White Paper

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Information and Insight into Breast Cancer in China

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China is in the middle of the biggest healthcare reform in its history and the government has set a goal of 100% healthcare coverage for all Chinese citizens by 2020.

China Overview

With 1.3 billion people[1], China accounts for about 20% of the world's population. In 2010 China surpassed Japan in terms of annual GDP to become the world's second largest economy. An analysis of the Chinese healthcare market highlights its many contradictions. On one hand, its average annual growth has been an astonishing 25.5%, in direct contrast to the slowing growth rates in other matured markets, including the United States, Japan and the five major European countries.

On the other hand, China is struggling with serious problems, such as uncontrollably high drug prices, poor medical insurance coverage (especially in rural Chinese and migrant populations), counterfeit and/or unsafe drugs, and a rather complicated (and constantly improving) regulatory environment. China is in the middle of the biggest healthcare reform in its history and the government has set a goal of 100% healthcare coverage for all Chinese citizens by 2020.

The paucity of healthcare in China is a serious issue that is only now starting to be addressed. Historically, the Chinese healthcare system was a self-pay system, with great disparity in the provision of medical services between China's urban and rural areas. However, the situation has steadily improved in the last few years with the establishment of the urban resident basic insurance and the countrywide adoption of the new countryside cooperative insurance for rural populations.

Drug reimbursement is primarily managed with two lists, the National Essential Drug List (NEDL) and the National Reimbursement Drug List (NRDL). For drugs listed on the NEDL and NRDL, insurance coverage will help patients by providing about 30% to 70% of the costs, depending on the providence/city. There are two categories in the NRDL: Type A and Type B. Drugs categorized as Type A are 100% reimbursable and cannot be changed by providence/city, whereas Type B drugs can be determined by regional districts and adjusted by providence/city for about 15% of all drugs (Figure 1). Overall, less than 100 oncology drugs are covered on the NRDL and innovative targeted agents are not on the list, making the insurance status irrelevant. The 2009 revision to the NRDL included a special "negotiation category" for high-priced premium drugs that have proven efficacy.

	Not on NRDL	NRDL Type A	NRDL Type B
bevacizumab	X	—	—
cetuximab	X	—	—
trastuzumab	X	—	—
gefitinib	X	—	—
rituximab	X	—	—
sorafenib	X	—	—
bortezomib	X	—	—
erlotinib	X	—	—
carboplatin	—	X	—
capecitabine	—	—	X
cisplatin	—	X	—
docetaxel	—	—	X
gemcitabine	—	—	X
oxaliplatin	—	—	X
topotecan	—	—	X
5-FU	—	X	—

Source: NRDL List, China, 2009.

Oncology Drug Coverage in the NRDL, China 2009 (Figure 1)

Breast Cancer in China

Breast cancer is a particularly good market to highlight the differences in the treatment practices between Western countries and China. This is despite the fact that the incidence of breast cancer in China was approximately 215,600 patients in 2011, which compares closely to the incidence in the United States[2]. Even with the high incidence, there has been a lack of emphasis on diagnosis and detection of breast cancer in its early stages. In Western countries, there are many resources available for patient education and awareness of breast cancer detection as well as many therapeutic options. In China, the majority of

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breast cancer patients are diagnosed with Stage III/IV disease, which contrasts with Western countries, where patients are more likely to be diagnosed in the early stages. Proper diagnosis is not the only limiting factor. Patients with well-defined disease (HER2-positive) struggle with the ability to gain access to traditional chemotherapeutic options that are considered the standard of care for their Western counterparts. This is discussed further in the Herceptin case study.

The other issue most often seen in emerging markets is lack of treatment options as patients relapse following their first line of therapy. In China, only about 40% of metastatic breast cancer patients who receive first-line therapy will go on to receive a second line of therapy. The situation gets dire in third-line, where only one-quarter of patients will receive third-line therapy. Fourth- and fifth-line therapies are virtually non-existent in China (Figure 2).

