



LEONARDO'S NOTEBOOK MARCH 2007 Volume 3, Issue 1

MATTSONJACK

MATTSONJACK DAVINCI'S ONCOLOGY E-NEWSLETTER

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This newsletter is intended to provide commercial organizations involved in the development and marketing of new cancer therapeutics topical articles and features relating to oncology. Each edition will include news and commentary about issues that may impact a company's development and commercialization strategies. MattsonJack DaVinci welcome your views and comments on this Oncology E-Newsletter and its content. If you would like to share your thoughts, please contact us:

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MEETING SUMMARIES

To support our *Cancer!MPact*[™] multiclient reports, MattsonJack DaVinci consistently attends most of the major oncology conferences in Europe and the U.S. This issue of *Leonardo's Notebook* highlights the research trends and the latest development from two of the most important U.S. conferences held in December 2006: the American Society of Hematology (ASH) meeting in Orlando, Florida and the San Antonio Breast Cancer Symposium (SABCS) in San Antonio, Texas. Please note that the highlights provided in the next section are not meant to be a comprehensive review of these conferences. Instead, MattsonJack DaVinci selected those data that, in our professional opinion, will have the greatest impact on the practice and business of oncology.

December 9–12, 2006
Orlando, Florida

THE AMERICAN SOCIETY OF HEMATOLOGY (ASH) 48TH ANNUAL MEETING

In 2006, more than 21,000 physicians, scientists, and others attend the four-day ASH meeting. Unlike most other conferences MattsonJack DaVinci attends, ASH is not strictly just a cancer conference but a general hematology conference. Even though only about 40% of the content at ASH is cancer-related, not all cancers had significant amounts of new or exciting data. For Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, and myelodysplastic syndrome, there was little new data, mainly updates on previously reported clinical trials.

From ASH 2006, MattsonJack DaVinci has highlighted the following key presentations:

- Novel agents for imatinib-resistance in CML
- New options for CLL: Campath/MabCampath and Revlimid
- Use of Velcade and Revlimid for induction therapy in multiple myeloma

Novel Agents for Imatinib Resistance in CML

Most CML patients can be in remission for many years following Gleevec[®]/Glivec[®] (imatinib mesylate, Novartis) treatment, but will eventually develop imatinib resistance, particularly when they are administered a 400 mg dose. The most recent review of imatinib resistance provided the following annual rates of patients becoming refractory or insensitive to imatinib: 3.3% in Year 1, 7.5% in Year 2, 4.8% in Year 3, 1.5% in Year 4, and 0.9% in Year 5.

For imatinib-resistant patients receiving the "standard" dose of 400 mg, the most common therapeutic option upon failure is to increase the dose of Gleevec to 600 mg or 800 mg. However, as more and more physicians use higher doses of the drug, the key clinical question is now "How should we treat those patients who relapse on 800 mg Gleevec (either as a first- or second-line of therapy), or those patients who cannot tolerate dose escalation?"

The current strategy is to use new agents that have proven effective in these patient populations.

The Newest Agents: Sprycel[®] and Tasigna[™]

Sprycel[®] (dasatinib, Bristol-Myers Squibb) was approved in the U.S and Europe in 2006, based on the data from the completed START (SRC/ABL Tyrosine kinase inhibition Activity: Research Trials) series of pivotal Phase II trials. START originally included four non-randomized Phase II studies:

- One trial in each phase (chronic, accelerated, and blast) of CML where patients have received at least 600 mg of Gleevec, and another trial in Ph+ ALL and lymphoid blast CML

The following table presents the most recent data for Sprycel in terms of hematologic and cytogenetic responses as presented at ASH 2006 and in the drug's prescribing information.

SPRYCEL'S DATA BY PATIENT TYPE AND TYPE OF RESPONSE

Phase of CML	Complete Hematologic Response ¹ (%)	Major Hematologic Response ¹ (%)	Complete Cytogenetic Response (%)	Major Cytogenetic Response ² (%)
Chronic (n=186)	91%	—	49%	59%
Accelerated (n=174)	45%	64%	32%	39%
Myeloid Blast (n=74)	24%	32%	27%	30%
Lymphoid Blast (n=42)	26%	31%	43%	50%
Ph+ ALL (n=30)	40%	50%	38%	—

¹ Hematologic response rates are noted as either "complete" or "major" (complete responses plus patients with no evidence of leukemia).

