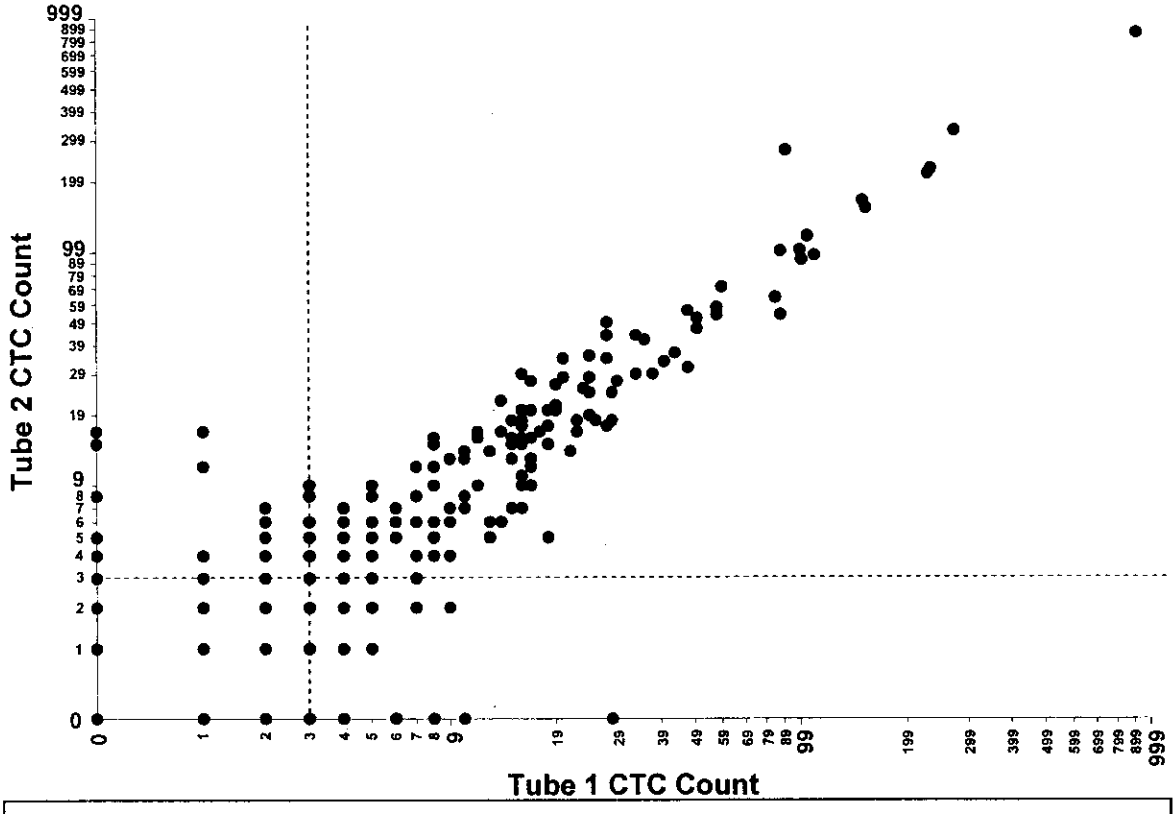


Figure 2 Note: There may be more than one point superimposed over another. For example, on this plot, there are 975 instances (60%) where both tubes had 0 CTC, 116 instances (7%) where Tube 1 had 0 CTC and Tube 2 had 1 CTC, and another 109 instances (7%) where Tube 1 had 1 CTC and Tube 2 had 0 CTC.

The tube-to-tube variation of CTC counts in blood samples from metastatic breast and colorectal cancer patients is shown in **Figures 1 & 2**. The distribution of infrequent events (such as tumor cells) within a given volume is random and independent of cell or disease type. This is best characterized by the Poisson distribution – a mathematical method employed for modeling systems where the probability of an event occurring is very low but the number of opportunities for such an event to occur is large. For tubes with very few prostatic CTC it is reasonable to expect variation in results similar to what is depicted in **Figures 1 & 2**. Because the two previous studies in MBC and MCRC patients showed almost identical results, a tube-to-tube comparison of CTC counts in blood samples from metastatic prostate cancer patients was not performed during the CellSearch™ CTC prostate clinical trial. However, results of an independent study using CellSearch™ technology conducted at the Memorial Sloan-Kettering Cancer Center demonstrated no systematic site-to-site or tube-to-tube variation in CTC counts across a range of 0 to 1192 CTC per tube in patients with metastatic prostate cancer.

807.92(b)(2): Brief Description of Clinical Data

Metastatic Prostate Cancer (MPC) Patients

A multi-center prospective, clinical trial was conducted to determine whether the number of CTC predicted disease progression and survival. 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. These patients are commonly described as having androgen-independent, hormone-resistant, or castration-resistant prostate cancer. 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. Patient demographic information is presented in **Table 3**.

Table 3: MPC Patient Demographics

Category	Mean ± Std. Deviation (Median)	Number of Subjects
Age at Baseline (in years)	70 ± 9 (70)	**231**
Pre-Therapy:		
PSA (ng/mL)	547 ± 1616 (144)	**231**
Hemoglobin (g/dL)	12.3 ± 1.6 (12.4)	**221**
Alkaline Phosphatase(AlkPhos) (IU/mL)	235 ± 271 (144)	**223**
Lactate dehydrogenase(LDH) (IU/mL)	293 ± 228 (224)	**219**
Albumin (g/dL)	3.9 ± 2.6 (3.8)	**214**
	Description of Categories	**Number of Subjects (% of total)**
Race	White	209 (90%)
	Black	17 (7%)
	Other	5 (3%)
Baseline ECOG Score	0	101 (44%)
	1	100 (43%)
	2	21 (9%)
	Unknown	9 (4%)
Gleason Score	≥5	18 (8%)
	6	28 (12%)
	7	63 (27%)
	8	45 (20%)
	≥9	54 (23%)
	Unknown	23 (10%)
Stage at Primary Diagnosis	1	14 (6%)
	2	30 (13%)
	3	58 (25%)
	4	19 (8%)
	Unknown	110 (48%)
Line of Therapy	1st	154 (67%)
	2nd	38 (16%)
	≥3rd	39 (17%)
Taxotere in Current Therapy Line?	No	67 (29%)
	Yes	162 (70%)
	Unknown	2 (1%)
Bone Metastasis	Negative	20 (8%)
	Positive	207 (90%)
	Unknown	4 (2%)
Measurable Disease	No	142 (62%)
	Yes	88 (38%)
	Unknown	1 (0%)
Visceral Metastasis	No	141 (61%)
	Yes	89 (39%)
	Unknown	1 (0%)

Baseline CTC count was determined prior to initiation of a new line of chemotherapy. The following timeframes were chosen for evaluation: baseline (prior to the initiation of therapy), 2-5 weeks (14 - 41 days from baseline), 6-8 weeks (42 - 62 days from baseline), 9-12 weeks (63 - 90 days from baseline), and 13-20 weeks (91 - 146 days from baseline) after the initiation of therapy. If more than one blood draw fell within the designated timeframes, the blood draw furthest from the baseline blood draw was used as the result for each timeframe.

CTC frequencies

All 231 evaluable MPC patients had a baseline blood draw. Two hundred and twenty-one of these MPC patients had one or more follow-up blood draws after the initiation of therapy. Of the ten MPC patients with only a baseline blood draw, three died before a follow-up blood draw could be obtained, one progressed and was sent to hospice, one stopped their chemotherapy due to a broken hip, one patient moved, three refused any further blood draws, and one withdrew their consent for the study. There were a total of 214, 171, 158, and 149 MPC patients with follow-up blood draws 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy, respectively.

In metastatic prostate cancer, disease progression is primarily determined using changes in PSA. For this study, disease progression was determined by the sites using PSA, imaging, and/or clinical signs and symptoms. 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. Patients with progression prior to the date of the blood draw being evaluated were excluded from the PFS analyses of that time point and all subsequent follow-up blood draws. Patients with no additional survival follow-up beyond the date of the blood draw being evaluated were excluded from the PFS & OS analyses of that time point. **Table 4** shows the numbers of patients at each time point excluded from the PFS or PFS & OS analyses and the reasons for their exclusion.

Table 4: Exclusions from PFS and OS Analyses in MPC Patients

Blood Draw Timing	MPC Patients Not Evaluable:					Total # of MPC Patients Evaluable	
	PFS & OS				PFS Only		
	Blood Not Drawn	Blood Drawn 1-7 days after therapy administration	No Follow-up Beyond Date of Blood Draw	No or Non-Evaluable CTC Results	Blood drawn after date of disease progression	PFS	OS
Baseline	0	6	0	6	0	219	219
2-5 Weeks	17	0	0	11	4	199	203
6-8 Weeks	60	0	0	8	22	141	163
9-12 Weeks	73	1	0	8	15	134	149
13-20 Weeks	82	0	1	5	27	116	143

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 CTC) or unfavorable (≥5 CTC). The PSA, Alkaline Phosphatase, and LDH levels summarized in the demographics table and used in the analyses were all measured at a central laboratory in serum samples collected at the same time as the blood samples used for CTC evaluation. The hemoglobin and albumin levels

summarized in the tables and used in the analyses were values provided by the sites and verified from the patient's medical records that were determined within ± 30 days of the baseline CTC evaluation.