These reported frequencies of later lines of chemotherapy among Chinese patients are significantly lower than those in Japan and the United States, where 80% of patients continue to second-line and 65% of those patients continue to third-line3. The main reasons for low use of later-line treatments are the lack of good therapeutic options and the financial burden of more expensive drugs. As their disease progresses, patients are more likely to turn to traditional Chinese medicine (TCM)[4].

Lines of Therapy	% of Patients
First-line who receive second-line	42.4%
Second-line who receive third-line	23.7%

Kantar Health and Draco Healthcare Consulting LLC. CancerMPact® Treatment Architecture China, Breast Cancer 2011.

Metastatic Breast Cancer Patients who Receive Later Lines of Chemotherapy (Figure 2)

Treatment Patterns in China Are Very Different Compared With Western Practices

Our CancerMPact® Treatment Architecture physician survey, conducted in partnership between Kantar Health and Draco Healthcare Consulting, showed that the overall use of chemotherapy in China is high compared with Western countries; however, there are differences in the preference of chemotherapy regimens or agents. In the adjuvant setting, fluoropyrimidine-containing regimens are common, which is similar to the practice in Japan but not in the United States[3]. In the metastatic setting, Chinese physicians are more likely to continue with the anthracycline plus taxane combination such as AC (cyclophosphamide plus doxorubicin) or CEF (cyclophosphamide, epirubicin plus 5-FU). This is somewhat similar to Japan, whereas in the United States physicians like to combine a targeted agent with their taxane. For example, paclitaxel is primarily combined with Avastin® (bevacizumab, Roche/Genentech) in HER2-negative patients or with Herceptin® (trastuzumab, Roche/Genentech) in HER2-positive patients[3].

In China, even though physicians test for a patient's HER2-status, only a small percent will receive a HER2-targeted agent. The lack of entrenchment of Herceptin into treatment practices in China is addressed in the Herceptin case study on page 6. Relapsed or refractory patients are more likely to receive combination chemotherapy with Xeloda® (capecitabine, Roche) or gemcitabine plus docetaxel (preferred over paclitaxel in China). The reliance on combination chemotherapy, even in a patient group that had received chemotherapy for earlier-stage disease, is in stark contrast to the practice in the United States and Japan. In both countries, patients in the relapsed setting are more likely to receive monotherapies such as Xeloda, taxane, vinorelbine or gemcitabine (Figure 3).

The use of Xeloda in China can be attributed to the unique packaging plan followed by Roche. Roche imports Xeloda as a bulk drug into China and repackages it to be sold at lower cost (Chinese Yuan 2,390 for a box of

Differences between practices in China versus Western countries and Japan arise more in postmenopausal women.

60 tablets at 500 mg each, approximately $374.60). This has helped significantly in the uptake of Xeloda in the Chinese market, where our survey shows frequent use of Xeloda. In addition, Xeloda is on the NRDL list for late-stage breast cancer and colorectal cancer. Sales of Xeloda have steadily increased in China, accounting for 3.29% of the total Chinese hospital cancer drug market in 2010 and making it the seventh best-selling cancer drug in the Chinese market in 20115.

In breast cancer, hormone therapy is used in several settings like chemotherapy. Hormonal agents are effective in patients whose cancer cells have high levels of hormone receptors. Several hormone agents are used, the two major classes being the hormone receptor antagonists tamoxifen and Faslodex® (fulvestrant, AstraZeneca; approved 2010) and the aromatase inhibitors Arimidex® (anastrozole, AstraZeneca; approved 2002), Aromasin® (exemestane, Pfizer; approved in 2002 for breast cancer treatment in postmenopausal women), and Femara® (letrozole, Novartis; approved 2009). Similar to other countries, tamoxifen is the leading agent for first-line premenopausal women in China. This is not surprising since tamoxifen is a Type A drug on the NRDL and is 100% reimbursed, unlike the aromatase inhibitors (Figure 5).

