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Final Report

Ludwig Boltzmann Institut
Health Technology Assessment

HTA-Projektbericht Nr:14
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Abbreviations

ASCO	American Society of Clinical Oncology
CADTH	Canadian Agency for Drugs and Technologies in Health
CAST	Centre for Applied Health Services and Technology Assessment
CDER	Centre for Drug Evaluation and Research
CHMP	Committee for Medicinal Products for Human Use
COMP	Committee for Orphan Medicinal Products
DKG	Deutsche Krebsgesellschaft
EC	European Commission
EMEA	European Medicines Agency
eTOC	Electronic table of contents
EU	European Union
EUnetHTA	European network for Health Technology Assessment
FDA	U.S. Food and Drug Administration
HONcode	Health On the Net Foundation code of conduct
HSS	Horizon Scanning System
HTA	Health Technology Assessment
ISOPP	International Society of Oncology Pharmacy Practitioners
LBI-HTA	Ludwig Boltzmann Institute for Health Technology Assessment
LKH	Landeskrankenhaus
NDPM	New Drug Pipeline Monitor
NHSC	National Horizon Scanning Centre
OODP	Office of Oncology Drug Products
OTC	Over-the-counter drug
PDF	Portable document format
PMPRB	Patented Medicine Prices Review Board
R&D	Research and Development
SMC	Scottish Medicines Consortium
UK	United Kingdom
WP7	Work package 7

Executive Summary

Background: Scientific and medical progress in oncology has led to the introduction of new medicines in rapid succession. In addition, the development of new therapy modalities, the so-called "targeted therapies" such as e.g. monoclonal antibodies or tyrosinekinase-inhibitors ("small molecules"), has resulted in swift increases in medicine costs in oncology in hospitals. The fast and, to some extent, uncontrolled implementation of these expensive cancer medicines has affected hospital drug budgets.

medical progress in oncology affects hospital drug budgets

The development of a Horizon Scanning System (HSS) which aims at identifying and evaluating new drug therapies in oncology early on, i.e. before their routine introduction for cancer treatment, could prepare Austrian hospitals (hospital administrators and drug commissions respectively) for new anticancer medicines, and could contribute to making rational decisions and planning prospective budgets.

Horizon Scanning for anticancer drugs to inform decision makers

The main components of such a Horizon Scanning System are the determination of relevant information sources for the systematic identification of emerging anticancer drugs, the establishment of a useful filtering and prioritisation instrument, the set up of a network of Austrian oncologists involved in the Horizon Scanning process and the definition of the parameters and the format of early assessment.

Objectives: This project was performed in order to develop a concept for the preparation of a HSS for anticancer drugs in Austria and to test the two important steps of identification and priority setting within a first feasibility study.

development of a concept for a Horizon scanning system in oncology

Methods: A literature and internet search based on the EUnetHTA WP7 HSS-review (overview of Horizon Scanning activities) was performed to identify existing Horizon Scanning Systems and relevant information sources for new anticancer drugs. Experts from established HSSs, mainly members of EuroScan, were contacted for information about their identification and prioritisation processes. Existing methods were then adapted to the needs of Horizon Scanning in oncology. Clinical experts were involved in the priority-setting process and the selection of new anticancer drugs for performing an early assessment. In a pilot run, we tested the feasibility of the concept.

methods include literature search, contact to experts and adaptation of existing methods

Results: In a time period of three months about sixty selected information sources for oncology were scanned weekly to identify emerging anticancer drugs or drugs with an extension of indication in phase II/ III of clinical testing. Our scanning revealed 116 different anticancer drugs for which we extracted relevant data. Three clinical experts in oncology then independently applied seven prioritisation criteria with an underlying score to the potentially important anticancer drugs. We analysed their preliminary estimations by calculating a mean score. The number of anticancer drugs relevant to the Austrian health care system could thereby be reduced to five, although this result has to be interpreted carefully. Prioritisations by the experts clearly differed. Therefore, a final decision about which anticancer drugs should undergo early assessment was not feasible after calculating a mean score. Instead, a multistage prioritisation process must be used to reach a consensus between oncologists. In addition, our experts have commented on the proposed procedures of drug identification and prioritisation.

feasibility study showed the need for slight changes in the identification and prioritisation process

Their suggestions mainly dealt with how drugs are identified (i.e. more restricted inclusion criteria) and who makes up the expert panel (more experts with expertise in specific tumour entities). Their input could now be used to optimize the Horizon Scanning System and serve as a basis for further discussions.

consideration of weak points to improve the existing concept and make HSS standard practice