² Major cytogenetic response rates are the sum of complete and partial ($\leq 35\%$ Ph+ metaphases) cytogenetic responses.

Sources: Baccarani (Abstract 164), Cortes (Abstract 2160), Sprycel prescribing information label, Dombret (Abstract 286)

In late 2006, Novartis completed its U.S. and European filings for Tasigna™ (nilotinib, Novartis) for the treatment of imatinib-resistant/intolerant CML in chronic and accelerated phases (but not blast phase). In general, the two drugs look similar in blast phase but in chronic and accelerated phase, as well as Ph+ ALL, the data suggest that Tasigna may be inferior to Sprycel (see table below). However, Tasigna appears to have a much lower rate of cytopenias compared to Sprycel, and pleural effusions and edemas that are of concern with Sprycel are virtually non-existent in Tasigna-treated patients. This safety benefit may help outweigh the efficacy issues, especially if we start to see a large Sprycel-intolerant population develop.

SPRYCEL VS. TASIGNA: BY PATIENT TYPE AND TYPE OF RESPONSE

Phase of CML	SPRYCEL (dasatinib)		TASIGNA (nilotinib)	
	Hematologic CR ¹	Cytogenetic CR	Hematologic CR ¹	Cytogenetic CR
Chronic	91% (n=186)	49% (n=186)	77% (n=132)	32% (n=132)
Accelerated	45% (n=174)	32% (n=174)	23% (n=64)	22% (n=64)
Blast	24-26% (n=116)	27-43% (n=116)	25% (n=101)	— ²
Ph+ ALL	40% (n=30)	38% (n=30)	29% (n=35)	— ²

¹ Includes patients with myeloid and lymphoid lineage.

² Cytogenetic data was not presented.

Sources: Baccarani (Abstract 164), Sprycel prescribing information label, Dombret (Abstract 286), le Coutre (Abstract 165), Kantarjian (Abstract 2169), Ottmann (Abstract 1862)

New Options in the Treatment of CLL: Expanding Campath Usage and Revlimid Data

In 2001, Campath®/MabCampath® (alemtuzumab, Berlex/Bayer Schering/Gemzyme) was approved in the U.S. and Europe for the third-line treatment of chronic lymphocytic (CLL). Although there are no agents currently approved in the front-line setting, the most commonly utilized regimens are FCR (fludarabine, cyclophosphamide, Rituxan® [rituximab, Genentech/Roche/Chugai]), FC, or chlorambucil.

At ASH 2006, mature data was presented for the Phase III CAM307 study (first presented at the 11th Congress of the European Society of Hematology in 2006) that clearly showed that Campath is superior to chlorambucil in previously-untreated patients (Abstract 301). The Campath arm had a progression-free survival (PFS) of 23.3 months compared to 14.7 months for the chlorambucil arm ($p=0.0001$, $HR=0.58$). Other efficacy endpoints include an overall response rate (ORR) of 83% for Campath vs. 55% for chlorambucil ($p<0.0001$) with the complete (CR) rate being 24% vs. 2% for Campath and chlorambucil, respectively. In addition, minimal residual

disease (MRD) was measured and observed in 26% (9 of 34) of the complete responses in the Campath arm versus 0% in the chlorambucil arm. Of the MRD patients, 89% (8/9) have not progressed at a median follow-up of 2 years. Based on this randomized Phase III trial, in early April 2007 Genzyme submitted a supplemental biologics license application to the U.S. FDA to expand Campath's indication to include first-line treatment of B-cell chronic lymphocytic leukemia. A similar filing in Europe is expected by the end of the month.