		China 2011	China 2010	Japan 2010	U.S. 2010
Top Three Chemotherapy Regimens					
Stage I/II Adjuvant	HER2-	CEF FAC (CAF) AC	FAC (CAF) CEF AC + docetaxel	TC CEF CEF + docetaxel	TC AC + paclitaxel AC
	HER2+	FAC (CAF) EC + docetaxel AC + docetaxel	AC + docetaxel EC + paclitaxel AC + paclitaxel	CEF + paclitaxel CEF + docetaxel paclitaxel	**docetaxel + carboplatin** AC + paclitaxel TC
Stage III Adjuvant	HER2-	EC + docetaxel AC + docetaxel CEF + docetaxel	EC + docetaxel AC + docetaxel AC + paclitaxel	CEF + docetaxel CEF + paclitaxel CEF	**AC + paclitaxel** TAC TC
	HER2+	EC + docetaxel AC + docetaxel AC + paclitaxel	EC + docetaxel AC + docetaxel AC + paclitaxel	CEF + paclitaxel CEF + docetaxel paclitaxel	docetaxel + carboplatin AC + paclitaxel TC
Stage IV 1st line	HER2-	AC + docetaxel AC + paclitaxel EC + docetaxel	AC + docetaxel AC + paclitaxel CEF	paclitaxel CEF + docetaxel CEF	**bevacizumab + paclitaxel** bevacizumab + paclitaxel paclitaxel
	HER2+	AC + docetaxel AC + paclitaxel EC + docetaxel	AC + docetaxel AC + paclitaxel CEF	**paclitaxel** CEF + docetaxel docetaxel	paclitaxel docetaxel+ carboplatin docetaxel
Stage IV 2nd line		capecitabine + docetaxel gemcitabine + docetaxel CEF + paclitaxel	capecitabine AC + docetaxel gemcitabine + docetaxel	paclitaxel capecitabine docetaxel	capecitabine gemcitabine vinorelbine
Stage IV 3rd line		capecitabine + docetaxel gemcitabine + docetaxel capecitabine	capecitabine + docetaxel gemcitabine + docetaxel capecitabine	vinorelbine capecitabine gemcitabine	capecitabine gemcitabine vinorelbine
Stage IV 4th line		N/A	N/A	capecitabine gemcitabine vinorelbine	capecitabine gemcitabine vinorelbine

Kantar Health and Draco Healthcare Consulting LLC. CancerMPact® Treatment Architecture China, Breast Cancer 2011 and CancerMPact® Treatment Architecture U.S. and Japan, Breast Cancer 2010.

Top Three Chemotherapy Regimens (Figure 3)

	China 2011	China 2010	Japan 2010	U.S. 2010
Top Three Hormone Therapies (Stage IV)				
First line	letrozole tamoxifen anastrozole	letrozole tamoxifen anastrozole	anastrozole letrozole exemestane	letrozole anastrozole tamoxifen
Second line	tamoxifen anastrozole exemestane	letrozole anastrozole tamoxifen	exemestane letrozole toremifene	fulvestrant letrozole anastrozole
Third line	tamoxifen anastrozole exemestane	letrozole anastrozole tamoxifen	medroxyprogesterone letrozole exemestane	fulvestrant exemestane anastrozole

Kantar Health and Draco Healthcare Consulting LLC. CancerMPact® Treatment Architecture China, Breast Cancer 2011 and CancerMPact® Treatment Architecture U.S. and Japan, Breast Cancer 2010.

Top Three Hormone Therapies (Figure 4)

Differences between practices in China versus Western countries and Japan arise more in postmenopausal women. In China, physicians will use tamoxifen even in postmenopausal women, which contrasts with Western practice where postmenopausal patients are more likely to be treated with aromatase inhibitors. There is no clear leader among aromatase inhibitors for postmenopausal women in China, and physicians may choose either anastrozole or letrozole (generic versions of aromatase inhibitors are available in the Chinese market). The use of aromatase inhibitors in China is somewhat similar to the practice in the United States and Japan, where there is equal preference for anastrazole and letrozole. In the relapsed setting, patients in Japan may receive either exemestane or letrozole, whereas in the United States the estrogen receptor antagonist fulvestrant is most often preferred for second- and third-line patients (Figure 4).

What differentiates China from Western markets is the predominance of generic versions, produced locally by Chinese companies that exist alongside the branded versions produced overseas and imported into China. Generic versions of drugs exist in China even though the drug might still be patent-protected in other parts of the world.