Conclusions: The establishment of a Horizon Scanning System for anticancer drugs is an important tool to prepare Austrian hospitals for new/ emerging medicines. In principle our first experiences with the Horizon Scanning System from the feasibility study were acceptable but several changes, especially regarding the collection of data on anticancer drugs and the priority setting process, were proposed by our experts. The next steps will be to work out an optimized, final concept with various stakeholders (e.g. hospital administrators, clinical experts, drug commissions) in consideration of the results of the feasibility study. Secondly, the Horizon Scanning System should be made standard practice to regularly provide Austrian hospitals (hospital management and drug commissions) with information about new/ emerging anticancer drugs to support their financial drug budget planning and rational decision making. Third, as an input for the international HTA-community, the Ludwig Boltzmann Institute for HTA will join EuroScan in 2008/ 2009.

Zusammenfassung

Einleitung: Der wissenschaftliche und medizinische Fortschritt in der Onkologie führt in rascher Abfolge zur Einführung neuer Medikamente. Mit der Entwicklung neuer Therapiemodalitäten, den so genannten „targeted therapies“ wie z.B. monoklonale Antikörper oder Tyrosinkinasehemmer („small molecules“), ist es in den Krankenhäusern zu einer rasanten Steigerung der Medikamentenkosten in der Onkologie gekommen. Die schnelle, teils unkontrollierte Implementierung dieser teuren Krebsmedikamente in die klinische Praxis hat Auswirkungen auf die Arzneimittelbudgets der Österreichischen Krankenhäuser.

Fortschritt in der Krebstherapie wirkt sich auf Arzneimittelbudgets der Krankenhäuser aus

Zielsetzung: Der Aufbau eines „Horizon-Scanning-Systems“ zur Früherkennung und Bewertung von neuen medikamentösen Therapiekonzepten in der Onkologie, d.h. bevor einer routinemäßigen Einführung in die Patientenbehandlung, soll Krankenanstalten (resp. Arzneimittelkommissionen) auf neue Krebsmedikamente gezielt vorbereiten, zur rationalen Entscheidungsfindung beitragen sowie die prospektiven Budgetplanung unterstützen und einen wissenschaftlich begründeten Einsatz von Krebsmedikamenten sicherstellen.

Entwicklung eines Konzeptes für ein Horizon Scanning System in der Onkologie

Horizon Scanning Systeme umfassen die folgenden sequentiellen Schritte: die Identifikation von geeigneten Informationsquellen für das Herausfiltern neuer Krebsmedikamente, die Festlegung eines geeigneten Priorisierungs-Instrumentes, die Zusammenstellung eines Expertenteams und die Erarbeitung des Formats und der Methode für die Durchführung von frühen Assessments. Das Ziel dieses Projektes war die Entwicklung eines Konzeptes für ein Horizon Scanning System (HSS) in der Onkologie sowie die Prüfung der Machbarkeit der Schritte „Identifikation“ und „Priorisierung“ im Rahmen einer Studie.

Methode: Ausgehend von EUnetHTA WP7 Horizon Scanning Bericht wurde eine Literatursuche durchgeführt, um bestehende HSS-Aktivitäten und geeignete Informationsquellen für den onkologischen Bereich zu identifizieren. Zusätzlich wurden Experten zu Informationsquellen und deren Priorisierungsprozessen befragt. Es konnten bestehende Methoden übernommen bzw. an ein HSS speziell für die Onkologie angepasst werden. Die Durchführbarkeit des HSS wurde in Zusammenarbeit mit klinischen Experten getestet.

Literatursuche und Expertenkontakt

Ergebnis: In einem Zeitraum von 3 Monaten wurden über 60 verschieden Informationsquellen einmal pro Woche gescannt und dabei Informationen zu neuen Krebsmedikamenten in der Entwicklung extrahiert. Es wurden 116 verschiedene Arzneistoffe identifiziert, welche anschließend von 3 unabhängigen klinischen Experten mittels 7 definierten Kriterien priorisiert wurden. Die drei Einschätzungen wurden anhand einer hinterlegten Punktezahl quantifiziert und dann ein durchschnittlicher Punktewert pro Arzneistoff ermittelt. Dadurch konnte die Anzahl der für das Österreichische Gesundheitssystem relevanten Arzneistoffe auf 5 eingeschränkt werden, wobei dieses Ergebnis durch die z.T. großen Unterschiede in der Einschätzung durch die Experten, nur beschränkt aussagekräftig ist. Eine endgültige Festlegung, welche Arzneistoffe nun einem frühen Assessment zugeführt werden sollen, muss demnach durch einen mehrstufigen Konsensfindungsprozess erreicht werden. Das Expertenteam wurde zur Machbarkeit des vorgeschlagenen HSS befragt und es zeigten sich notwendige Änderungen in den Ein-

machbares Konzept aber Optimierung bei Identifikation und Priorisierungsprozess notwendig

schlusskriterien bei der Identifikation von Krebsmedikamenten sowie in der Zusammensetzung des Expertenteams.