Another potential indication expansion for Campath is as consolidation chemotherapy, where Campath appeared to demonstrate a significant PFS benefit in the German CLL4B trial (observation vs. Campath consolidation) (Abstract 33). The PFS (the primary endpoint) at 48 months was 20.6 months for the observation arm; the PFS has not been reached in the Campath arm ($p=0.0035$). This data should be interpreted with caution given that only 21 patients were evaluated in this early-closure Phase III study. Any significant increase in the use of Campath as consolidation therapy will require positive data from the ongoing Phase III studies (CALGB-10101 and ECOG-2903)

Revlimid[®] (lenalidomide, Celgene) is a potent analogue of thalidomide that has recently gained approval by the FDA for the treatment of multiple myeloma and myelodysplastic syndrome. Two separate Phase II studies have also confirmed the benefit of Revlimid in patients with relapsed or refractory CLL (see table below). A Phase III study (CLL001) has been initiated in relapsed patients who have previously been treated with an alkylating agent with or without fludarabine. Patients will be randomized to two different dose of Revlimid: 25 mg or 10 mg daily on days 1 through 28 in a 28-day cycle. The primary endpoint is response rate.

TWO PHASE II TRIALS OF REVLMID IN RELAPSED/REFRACTORY CLL

Sample (n)	35 patients	31 patients
Revlimid Dose	10 mg/day	25 mg/day
ORR (CR + PR)	37%	57.7%
CR	6%	23.3% (11% mCR)
PR	31%	44.4%
SD	29%	5%
Reference	Ferrajoli, Abstract 305	Chanan-Khan, Abstract 306

Multiple Myeloma: Use of Velcade and Revlimid in Induction Chemotherapy

In general, current treatment trends for myeloma in the front-line setting vary based upon a patient's eligibility for transplantation. Transplant eligible patients should not receive alkylating agents (like melphalan) since this may hinder stem cell mobilization. At this time, ThalDex—Thalomid[®] (thalidomide, Celgene; Thalidomide Pharmion by Pharmion in Europe) plus dexamethasone—is the standard of care for these patients in the general community setting. Transplant ineligible patients could alternatively receive a melphalan-containing regimen, such as MP (melphalan plus prednisone) or MPT (MP plus Thalomid).

The key issue in induction chemotherapy is determining the appropriate role for Velcade and Revlimid in both the transplant-eligible and transplant-ineligible patient groups. The following table presents a relative comparison of the first-line data for Thalomid, Velcade, and Revlimid in combination with dexamethasone in transplant-eligible myeloma patients. While these studies are difficult to compare directly, the table does illustrate that the overall response rate appears improved with either Velcade or Revlimid compared to the current standard of care of ThalDex. Determining if either Revlimid or Velcade is superior to the other will require larger datasets and randomized trial data.

Interestingly, the Mayo Clinic's internal consensus guidelines (which have not yet been validated or widely accepted outside the Mayo Clinic) recommend the use of Revlimid with low-dose dexamethasone for induction therapy in patients who are transplant eligible.

FIRST-LINE DATA COMPARISON: THALOMID, VELCADE, AND REVLIMID PLUS DEXAMETHASONE

	ThalDex	VelDex	RevDex
Sample (n)	234	49	35
CR + VGPR	43.8%	38%	56%
CR	8.1%	18%	18%
ORR (CR/VGPR/PR)	69.4%	88%	91%
PFS	15 months	—	83% at 24 months
OS	—	85% at 24 months	90% at 24 months
Reference	Rajkumar, Blood, 108(11): Abstract 795, 2006.	Jagannath, Blood, 108(11): Abstract 796, 2006.	Lacy, Blood, 108(11): Abstract 798, 2006.

Currently there are two international Phase III trials ongoing to evaluate the activity of Velcade combinations as induction chemotherapy in newly-diagnosed myeloma patients:

- The French IFM-2005-01 study is comparing Velcade/dexamethasone vs. the PAD regimen (prednisone, doxorubicin, dexamethasone). This trial was initiated in June 2005 and will compare complete response rate in 480 patients
- The second study is the HOVON (Hemato-Oncologie voor Volwassenen Nederland) study initiated in mid-2005; it plans to enroll 800 patients randomized to VAD induction followed by transplantation and Thalomid maintenance vs. PAD induction followed by transplantation and Velcade maintenance

For Revlimid, there are several studies looking at induction therapy:

