

In addition to the data relied upon by the FDA, the attached article, published in the New England Journal of Medicine on July 29, 2010, presents the results of the double-blind, placebo-controlled phase III trial for PROVENGE, as well as summarizes the findings from 2 earlier phase III trials. The article concludes that the "use of sipuleucel-T prolonged overall survival among men with metastatic castration-resistant prostate cancer." [3]

As described in the New England Journal of Medicine article, sipuleucel-T has shown evidence of efficacy in reducing the risk of death among men with metastatic castration-resistant prostate cancer. In the randomized double-blind, placebo-controlled, multicenter phase III "IMPACT" trial, we randomly assigned 512 patients with median age of 71, in a 2:1 ratio to receive either sipuleucel-T (341 patients) or placebo (171 patients) administered intravenously every 2 weeks, for a total of 3 infusions.

The primary endpoint of this study was overall survival, the most meaningful clinical outcome for patients, analyzed by means of a stratified Cox regression model adjusted for baseline levels of serum prostate-specific antigen (PSA) and lactate dehydrogenase. In the sipuleucel-T group, there was a relative reduction of 22% in the risk of death as compared with the placebo group (hazard ratio (HR), 0.78; 95% confidence interval (CI), 0.61 to 0.98;  $P = 0.03$ ). There was a 4.1-month improvement in median survival (25.8 months in the sipuleucel-T group vs. 21.7 months in the placebo group). The 36-month survival probability was 31.7% in the sipuleucel-T group versus 23.0% in the placebo group. The treatment effect was also observed with the use of an unadjusted Cox model and a log-rank test (HR, 0.77; 95% CI, 0.61 to 0.97;  $P = 0.02$ ) and after adjustment for use of docetaxel after the study therapy (HR, 0.78; 95% CI, 0.62 to 0.98;  $P = 0.03$ ).

Importantly, the results of the IMPACT trial confirmed the results of the earlier D9901 study, published in the attached article in the Journal of Clinical Oncology. [4] Specifically, in this study there was a relative reduction of 41% in the risk of death in the sipuleucel-T group compared with the placebo group (HR, 0.586; 95% CI, 0.388 to 0.884;  $P=0.010$ ). There was a 4.5 month improvement in median survival (25.9 months in the sipuleucel-T group vs. 21.4 months in the placebo group). In this study, 34% of the men were alive at the 3 year follow-up compared to 11% in the placebo group. An integrated survival analysis completed with these results together with the results from the D9902A [5] trial and IMPACT demonstrated a p-value of  $<0.001$ , suggesting a less than 1 in 1000 chance that the results would have been observed by chance alone.

Additionally, PROVENGE has a favorable side effect profile. The most common adverse events (AEs), reported in patients in the sipuleucel-T group at a rate  $\approx$  15%, were chills, fatigue, fever, back pain, nausea, joint ache, and headache. The majority of AEs in trials were grades 1 or 2. The most common ( $\approx$  2%) Grade 3-5 adverse events reported in the sipuleucel-T group were back pain and chills. The percentage of patients in each arm experiencing serious AEs (SAEs) was comparable, including the percentage with cerebral vascular accidents (CVAs), of which none were attributed to sipuleucel-T. Safety concerns raised earlier by the FDA about the incidence of CVAs are addressed by a Risk Management Plan submitted as part of the amendment to the BLA and a post-marketing registry study.

In conclusion, multiple randomized trials have shown that PROVENGE prolonged survival among men with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. This strong clinical evidence led to FDA approval and should serve as the foundation for coverage by CMS. There is a current unmet need for the treatment of men with metastatic castrate resistant prostate cancer who have yet become symptomatic enough to receive traditional chemotherapy manipulation. PROVENGE provides a new, innovative, safe, and proven opportunity for such patients to extend their lives with minimal daily interruptions.

The evidence provided to CMS and contained in the New England Journal of Medicine article, demonstrates that PROVENGE is reasonable and necessary for patients with asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer and that the NCA is not warranted. More important, it creates an unnecessary additional hurdle for patients to navigate as they seek treatment for this deadly disease. Now that CMS has adequately gathered "comments and additional information or evidence of studies" about the policy under consideration,[6] the agency need not invest additional time and resources into evaluating coverage of PROVENGE. This is particularly true as the primary endpoint of the IMPACT trial was overall survival, and the median age of patients enrolled was 71 years, with 75% of the patients being 65 years of age or older and eligible for Medicare. The subgroup analysis of patients 65 years of age or older in the integrated dataset for the 3 randomized trials in metastatic castrate resistant prostate cancer demonstrated consistency of the PROVENGE treatment effect. The median survival was 23.4 months in the PROVENGE group and 17.1 months in the placebo group. PROVENGE clearly shows effectiveness in the Medicare population and improves health outcomes in patients with prostate cancer. Accordingly, we request that CMS close this NCA and instead allow its local contractors to cover PROVENGE, applying the same coverage criteria as they apply to any other new cancer drug or biological. We believe that CMS should rely on its local contractors and physicians, through its local processes to determine appropriate use. CMS should not stand in the way of the adoption of new technologies and perhaps a new standard of care; rather, it should partner with its local contractors and physicians to educate Medicare beneficiaries on the clinical benefits and appropriate use of PROVENGE.

To the extent that CMS initiated this NCA based on concerns about "health inequalities" and "local variation" and a desire to ensure that this "substantial clinical advance . . . diffuses more rapidly to all patients for whom it is indicated,"[7] this uniformity and diffusion already is occurring. Although we expressed concerns during our most recent meeting with you about the variations in coverage of PROVENGE between contractors, these variations have subsided. Currently most Medicare contractors have published guidelines or verbally indicated they are/will cover PROVENGE as a biological product for its on-label indication, and Medicare beneficiaries across the country have access to PROVENGE in their battle against metastatic castrate resistant prostate cancer. Again, this reinforces why the NCA is not necessary at this time.