Diskussion des HSS-Konzeptes mit Entscheidungsträgern und Implementierung in die Praxis

Schlussfolgerung: Der Aufbau und die Einführung eines Horizon Scanning Systems für den Bereich der Onkologie ist ein wichtiger Beitrag zur Vorbereitung von Krankenhäusern auf neue Medikamente in der Krebstherapie. Die erste Testung des Konzeptes verlief gut, allerdings wurden Änderungen zur Verbesserung des HSS von den Experten vorgeschlagen. Die nächsten Schritte umfassen deshalb die Ausarbeitung eines optimierten Konzeptes unter Einbeziehung verschiedener Entscheidungsträger (z.B. Krankenhausverwaltungen, Arzneimittelkommissionen, Ärzte) sowie die nachfolgende Implementierung des HSS in die Praxis. Als internationalen Beitrag auf dem Gebiet Health Technology Assessment bzw. Horizon Scanning wird das Ludwig Boltzmann Institut für HTA noch im Jahre 2008 EuroScan beitreten.

1 Introduction

1.1 Background

cancer is one of the major health problems

Around 35,000 people are diagnosed with cancer each year in Austria and after cardiovascular diseases, malignant cancer is the second most common cause of death in both sexes [1]. These facts illustrate that cancer is one of the major health problems Austria, as many other countries, has to face.

new therapy modalities in oncology

Over the past years basic and clinical research in oncology has been steadily increasing and is still expanding. Scientific and medical progress in this field has led in rapid succession to the introduction of many new medicines and the development of new therapy modalities, the so-called "targeted therapies" (e.g. monoclonal antibodies, tyrosinekinase-inhibitors). According to the annual report of the European Medicines Agency (EMEA) from the year 2007, cancer treatment was the most-represented therapeutic area for which positive orphan-designation opinions were adopted (55% of COMP/ Committee for Orphan Medicinal Products opinions), for which the highest proportion of initial marketing-authorisation applications was received (26% of applications for new products) and for which the highest number of positive CHMP/ Committee for Medicinal Products for Human Use opinions were adopted (28% of positive opinions)[2]. However, there are large differences between countries with regard to the level of uptake and the time period over which cancer drugs become available to patients. Austria was one of the three countries which have been shown to be leaders in terms of adoption and availability of new cancer drugs [3].

increasing expenses for cancer therapy effect on hospitals' drug budget

The variety of new anticancer drugs available for therapy not only offers improved cancer treatments but also brings about means new challenges. On the one hand, clinicians have to have an overview of medical progress and choose the best suitable therapy regime for each patient. On the other hand, the health system (i.e. hospitals) has to deal with increasing expenditures because cancer therapy is one of the major cost drivers of medicine costs in Austrian hospitals [4]. The fast and, to some extent, uncontrolled implementation of these mostly expensive cancer medicines into clinical practice has already dramatically affected hospital drug budgets.

1.2 Horizon Scanning Systems

1.2.1 Introduction

support decision makers with information about new/ emerging health technologies

New health technologies (e.g., drugs) raise a lot of questions concerning managed introduction, financial burdens, organisational requirements, and clinical practice changes. They also require consideration of social or ethical aspects as well as their effect on health care systems. Some countries (e.g. UK, Norway, Sweden, Belgium, Canada, and Australia) have established so called Horizon Scanning Systems (HSS), Early Warning Systems or Alert Systems to support decision makers with early information about new health technologies prior to their adoption and introduction into the national health system [5].

international network called EuroScan

Since 1999 these HSS have been collaborating in an information network called EuroScan, which is hosted by the National Horizon Scanning Centre (NHSC), the British HSS [6, 7]. The long-term aim of EuroScan is to establish a permanent network among agencies and organisations in the field of HTA to evaluate and exchange information on new and changing technologies, to develop the sources of information used, to share applied methods for early assessment, and to disseminate information on early identification and assessment activities [8].

five sequenced main components of a HSS

According to EuroScan, HSS focuses on health technologies that are new (in the phase of adoption, i.e. in the launch or early post-marketing stages) or emerging (pharmaceuticals in phase II or phase III clinical trials) or that represent a change in indication of an existing technology, or that are part of a group of developing technologies that, as a whole, may have an impact. Such a HSS consists of 5 sequenced main components and work steps:

- **Identification** of technologies that have the potential to make a large impact on health and/ or health services
- **Prioritisation** i.e. to filter and prioritise these technologies to select those most likely to have a significant future impact
- Early **assessment** of likely impact in terms of health, service and financial impact
- **Dissemination** of the resulting information to relevant decision-makers
- **Monitoring** of assessed technologies.