- The Phase III ECOG (E4A03) trial is evaluating Revlimid plus either high-dose dexamethasone or low-dose dexamethasone in newly-diagnosed myeloma patients. For patients who achieve a PR or CR, they have the option to continue their therapy or move to transplant. Patients with progressive disease are given ThalDex. This additional treatment phase was established to see if patients would respond to Thalomid after receiving Revlimid; from prior studies, we know that patients will respond to Revlimid therapy after the failure of Thalomid therapy, but the converse, while expected, has never been tested in a randomized trial
- The Southwest Oncology Group initiated a randomized study (S0232) of dexamethasone with or without Revlimid as first-line therapy. This study was initiated in November 2004 and will randomize 500 patients to receive dexamethasone with or without Revlimid

For transplant-ineligible patients, the historical standard has been MP. Recent data have shown the value of adding Thalomid to MP. However, the additional efficacy was coupled with significantly increased toxicity associated with the addition of Thalomid.

The following table presents the most recent datasets for the front-line use of Thalomid, Velcade or Revlimid in combination with MP for elderly (transplant-ineligible) myeloma patients. From the data available, the Velcade plus MP regimen appears to be most active in this elderly population, although we lack comparative data of these three agents plus dexamethasone in elderly patients. Interestingly, during the ASH 2006 education session on myeloma, intermediate- and high-risk patients are recommended to receive MPV given the relative efficacy levels seen with this combination.

**FRONT-LINE DATA COMPARISON OF MP PLUS THALOMID, VELCADE, AND REVLIMID
IN TRANSPLANT-INELIGIBLE MYELOMA PATIENTS**

	MP + Thalomid		MP + Thalomid		MP + Velcade		MP + Revlimid	
Sample (n)	129		124		60		53	
Age (years)	Median: 72		41% ≥ 70		Median: 74		Median: 71	
CR + PR	76%		81%		89%		81%	
CR	15.5%		16%		32%		13.2%	
EFS	54% at 24 months		—		83% at 16 months		87% at 16 months	
PFS	—		27.6 months		91% at 16 months		—	
OS	80% at 36 months		53.6 months		86% at 24 months		—	
Follow-up	18 months		—		16 months		10 months	
Grade 3 & 4 Toxicities	Hematologic	22%	Neutropenia	48%	Thrombocytopenia	52%	Neutropenia	66%
	Thromboembolism	12%	Anemia	14%	Neutropenia	43%	Thrombocytopenia	34%
	Infection	10%	Thrombocytopenia	14%	Neuropathy (PN)	18%	Anemia	17%
	Neuropathy (PN)	8%	Infection	13%	Infection	17%	Cutaneous	10%
			DVT	12%			Neutropenic Fever	8%
		Neuropathy	6%					
Reference	Palumbo, Lancet, 367:825-831, 2006.		Facon, JCO, 24:1s (Abstract 1), 2006.		Mateos, Blood, 108:2165-2172, 2006.		Palumbo, Blood, 108(11): Abstract 800, 2006.	

Based on the promising results with Velcade, Millennium and its European partner, Janssen (Johnson & Johnson), have initiated an international Phase III study administering the MP regimen with or without Velcade (MMY-3002). This study was initiated in December 2004 will enroll 680 newly-diagnosed patients who are not eligible for stem cell transplantation.

Celgene has also recently initiated an international (ex-U.S.) Phase III trial (CC-5013-MM-015) that will randomize 450 newly-diagnosed myeloma patients aged 65 or older to treatment with either MPR or MP-placebo. This trial is not yet open for enrollment, but is expected to open soon.

A key issue for the future of front-line therapy in myeloma will be the continuing need to classify patients by transplant eligibility. The novel combinations with Velcade and Revlimid plus dexamethasone apparently have higher complete response (CR) and very good partial response (VGPR) rates, which are the most important response endpoints in myeloma, compared to current standards of care. It has been postulated that all patients should receive these induction therapies to maximize the response rates to initial therapy and that perhaps we should save the alkylating agent regimens (MP, MPT, MPR, and MPV) until first- or second-relapse. While the MPV regimen appears to be most active in the elderly, transplant-ineligible population, using the RevDex or VelDex induction regimens should achieve similar ORR, CR, and VGPR rates without eliminating the option of transplant for older patients. Thus, while current guidelines still arbitrarily separate “transplant eligible” from “transplant ineligible”, from our treatment data, MattsonJack DaVinci sees that patients in both settings are currently receiving ThalDex as their standard of care. Thus, the trend towards using novel agent induction regimens appears to be the general treatment approach for all newly diagnosed myeloma patients, irrespective of their potential transplant status. This is a trend that we will continue to monitor over the coming year.