Progression Free Survival (PFS) Analysis of MPC Patients

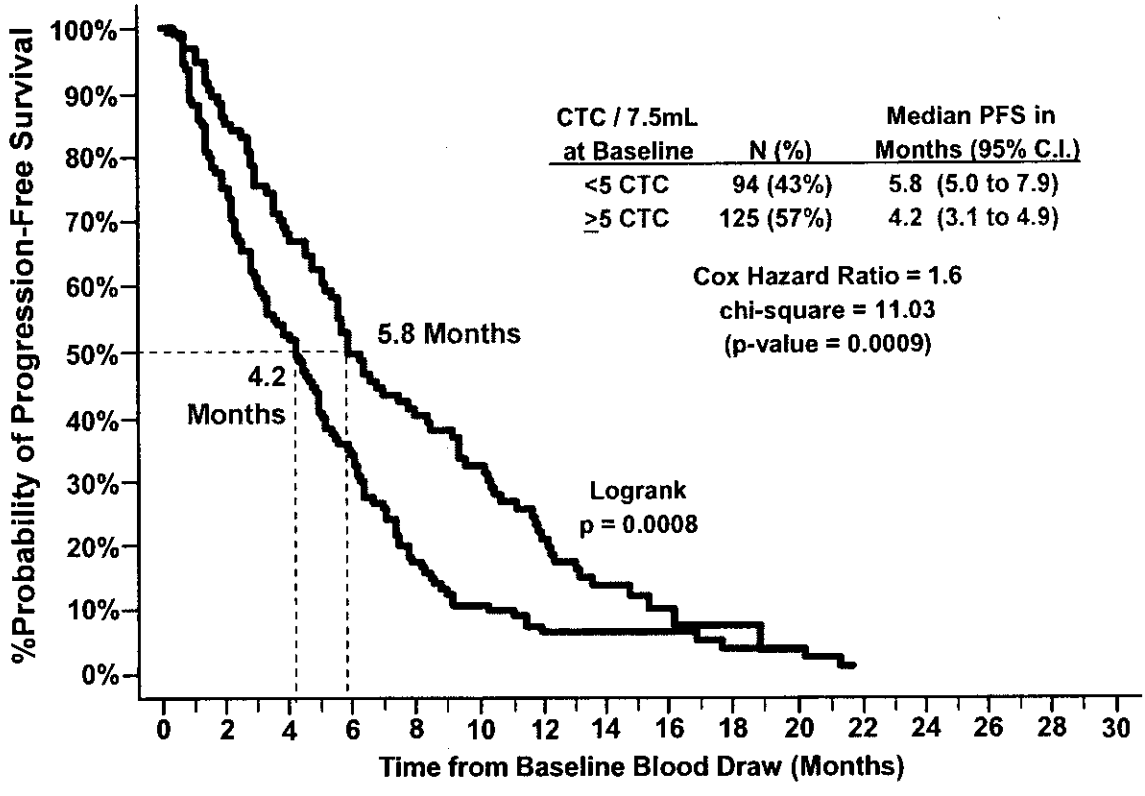
PFS Using Baseline CTC Results

Two hundred nineteen of the 231 evaluable patients had a baseline CTC result available. For Kaplan-Meier analysis, patients were segmented into two groups based upon their CTC count at baseline:

- The Favorable group (N=94), represented in **green**, consisted of patients with <5 CTC.
- The Unfavorable group (N=125), represented in **red**, consisted of patients with ≥5 CTC.

Median PFS was longer in the Favorable group compared to the Unfavorable group (5.8 vs. 4.2 months, respectively.) These results are illustrated in **Figure 3** or **Table 5.**

Figure 3: PFS of MPC Patients with < 5 or ≥ 5 CTC at Baseline (N = 219).



PFS Using Follow-up CTC Results

For Kaplan-Meier analysis, MPC patients were segmented into two groups based upon their CTC count at each of the various follow-up blood draws. Both patient groups at each of the different follow-up blood draws after initiation of therapy for PFS are illustrated in **Figure 4**. This figure illustrates the ability of CTC in MPC patients with <5 and ≥5 CTC to predict time to clinical progression or death at 2-5 weeks (n=199), 6-8 weeks (n=141), 9-12 weeks (n=134) and 13-20 weeks (n=116) after the initiation of therapy.

- The Favorable group represented in **olive green, blue, purple,** and cyan consisted of patients with <5 CTC at 2-5, 6-8, 9-12, and 13-20 weeks after the initiation of therapy, respectively.
- The Unfavorable group, represented in **brown, black,** grey, and orange consisted of patients with ≥5 CTC at 2-5, 6-8, 9-12, and 13-20 weeks after the initiation of therapy, respectively.

Figure 4: PFS of MPC Patients with < 5 or ≥ 5 CTC at different times of Follow-Up

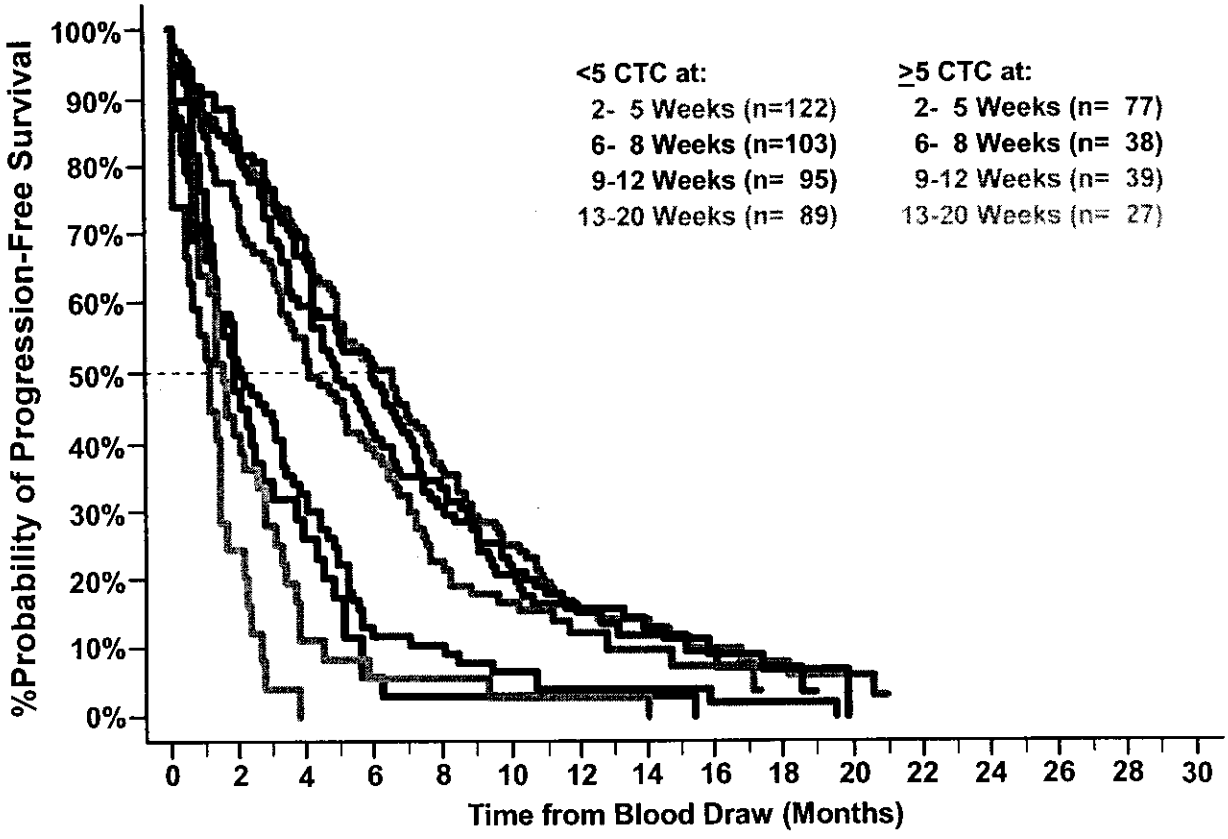


Table 5 summarizes the results of the PFS analysis using the CTC levels and a threshold of ≥5 CTC/7.5mL at each of the different blood draw time points.

Table 5: Progression Free Survival (PFS) for MPC patients with <5 or ≥5 CTC at different time points

1	2	3	4	5	6
Sampling Time After Tx Initiation	**N**	**≥5 CTC**	**Median PFS in Months (95% CI)**		**Log-rank p-value**
			<5 CTC	**≥5 CTC**	
Baseline	219	125 (57%)	5.8 (5.0 – 7.9)	4.2 (3.1 – 4.9)	0.0008
2-5 Weeks	199	77 (39%)	6.5 (4.9 – 7.4)	2.1 (1.4 – 3.3)	<0.0001
6-8 Weeks	141	38 (27%)	5.9 (4.2 – 7.0)	1.9 (1.3 – 2.7)	<0.0001
9-12 Weeks	134	39 (24%)	4.9 (3.8 – 6.2)	1.6 (0.9 – 2.6)	<0.0001
13-20 Weeks	116	27 (23%)	4.1 (3.3 – 5.8)	1.2 (0.5 – 1.5)	<0.0001

As illustrated in **Figure 4** and **Table 5**, MPC patients with elevated CTC (≥5 CTC/7.5mL whole blood) at any of the time points had a much higher likelihood of rapid progression than did those with <5 CTC. **Table 5** column 4 shows the median PFS times for those patients with <5 CTC ranged from 4.1 to 6.5 months and were substantially longer than the median PFS times for those patients with ≥5 CTC, which ranged from 1.2 to 4.2 months (column 5).

Reduction or Increase in CTC Predicts Improved or Decreased PFS

Elapsed PFS times were calculated from the baseline blood draw. For the Kaplan-Meier analysis shown in **Figure 5**, MPC patients were segmented into four groups based upon their CTC counts at baseline, 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy:

- Group 1 (**green** curve), 88 (38%) patients with <5 CTC at all time points. Five (6%) of these patients only had a baseline blood draw while seven (8%) had a single blood draw between their first and last blood draw that had ≥5 CTC;
- Group 2 (**blue** curve), 45 (20%) patients with ≥5 CTC prior to the initiation of therapy but who had decreased to <5 CTC at the time of their last blood draw;
- Group 3 (orange curve), 26 (11%) patients with <5 CTC at an early draw (baseline, 2-5 weeks, and/or 6-8 weeks) but who increased to ≥5 CTC at the time of their last blood draw;
- Group 4 (**red** curve), 71 (31%) patients with ≥5 CTC at all draw time points. Eight (11%) of these patients had only a baseline blood draw and two (3%) had a single blood draw between their first and last blood draw that had <5 CTC.