We believe that if CMS does decide to move forward with this NCA, it should conclude the process quickly, without a TA or a MedCAC meeting. We believe that a TA is not needed because none of the conditions listed in the guidance document regarding factors CMS considers in commissioning a TA exist. In particular, there are no "significant differences in opinion among experts," as shown by the fact that soon after PROVENGE was approved by the FDA, the National Comprehensive Cancer Network (NCCN) listed PROVENGE in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>T</sup>) for Prostate Cancer (version 2.2010) and

NCCN Drugs & Biologics Compendium (NCCN CompendiumT) as a category 1 treatment recommendation for patients with castration-recurrent prostate cancer.[8] A category 1 recommendation means that "the recommendation is based on high level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus." [9] NCCN is a not-for-profit alliance of 21 of the world's leading cancer centers. Its experts are world renowned, and its Prostate Cancer Panel includes 28 members from the best cancer hospitals across the country. NCCN's rapid inclusion of PROVENGE in its Guidelines and Compendium with a category 1 recommendation shows the high level of consensus that exists regarding PROVENGE's clinical data as well as PROVENGE's role in the treatment regimen for prostate cancer.

Furthermore, although the description of the TA on the Agency for Healthcare Research and Quality (AHRQ) website recently was changed from "The Efficacy and Safety of Sipuleucel T" to "The Outcomes of Sipuleucel T," [10] we continue to be concerned that the scope of the assessment duplicates the review already conducted by the FDA. For the same reasons, we believe that a meeting of the MedCAC is not needed to assess the data on PROVENGE, all of which already has been reviewed by CMS.

If CMS proceeds with the NCA, we believe the agency should issue a proposed decision as soon as possible covering PROVENGE under the same standards as apply to any other drug or biological used in an anticancer chemotherapeutic regimen. Under the Social Security Act (SSA), any FDA-approved use of a drug or biological in an anticancer chemotherapeutic drug regimen is a "medically accepted indication" that is included in the definition of "drugs and biologicals" that may be covered by Medicare.[11] The use of PROVENGE for asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer is approved by the FDA and thus is a "medically accepted indication" used in an anticancer chemotherapeutic drug regimen that should be covered by Medicare. In addition, other uses of FDA-approved drugs used in anticancer chemotherapeutic drug regimens are "medically accepted indications" if the use is supported by authoritative compendia recognized by the Secretary of Health and Human Services.[12] The NCCN Drugs and Biologics Compendium is one of these compendia,[13] and it supports use of PROVENGE for "asymptomatic or minimally symptomatic patients with performance status 0-1 and a life expectancy of greater than 6 months and no visceral disease." [14] By virtue of this listing in the NCCN Compendium, PROVENGE would satisfy the criteria for coverage even if it had not been approved for asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer; therefore, it undoubtedly should be covered for its FDA-approved use.

Thank you for your thoughtful consideration of our comments. We remind you that the patients we serve have late-stage cancer and few, if any, appealing treatment options available to them, with only chemotherapy as an FDA-approved alternative. Not only is PROVENGE clearly reasonable and necessary for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer, but it provides an unambiguous survival benefit and real hope for patients battling their disease. At Dendreon, so many of us have been affected by cancer, which is why we have dedicated our lives to transforming the way cancer is treated. The patients PROVENGE treats are our fathers, our husbands, our brothers and sons, our teachers and physicians, our veterans and our friends. We urge you not to deny them access to PROVENGE and recognize that survival is more than just surviving: it allows cancer patients the freedom to live. We appreciate the opportunity to submit these comments and would be pleased to meet with the agency again to address any questions you may have.

Sincerely,

Hans Bishop, Chief Operating Officer of Dendreon

Mark Frohlich, Chief Medical Officer of Dendreon

[1] NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N), June 30, 2010, <http://www.cms.gov/mcd/viewtrackingsheet.asp?id=247>.

2 Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006, [http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6).

3 Kantoff PW, Higano CS, et al. Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. *N Engl J Med* 2010;363:411-22.

4 Small EJ, Schellhammer PF, Higano CS, et al. Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J Clin Oncol* 2006; 24:3089-94.

5 Higano CS, Schellhammer PF, Small EJ, et al. Integrated data from 2 randomized double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* 2009;115:3670-9.

6 68 Fed. Reg. 55634, 55639; see also Guidance Document on Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006,

[http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6)  
<[http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6)> .

7 Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006,  
[http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6).

8 NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer, v.2.2010, May 12, 2010.

9 NCCN Categories of Evidence and Consensus,  
[http://www.nccn.org/professionals/physician\\_gls/categories\\_of\\_consensus.asp](http://www.nccn.org/professionals/physician_gls/categories_of_consensus.asp)  
<[http://www.nccn.org/professionals/physician\\_gls/categories\\_of\\_consensus.asp](http://www.nccn.org/professionals/physician_gls/categories_of_consensus.asp)> .

10 Technology Assessments in Progress, <http://www.ahrq.gov/clinic/techix.htm#progress>.

11 SSA § 1861(t)(2)(A)-(B).

12 SSA § 1861(t)(2)(B)(ii).

13 Medicare Benefit Policy Manual, ch. 15, § 50.4.5.

14 NCCN Drugs & Biologics Compendium, "Sipuleucel-T," current as of July 26, 2010.

#### Attachments

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[1] NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N), June 30, 2010, <http://www.cms.gov/mcd/viewtrackingsheet.asp?id=247>.

[2] Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006,  
[http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6).

[3] Kantoff PW, Higano CS, et al. Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. *N Engl J Med* 2010;363:411-22.

[4] Small EJ, Schellhammer PF, Higano CS, et al. Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J Clin Oncol* 2006; 24:3089-94.

[5] Higano CS, Schellhammer PF, Small EJ, et al. Integrated data from 2 randomized double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* 2009;115:3670-9.

[6] 68 Fed. Reg. 55634, 55639; see also Guidance Document on Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006, [http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6)  
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[7] Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006, [http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6).

[8] NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer, v.2.2010, May 12, 2010.