December 14–17, 2006

San Antonio, Texas

THE 29TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM (SABCS)

The San Antonio Breast Cancer Symposium (SABCS; www.sabcs.org) is the leading breast cancer conference in the world. Its mission is to provide comprehensive coverage of the latest information about the biology, etiology, prevention, diagnosis, and therapy of breast cancer. SABCS is sponsored by the Cancer Therapy & Research Center (CTRC), University of Texas Health Science Center at San Antonio (UTHSCSA), the San Antonio Cancer Institute (SACI, an NCI-designated Clinical Cancer Research Center that was created to provide organizational support to CTRC and UTHSCSA) and Baylor College of Medicine. Since the symposium's humble origin in the late 1970s as a small regional meeting with less than 150 physicians, attendance has grown quickly in recent years to more than 8,000 participants in 2006 with approximately half of the attendees from outside of the United States. Our clients should be aware, however, that the organizers do not allow industry-sponsored market research (e.g., interviews and surveys) during this conference.

From SABCS 2006, MattsonJack DaVinci has highlighted the following key presentations:

- Declining incidence of breast cancer
- Second interim results of the BCIRG 006 trial: further evidence supporting the use of Herceptin in the adjuvant setting and questioning the use of anthracyclines regardless of HER2 status
- Combining Targeted Agents: Herceptin plus Avastin

Declining Incidence of Breast Cancer

The most widely-reported news from SABCS, even in the lay press, was the 2003 reported 7% decline in the incidence rates of breast cancer, the first major decline to be reported for this disease (Abstract 5). The “stunning” decline was reported across U.S. SEER cancer registries for both *in situ* and malignant breast cancer and was equivalent to 14,000 fewer women diagnosed in 2003 versus 2002. The decrease was most evident in estrogen receptor (ER)-positive tumors, especially among the postmenopausal women—the decline in this latter subgroup was 15%.

The timing of the decline correlates with the reported findings from the Women's Health Initiative (WHI) of the association between hormone replacement therapy (HRT) and increased breast cancer and other adverse events. Following the announcement of these findings in July 2001, many women stopped HRT. The presenter, Dr. Ravdin, proposed that one could calculate:

*If 30% of postmenopausal women were taking HRT,
if half of these women stopped taking HRT, and
if the risk of developing breast cancer in the subsequent year decreased by half?
then overall breast cancer rates would fall by $30\% * 0.5 * 0.5 = 7.5\%$*

Since the apparent effect of ceasing HRT occurred within months, not years, the researchers proposed that the effect was on progression of pre-existing tumors just below the level of detection, rather than initiation of tumors—tumors either stopped growing, grew more slowly, shrank or even disappeared.

Early registry data appear to show a continued decline in incidence in 2004, though perhaps slightly less than in 2003. The researchers proposed that one would expect to see an additional drop in incidence in 2007 due additional women ceasing HRT based on this latest news. MattsonJack DaVinci expects similar results in Europe and Japan, which also participated in the WHI.

This decline in breast cancer patients will impact our client's forecasts of all agents in breast cancer to some extent, but the impact will be most notable in the forecasts of hormonal agents such as aromatase inhibitors (AIs) utilized in postmenopausal, ER-positive patients. Additionally, the forecasts of agents such as Herceptin[®] (trastuzumab, Genentech/Roche/Chugai) and Tykerb[®]/Tyverb[®] (lapatinib, GlaxoSmithKline) in combination with hormonal agents will also be affected.

No Need for Anthracyclines in the Adjuvant Setting?