For example, docetaxel from sanofi-aventis and Ai Su (generic docetaxel) from Jiangsu Hengri coexist in the Chinese market. Docetaxel accounts for about 32% of the market in total sales, immediately following market leader Ai Su, which had 39% of the total docetaxel market in China in 20106. This predominant

Chinese physicians can prescribe either the branded or the local generic version of a drug, and reimbursement is dependent on whether the drug is on the NRDL

use of generics is not surprising, considering the distinct price differences between generic and "branded" docetaxel (from sanofi-aventis at RMB 1,924 for every 20 mg, while from Ai Su at RMB 460 per 20 mg).

Chinese physicians can prescribe either the branded or the local generic version of a drug, and reimbursement is dependent on whether the drug is on the NRDL. Maximum retail price is determined by the National Development and Reform Commission (NDRC). The key decision-maker for which drug is ultimately administered is the patient. Most often the patient's decision is influenced by affordability and access to the drug, as well as the perceived quality of the imported (branded) version versus the locally manufactured generic version[6].

Figure 5 gives an overview of drugs for breast cancer that have generic or branded versions, and indicates whether they are listed on the NRDL and can be reimbursed.

Drug	Branded	Generic	On NRDL
paclitaxel	X	—	—
trastuzumab	X	—	—
capecitabine	X	—	Type B
cyclophosphamide	—	X	Type A
doxorubicin	X	X	Type A
docetaxel	X	X	Type B
paclitaxel	X	X	Type B
vinorelbine	—	X	Type A
epirubicin	—	X	Type B
gemcitabine	X	X	Type B
anastrozole	X	X	Type B
letrozole	X	X	Type B
exemestane	X	X	Type B
tamoxifen	—	X	Type A

Type A: 100% reimbursed; Type B: Coverage can be 30-70% dependent on regional districts

Breast Cancer Drugs Available in China (Figure 5)

Stage	Western Medicine only	TCM Only	TCM in Combination with Western Treatments
Stage 0, I, II	55.9%	6.2%	37.9%
Stage III	50.1%	7.7%	42.2%
Stage IV 1st line	52.6%	8.0%	39.5%
Stage IV 2nd line	49.7%	9.5%	40.8%
Stage IV 3rd line	43.8%	13.5%	42.7%

Kantar Health and Draco Healthcare Consulting LLC. CancerMPact® Treatment Architecture China, Breast Cancer 2011.

Traditional Chinese Medicine (Figure 6)

In China, TCM is well accepted by physicians and patients as supportive therapy in combination with other modalities (Figure 6). TCM also represents an alternative to the palliative care (or best supportive care) that Western medicine employs, and there are more than 100 formulas of TCM for breast cancer. TCM is thought to alleviate toxicity associated with Western treatments, improve quality of life, and is relatively cheaper compared with other treatment options. Many inexpensive TCM options are made even more affordable by being listed as Type B on the NRDL or even fully reimbursable to patients by being listed as Type A on the NRDL. The other and potentially more influential reason that TCM is utilized to such a large extent is that it is part of the culture even outside of oncology.

Summary

In summary, understanding the Chinese market and differences in cancer treatment is key for successful planning. Pharmaceutical companies need the clinical depth and insight to support actionable decisions to take advantage of this dynamic market on the verge of introducing universal healthcare coverage.

Kantar Health's CancerMPact® Treatment Architecture China can help you produce more accurate market assessments (forecasting), leading to targeted sales approaches; capitalize on opportunities, such as where to introduce new therapeutic regimens; understand current treatment practices and market dynamics specific to China; and gain perspective on target audiences regarding whom they treat and how they treat them.

Our expertise is highlighted in the case study below on Herceptin use in China.