Figure 5: A Reduction in CTC Below 5 After the Initiation of Therapy Predicts Longer PFS in MPC Patients

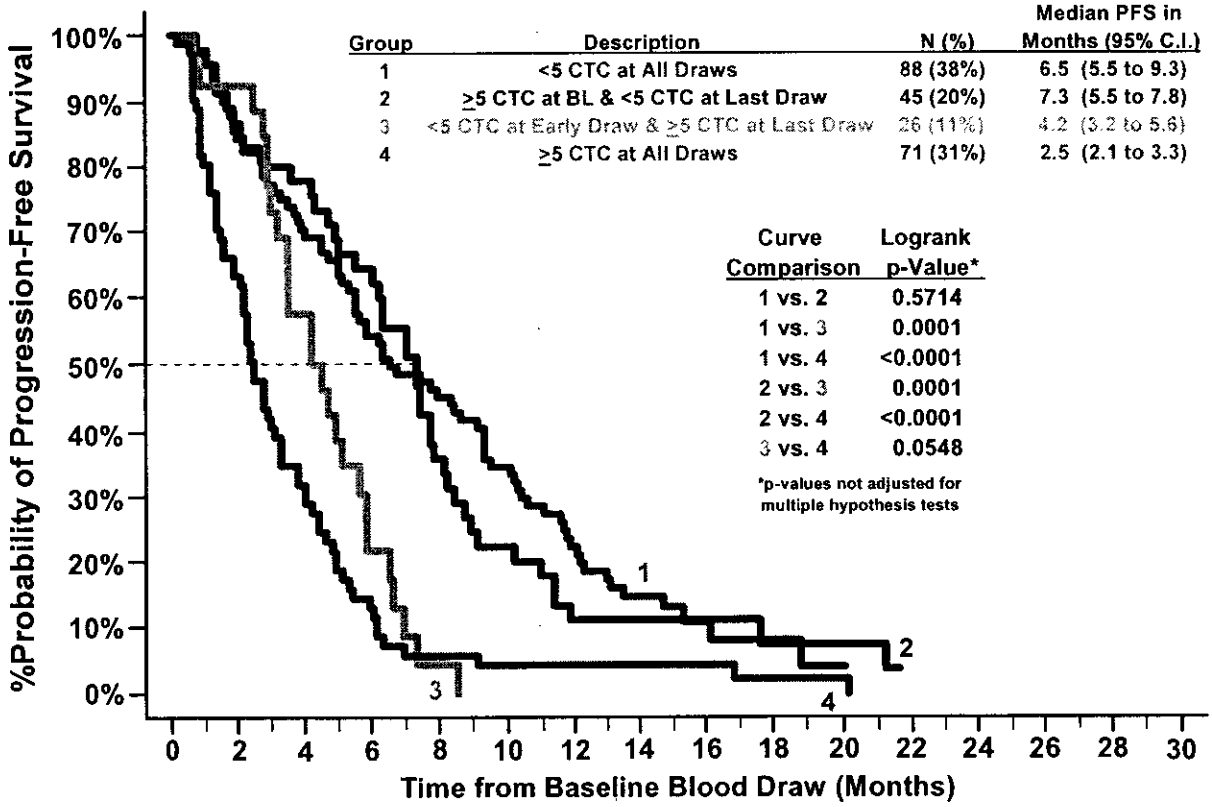


Figure 5 shows that MPC patients with ≥5 CTC at all time points (**Group 4**) had the shortest median PFS, which was significantly different compared to the median PFS of Group 3, **Group 2** and **Group 1**. The difference in the median PFS between those patients who showed a CTC reduction after the initiation of therapy (**Group 2**) was significantly longer compared to those patients who showed a CTC increase (Group 3).

Overall Survival (OS) Analysis of MPC Patients

OS Analysis Using Baseline CTC Results

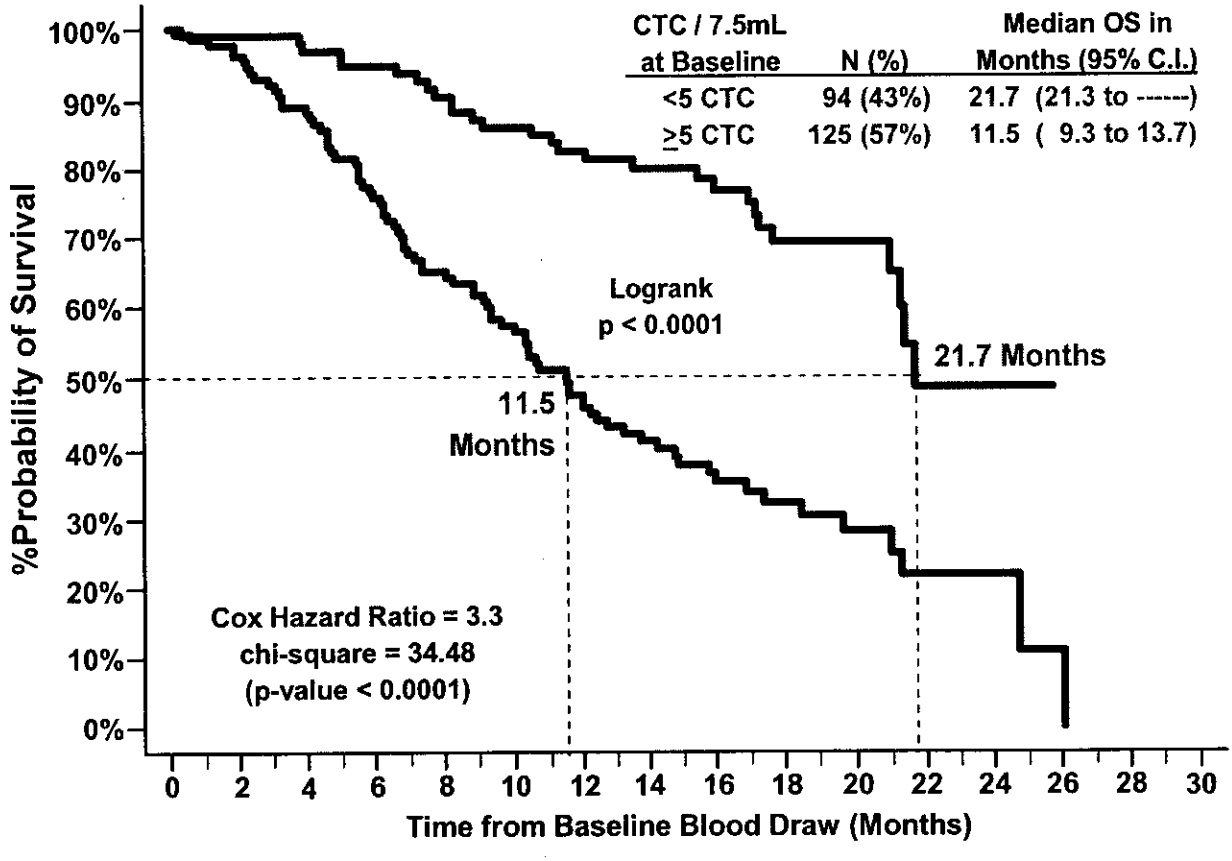
Death occurred in 119 (52%) of the 231 MPC patients, with a mean follow-up time for the 112 (48%) patients still alive of 16.1 ± 4.9 months (median = 16.5 months, range = 1.9 to 25.7 months). At the time of these analyses, 28 (30%) of 94 patients from the Favorable group (<5 CTC at baseline) compared to 83 (66%) of 125 from the Unfavorable group (≥5 CTC at baseline) had died.

For Kaplan-Meier analysis, the 219 of the 231 evaluable patients that had baseline results were segmented into two groups based upon their CTC count at baseline:

- The Favorable group (N=94), represented in **green**, consisted of patients with <5 CTC.
- The Unfavorable group (N=125), represented in **red**, consisted of patients with ≥5 CTC.

Median OS was significantly longer in the Favorable group compared to the Unfavorable group (21.7 vs. 11.5 months, respectively). These results are illustrated in **Figure 6**.

Figure 6: OS of MPC Patients with <5 or ≥5 CTC at Baseline (N = 219).



OS Using Follow-up CTC Results

The Kaplan-Meier analyses of both MPC patient groups at each of the different follow-up blood draw times after initiation of therapy are illustrated in **Figure 7**. This figure illustrates the ability of CTC in MPC patients with <5 and ≥5 CTC 2-5 weeks (n=203), 6-8 weeks (n=163), 9-12 weeks (n=149) and 13-20 weeks (n=143) after the initiation of therapy to predict time to death. OS times were calculated from the time of each blood draw.

- The Favorable group, represented in **olive green**, **blue**, **purple**, and cyan, consisted of patients with <5 CTC,
- The Unfavorable group, represented in **brown**, **black**, grey, and orange, consisted of patients with ≥5 CTC.

Figure 7: OS of MPC Patients with < 5 or ≥ 5 CTC at different times of Follow-Up.