As previously presented at SABCS 2005, the first interim results of the BCIRG 006 trial in early-stage HER2(+) breast cancer patients demonstrated the clear superiority of two Herceptin-containing regimens—TCH (Taxotere[®] [docetaxel, sanofi-aventis], carboplatin, and Herceptin) and AC → TH (doxorubicin plus cyclophosphamide followed by Taxotere plus Herceptin)—in terms of disease free survival (DFS) (the primary endpoint) in comparison to the non-Herceptin-containing regimen AC → T.

At the second interim analysis presented at SABCS 2006, the TCH arm now appears similar in terms of efficacy to the AC → TH arm than in the first interim analysis, as presented in the table below (Abstract 52). The two arms now differ primarily by toxicity:

- TCH results in less neutropenia, nausea and vomiting, neuropathy, and, most importantly, cardiotoxicity
- AC → TH results in less anemia and thrombocytopenia

HERCEPTIN IN THE ADJUVANT SETTING: BCIRG 006 RESULTS

Regimen	Number of Patients	First Interim Analysis			Second Interim Analysis		
		2-year DFS	3-year DFS	4-year DFS	2-year DFS	3-year DFS	4-year DFS
AC → TH	1,074	93%	86%	84%	93%	87%	83%
TCH	1,075	91%	80%	80%	92%	86%	82%
AC → T	1,073	86%	77%	73%	87%	81%	77%

T = Taxotere (docetaxel); C = carboplatin in TCH, cyclophosphamide in AC and TC; H = Herceptin (trastuzumab);

A = Adriamycin (doxorubicin)

Source: Oral presentation of Abstract #52, SABCS, 2006.

The results support the selection of TCH as the adjuvant regimen of choice for HER2(+) patients, as it has all the benefit of Herceptin without the cardiac damage associated with its combined use with anthracyclines. Based on recent trials, approximately 5 to 7% of patients who plan to receive a Herceptin-containing regimen in the adjuvant setting never receive Herceptin because of decreased heart function while on AC.

The presenter, Dr. Slamon then reminded the audience of a recently-published Phase III study (Jones, *J Clin Oncol*, 2006) in which TC was demonstrated to be superior to AC as adjuvant therapy in terms of disease-free survival in primarily HER2(-) breast cancer patients. (Notably, the toxicity profile of the TC arm was also better than that of the AC arm.) He then proposed that perhaps there is no longer a role for anthracyclines in any type of breast cancer patient in the adjuvant setting.

MattsonJack DaVinci expects a modest shift away from anthracycline-containing regimens in the future, especially in HER2(+) patients, but we do not expect these regimens to “disappear” as they are a cornerstone of treatment and have a relatively high comfort level with physicians.

Combining Targeted Agents: Herceptin Plus Avastin

Combinations of targeted agents are a hot area of investigation, particularly in colorectal cancer and renal cell carcinoma where these agents—such as Avastin[®] (bevacizumab, Genentech/Roche/Chugai) and Erbitux[®] (cetuximab, ImClone/BMS/Merck KGaA) in colorectal cancer, and Nexavar[®] (sorafenib, Bayer Schering Pharma) and Sutent[®] (sunitinib, Pfizer) in renal cell carcinoma—have become standards of care. By successfully combining targeted agents, the goal is to eliminate traditional cytotoxic chemotherapy and its side effects.

We already know that Avastin has activity in breast cancer based on the results from the ECOG-sponsored E2100 study. In this randomized study, Avastin added to paclitaxel increased the median progression-free survival from 6 months for paclitaxel alone to 11 months.

Genentech and Roche are currently studying the combination of Avastin with Herceptin. The first results of the combination of Herceptin plus Avastin in the first-line metastatic/advanced setting (Abstract 301) was the highest profile presentation for Herceptin other than the BCIRG 006 update. The goal is to target both HER2 and VEGF, as overexpression of HER2 is associated with up-regulation of VEGF in breast cancer cells; there is also a strong association between HER2 and VEGF, which predicts clinical outcome, in primary breast tumors. Among the 37 patients who have **either** HER2-amplified metastatic **or** locally-relapsed, surgically-unresectable breast cancer, the complete response rate was 3% and the partial response rate was 51%.