[9] NCCN Categories of Evidence and Consensus, [http://www.nccn.org/professionals/physician\\_gls/categories\\_of\\_consensus.asp](http://www.nccn.org/professionals/physician_gls/categories_of_consensus.asp)  
<[http://www.nccn.org/professionals/physician\\_gls/categories\\_of\\_consensus.asp](http://www.nccn.org/professionals/physician_gls/categories_of_consensus.asp)> .

[10] Technology Assessments in Progress, <http://www.ahrq.gov/clinic/techix.htm#progress>.

[11] SSA § 1861(t)(2)(A)-(B).

[12] SSA § 1861(t)(2)(B)(ii).

[13] Medicare Benefit Policy Manual, ch. 15, § 50.4.5.

[14] NCCN Drugs & Biologics Compendium, "Sipuleucel-T," current as of July 26, 2010.

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**Rollins, James (CMS/OCSQ)**

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**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Thursday, July 29, 2010 8:30 AM  
**To:** PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Attachments:** IMPACT NEJM manuscript 2010.pdf

Please find the pivotal study published in the NEJM today. I received it from Dendreon. It has been saved on the G drive.

**Rollins, James (CMS/OCSQ)**

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Thursday, July 29, 2010 8:30 AM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Dolina, Elaine L. (CMS/OCSQ)  
**Subject:** RE: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

The IMPACT publication in the NEJM has been sent to you and saved on the G drive. I have forwarded this to Elaine to be posted.

-----Original Message-----

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Wednesday, July 28, 2010 11:23 PM  
**To:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Dolina, Elaine L. (CMS/OCSQ)  
**Subject:** FW: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

-----Original Message-----

**From:** Larson, Tricia [mailto:tlarson@Dendreon.com]  
**Sent:** Wed 7/28/2010 10:25 PM  
**To:** Jacques, Louis B. (CMS/OCSQ)  
**Cc:** Bishop, Hans; Frohlich, Mark; Lockett, Chris  
**Subject:** NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N).

July 28, 2010

Louis Jacques, MD

Director, Coverage and Analysis Group

Centers for Medicare & Medicaid Services

Mail Stop S3-02-01

7500 Security Blvd.

Baltimore, MD 21244

**Re:** NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

Dear Dr. Jacques:

On behalf of Dendreon Corporation (Dendreon), I am submitting the following comments on the opening of a national coverage analysis (NCA) for autologous cellular immunotherapy treatment of metastatic prostate cancer.[1] Dendreon is the manufacturer of PROVENGE® (sipuleucel-T), an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. PROVENGE is the first in a new class of biological products designed to induce a tumor-specific immune response. The Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration (FDA) approved PROVENGE on April 29, 2010 under a biologic license application (BLA, license number 1749). Bringing PROVENGE to market has been a 15-year journey that has involved more than a thousand courageous patients, 15 clinical trials, and nearly one billion dollars of funding of research and development.

Dendreon appreciates the numerous opportunities we have had to meet with the Centers for Medicare and Medicaid Services (CMS) to discuss PROVENGE both pre- and post- FDA approval. We believe that the agency should be very familiar with PROVENGE's clinical benefits and manufacturing process as a result of these meetings and all of the additional information we have provided in other various forms. Specifically, in just the past few months, Dendreon applied for a Healthcare Common Procedure Coding System (HCPCS) code and for pass-through biological status under the hospital outpatient prospective payment system (OPPS). Each application requires substantial clinical and product information that further demonstrates the appropriateness and reasonableness of immediate Medicare coverage. As we describe in further detail below, we are now enhancing the breadth and depth of evidence of PROVENGE's effectiveness in the Medicare population by including a recently published study in the New England Journal of Medicine. Based upon the overwhelming clinical evidence showing a significant improvement in overall survival in this patient population, the "gold standard" of all endpoints in oncology clinical trials, we ask CMS to reconsider whether a NCA is necessary. We make this request based on the fact that CMS's initiation of this process was highly unusual. Since the current NCA process was implemented after the Medicare Modernization Act of 2003 (MMA), this is the first time CMS has internally initiated a NCA for an approved use of an innovative new cancer biological. The evidence we have submitted demonstrates that consistent with other drugs and biologicals CMS currently covers, PROVENGE clearly is reasonable and necessary for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer. Dendreon believes that upon further review, CMS should conclude that the NCA can be closed at this time, without the need for further evaluation, a technology assessment (TA), or a Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting.

Under CMS's Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, CMS identifies several circumstances in which CMS could internally initiate a NCA for a new technology. Although we do not know the precise reason CMS opened this NCA, we think the agency may have initiated it based on a belief that "significant uncertainty exists concerning the health benefits, patient selection, or appropriate facility and staffing requirements for the new technology." [2] As stated above, we believe that any uncertainty about the health benefits, patient selection, and appropriate provision of PROVENGE can be addressed without further analysis by CMS. FDA's review of PROVENGE was comprehensive and rigorous. The agency reviewed data from 4 randomized trials involving over 900 patients. The pivotal registration study was conducted under a Special Protocol Assessment agreement with the FDA and demonstrated a statistically significant survival benefit. Similar results were seen in a previous smaller randomized trial.

In addition to the data relied upon by the FDA, the attached article, published in the New England Journal of Medicine on July 29, 2010, presents the results of the double-blind, placebo-controlled phase III trial for PROVENGE, as well as summarizes the findings from 2 earlier phase III trials. The article concludes that the "use of sipuleucel-T prolonged overall survival among men with metastatic castration-resistant prostate cancer." [3]

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that "the recommendation is based on high level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus." [9] NCCN is a not-for-profit alliance of 21 of the world's leading cancer centers. Its experts are world renowned, and its Prostate Cancer Panel includes 28 members from the best cancer hospitals across the country. NCCN's rapid inclusion of PROVENGE in its Guidelines and Compendium with a category 1 recommendation shows the high level of consensus that exists regarding PROVENGE's clinical data as well as PROVENGE's role in the treatment regimen for prostate cancer.

Furthermore, although the description of the TA on the Agency for Healthcare Research and Quality (AHRQ) website recently was changed from "The Efficacy and Safety of Sipuleucel T" to "The Outcomes of Sipuleucel T," [10] we continue to be concerned that the scope of the assessment duplicates the review already conducted by the FDA. For the same reasons, we believe that a meeting of the MedCAC is not needed to assess the data on PROVENGE, all of which already has been reviewed by CMS.