HSS as part of HTA agencies

Most HSS units are part of a HTA agency and HSS can be seen as the first stage of a comprehensive HTA process [6]. The main difference is that HSSs focus on technologies early in the life cycle (identifying and assessing technologies that potentially might have an impact on the health care system), whereas HTA in general primarily focus on assessing established health technologies.

1.2.2 Horizon Scanning in Oncology

establishment of a HSS for the identification of new/ emerging anticancer drugs

Due to the increasing interest in emerging and new health technologies relevant to the Austrian health care system, in particular in the clinical field of oncology, interest was expressed to establish a Horizon Scanning System in oncology as part of the research program in the Austrian Ludwig Boltzmann Institute of Health Technology Assessment (LBI-HTA).

We decided to establish a separate Austrian Horizon Scanning System in oncology only because most of the institutions collaborating within EuroScan operate at a national level (e.g. differences in priority setting between health care systems), with additional awareness to the internationality of Horizon Scanning and secondly, oncology is one of the major fields of medical research with the lead in many (highly-expensive) new/ emerging drugs. Hence a HSS with a special focus on anticancer drugs is of great national and international importance and relevance.

Therefore, the development of a national Horizon Scanning System for the early identification and evaluation of new drug therapies in oncology, i.e. prior to routine introduction to cancer treatment should purposefully prepare decision-makers in hospitals (hospital administration, drug commissions, oncologists) for new cancer medicines with potential impact (clinical, economic) and should contribute to making rational decisions as well as planning prospective budgets. After the successful establishment of the HSS by the LBI-HTA in Austria, the institute will make an important contribution to the international HTA-community through joining the EuroScan Network. In exchange, the Network will grant access to the EuroScan database in other fields of medicine as well.

target groups: decision-makers in hospitals (hospital administration, drug commissions, oncologists)

1.3 Objectives

The aim of this project, which was carried out between July 2007 and May 2008, was to develop a concept for setting up a Horizon Scanning System in Austria which places special emphasis on anticancer drugs. The methods and knowledge from existing HSS should be used and adapted to the challenges in oncology.

development of a concept for a HSS in oncology and the testing of its feasibility

The project focussed on the following:

- The identification of information sources which provide timely information on new/ emerging anticancer drugs,
- The identification and presentation of the most important parameters on which information should be extracted from the identified sources,
- The selection of relevant and useful criteria for the prioritisation process,
- The establishment of a group of clinical experts in oncology who support and perform the selection/ prioritisation of anticancer drugs with potential impact (e.g., clinical, economic) on the Austrian health care system,
- The testing of the two major steps involved in the HSS (identification and prioritisation) within a short pilot feasibility study,
- The preparation of a basis for discussion with stakeholders about the concrete implementation of the HSS into practice.

2 Methods

Search of the literature, contact to experts and a feasibility study to explore two important steps in the process of HSS (identification of health technologies and priority setting for early assessment) were used as methods within this project.

literature search and contact to experts

2.1 Definition of Drugs to be identified by the HSS

The first step was to determine an exact definition of the drugs which should be identified by systematically scanning several sources within the framework of our HSS:

inclusion criteria: anticancer drugs in phase II/III of clinical testing

- Drugs that are designed for cancer therapy in adults concerning solid malignancies as well as leukaemia and lymphoma ,
- Anticancer drugs that are new (in the phase of adoption, i.e. in the launch or early post-marketing stages) or emerging (in phase II or phase III of clinical testing),
- Approved anticancer drugs that represent a change in indication (extension of indication),
- Anticancer drugs which will be in clinical use in Austria within a time period of 0 to 4 years,
- Excluded are drugs used for only supportive therapy like antiemetics, bisphosponates etc. ,
- Excluded are other anticancer treatments other than drugs.

exclusion criteria: drugs used for supportive therapy, other anticancer treatments other than drugs