The overall response rate (54%) is encouraging, but it is slightly lower than the 70% range observed in many previous studies of Herceptin plus chemotherapy, including BCIRG 007 (Herceptin plus Taxotere with or without carboplatin). However, response rates do not always correlate to survival.

As for cardiotoxicity, one patient had a Grade 4 cardiac event, and five patients had Grade 2 cardiac events. In early studies, combinations of targeted therapies have lead to an exacerbation of side effects, particularly when antiangiogenic agents, such as Avastin, have been combined. In comparison to BCIRG 007, the rate of cardiac events may be elevated in the Avastin combination, such that more strict cardiac surveillance has been added for future enrollment (50 total are planned).

While Avastin plus Herceptin without a chemotherapeutic does not look to be as active as hoped, this study provides preliminary safety data for the combination of Avastin plus Herceptin as a component of further combination with chemotherapy. These data are particularly important with the on-going Phase III study sponsored by Roche (nicknamed AVEREL) examining the combination of Herceptin plus Taxotere with or without Avastin.

2007 CANCER MEETINGS

MATTSONJACK DAVINCI'S CANCER MEETING ATTENDANCE

In order to “stay at the cutting edge of oncology research,” MattsonJack DaVinci attend as many major cancer meetings as possible. Our Oncology E-Newsletter, *Leonardo's Notebook*, will bring you highlights and breaking news from most of the following 2007 oncology meetings:

- **April 14–18, 2007, Los Angeles, California:** The Centennial American Association for Cancer Research (AACR) Annual Meeting
- **May 16–19, 2007, Florence, Italy:** 9th International Symposium on Myelodysplastic Syndromes
- **June 1–5, 2007, Chicago, Illinois:** 43rd American Society of Clinical Oncology (ASCO) Annual Meeting
- **June 7–10, 2007, Vienna, Austria:** 12th Conference for European Hematology Association (EHA–tentative)
- **June 27–30, 2007, Barcelona, Spain:** 9th World Congress on Gastrointestinal Cancer (WGCG)
- **June 28–30, 2007, St. Gallen, Switzerland:** 20th International Symposium on Supportive Care in Cancer
- **September 2–6, 2007, Seoul, South Korea:** 12th World Conference on Lung Cancer (WCLC)
- **September 7–8, 2007, San Francisco, California:** 2007 ASCO Breast Cancer Symposium
- **September 7–9, 2007, San Francisco, California:** 2nd Oncology World Congress (OWC)
- **September 23–27, 2007, Barcelona, Spain:** The 14th European Cancer Conference (ECCO)
- **October 22–26, 2007, San Francisco, California:** The 19th AACR-NCI-EORTC: International Conference on Molecular Targets and Cancer Therapeutics
- **October 24–26, 2007, Kyoto, Japan:** 45th Annual Meeting of the Japan Society of Clinical Oncology (JSCO)
- **November 8–10, 2007, New York, New York:** 4th International Congress on MPD and MDS
- **November 7–10, 2007, New York, New York:** Chemotherapy Foundation Symposium XXV (CFS)
- **December 7–11, 2007, Atlanta, Georgia:** 49th Annual Meeting of the American Society of Hematology (ASH)
- **December 13–16, 2007, San Antonio, Texas:** 30th Annual San Antonio Breast Cancer Symposia (SABCS)

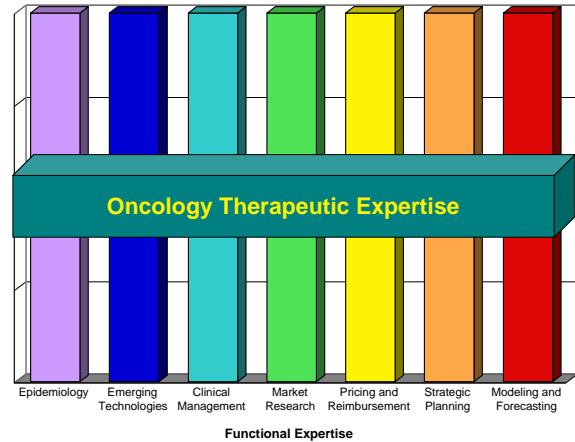
Let us know if there are other oncology events you would like us to cover through 2007 that perhaps you are not able to attend, and we will do our best to include them.