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Thank you for your thoughtful consideration of our comments. We remind you that the patients we serve have late-stage cancer and few, if any, appealing treatment options available to them, with only chemotherapy as an FDA-approved alternative. Not only is PROVENGE clearly reasonable and necessary for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer, but it provides an unambiguous survival benefit and real hope for patients battling their disease. At Dendreon, so many of us have been affected by cancer, which is why we have dedicated our lives to transforming the way cancer is treated. The patients PROVENGE treats are our fathers, our husbands, our brothers and sons, our teachers and physicians, our veterans and our friends. We urge you not to deny them access to PROVENGE and recognize that survival is more than just surviving: it allows cancer patients the freedom to live. We appreciate the opportunity to submit these comments and would be pleased to meet with the agency again to address any questions you may have.

Sincerely,

Hans Bishop, Chief Operating Officer of Dendreon

Mark Frohlich, Chief Medical Officer of Dendreon

[1] NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N), June 30, 2010, <http://www.cms.gov/mcd/viewtrackingsheet.asp?id=247>.

2 Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006, [http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6).

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4 Small EJ, Schellhammer PF, Higano CS, et al. Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J Clin Oncol* 2006; 24:3089-94.

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6 68 Fed. Reg. 55634, 55639; see also Guidance Document on Factors CMS Considers in Opening a National Coverage Determination, April 11, 2006, [http://www.cms.gov/mcd/ncpc\\_view\\_document.asp?id=6](http://www.cms.gov/mcd/ncpc_view_document.asp?id=6)  
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11 SSA § 1861(t)(2)(A)-(B).

12 SSA § 1861(t)(2)(B)(ii).

13 Medicare Benefit Policy Manual, ch. 15, § 50.4.5.

14 NCCN Drugs & Biologics Compendium, "Sipuleucel-T," current as of July 26, 2010.

#### Attachments

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**Rollins, James (CMS/OCSQ)**

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**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Thursday, July 29, 2010 8:30 AM  
**To:** Dolina, Elaine L. (CMS/OCSQ); Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ)  
**Subject:** RE: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

Please add all attachments since they are published literature and one was published today. Thanks!

-----Original Message-----

**From:** Dolina, Elaine L. (CMS/OCSQ)  
**Sent:** Thursday, July 29, 2010 6:58 AM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Subject:** RE: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

Would you like me to add this comment to the database? If so, which attachments (if any) should I include?

Elaine

-----Original Message-----

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Wednesday, July 28, 2010 11:23 PM  
**To:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Dolina, Elaine L. (CMS/OCSQ)  
**Subject:** FW: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

-----Original Message-----

**From:** Larson, Tricia [mailto:tlarson@Dendreon.com]  
**Sent:** Wed 7/28/2010 10:25 PM  
**To:** Jacques, Louis B. (CMS/OCSQ)  
**Cc:** Bishop, Hans; Frohlich, Mark; Lockett, Chris  
**Subject:** NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

July 28, 2010

Louis Jacques, MD

Director, Coverage and Analysis Group

Centers for Medicare & Medicaid Services

Mail Stop S3-02-01

7500 Security Blvd.

Baltimore, MD 21244

Re: NCA Tracking Sheet for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N)

Dear Dr. Jacques:

On behalf of Dendreon Corporation (Dendreon), I am submitting the following comments on the opening of a national coverage analysis (NCA) for autologous cellular immunotherapy treatment of metastatic prostate cancer.[1] Dendreon is the manufacturer of PROVENGE® (sipuleucel-T), an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. PROVENGE is the first in a new class of biological products designed to induce a tumor-specific immune response. The Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration (FDA) approved PROVENGE on April 29, 2010 under a biologic license application (BLA, license number 1749). Bringing PROVENGE to market has been a 15-year journey that has involved more than a thousand courageous patients, 15 clinical trials, and nearly one billion dollars of funding of research and development.

Dendreon appreciates the numerous opportunities we have had to meet with the Centers for Medicare and Medicaid Services (CMS) to discuss PROVENGE both pre- and post- FDA approval. We believe that the agency should be very familiar with PROVENGE's clinical benefits and manufacturing process as a result of these meetings and all of the additional information we have provided in other various forms. Specifically, in just the past few months, Dendreon applied for a Healthcare Common Procedure Coding System (HCPCS) code and for pass-through biological status under the hospital outpatient prospective payment system (OPPS). Each application requires substantial clinical and product information that further demonstrates the appropriateness and reasonableness of immediate Medicare coverage. As we describe in further detail below, we are now enhancing the breadth and depth of evidence of PROVENGE's effectiveness in the Medicare population by including a recently published study in the New England Journal of Medicine. Based upon the overwhelming clinical evidence showing a significant improvement in overall survival in this patient population, the "gold standard" of all endpoints in oncology clinical trials, we ask CMS to reconsider whether a NCA is necessary. We make this request based on the fact that CMS's initiation of this process was highly unusual. Since the current NCA process was implemented after the Medicare Modernization Act of 2003 (MMA), this is the first time CMS has internally initiated a NCA for an approved use of an innovative new cancer biological. The evidence we have submitted demonstrates that consistent with other drugs and biologicals CMS currently covers, PROVENGE clearly is reasonable and necessary for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer. Dendreon believes that upon further review, CMS should conclude that the NCA can be closed at this time, without the need for further evaluation, a technology assessment (TA), or a Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting.

Under CMS's Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination, CMS identifies several circumstances in which CMS could internally initiate a NCA for a new technology. Although we do not know the precise reason CMS opened this NCA, we think the agency may have initiated it based on a belief that "significant uncertainty exists concerning the health benefits, patient selection, or appropriate facility and staffing requirements for the new technology." [2] As stated above, we believe that any uncertainty about the health benefits, patient selection, and appropriate provision of PROVENGE can be addressed without further analysis by CMS. FDA's review of PROVENGE was comprehensive and rigorous. The agency reviewed data from 4 randomized trials involving over 900 patients. The pivotal registration study was conducted under a Special Protocol Assessment agreement with the FDA and demonstrated a statistically significant survival benefit. Similar results were seen in a previous smaller randomized trial.