2.2 Constitution of an Expert Panel

Clinical oncologists are important for our HSS because they represent the expert panel that is responsible for the prioritisation of identified anticancer drugs. In our pilot study, we started with three well-reputed experts in oncology recommended by medical directors from three different Austrian hospitals which work closely with the LBI-HTA. They have graciously volunteered to participate in the pilot process of developing a concept for an Austrian HSS in oncology:

experts from 3 different Austrian hospitals

Prim. Univ. Doz. Dr. Peter Krippl, Department of Internal Medicine– Centre for Oncology and Haematology, LKH Fürstenfeld,

Dr. Clemens Leitgeb, 1. Medical Department – Centre for Oncology and Haematology, Wilhelminenspital Vienna and

Dr. Wolfgang Willenbacher, Department of Internal Medicine – Centre for Oncology and Haematology, University Hospital Innsbruck.

2.3 Identification of Information Sources which provide timely Information on new/ emerging Anticancer Drugs

2.3.1 Searching for information sources

identification of information sources for oncology by literature search

Due to limited financial resources for this initial study, we included only information sources that are easily and freely accessible on the internet. We began by scanning internet sites already familiar to us, such as the American Society of Clinical Oncology homepage. From there we explored other useful sources (i.e. including predominantly and reliable oncology-related information) for identifying new/ emerging anticancer drugs. Moreover, we searched for information sources used within the identification process of other Horizon Scanning- / Early Warning Systems by reading publications cited in the EUnetHTA WP7 Project Report (overview of horizon scanning activities [6]) and hand-searching their reference lists for further literature on this topic. In addition, based on recommendations of clinical oncologists regarding sources which they use to stay informed about state-of-the-art science, various internet sites were included.

We collected and tabulated all potential information sources (see chapter 2.3.2) that provide predominately information about anticancer drugs. In a feedback process we contacted four experts well known to the LBI-HTA from established HSSs to comment on our list of sources, to report their experiences with the mentioned sources and to suggest additional ones.

The following experts from HSSs provided us with their support and advice:

Karla Douw, PhD, Centre for Applied Health Services Research and technology Assessment (CAST) at the University of Southern Denmark

Anne Lee, MPhil, MRPharmS, Horizon Scanning, Scottish Medicines Consortium (SMC), Scotland

Dr. Sue Simpson, National Horizon Scanning Centre (NHSC) at the University of Birmingham, UK

Leigh-Ann Topfer, Emerging Health Technologies, Canadian Agency for Drugs and Technologies in Health (CADTH), Canada

2.3.2 Selection criteria for information sources

defined criteria for information sources on the Internet

Due to the fact that we used information sources mainly available to the public on the internet, we used the following criteria to judge a site as suitable for our scanning process [9].

- Timeliness of information (periodical updates)
- Quality of information provided (objectivity, transparency of primary source and credibility)
- Accessibility (available free or with free subscription)
- Oncology-related content
- Usability (easy to scan, not too time consuming, electronic alerts or newsletters available)
- Geographic coverage (international or national coverage)

Information sources were included in our list of internet sites if all the criteria were fulfilled.

2.4 Data Extraction

format for data extraction: Excel spreadsheet

After completing the selection of internet sources we generated an Excel spreadsheet that included a set of parameters for extracting relevant information on new/ emerging anticancer drugs during the scanning process. The preparation and format of the available information on anticancer drugs is an essential step within the HSS, because the expert panel (see chapter 2.2) has to appraise the identified anticancer drugs on the basis of the provided information by applying defined criteria. The more comprehensive the information, the easier it is to do the priority setting process. We listed a set of parameters which we regarded as being important, and discussed our proposal face to face with the experts.

2.5 Definition of Criteria for Priority Setting

use of established criteria and adaptation to our needs

Existing HSS, i.e. EuroScan, have already defined and established priority setting criteria [8]. We collected comprehensively the criteria that were described in literature [10-13] and by EuroScan and assigned them to our predefined categories. The definition of our final priority setting instrument comprising a useful and manageable set of criteria was reached in agreement with the expert panel and was tested in the context of the feasibility study.

2.6 Feasibility Study

testing of the identification and prioritisation process and answering questions regarding its feasibility

Before a final implementation of a new Horizon Scanning System to support administrative and medical decision-making, the theoretical concept must be tested in the context of a feasibility study [13]. Therefore, in a pilot study between January and March 2008 we regularly scanned the predefined information sources and collected data about anticancer drugs. According to the selected parameters we tabulated the recorded information in an Excel spreadsheet and asked our expert panel to apply the prioritisation criteria to the identified anticancer drugs. The task was to narrow the topic list to a manageable number of anticancer drugs which could be further evaluated in the context of an early assessment. Moreover, the study was performed to answer the following questions:

- Are the specified information sources suitable for an HSS in oncology (i.e. manageable and not too time consuming)?
- What is the optimal scanning frequency (e.g. daily, weekly or monthly) and how much time is needed to scan the sources and extract data?
- Are the extracted data detailed enough (is enough information provided) to apply the priority setting criteria?