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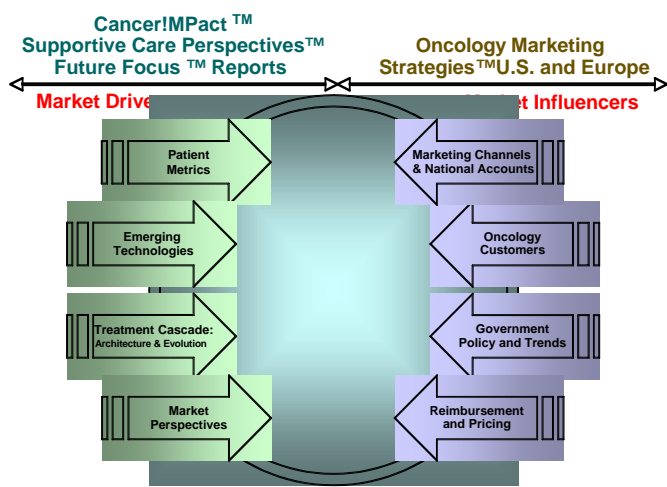
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- Business Development and Licensing

MattsonJack DaVinci is the Oncology Center of Excellence for The Mattson Jack Group and provides unparalleled depth and breadth of oncology experience to the areas of functional expertise.



MattsonJack DaVinci's syndicated reports, as shown in the following graphic, provide a comprehensive review of the market drivers and influencers for the U.S., European, and Japanese oncology markets. In addition to the reports, MattsonJack DaVinci also offers clients innovative custom consulting solutions in the oncology arena.



Existing Syndicated Reports and Services

- **Cancer!MPact™:** Premier global oncology resource to assist clients with all aspects of strategic planning, market analysis, and identification of commercial opportunities. Available for the United States, Europe, and Japan
- **Oncology Marketing Strategies™:** Unique service designed to guide marketing and sales professionals to succeed in the evolving and complex cancer marketplace. Only report of its kind focused on oncology; available for the United States and Europe
- **Supportive Care Perspectives™:** Report covering the major supportive care issues like anemia, neutropenia, nausea and vomiting, mucositis, and thrombosis. Available for the United States only
- **Future Focus™ Reports:** Series of reports on focused topics or smaller tumor types. Recent topics include generics in the U.S. oncology market, the U.S. MDS market, and the U.S. GIST market

MattsonJack DaVinci's Custom Oncology Consulting provides clients with actionable intelligence to assist in making better decisions faster.

The topics covered include:

- Strategic pricing plans
- Indication prioritization and selection for novel agents
- Conference reviews for key topics and cancers
- Comprehensive and insightful forecast models for novel agents and competitors
- Assessment of specific indications regarding current standards, new agents, and future treatment trends
- Analysis of oncology in-licensing opportunities and strategies

Custom Consulting Case Study

CLIENT CHALLENGE: A biotechnology company with a new agent in late-stage development requested assistance with strategic launch planning activities including forecasting, strategic positioning, and pricing and reimbursement issues.

MATTSONJACK DAVINCI'S SOLUTION: MattsonJack DaVinci comprehensive coverage of the oncology marketplace allowed for the formation of a project team that included professionals with technical, clinical, marketing, sales, and reimbursement expertise. The team conducted primary research in combination with MattsonJack DaVinci's detailed reports to generate strategic plans to assist with client launch planning activities. Forecasting and preparation of materials for financial analysts were also part of the project's final deliverables.

CLIENT RESPONSE: The client was pleased with the team's expertise, analysis, and planning. Additional project work is on-going to provide more detailed tactical launch coverage for the U.S. and European launches anticipated within the next 12 months

This newsletter is intended to provide commercial organizations involved in the development and marketing of new cancer therapeutics topical articles and features relating to oncology. Each edition will include news and commentary about issues that may impact a company's development and commercialization strategies. MattsonJack DaVinci welcome your views and comments on this Oncology E-Newsletter and its content. If you would like to share your thoughts, please contact us:

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