In addition to the data relied upon by the FDA, the attached article, published in the New England Journal of Medicine on July 29, 2010, presents the results of the double-blind, placebo-controlled phase III trial for PROVENGE, as well as summarizes the findings from 2 earlier phase III trials. The article concludes that the "use of sipuleucel-T prolonged overall survival among men with metastatic castration-resistant prostate cancer." [3]

As described in the New England Journal of Medicine article, sipuleucel-T has shown evidence of efficacy in reducing the risk of death among men with metastatic castration-resistant prostate cancer. In the randomized double-blind, placebo-controlled, multicenter phase III "IMPACT" trial, we randomly assigned 512 patients with median age of 71, in a 2:1 ratio to receive either sipuleucel-T (341 patients) or placebo (171 patients) administered intravenously every 2 weeks, for a total of 3 infusions.

The primary endpoint of this study was overall survival, the most meaningful clinical outcome for patients, analyzed by means of a stratified Cox regression model adjusted for baseline levels of serum prostate-specific antigen (PSA) and lactate dehydrogenase. In the sipuleucel-T group, there was a relative reduction of 22% in the risk of death as compared with the placebo group (hazard ratio (HR), 0.78; 95% confidence interval (CI), 0.61 to 0.98;  $P = 0.03$ ). There was a 4.1-month improvement in median survival (25.8 months in the sipuleucel-T group vs. 21.7 months in the placebo group). The 36-month survival probability was 31.7% in the sipuleucel-T group versus 23.0% in the placebo group. The treatment effect was also observed with the use of an unadjusted Cox model and a log-rank test (HR, 0.77; 95% CI, 0.61 to 0.97;  $P = 0.02$ ) and after adjustment for use of docetaxel after the study therapy (HR, 0.78; 95% CI, 0.62 to 0.98;  $P = 0.03$ ).

Importantly, the results of the IMPACT trial confirmed the results of the earlier D9901 study, published in the attached article in the Journal of Clinical Oncology. [4] Specifically, in this study there was a relative reduction of 41% in the risk of death in the sipuleucel-T group compared with the placebo group (HR, 0.586; 95% CI, 0.388 to 0.884;  $P=0.010$ ). There was a 4.5 month improvement in median survival (25.9 months in the sipuleucel-T group vs. 21.4 months in the placebo group). In this study, 34% of the men were alive at the 3 year follow-up compared to 11% in the placebo group. An integrated survival analysis completed with these results together with the results from the D9902A [5] trial and IMPACT demonstrated a p-value of  $<0.001$ , suggesting a less than 1 in 1000 chance that the results would have been observed by chance alone.

Additionally, PROVENGE has a favorable side effect profile. The most common adverse events (AEs), reported in patients in the sipuleucel-T group at a rate of 15%, were chills, fatigue, fever, back pain, nausea, joint ache, and headache. The majority of AEs in trials were grades 1 or 2. The most common (2%) Grade 3-5 adverse events reported in the sipuleucel-T group were back pain and chills. The percentage of patients in each arm experiencing serious AEs (SAEs) was comparable, including the percentage with cerebral vascular accidents (CVAs), of which none were attributed to sipuleucel-T. Safety concerns raised earlier by the FDA about the incidence of CVAs are addressed by a Risk Management Plan submitted as part of the amendment to the BLA and a post-marketing registry study.

In conclusion, multiple randomized trials have shown that PROVENGE prolonged survival among men with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. This strong clinical evidence led to FDA approval and should serve as the foundation for coverage by CMS. There is a current unmet need for the treatment of men with metastatic castrate resistant prostate cancer who have yet become symptomatic enough to receive traditional chemotherapy manipulation. PROVENGE provides a new, innovative, safe, and proven opportunity for such patients to extend their lives with minimal daily interruptions.

The evidence provided to CMS and contained in the New England Journal of Medicine article, demonstrates that PROVENGE is reasonable and necessary for patients with asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer and that the NCA is not warranted. More important, it creates an unnecessary additional hurdle for patients to navigate as they seek treatment for this deadly disease. Now that CMS has adequately gathered "comments and additional information or evidence of studies" about the policy under consideration,[6] the agency need not invest additional time and resources into evaluating coverage of PROVENGE. This is particularly true as the primary endpoint of the IMPACT trial was overall survival, and the median age of patients enrolled was 71 years, with 75% of the patients being 65 years of age or older and eligible for Medicare. The subgroup analysis of patients 65 years of age or older in the integrated dataset for the 3 randomized trials in metastatic castrate resistant prostate cancer demonstrated consistency of the PROVENGE treatment effect. The median survival was 23.4 months in the PROVENGE group and 17.1 months in the placebo group. PROVENGE clearly shows effectiveness in the Medicare population and improves health outcomes in patients with prostate cancer. Accordingly, we request that CMS close this NCA and instead allow its local contractors to cover PROVENGE, applying the same coverage criteria as they apply to any other new cancer drug or biological. We believe that CMS should rely on its local contractors and physicians, through its local processes to determine appropriate use. CMS should not stand in the way of the adoption of new technologies and perhaps a new standard of care; rather, it should partner with its local contractors and physicians to educate Medicare beneficiaries on the clinical benefits and appropriate use of PROVENGE.

To the extent that CMS initiated this NCA based on concerns about "health inequalities" and "local variation" and a desire to ensure that this "substantial clinical advance . . . diffuses more rapidly to all patients for whom it is indicated,"[7] this uniformity and diffusion already is occurring. Although we expressed concerns during our most recent meeting with you about the variations in coverage of PROVENGE between contractors, these variations have subsided. Currently most Medicare contractors have published guidelines or verbally indicated they are/will cover PROVENGE as a biological product for its on-label indication, and Medicare beneficiaries across the country have access to PROVENGE in their

battle against metastatic castrate resistant prostate cancer. Again, this reinforces why the NCA is not necessary at this time.