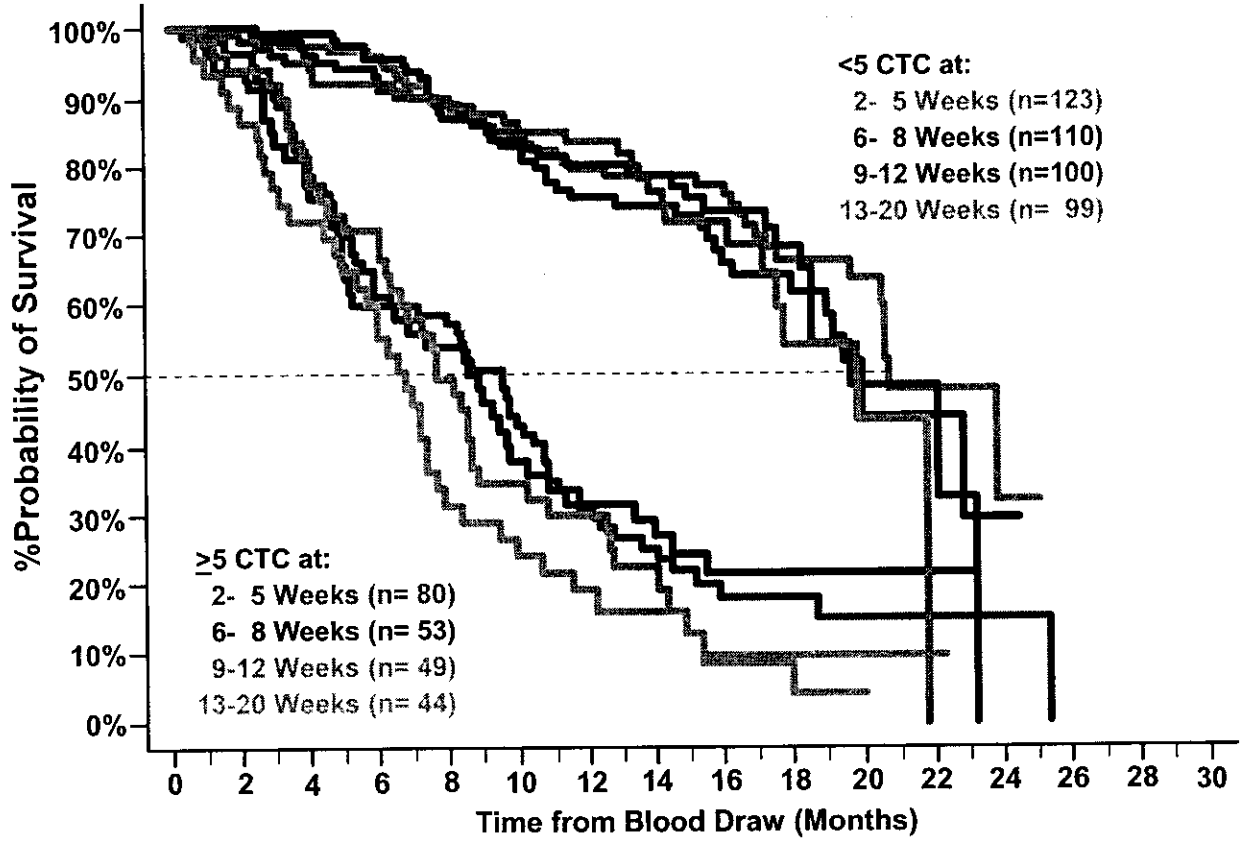


Table 6 summarizes the results of the OS analysis using the CTC levels and a threshold of ≥5 CTC/7.5mL at each of the different blood draw time points.

Table 6: Overall Survival (OS) for MPC patients with <5 or ≥5 CTC at different time points

1	2	3	4	5	6
Sampling Time After Tx Initiation	**N**	**≥5 CTC**	**Median OS in Months (95% CI)**		**Log-rank p-value**
			<5 CTCs	**≥5 CTCs**	
Baseline	219	125 (57%)	21.7 (21.3 - NR)	11.5 (9.3 - 13.7)	<0.0001
2-5 Weeks	203	80 (39%)	20.7 (20.5 - NR)	9.5 (5.8 - 10.7)	<0.0001
6-8 Weeks	163	53 (33%)	19.9 (17.9 - NR)	8.5 (5.0 - 10.2)	<0.0001
9-12 Weeks	149	49 (33%)	19.6 (18.5 - NR)	7.6 (6.2 - 8.6)	<0.0001
13-20 Weeks	143	44 (31%)	19.8 (17.1 - NR)	6.7 (4.9 - 7.6)	<0.0001

As illustrated in **Figure 7** and **Table 6** in columns 4 & 5, MPC patients with ≥5 CTC at any of the time points had a much higher likelihood of dying sooner than did those with <5 CTC. The median OS times for those patients with <5 CTC ranged from 19.6 to 21.7 months and were substantially longer than the median OS times for those patients with ≥5 CTC, which ranged from 6.7 to 11.5 months.

Reduction or Increase of CTC Predicts Improved or Decreased OS

Elapsed OS times were calculated from the baseline blood draw. For Kaplan-Meier analysis (**Figure 8**), patients were segmented into four groups based upon their CTC counts at baseline, 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy:

- Group 1 (**green** curve), 88 (38%) patients with <5 CTC at all time points. Five (6%) of these patients had only a baseline blood draw while seven (8%) had a single blood draw between their first and last blood draw that had ≥5 CTC;
- Group 2 (**blue** curve), 45 (20%) patients with ≥5 CTC prior to the initiation of therapy but who had decreased to <5 CTC at the time of their last blood draw;
- Group 3 (orange curve), 26 (11%) patients with <5 CTC at an early draw but who increased to ≥5 CTC at the time of their last blood draw;
- Group 4 (**red** curve), 71 (31%) patients with ≥5 CTC at all draw time points. Eight (11%) of these patients had only a baseline blood draw and two (3%) had a single blood draw between their first and last blood draw that had <5 CTC.

Figure 8: A Reduction in CTC Below 5 After the Initiation of Therapy Predicts Longer OS whereas an Increase in CTC Count to 5 or above Predicts Shorter OS in MPC Patients

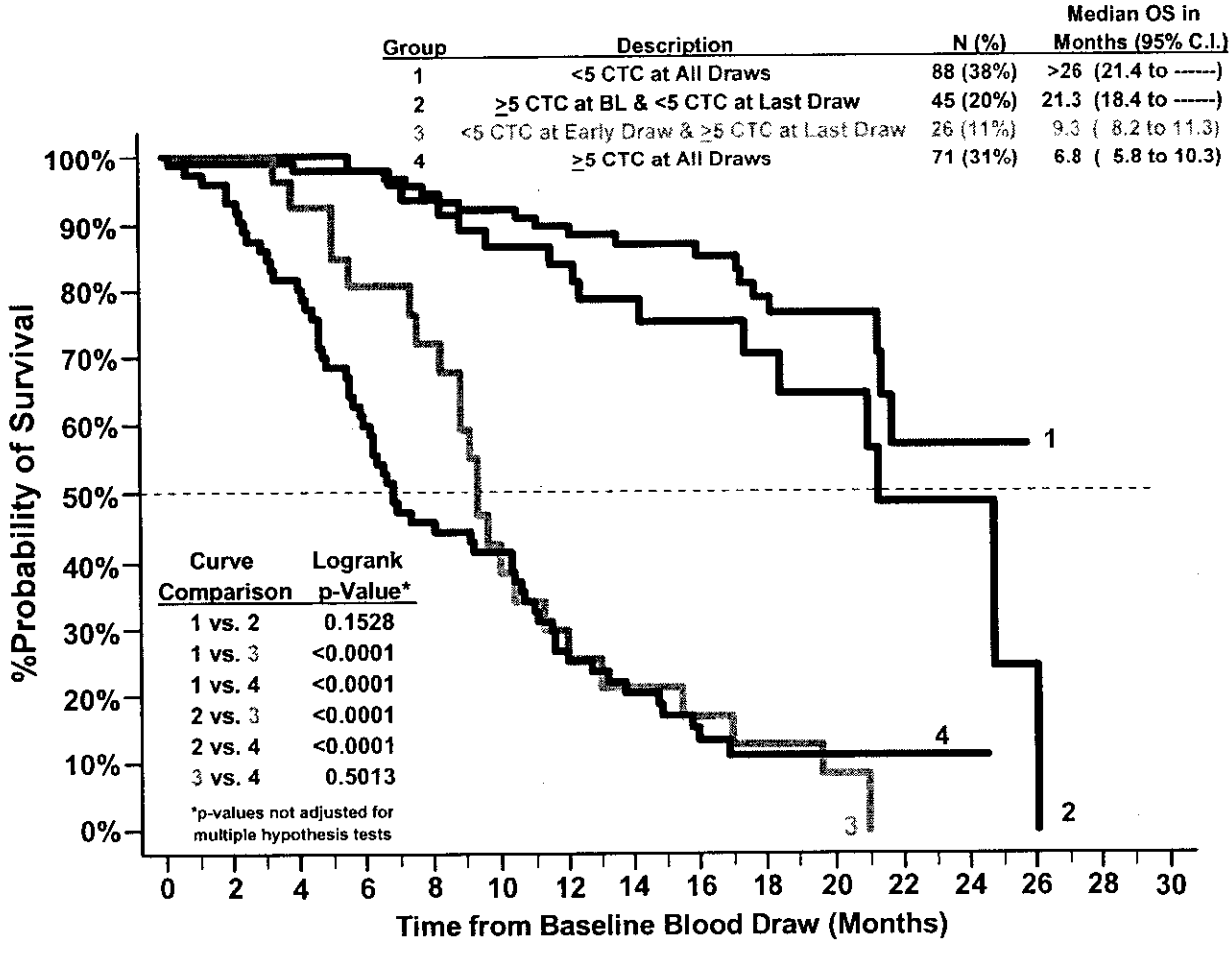


Figure 8 shows that those patients with ≥5 CTC at any point after the initiation of therapy had a much higher likelihood of dying sooner. Patients with ≥5 CTC at all time points (**Group 4**) had the shortest median OS, which was significantly different compared to the median OS of **Group 2**, and **Group 1** but not Group 3. Patients with <5 CTC at all time points (**Group 1**) had the longest median OS, which was significantly different compared to the median OS of **Group 4** and Group 3, but not **Group 2**. **Figure 8** also demonstrated that patients who showed a decrease in CTC (**Group 2**) improve their survival chances and had a median OS similar to those patients with favorable CTC at all draws (**Group 1**). The figure also shows that unfavorable CTC levels after the initiation of therapy significantly decreased overall survival (Group 3 and **Group 4**).

Univariate Cox Regression Analysis in MPC Patients

Univariate Cox proportional hazards regression analysis was used to evaluate the association of the following pre-treatment parameters with PFS and OS: stage of disease at diagnosis (1-4), patient age (≥70 or <70 years), ECOG status before initiation of a new line of therapy (0-2), Gleason score (2-10), hemoglobin level within ± 30 days of baseline draw (g/dL, continuous), albumin level within ± 30 days of baseline draw (g/dL, continuous), testosterone level at the time of the baseline draw (ng/mL, continuous), LDH level at the time of the baseline draw (IU/mL, continuous), alkaline phosphatase level at the time of the baseline draw (IU/mL, continuous), PSA level at the time of the baseline draw (ng/mL, continuous),

pre-treatment PSA doubling time (months, continuous), pre-treatment PSA velocity (ng/mL/month, continuous), line of therapy (1st, 2nd, 3rd, 4th, 5th, or 6th), type of therapy (taxotere included or not), presence of measurable disease (yes or no), presence of bone metastasis (yes or no), presence of visceral metastasis (yes or no), and baseline CTC level (≥5 CTC/7.5mL or <5 CTC/7.5mL) and follow up CTC counts at 2-5, 6-8, 9-12 and 13-20 weeks.