- Are the prioritisation criteria and the underlying score appropriate to reduce the initially large amount of identified anticancer drugs to a manageable number of substances?
- How much time does it take to do the prioritisation?
- What is the optimal size of an expert panel? Can three experts cover the wide field of oncology?
- Which changes are necessary to optimize the HSS?
- What are the next important steps to make the HSS standard practice and to support decision makers with relevant information about relevant anticancer drugs?

2.7 Early Assessment of Anticancer Drugs

early assessment as main output of a HSS

Early assessments of relevant new/ emerging anticancer drugs are the main output of this and other HSS to support decision makers. Information on the format and methods of different agencies with existing HSS was collected from websites and published literature and was used to propose a preliminary concept for this next step of the HSS, which has yet to be conducted.

3 Results

3.1 Information Sources

3.1.1 General Classification

63 different information sources from 7 categories

The identified information sources based on the recommendations of experts and on published reports [9, 14-19] were summarized. To obtain a useful combination of sources and to be comprehensive enough, we finally included 63 different information sources available on the internet, which can be divided into 7 main categories (Figure 3.1-1).

- Regulatory Authorities
- Societies of Clinical Oncology (incl. Conference Abstracts)
- Clinical Trial Registries
- HTA Agencies with existing HSS
- Newswires (medical and/ or oncology news)
- Medical Journals
- Pharmaceutical Companies

Figure 3.1-1: Main categories of information sources

3.1.2 Regulatory Authorities

FDA – U.S. Food and Drug Administration

FDA homepage provides information about drug approvals in the USA

The U.S. Food and Drug Administration (FDA) is an agency within the Department of Health and Human Services and is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health [20]. Concerning drugs, FDA regulates product approvals, OTC and prescription drug labelling and drug manufacturing standards. Especially the Centre for Drug Evaluation and Research (CDER) and the Office of Oncology Drug Products (OODP) which oversees development, approval, and regulation of drug treatments for cancer provide a lot of useful information on drugs on their homepages. See Table 3.1-1 for a detailed description of FDA's information sources regarding anticancer drugs.

Table 3.1-1: Details of information sources provided by FDA

Name	URL	Information
FDA Homepage	www.fda.gov	see CDER
CDER Homepage	http://www.fda.gov/cder/	1) CDER Listserv mailing lists (one weekly email containing new updates to CDER website)
	http://www.fda.gov/cder/Offices/OODP/default.htm	2) OODP – Office of Oncology Drug products (occasional notifications of new approvals, meetings, presentations, and other information from OODP – see "What's New"
FDAnews	http://www.fdanews.com/	2 free newsletter available via email after free subscription (FDAnews is the premier provider of domestic and international regulatory, legislative and business news and information for executives in industries regulated by the U.S. Food and Drug Administration)
		1) FDAnews Drug Daily Bulletin*
		2) RxTrials Institute Drug Pipeline Alert**

**targeted FDA regulatory, legislative and business news briefs in the pharmaceutical and biologics industries (daily newsletter)*

***latest news on research and development of new drugs in high-cost therapeutic areas such as oncology/haematology, cardiovascular, paediatrics, respiratory and others; issues cover U.S. and international clinical trials, medical research, drug applications and co-development activities (weekly newsletter)*

EMEA – European Medicines Agency

EMEA provides information about orphan drug designations and approved medicinal products

The European Medicines Agency (EMEA) is a decentralised body of the European Union with its headquarter in London and was established in 1995 according to the Regulation (EC) 2309/93. Its main responsibility is the protection and promotion of public and animal health through the evaluation and supervision of medicines for human and veterinary use [21]. The EMEA is responsible for the scientific evaluation of applications for European marketing authorisation for medicinal products (centralised procedure). Under the centralised procedure, companies submit a single marketing authorisation application to the EMEA. Once granted by the European Commission, a centralised (or 'Community') marketing authorisation is valid in all European Union (EU) and EEAEFTA states (Iceland, Liechtenstein and Norway).