We believe that if CMS does decide to move forward with this NCA, it should conclude the process quickly, without a TA or a MedCAC meeting. We believe that a TA is not needed because none of the conditions listed in the guidance document regarding factors CMS considers in commissioning a TA exist. In particular, there are no "significant differences in opinion among experts," as shown by the fact that soon after PROVENGE was approved by the FDA, the National Comprehensive Cancer Network (NCCN) listed PROVENGE in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>T</sup>) for Prostate Cancer (version 2.2010) and NCCN Drugs & Biologics Compendium (NCCN Compendium<sup>T</sup>) as a category 1 treatment recommendation for patients with castration-recurrent prostate cancer.[8] A category 1 recommendation means that "the recommendation is based on high level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus." [9] NCCN is a not-for-profit alliance of 21 of the world's leading cancer centers. Its experts are world renowned, and its Prostate Cancer Panel includes 28 members from the best cancer hospitals across the country. NCCN's rapid inclusion of PROVENGE in its Guidelines and Compendium with a category 1 recommendation shows the high level of consensus that exists regarding PROVENGE's clinical data as well as PROVENGE's role in the treatment regimen for prostate cancer.

Furthermore, although the description of the TA on the Agency for Healthcare Research and Quality (AHRQ) website recently was changed from "The Efficacy and Safety of Sipuleucel T" to "The Outcomes of Sipuleucel T," [10] we continue to be concerned that the scope of the assessment duplicates the review already conducted by the FDA. For the same reasons, we believe that a meeting of the MedCAC is not needed to assess the data on PROVENGE, all of which already has been reviewed by CMS.

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Mark Frohlich, Chief Medical Officer of Dendreon

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- [14] NCCN Drugs & Biologics Compendium, "Sipuleucel-T," current as of July 26, 2010.

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**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, July 30, 2010 7:40 AM  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Re: Meeting with Dendreon at CMS

I will respond to him and cc the team  
Sent from my Blackberry

---

**From:** Lockett, Chris <[clockett@Dendreon.com](mailto:clockett@Dendreon.com)>  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ); Jacques, Louis B. (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Sent:** Thu Jul 29 23:42:14 2010  
**Subject:** RE: Meeting with Dendreon at CMS

Leslye,

When we confirmed our meeting last week you informed us that you would provide us with your questions in advance. Having these questions will allow us to prepare the most relevant slide presentation for your analysis. You also stated that the NCA was initiated to determine the "effectiveness" of Provenge (see Below). We are still struggling to understand the rationale CMS has used to initiate the NCA and we were hoping your clarification of "effectiveness" would provide us some of that understanding. Dendreon wants to provide CMS with any additional evidence that the agency needs for this analysis, at this point we are still unclear as to exactly what evidence the agency is seeking. Any further guidance would be greatly appreciated.

Regards,

Chris

---

**From:** Fitterman, Leslye (CMS/OCSQ) [<mailto:Leslye.Fitterman3@CMS.hhs.gov>]  
**Sent:** Thursday, July 22, 2010 4:20 PM  
**To:** Lockett, Chris  
**Cc:** Rollins, James (CMS/OCSQ); Jacques, Louis B. (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Meeting with Dendreon at CMS

Dear Mr. Lockett:

We have scheduled a meeting with you and your colleagues at our office in Baltimore, MD for August 3, 2010 11:00 am to 12 noon. I will follow-up with you early next week when we have composed questions. I will also clarify what I mean by "effectiveness" and "comparative effectiveness".

We looking forward to meeting with you on August 3<sup>rd</sup>.

Regards, Leslye

Leslye Fitterman, PhD.  
Centers for Medicare and Medicaid Services  
Office of Clinical Standards and Quality  
Coverage and Analysis Group  
7500 Security Boulevard  
C1-09-06  
Fax - 410-786-9286  
Phone - 410-786-1806  
Email - [Leslye.Fitterman3@cms.hhs.gov](mailto:Leslye.Fitterman3@cms.hhs.gov)

---

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**Rollins, James (CMS/OCSQ)**

---

**From:** Wittenberg, Kim (AHRQ/COE)  
**Sent:** Thursday, July 29, 2010 11:08 AM  
**To:** Rollins, James (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Subject:** Provenge MedCAC

Good morning,

Do we have a confirmed date for the Provenge MedCAC? Thank you in advance for this information.

Sincerely,  
Kim

Kim Marie Wittenberg, MA

Agency for Healthcare Research and Quality

Center for Outcomes and Evidence

540 Gaither Road, Room 6018

Rockville, MD 20850

Ph: 301-427-1488

Fax: 301-427-1639

E-mail: [Kim.Wittenberg@ahrq.hhs.gov](mailto:Kim.Wittenberg@ahrq.hhs.gov)

## **Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, July 30, 2010 9:13 AM  
**To:** Syrek Jensen, Tamara S. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Subject:** Provenge News

### **Provenge Study May Not Reveal How It Extends Patients' Lives.**

The NPR (7/29, Knox) "Shots" blog reported that this week's New England Journal of Medicine includes "the study that led to FDA approval" of Provenge [sipuleucel-T] to treat prostate cancer, but "it's clear that experts are still scratching their heads about just how Provenge works." NPR added, "The primary mystery is how Provenge extends life, since it doesn't shrink prostate tumors, as far as anyone can tell. 'Prolongation of survival without a measurable antitumor effect is surprising,' writes Dr. Dan Longo of the National Institute on Aging in a NEJM editorial." Still, "study shows that patients who got Provenge were indeed more likely to mount immune-cell responses to a prostate cancer antigen in the test tube. But oddly, the patients who had these activated immune cells didn't survive any longer than those who didn't."