For these analyses, the elapsed times for both PFS and OS were calculated from the time of the baseline blood draw. The Cox regression results (i.e. the hazards ratio and associated 95% confidence interval, chi-square value, and associated p-values) for the ability of the parameters to independently predict PFS and OS are provided in **Table 7** as well as the number of patients in each evaluation.

Table 7: Univariate Cox Regression Analysis in MPC Patients

Parameter	Categories		# of MPC Patients	PFS Risk from Baseline		OS Risk From Baseline	
	Positive	Negative		HR	p-value [2]	HR	p-value [2]
Stage at Primary Diagnosis	4 vs. 3 vs. 2 vs. 1		121	0.88	0.206	0.83	0.174
Age at Baseline Blood Draw	≥70	<70	231	0.96	0.764	1.28	0.178
ECOG Status at Study Entry	2 vs. 1 vs. 0		222	1.34	0.011	2.36	<0.001
Gleason Score	10 to 2		208	1.01	0.919	1.02	0.717
Pre-treatment PSA Doubling Time (Months)	Continuous		230	0.97	0.542	0.97	0.664
Pre-treatment PSA Velocity (ng/mL/Month)	Continuous		230	1.00	0.200	1.00	0.544
Baseline Hemoglobin (g/dL)	Continuous		221	0.87	0.002	0.71	<0.001
Baseline Albumin (g/dL)	Continuous		214	0.99	0.748	1.02	0.557
Baseline Testosterone (ng/mL) [1]	Continuous		223	1.07	0.900	2.71	0.060
Baseline LDH (IU/mL) [1]	Continuous		219	1.001	<0.001	1.002	<0.001
Baseline Alkaline Phosphatase (IU/mL) [1]	Continuous		223	1.00	0.158	1.0008	0.001
Line of Therapy	Continuous (1 - 6)		231	1.23	0.003	1.28	0.003
Type of Therapy (Taxotere: Yes/No)	Yes	No	229	0.57	<0.001	0.59	0.006
Measurable Disease?	Yes	No	230	1.00	0.993	1.28	0.181
Bone Metastasis?	Yes	No	227	1.02	0.933	2.22	0.057
Visceral Metastasis?	Yes	No	230	1.01	0.918	1.26	0.216
Baseline PSA (ng/mL) [1]	Continuous		231	1.00	0.746	1.00	0.907
2 - 5 Week PSA (ng/mL) [1]	Continuous		207	1.00	0.819	1.00	0.794
6 - 8 Week PSA (ng/mL) [1]	Continuous		167	1.00	0.426	1.00	0.654
9 - 12 Week PSA (ng/mL) [1]	Continuous		155	1.00	0.684	1.00	0.324
13 - 20 Week PSA (ng/mL) [1]	Continuous		143	1.00	0.639	1.00	0.205
2 - 5 Week PSA Reduction from BL (%) [1]	<30%	≥30%	207	1.56	0.006	1.24	0.318
6 - 8 Week PSA Reduction from BL (%) [1]	<30%	≥30%	167	2.21	<0.001	2.27	0.001
9 - 12 Week PSA Reduction from BL (%) [1]	<30%	≥30%	155	2.76	<0.001	2.30	<0.001
13 - 20 Week PSA Reduction from BL (%) [1]	<30%	≥30%	143	2.69	<0.001	3.19	<0.001

Parameter	Categories		# of MPC Patients	PFS Risk from Baseline		OS Risk From Baseline	
	Positive	Negative		HR	p-value [2]	HR	p-value [2]
Baseline CTC Number	≥5	<5	219	1.62	0.001	3.33	<0.001
2 - 5 Week CTC Number	≥5	<5	203	2.34	<0.001	4.46	<0.001
6 - 8 Week CTC Number	≥5	<5	163	3.29	<0.001	3.66	<0.001
9 - 12 Week CTC Number	≥5	<5	149	3.23	<0.001	5.82	<0.001
13 - 20 Week CTC Number	≥5	<5	144	4.82	<0.001	7.18	<0.001

[1] **Determined from Serum Drawn on the Same Date as the Blood Drawn for CTC**
[2] **p-value from Wald test of Z statistic**
[3] **p-value from chi-squared test**

Multivariate Cox Regression Analysis in MPC Patients

Multivariate Cox regression analyses were conducted to evaluate the independent predictive power of CTC count by adjusting for the effects of the known important clinical factors that are statistically significant in the univariate analyses. CTC were found to be strongest predictors at most time points of PFS and OS (**Table 8**).

Table 8: Multivariate Cox Regression Analysis in MPC Patients

Parameter	# of Patients	PFS Risk from Baseline		OS Risk from Baseline	
		HR	p-value [2]	HR	p-value [2]
Baseline CTC (<5 vs. ≥5)	188	1.14	0.455	1.92	0.009
Baseline ECOG Status (0 vs. 1 vs. 2)		1.00	0.982	1.46	0.032
Baseline Hemoglobin (g/dL) [3]		0.88	0.027	0.81	0.007
Baseline LDH (IU/mL) [1, 3]		1.0007	0.018	1.002	<0.001
Baseline Alkaline Phosphatase (IU/mL) [1, 3]		---	---	1.00	0.410
Line of Therapy (1st through 6th)		1.14	0.145	1.07	0.547
Type of Therapy (Taxotere: Yes/No)		0.63	0.009	0.70	0.139
2 - 5 Week CTC (<5 vs. ≥5)	173	1.48	0.041	2.91	<0.001
2 - 5 Week PSA Reduction from Baseline (≥30% vs. <30%) [1]		1.40	0.077	1.13	0.637
Baseline ECOG Status (0 vs. 1 vs. 2)		0.97	0.836	1.46	0.054
Baseline Hemoglobin (g/dL) [3]		0.93	0.246	0.89	0.141
Baseline LDH (IU/mL) [1, 3]		1.002	0.002	1.003	<0.001
Baseline Alkaline Phosphatase (IU/mL) [1, 3]		---	---	1.00	0.622
Line of Therapy (1st through 6th)		1.11	0.274	1.11	0.399
Type of Therapy (Taxotere: Yes/No)		0.75	0.133	0.80	0.397
6 - 8 Week CTC (<5 vs. ≥5)	139	2.14	<0.001	2.13	0.009
6 - 8 Week PSA Reduction from Baseline (≥30% vs. <30%) [1]		1.88	0.002	2.38	0.007
Baseline ECOG Status (0 vs. 1 vs. 2)		1.04	0.810	1.52	0.088
Baseline Hemoglobin (g/dL) [3]		0.97	0.695	0.79	0.013
Baseline LDH (IU/mL) [1, 3]		1.002	0.003	1.004	<0.001

Parameter	# of Patients	PFS Risk from Baseline		OS Risk from Baseline	
		HR	p-value [2]	HR	p-value [2]
Baseline Alkaline Phosphatase (IU/mL) [1, 3]		---	---	1.00	0.780
Line of Therapy (1st through 6th)		1.37	0.001	1.35	0.035
Type of Therapy (Taxotere: Yes/No)		0.80	0.278	1.45	0.276
9 - 12 Week CTC (<5 vs. ≥5)	125	1.74	0.015	3.94	<0.001
9 - 12 Week PSA Reduction from Baseline (≥30% vs. <30%) [1]		2.23	<0.001	1.46	0.221
Baseline ECOG Status (0 vs. 1 vs. 2)		1.21	0.307	1.89	0.004
Baseline Hemoglobin (g/dL) [3]		0.93	0.322	0.97	0.758
Baseline LDH (IU/mL) [1, 3]		1.00	0.190	1.003	<0.001
Baseline Alkaline Phosphatase (IU/mL) [1, 3]		---	---	1.00	0.989
Line of Therapy (1st through 6th)		1.25	0.052	1.11	0.499
Type of Therapy (Taxotere: Yes/No)		0.97	0.903	1.26	0.486
13 - 20 Week CTC (<5 vs. ≥5)	123	2.95	<0.001	3.75	0.001
13-20 Week PSA Reduction from Baseline (≥30% vs. <30%) [1]		1.97	0.002	1.52	0.275
Baseline ECOG Status (0 vs. 1 vs. 2)		0.98	0.919	1.98	0.002
Baseline Hemoglobin (g/dL) [3]		1.03	0.723	0.87	0.232
Baseline LDH (IU/mL) [1, 3]		1.00	0.380	1.003	<0.001
Baseline Alkaline Phosphatase (IU/mL) [1, 3]		---	---	1.00	0.078
Line of Therapy (1st through 6th)		1.25	0.050	1.06	0.751
Type of Therapy (Taxotere: Yes/No)		1.04	0.882	0.90	0.770

[1] Determined from Serum Drawn on the Same Date as the Blood Drawn for CTC

[2] p-value from Wald test of Z statistic

[3] Assessed as a continuous parameter

Use of CTC to Monitor Clinical Status of Metastatic Prostate Cancer Patients

Relationship between survival, CTCs and disease assessment by PSA

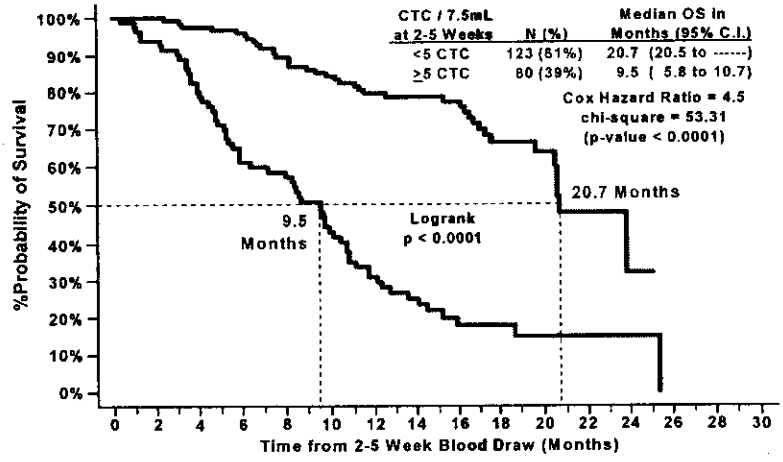
At present, a reduction in PSA is one of the primary means to determine response to therapy in MPC patients. To establish the relationship of clinical status as determined by a PSA to CTC, reduction of ≥30% or ≥50% PSA and CTC were measured 2-5 weeks, 6-8 weeks, 9-12 weeks and 13-20 weeks after initiation of therapy and compared to overall survival.