The agency consists of five scientific committees, composed of members of all EU and EEAEFTA states, which conduct the main scientific work of the Agency: the Committee for Medicinal Products for Human Use (CHMP), the Committee for Medicinal Products for Veterinary Use (CVMP), the

Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC) and the Paediatric Committee (PDCO). A sixth scientific committee – the Committee for Advanced Therapies (CAT) – will be established at the end of 2008. Information about Orphan medicinal products, applications for new products, positive opinions adopted by the Committee of Medicinal Products for Human Use (CHMP) are available on EMEA's homepage (Table 3.1-2).

Table 3.1-2: Details of information sources provided by EMEA

Name	URL	Information
EMEA	http://www.emea.europa.eu/	EMEA Mailing Lists – 3 newsletters available via email 1) Human Medicinal products list* 2) Orphan Medicinal products list** 3) Press Releases*** (CHMP, COMP)

** Information about authorised products, Opinion Summaries, Product safety Alerts, Market Withdrawals, Referrals, Orphan Medicinal Products, Herbal Medicinal Products Guidance Documents*

*** Information about Orphan Product Designation, Orphan Incentives, Committee for Orphan Medicinal Products (COMP), Quality Management*

**** EMEA Press Releases, Management Board Press Releases, CHMP Press Releases, CHMP Product Safety announcements, COMP Press Releases, HMPC Press Releases, CVMP Press Releases, CVMP Product Safety announcements, PDCO Press Releases*

PMPRB – Patented Medicine Prices Review Board

Canadian agency for drug price regulation releases semi-annually Drug Pipeline Monitor

The Patented Medicine Prices Review Board (PMPRB) is an independent quasi-judicial body established by the Canadian Parliament in 1987 under the *Patent Act* (Act). The PMPRB has a dual role, a regulatory role to protect consumers and contribute to Canadian health care by ensuring that prices charged by manufacturers for patented medicines are not excessive and a reporting role to contribute to informed decisions and policy making by reporting on pharmaceutical trends and on the R&D spending by pharmaceutical patentees. In Canada, Health Canada assesses new medicines to ensure that they conform to the Food and Drugs Act and Regulations and the PMPRB is responsible for regulating the prices [22].

The PMPRB released its first New Drug Pipeline Monitor (NDPM) in June 2007. The NDPM is a new web-based, semi-annually publication that summarizes information on new drugs that are expected to be launched in Canada within the next two to five years and could potentially have a significant impact on federal, provincial and territorial (F/P/T) drug plan expenditures (Table 3.1-3).

Table 3.1-3: Details of PMPRB Homepage

Name	URL	Information
New Drug Pipeline Monitor by PMPRB	http://www.pmprb-cepmb.gc.ca/	Bi-annual publication of NDPM – available as PDF-format on the PMPRB homepage in June and December

3.1.3 Societies of Clinical Oncology

ASCO – American Society of Clinical Oncology

leading Society in oncology provides relevant cancer news

The American Society of Clinical Oncology (ASCO) is a non-profit organization, founded in 1964, with overarching goals of improving cancer care and prevention. ASCO is the world's leading professional organization representing physicians who treat people with cancer. ASCO's members set the standard for patient care worldwide and lead the way in carrying out clinical research aimed at improving the prevention, diagnosis, and treatment of cancer [23]. The ASCO Annual Meeting is the premier event in the oncology community and the research and education presented at ASCO meetings enhance oncologists' knowledge, thereby advancing high-quality cancer care. ASCO's homepage contains a lot of oncology-related news and reports (Table 3.1-4).

Table 3.1-4: Details of ASCO Homepage

Name	URL	Information
ASCO	www.asco.org	1) see News – Cancer News - professionals (Headline news on the latest cancer research) 2) Annual ASCO Meeting* – Abstracts and "virtual meeting" are available on the homepage

**Comprehensive database of Annual Meeting abstracts and online access to lecture/slide presentations and posters from ASCO Annual Meetings*

German Society of Cancer (Deutsche Krebsgesellschaft)

society in oncology provides relevant cancer news for Germany

The German Society of Cancer (Deutsche Krebsgesellschaft, DKG) is the leading scientific-oncological society in Germany and is based in Berlin. Extensive interesting and useful information regarding meeting-highlights in oncology and anticancer drug research are available with a free subscription (DocCheck-password [24]) on the society's homepage (Table 3.1-5).