Louis B. Jacques, MD  
Director, Coverage & Analysis Group  
Office of Clinical Standards and Quality  
Centers for Medicare & Medicaid Services  
Mailstop C1-09-06  
7500 Security Blvd  
Baltimore MD 21244  
(410) 786-4512  
(410) 786-9286 (FAX)  
[Louis.Jacques@CMS.HHS.GOV](mailto:Louis.Jacques@CMS.HHS.GOV)

## Rollins, James (CMS/OCSQ)

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, July 30, 2010 11:27 AM  
**To:** Lockett, Chris; Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Meeting with Dendreon at CMS

Chris,

We'd like to focus our discussion at the upcoming meeting on the following topics.

- The criteria used in the trials to identify subjects with "asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer." More specifically, how were symptoms assessed, did the symptoms have to be secondary to prostate CA or prior or current CA treatment, and what cutoffs were applied to differentiate these men from more symptomatic subjects?
- How do the characteristics of the actual enrolled study population compare to the affected Medicare beneficiary population, in light of the apparent disparate impact of prostate CA on particular populations? As the unclear biologic mechanism of action of Provenge is still being debated/discussed in the press, is there any reason to believe that Provenge would be more or less effective in the impacted populations?
- I recall that there was discussion of a Provenge registry. We'd like to hear more about its design, the included data elements, and the plans for downstream analysis.

In addition, as we discuss the above we may have more questions on the evidence you present.

Louis

---

**From:** Lockett, Chris [<mailto:clockett@Dendreon.com>]  
**Sent:** Thursday, July 29, 2010 11:42 PM  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ); Jacques, Louis B. (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Meeting with Dendreon at CMS

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Regards,

Chris

**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, July 30, 2010 2:59 PM  
**To:** Syrek Jensen, Tamara S. (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Subject:** FW: Meeting with Dendreon at CMS

Just FYI

---

**From:** Lockett, Chris [<mailto:clockett@Dendreon.com>]  
**Sent:** Friday, July 30, 2010 2:57 PM  
**To:** Jacques, Louis B. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Subject:** RE: Meeting with Dendreon at CMS

Dr Jacques,

Thank you for this guidance, we will prepare accordingly. I will send you our attendee list for the meeting by Monday morning. We look forward to meeting with your team next Tuesday at 11am.

Regards,

Chris

---

**From:** Jacques, Louis B. (CMS/OCSQ) [<mailto:Louis.Jacques@cms.hhs.gov>]  
**Sent:** Friday, July 30, 2010 11:27 AM  
**To:** Lockett, Chris; Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Meeting with Dendreon at CMS

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---

**From:** Lockett, Chris [mailto:clockett@Dendreon.com]

**Sent:** Thursday, July 29, 2010 11:42 PM

**To:** Fitterman, Leslye (CMS/OCSQ)

**Cc:** Rollins, James (CMS/OCSQ); Jacques, Louis B. (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)

**Subject:** RE: Meeting with Dendreon at CMS

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Regards,

Chris

---

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**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, July 30, 2010 3:56 PM  
**To:** Fitterman, Leslye (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 073010 lbj.doc  
**Attachments:** Provenge MEDCAC questions 073010 lbj.doc

We need to get closer to this model. There is room to integrate your questions, which were good. Let's discuss next week.

**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Monday, August 02, 2010 11:44 AM  
**To:** Rollins, James (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080210 lbj.doc  
**Attachments:** Provenge MEDCAC questions 080210 lbj.doc

Revised (see added questions) to bring in the team's question ideas. Let's discuss.

**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Tuesday, August 03, 2010 9:06 AM  
**To:** Rollins, James (CMS/OCSQ)  
**Subject:** Dendreon

With Sebelius here today, pls make sure Leslye is out in time to get Dendreon at security. Thanks.

---

**From:** Rollins, James (CMS/OCSQ)  
**Sent:** Tuesday, August 03, 2010 8:08 AM  
**To:** Jacques, Louis B. (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ)  
**Subject:** FW: Web Posting

Louis, here is the January MEDCAC minutes and transcripts to be posted. Jarollins

---

**From:** Ellis, Maria A. (CMS/OCSQ)  
**Sent:** Tuesday, March 16, 2010 11:01 AM  
**To:** Rollins, James (CMS/OCSQ)  
**Cc:** Roche, Jeffrey (CMS/OCSQ); Eggleston, Lisa J. (CMS/OCSQ); Miller, Susan (CMS/OCSQ)  
**Subject:** Web Posting

*Good Morning!*

*Please find attached the signed meeting minutes and transcript from the January 27<sup>th</sup> MEDCAC meeting on Pharmacogenomic for clearance/approval for web posting. Please let me know if I can be of further assistance.*

*Maria A. Ellis*

*Health Insurance Specialist  
Division of Operations and Information Management  
Coverage and Analysis Group, OCSQ  
(410) 786-0309*

*[Maria.Ellis@cms.hhs.gov](mailto:Maria.Ellis@cms.hhs.gov)*

**Rollins, James (CMS/OCSQ)**

---

**From:** Pencek, Eileen (CMS/OCSQ)  
**Sent:** Tuesday, August 03, 2010 10:11 AM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions 080210 lbj.doc

I like this format, and I think these questions are good.

The vast majority of comments from the general public (and many treating physicians) are using Taxotere as the only comparator. Used on-label, Provenge and Taxotere with associated health outcomes such as overall survival, avoidance of adverse effects of anticancer therapy, and control of symptoms would not be compared. (b)(5) - Predecisional

(b)(5) - Predecisional

Eileen

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Monday, August 02, 2010 11:44 AM  
**To:** Rollins, James (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080210 lbj.doc

Revised (see added questions) to bring in the team's question ideas. Let's discuss.

## Rollins, James (CMS/OCSQ)

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Tuesday, August 03, 2010 10:18 AM  
**To:** Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions 080210 lbj.doc

Question 5b gets to the symptomatic folks. The MEDCAC chair and co chair always have suggestions regarding the questions when we share a few mos before the meeting.

---

**From:** Pencek, Eileen (CMS/OCSQ)  
**Sent:** Tuesday, August 03, 2010 10:11 AM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions 080210 lbj.doc

I like this format, and I think these questions are good.