For the Kaplan-Meier analysis the elapsed OS times were calculated from the time of blood draw. Patients were segmented into Favorable groups based upon a CTC of <5 at the time of evaluation and a ≥30% reduction of PSA from baseline to the time of evaluation. Patients were segmented into Unfavorable groups based upon a CTC of ≥5 and <30% reduction of PSA from baseline to the time of evaluation.

Figure 9 shows the results of the analysis 2-5 weeks after initiation of therapy, **Figure 10** the analysis 6-8 weeks after initiation of therapy, **Figure 11** the analysis 9-12 weeks after initiation of therapy and **Figure 12** the analysis 13-20 weeks after initiation of therapy.

Figure 9: OS of MPC Patients 2-5 weeks after the Initiation of Therapy

A. 2-5 Week CTC



B. ≥30% PSA Reduction at 2-5 Weeks

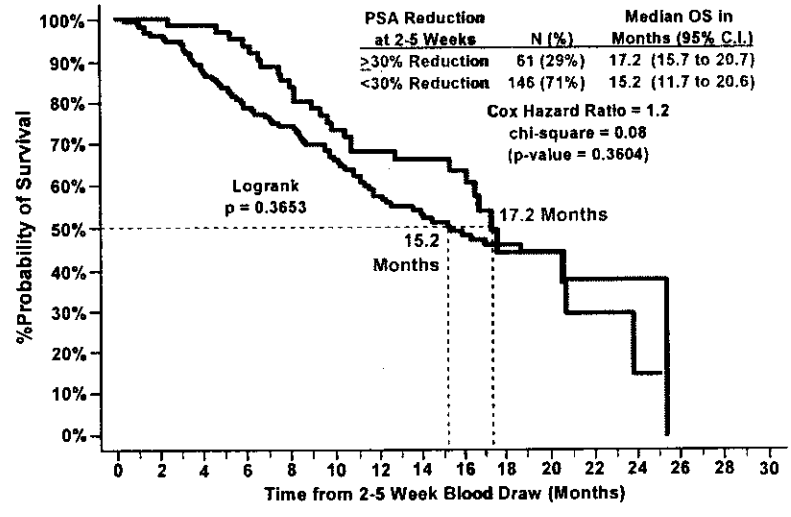
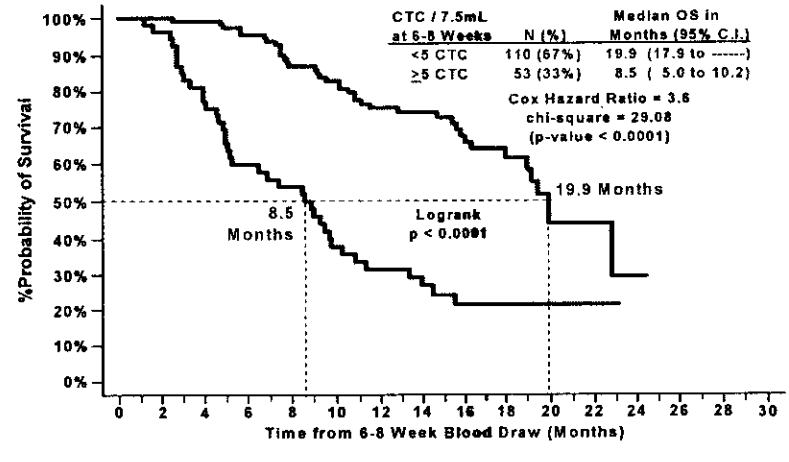


Figure 10: OS of MPC Patients 6-8 weeks after the Initiation of Therapy

A. 6-8 Week CTC



B. ≥30% PSA Reduction at 6-8 Weeks

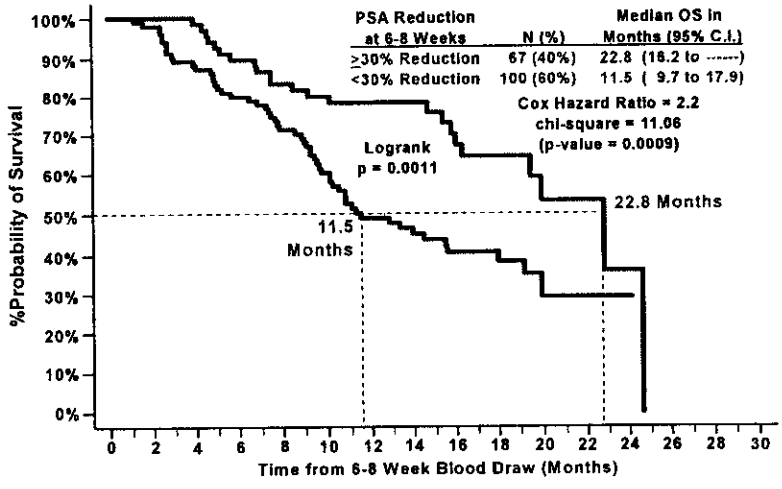
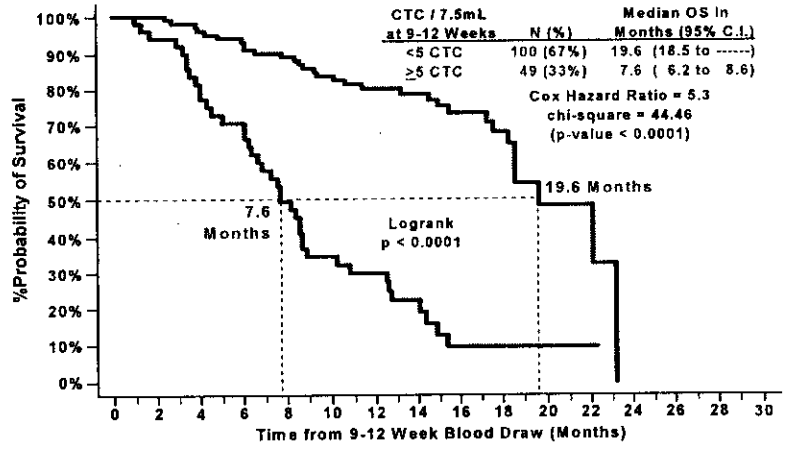


Figure 11: OS of MPC Patients 9-12 weeks after the Initiation of Therapy

A. 9-12 Week CTC



B. ≥30% PSA Reduction at 9-12 Weeks

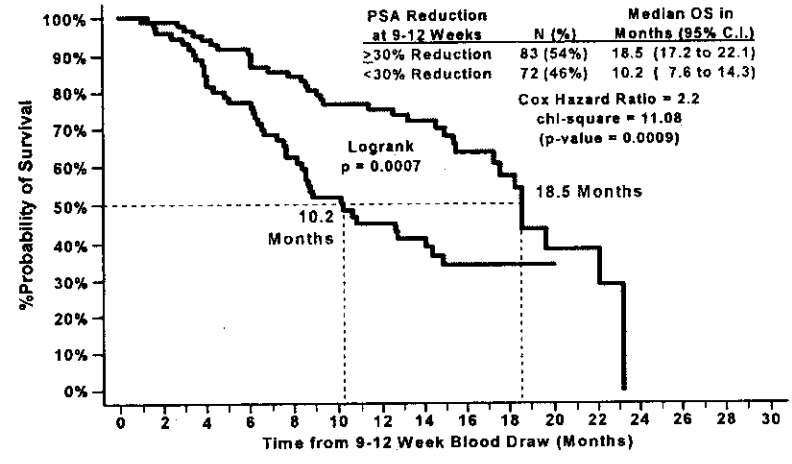
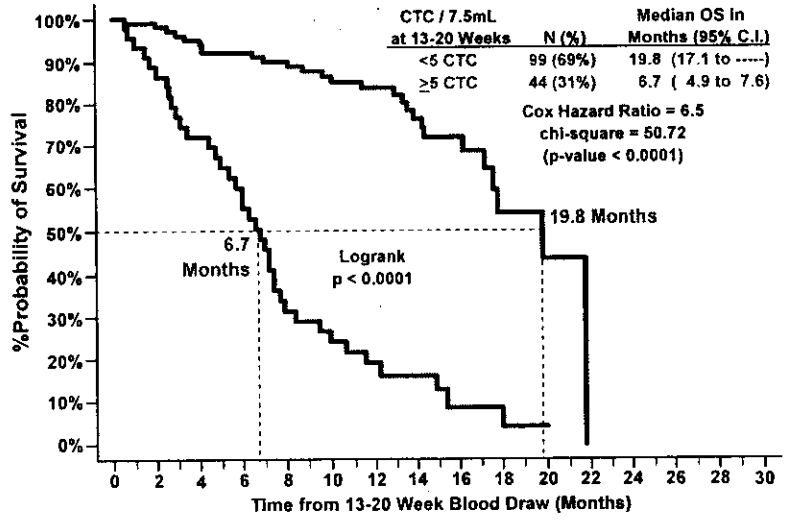


Figure 12: OS of MPC Patients 13-20 weeks after the Initiation of Therapy

A. 13-20 Week CTC



B. ≥30% PSA Reduction at 13-20 Weeks

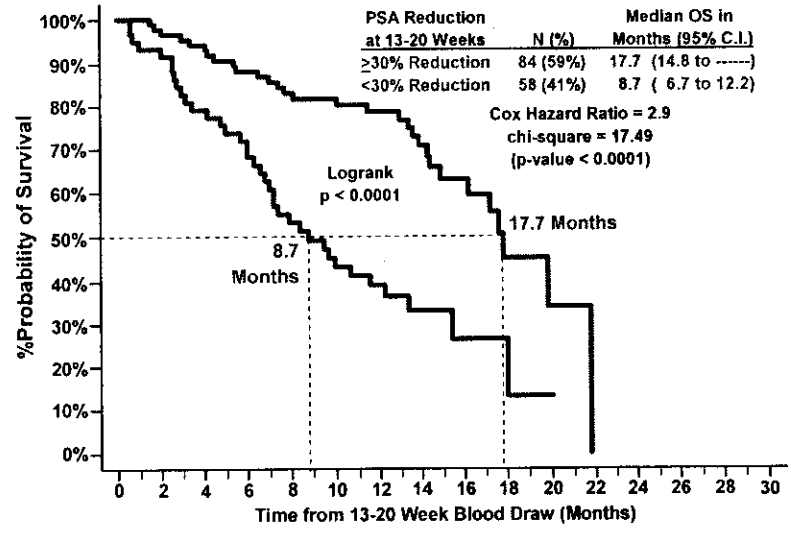


Table 9 illustrates the comparison of median overall survival at different time points after therapy with CTC, a 30% PSA reduction and a 50% PSA reduction.