Cancer Treatment in China, a Case Study: Herceptin

In Western countries and Japan, testing for HER2 status is common for all breast cancer patients, and Herceptin is the current standard

Getting Herceptin and other life-saving cancer agents into the hands of physicians, and ultimately patients, will need support far beyond what insurance can cover.

of care for HER2-positive patients; however, the same is not true for China. According to the Chinese Medical Association survey conducted in 2008, only 57% of Chinese breast cancer patients were tested for HER2 status, despite the relatively low cost of conducting the HER2 test, ranging from 80-100 Yuan (US: $12-15). Reasons for the low testing rate included lack of awareness of the test and its value, and low quality of testing (lack of standardized testing techniques). In 2009, the Pathological Society of China (PSC) sponsored a national program, "National HER2 Testing Quality Certification," with the goal of providing more accuracy and information on HER2 testing in breast cancer. The 2011 physician survey conducted by Kantar Health/Draco showed that 86% of patients were tested for HER2 status. Although the testing rate has increased, the Kantar Health/Draco survey reported very low utilization of Herceptin for both the adjuvant and the metastatic settings. So while over two-thirds of all HER2-positive patients in the United States or Japan will receive Herceptin with or without chemotherapy, only about one-third of HER2-positive patients in China will receive Herceptin-based chemotherapy.

Currently, Herceptin is not on the reimbursable list of the National Basic Insurance Program (Ministry of Labor and Social Security, MoLSS, Figure 5). Also, no patient assistance programs are in place for Herceptin. The cost of one cycle of Herceptin is about $3,500, which is a highly expensive out-of-pocket cost for the majority of patients. Due to the high costs, most HER2 expressors will receive chemotherapy only. Our data also shows that of the patients who receive Herceptin-based chemotherapy, most will be given a Herceptin-based chemotherapy for a fixed duration of time – typically 6 months. In contrast, their Western counterparts will typically receive Herceptin until progression. In some respects, this seems like a great disservice for breast cancer patients in China and possibly reflects the story in other emerging markets: lack of good therapeutic options due to economic constraints. It is no surprise that about half of breast cancer patients in China will die before getting a third line of therapy, reflecting on the lack of availability for these agents. This situation may change after healthcare reform takes effect, but getting Herceptin and other life-saving cancer agents into the hands of physicians, and ultimately patients, will need support far beyond what insurance can cover.

Sources:

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About Draco Healthcare Consulting, LLC

Draco Healthcare Consulting, LLC is a leader in healthcare consulting focusing on the Greater China region, and is committed to providing consulting service of highest-quality to leading pharmaceutical and biotech companies worldwide. Draco focuses exclusively on China's healthcare market, including pharmaceutical industry analysis, Chinese drug regulatory environment, China's unique hospital systems and complicated epidemiology data. Draco has a dedicated professional team composed of experienced healthcare consultants from pharmaceuticals and biotech industry veterans, experts on State Food and Drug Administration (SFDA) and on clinical trials in China.

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About CancerMPact®

The CancerMPact® Treatment Architecture China series is the result of an intensive collaborative effort between Kantar Health and Draco Healthcare Consulting, LLC (Draco). Draco has extensive experience in the Chinese pharmaceutical market and resources in China, while Kantar Health has comprehensive experience and resources in the epidemiology and treatment of cancer. Their respective strengths provide clients with unsurpassed depth, breadth, and insight into the treatment of cancer in the emerging and ever-growing Chinese market. Click here to download the CancerMPact® Treatment Architecture China factsheet.

About Kantar Health

Kantar Health is a global, evidence-based decision support partner to the world's leading pharmaceutical, biotech, device and diagnostic companies. Our 700+ staff act as catalysts, working closely with customers to drive distinctive decision-making that help them prioritize product development and portfolios, differentiate their brands and ensure product profitability after launch. We are unique in that we bring together clinical, medical and methodological expertise, commercial/marketing know-how and proprietary data. It is this rare combination, together with our unparalleled stakeholder reach, that enables us to mobilize incisive, imaginative and timely ROI-driven solutions, empowering clients to deliver better healthcare options to their customers.

With staff in over 40 countries, we excel at solving technically or logistically challenging projects around the world and across the product lifecycle, combining on-the-ground know-how and global and national proprietary data to quickly identify value drivers. As part of WPP, we can also incorporate highly innovative thinking from outside the industry into our solutions.

About the author

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