The vast majority of comments from the general public (and many treating physicians) are using Taxotere as the only comparator. Used on-label, Provenge and Taxotere with associated health outcomes such as overall survival, avoidance of adverse effects of anticancer therapy, and control of symptoms would not be compared. (b)(5) - Predecisional  
(b)(5) - Predecisional

Eileen

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Monday, August 02, 2010 11:44 AM  
**To:** Rollins, James (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080210 lbj.doc

Revised (see added questions) to bring in the team's question ideas. Let's discuss.

**Rollins, James (CMS/OCSQ)**

---

**From:** PASERCHIA, LORI A. (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 1:22 PM  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions  
**Attachments:** Provenge MEDCAC questions 080210 lbj LP rev.doc

Hi. Please see the attachment for potential revisions to the questions based on our meeting today.

Lori A. Paserchia, MD  
Coverage and Analysis Group  
Centers for Medicare and Medicaid Services  
[Lori.Paserchia@cms.hhs.gov](mailto:Lori.Paserchia@cms.hhs.gov)  
410.786.2115

**Rollins, James (CMS/OCSQ)**

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 1:24 PM  
**To:** PASERCHIA, LORI A. (CMS/OCSQ)  
**Cc:** Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions

Thanks-

---

**From:** PASERCHIA, LORI A. (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 1:22 PM  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions

Hi. Please see the attachment for potential revisions to the questions based on our meeting today.

Lori A. Paserchia, MD  
Coverage and Analysis Group  
Centers for Medicare and Medicaid Services  
[Lori.Paserchia@cms.hhs.gov](mailto:Lori.Paserchia@cms.hhs.gov)  
410.786.2115

**Rollins, James (CMS/OCSQ)**

---

**From:** Pencek, Eileen (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 3:54 PM  
**To:** PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Rollins, James (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions

Lori,

I think it looks good. The only comment (b)(5) - Predecisional

(b)(5) - Predecisional

Eileen

---

**From:** PASERCHIA, LORI A. (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 1:22 PM  
**To:** Fitterman, Leslye (CMS/OCSQ)  
**Cc:** Pencek, Eileen (CMS/OCSQ); Rollins, James (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions

Hi. Please see the attachment for potential revisions to the questions based on our meeting today.

Lori A. Paserchia, MD  
Coverage and Analysis Group  
Centers for Medicare and Medicaid Services  
[Lori.Paserchia@cms.hhs.gov](mailto:Lori.Paserchia@cms.hhs.gov)  
410.786.2115

**Rollins, James (CMS/OCSQ)**

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Wednesday, August 04, 2010 5:09 PM  
**To:** Rollins, James (CMS/OCSQ)  
**Subject:** Re: provenge inquest

Agree

Sent from my iPhone

On Aug 4, 2010, at 5:02 PM, "Rollins, James (CMS/OCSQ)" <[James.Rollins2@CMS.hhs.gov](mailto:James.Rollins2@CMS.hhs.gov)> wrote:

> Got a letter from representative Dana Rohrabacher that CMS carefully  
> consider the inquires related to a national coverage for provenge.

(b)(5) - Predecisional

> Jarollins

**Rollins, James (CMS/OCSQ)**

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 1:52 PM  
**To:** Rollins, James (CMS/OCSQ)  
**Cc:** PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080610 team.doc  
**Attachments:** Provenge MEDCAC questions 080610 team.doc

Revised as discussed.

**Rollins, James (CMS/OCSQ)**

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:28 PM  
**To:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080610 team lbj.doc  
**Attachments:** Provenge MEDCAC questions 080610 team lbj.doc

Looks ready for Cliff and Saty next week if possible. Redline attached as FYI. (b)(5) - Predecisional

(b)(5) - Predecisional

How are we doing on the website and FR notices?

**Rollins, James (CMS/OCSQ)**

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:36 PM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions 080610 team lbj.doc

Louis:

I agree with your changes and have saved this version on the G drive.

I will talk with Maria next week to establish the timeline to select MEDCAC attendees and invited guests and preparation and submission of the FR notice. Am I correct in assuming that Cliff and Saty will want to review and weigh in on the attendees?

Leslye

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:28 PM  
**To:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
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**Sent:** Friday, August 06, 2010 3:36 PM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
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(b)(5) - Predecisional

How are we doing on the website and FR notices?

## Rollins, James (CMS/OCSQ)

---

**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:42 PM  
**To:** Fitterman, Leslye (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** RE: Provenge MEDCAC questions 080610 team lbj.doc

The panel selection is a CAG process. I would like to get their input on the overall flow of the meeting, i.e. which questions will be specifically addressed by the TA, which are likely to be addressed by guest speakers, like the minimally symptomatic criteria. Also do they think some draft questions are missing the point, or missing entirely? That may lead us to choose guest panelists to address any expertise gaps if any. It's always been a good hour well spent with them.

---

**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:36 PM  
**To:** Jacques, Louis B. (CMS/OCSQ); Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
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**From:** Jacques, Louis B. (CMS/OCSQ)  
**Sent:** Friday, August 06, 2010 3:28 PM  
**To:** Rollins, James (CMS/OCSQ); PASERCHIA, LORI A. (CMS/OCSQ); Fitterman, Leslye (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Cc:** Ellis, Maria A. (CMS/OCSQ); Syrek Jensen, Tamara S. (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080610 team lbj.doc

Looks ready for Cliff and Saty next week if possible. Redline attached as FYI. (b)(5) - Predecisional

(b)(5) - Predecisional

How are we doing on the website and FR notices?

**Rollins, James (CMS/OCSQ)**

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**From:** Fitterman, Leslye (CMS/OCSQ)  
**Sent:** Monday, August 09, 2010 1:30 PM  
**To:** PASERCHIA, LORI A. (CMS/OCSQ); Rollins, James (CMS/OCSQ); Pencek, Eileen (CMS/OCSQ)  
**Subject:** Provenge MEDCAC questions 080910 team lbj lf.doc  
**Attachments:** Provenge MEDCAC questions 080910 team lbj lf.doc

Please see changes I made to question 7 and will verify with the FDA review documents.