Table 9: Comparison of Median OS between Favorable and Unfavorable CTC and PSA Reduction Groups.

	CTC / 7.5mL						30% PSA Reduction from Baseline						50% PSA Reduction from Baseline					
Time Point	N	≥5 (%)	Median OS <5	Median OS ≥5	logrank p-value	HR	N	<30% (%)	Median OS ≥30%	Median OS <30%	logrank p-value	HR	N	<50% (%)	Median OS ≥50%	Median OS <50%	logrank p-value	HR
2-5 Weeks	203	39%	20.7	9.5	<0.0001	4.5	207	71%	17.2	15.2	0.3653	1.2	207	83%	17.5	16.2	0.5599	1.2
6-8 Weeks	163	33%	19.9	8.5	<0.0001	3.6	167	60%	22.8	11.5	0.0011	2.2	167	75%	22.8	14.4	0.0117	2.1
9-12 Weeks	149	33%	19.6	7.6	<0.0001	5.3	155	46%	18.5	10.2	0.0007	2.2	155	59%	19.6	10.8	0.0006	2.3
13-20 Weeks	143	31%	19.8	6.7	<0.0001	6.5	142	41%	17.7	8.7	<0.0001	2.9	142	46%	17.7	9.9	0.0001	2.6

Concordances between CTC and PSA Changes in MPC Patients

The data in **Figure 9** through **12** and in **Table 9**, illustrate a highly significant difference in overall survival between patients with Unfavorable CTC and Favorable CTC at all time points tested, whereas PSA evaluations were not significant until 6-8 weeks after the initiation of therapy. Although the differences in median OS between the Favorable (≥30% or ≥50% PSA reduction from baseline) and Unfavorable (<30% or <50% PSA reduction from baseline) PSA reduction groups were significant, the separation between the Favorable (<5 CTC) and Unfavorable (≥5 CTC) CTC groups appeared greater and was significant at all time points after the initiation of therapy.

At present, either a ≥30% or ≥50% reduction in PSA is commonly used to evaluate disease progression in metastatic prostate cancer patients. Therefore, to establish the relationship between CTC and changes in PSA two by two tabulations of concordant and discordant observations between CTC and PSA changes for each time point after the initiation of therapy were constructed. Although comparisons of CTC to PSA change at both magnitudes were calculated, only data from the CTC vs. ≥30% PSA change are reported. This decision was based on a recent publication (*J Nat Ca Inst.* 98 (8):p.516-521, 2006) demonstrating that a 3-month 30% PSA decline showed a stronger association with decrease in risk of death than did a 50% decrease in PSA. Furthermore, a comparison of patient–wise and observation-wise results from the 30% and 50% PSA decline vs. CTC analyses did not demonstrate substantial differences in the Positive % Agreement, Negative % Agreement and Overall Agreement at any of the observed time points.

A total of 197, 159, 146, and 138 patients had serum samples analyzed by the central laboratory and had evaluable CTC results 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy, respectively. To determine a patient's response to therapy, the percent change in PSA from the baseline value was calculated for each of the time points after the initiation of therapy. For PSA changes at each time point, the Favorable group was defined as patients with a ≥30% reduction in PSA and the Unfavorable group was defined as patients with a <30% reduction in PSA. For CTC at each time point, the Favorable group was defined as patients having <5 CTC per 7.5mL of blood and the Unfavorable group was defined as patients having ≥5 CTC.

Because CTC vs. PSA results of the patient-wise comparisons between CTC and a ≥30% PSA reduction at 2-5 weeks and 13-20 weeks after the initiation of therapy showed the most significant discordance and concordance, respectively, these data are presented in **Table 10** and **Table 11**, respectively.

Table 10: MPC Patient-Wise Comparison of CTC and 30% PSA Reduction at 2-5 Weeks

% Reduction in PSA from Baseline at 2-5 Weeks After Initiation of Therapy	CTCs 2-5 Weeks after the Initiation of Therapy		Total
	< 5 CTCs/7.5mL	≥ 5 CTCs/ 7.5mL	
≥30% Reduction in PSA	50	11	**61**
<30% Reduction in PSA	69	67	**136**
Total	**119**	**78**	**197**

Measurement	Estimate	Lower 95% CI	Upper 95% CI
Positive % Agreement	49%	41%	58%
Negative % Agreement	82%	70%	91%
Positive Predictive Value	86%	76%	93%
Negative Predictive Value	42%	33%	51%
Overall Agreement	59%	52%	66%
Odds Ratio	4.4	2.1	9.2

Table 11: MPC Patient-Wise Comparison of CTC and 30% PSA Reduction at 13-20 Weeks.

% Reduction in PSA from Baseline at 13-20 Weeks After Initiation of Therapy	CTC 13-20 Weeks after the Initiation of Therapy		Total
	< 5 CTC	≥ 5 CTC	
≥30% Reduction in PSA	72	9	**81**
<30% Reduction in PSA	23	34	**57**
Total	**95**	**43**	**138**

Measurement	Estimate	Lower 95% CI	Upper 95% CI
Positive % Agreement	60%	46%	72%
Negative % Agreement	89%	80%	95%
Positive Predictive Value	79%	64%	90%
Negative Predictive Value	76%	66%	84%
Overall Agreement	77%	69%	84%
Odds Ratio	11.8	4.9	28.3

The results of an "observation-wise" comparison of CTC and PSA changes using a ≥30% reduction threshold at 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy combined are shown in **Table 12.**

Table 12: MPC Observation-Wise Comparison of CTC and 30% PSA Reduction.

% Reduction in PSA from Baseline After Initiation of Therapy	CTC after the Initiation of Therapy		Total
	< 5 CTC	≥ 5 CTC	
≥30% Reduction in PSA	243	41	**284**
<30% Reduction in PSA	175	181	**356**
Total	**418**	**222**	**640**

Measurement	Estimate	Lower 95% CI	Upper 95% CI
Positive % Agreement	51%	46%	56%
Negative % Agreement	86%	81%	89%
Positive Predictive Value	82%	76%	86%
Negative Predictive Value	58%	53%	63%
Overall Agreement	66%	62%	70%
Odds Ratio	6.1	4.1	9.1

The overall concordance between CTC and PSA changes at the various time points after the initiation of therapy ranged from 59% to 77% when comparing to a ≥30% PSA reduction and from 52% to 75% when comparing to a ≥50% PSA reduction, showing that there was discordance between CTC and PSA changes in ~25% to 40% of the patients.

CTC Levels and PSA Reduction Combined to Predict OS in MPC Patients

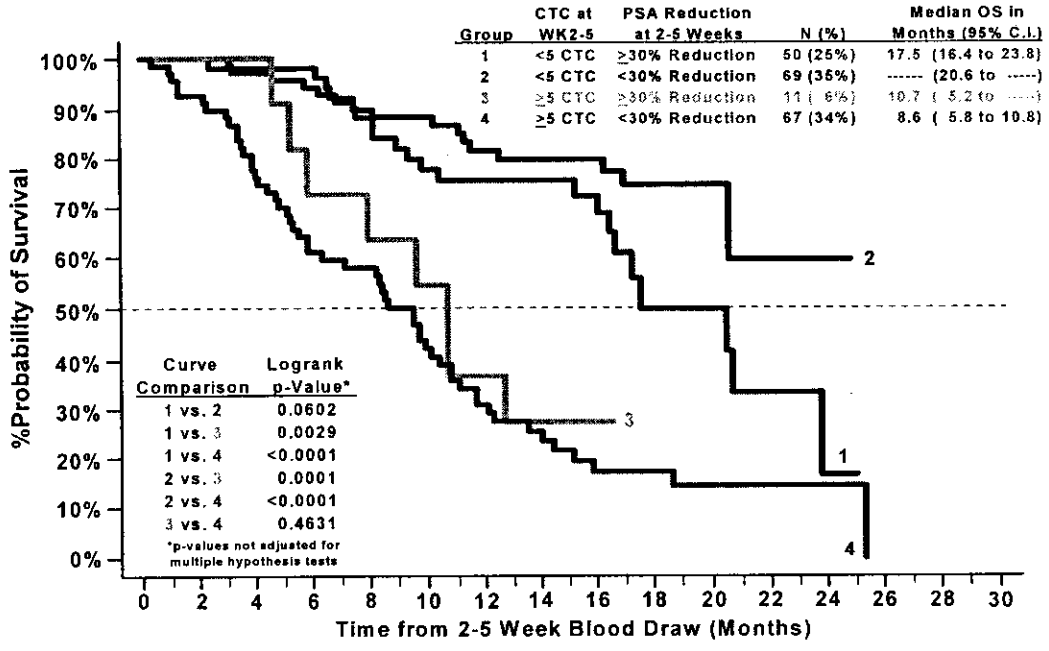
To determine which of the discordant results better reflected the prognosis of the patient, CTC assessment and changes in PSA 2-5 weeks, 6-8 weeks, 9-12 weeks and 13-20 weeks after initiation of therapy were compared to overall survival. Elapsed OS times were calculated from the blood draw being evaluated. For the Kaplan-Meier analysis **Figure 13 (Panels A, B, C and D)** patients were segmented into four groups based upon their CTC counts and PSA reduction at 2-5 weeks, 6-8 weeks, 9-12 weeks, and 13-20 weeks after the initiation of therapy, respectively:

:

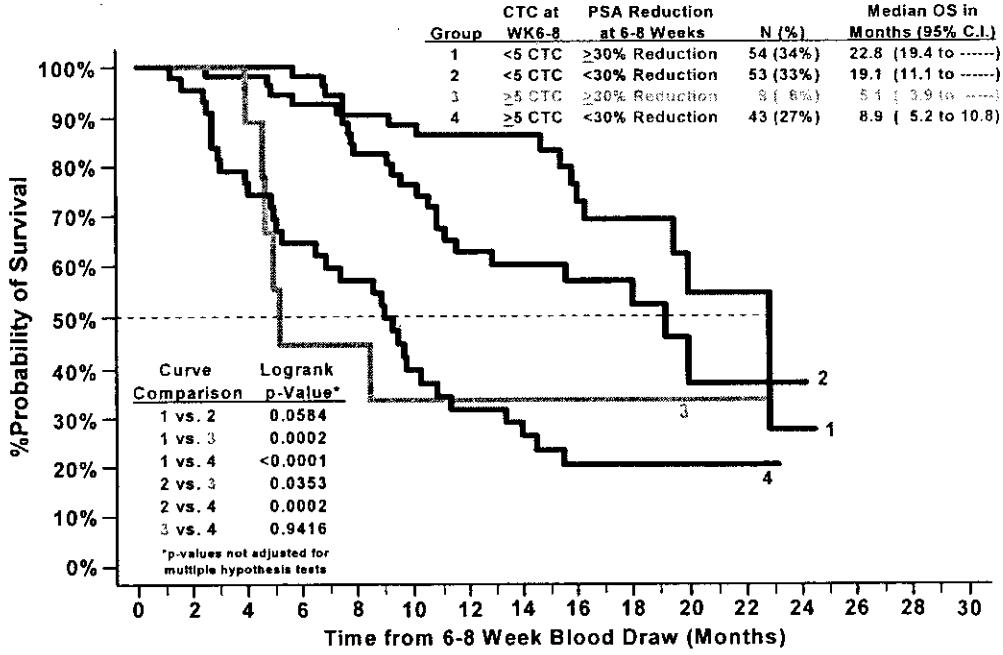
- Group 1 (**green** curve), patients with <5 CTC at the time of evaluation and a ≥30% reduction of PSA from baseline to the time of evaluation;
- Group 2 (**blue** curve), patients with <5 CTC at the time of evaluation and a <30% reduction of PSA from baseline to the time of evaluation;
- Group 3 (orange curve), patients with ≥5 CTC at the time of evaluation and a ≥30% reduction of PSA from baseline to the time of evaluation
- Group 4 (**red** curve), patients with ≥5 CTC at the time of evaluation and a <30% reduction of PSA from baseline to the time of evaluation.

Figure 13: CTC Levels and PSA Changes Combined to Predict OS 2-5 Weeks (Panel A), 6-8 Weeks (Panel B), 9-12 Weeks (Panel C), and 13-20 Weeks (Panel D) After the Initiation of Therapy

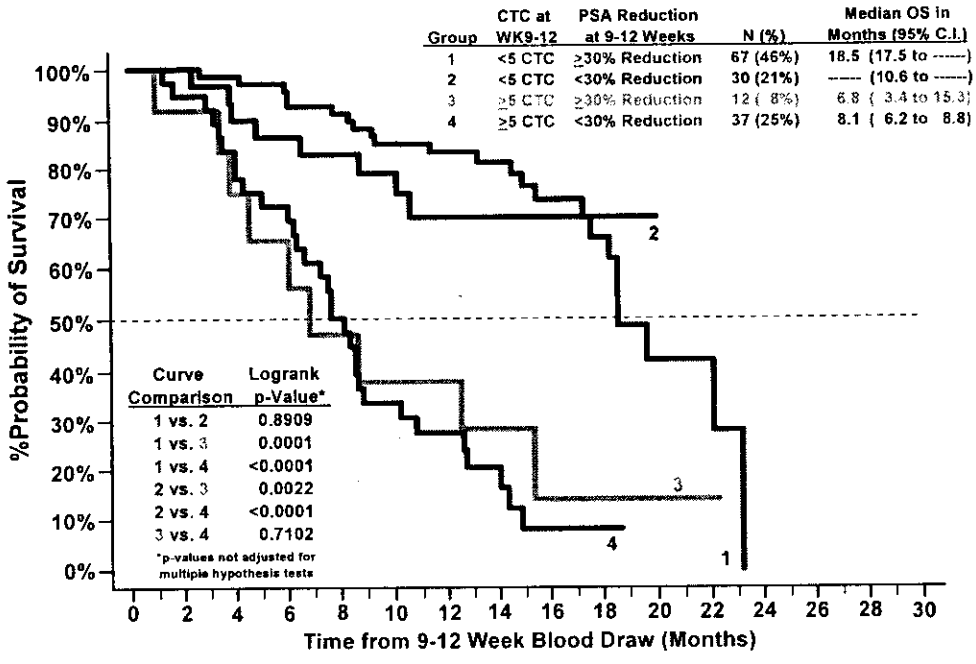
A. 2-5 Weeks



B. 6-8 Weeks



C. 9-12 Weeks



D. 13-20 Weeks

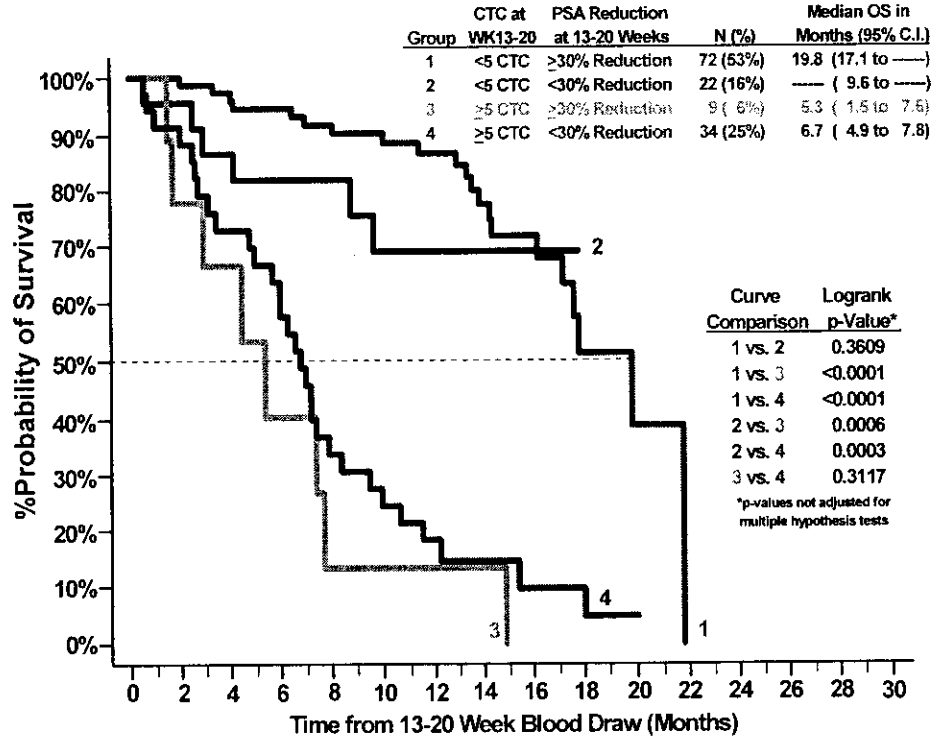


Figure 13 shows that patients with ≥5 CTC at any point after the initiation of therapy had a much higher likelihood of dying sooner, irrespective of the changes in PSA levels from baseline. Patients with ≥5 CTC at all time points (**Group 3** and **Group 4**) had the shortest median overall survivals, which were not significantly different. However, the median OS of these two groups was significantly different compared to the median OS of the patients with <5 CTC at all time points (**Group 1** and **Group 2**). These two groups (**Group 1** and **Group 2**) had the longest median overall survivals, which were not significantly different. The important finding illustrated in **Figure 13** is that although a reduction of PSA at some points after initiation of therapy may reach significance for prediction of survival, Favorable CTC at any time point were more accurate than the PSA evaluation. The practical implication is the use of CTC analysis for the evaluation of the probability of survival of MPC patients. In cases where CTC and PSA change were discordant, CTC provided the most accurate assessment of prognosis.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 26 2008

Veridex, LLC
c/o Ms. Debra J. Rasmussen
Worldwide Executive Director Regulatory Affairs
1001 US Highway 202
Raritan, NJ 08869

Re: k073338
Trade/Device Name: CellSearch™ Circulating Tumor Cell Kit (Epithelial)
Regulation Number: 21 CFR 866.6020
Regulation Name: Immunomagnetic Circulating Cancer Cell Selection and Enumeration System
Regulatory Class: Class II
Product Code: NQI
Dated: November 27, 2007
Received: November 28, 2007

Dear Ms. Rasmussen:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The

FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE

510(K) Number (if known): K073338

Device Name: CellSearch™ Circulating Tumor Cell Kit

Indications for Use:

The CellSearch™ Circulating Tumor Cell Kit is intended for the enumeration of circulating tumor cells (CTC) of epithelial origin (CD45-, EpCAM+, and cytokeratins 8, 18+, and/or 19+) in whole blood.

The presence of CTC 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 breast, colorectal or prostate* cancer. The test is to be used as an aid in the monitoring of patients with metastatic breast, colorectal or prostate cancer. Serial testing for CTC should be used in conjunction with other clinical methods for monitoring metastatic breast, colorectal and prostate cancer. Evaluation of CTC at any time during the course of disease allows assessment of patient prognosis and is predictive of progression free survival and overall survival.

**Metastatic prostate cancer patients in this study were defined as having two consecutive increases in the serum marker PSA above a reference level, despite standard hormonal management. These patients are commonly described as having androgen-independent, hormone-resistant, or castration-resistant prostate cancer.*

The CellSearch system includes: CellSave Preservative Tubes, the CellTracks® AutoPrep® System, the CellTracks® Analyzer II or the CellSpotter® Analyzer, and the CellSearch™ Circulating Tumor Cell Control Kit

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(PLEASE DO NOT WRITE BELOW THIS LINE- CONTINUE ON ANOTHER PAGE AS NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _X_ AND/OR Over –the-Counter Use ___
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K073338