Table 3.1-5: Details of German Society of Cancer

Name	URL	Information
Deutsche Krebsgesellschaft e.V.	www.krebsgesellschaft.de/	News and Meeting-Highlights* 1) Ärzte – Aktuelles - Nachrichtenüberblick 2) Ärzte - Kongressberichte (access with DocCheck Password)

** No English version available*

ISOPP – International Society of Oncology Pharmacy Practitioners

cancer therapy-related news service

The International Society of Oncology Pharmacy Practitioners (ISOPP) will promote and enhance oncology pharmacy practice worldwide in order to improve cancer patient care. The ISOPP website contains relevant cancer therapy-related news (Table 3.1-6).

Table 3.1-6: Details of ISOPP

Name	URL	Information
ISOPP	www.isopp.org	Cancer News are available on its homepage

3.1.4 Clinical Trial Registries

ClinicalTrials

information about ongoing and completed clinical trials for anticancer drugs

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives information about a trial's purpose, who may participate, and locations. ClinicalTrials.gov is a Service of the U.S. National Institute of Health. ClinicalTrials.gov contains thousands of studies and new clinical trials are received daily but there is an option to search free of charge within the recently (within the last 60 or 14 days) added studies (Table 3.1-7).

Table 3.1-7: Details of Clinicaltrials.gov

Name	URL	Information
ClinicalTrials	www.clinicaltrials.gov	recently added studies can be easily searched - see "What's new" – added the last 60 or 14 days (sort by condition "cancer/neoplasm")

3.1.5 HTA Agencies with existing Horizon Scanning Systems

The following institutions are adept at Horizon Scanning activities and provide useful information about new/ emerging technologies including anticancer drugs on their homepages.

EuroScan

international collaboration, development of methodology and common understanding

EuroScan (International Information Network on New and Changing Health Technologies) is a collaborative network of health technology assessment agencies to exchange information and to evaluate emerging technologies [8]. Since the first meeting of EuroScan members in February 1998, the collaboration has been working together to promote a common understanding of early warning activities, develop the methodology involved in this discipline and produce a system in which experiences and findings can be shared. EuroScan developed a publicly-accessible search of the EuroScan database to facilitate access to reports published by member agencies (Table 3.1-8).

NHSC – National Horizon Scanning Centre

service for Department of Health and national policy makers in England

The National Horizon Scanning Centre (NHSC) is a member of EuroScan and part of the National Institute for Health Research. NHSC hosts the secretariat of EuroScan. The NHSC aims to provide advanced notice to the Department of Health and national policy makers in England of selected new and emerging health technologies (including changing applications and uses of existing technologies) that might require urgent evaluation, consideration of clinical and cost impact or modification of clinical guidance around 2-3 years prior to launch on the National Health Service in UK. Technology Briefings and notes produced by the NHSC since January 2000 are available on its homepage (Table 3.1-8).

CADTH – Canadian Agency for Drugs and Technologies in Health

different products: Emerging Health Technologies, Emerging Drug List

The Canadian Agency for Drugs and Technologies in Health (CADTH) is an independent, not-for-profit agency funded by Canadian federal, provincial, and territorial governments to provide credible, impartial advice and evidence-based information about the effectiveness of drugs and other health technologies to Canadian health care decision makers. CADTH is a member of EuroScan. A Horizon Scanning Service which alerts decision makers to new and emerging health technologies that are likely to have a significant impact on the delivery of health care in Canada exist since 1997 within the Health Technology Assessment Program (HTA).

The Canadian Agency for Drugs and Technologies in Health's horizon scanning products include "Issues in Emerging Health Technologies" and "Emerging Drug List" (Table 3.1-8). **Issues in Emerging Health Technologies** is a series of concise bulletins describing drug and non-drug technologies that are not yet used (or widely diffused) in Canada. **Emerging Drug List** is an online series that profiles new drugs and vaccines while they are at an early stage of development, prior to Health Canada approval. Both issues

are available to be downloaded in an electronic format (PDF) on CADTH's Homepage [25].

Table 3.1-8: Details of HTA Agencies with existing HSS

Name	URL	Information
EuroScan	http://www.euroscan.bham.ac.uk/	See "Technology Reports"
NHSC	http://pcpoh.bham.ac.uk/publichealth/horizon/index.htm	See "Technology Briefings" – restriction to „Cancer"
CADTH	http://www.cadth.ca	General homepage – see Horizon Scanning Program
	http://www.cadth.ca/index.php/en/hta/programs/horizon-scanning	1) Issues in Emerging Health Technologies 2) Emerging drug list Both issues can be downloaded as electronic version (PDF)

3.1.6 Newswires (Cancer/ Oncology/ Medical News)

Several internet information sources which provide oncology-related, cancer or medical news can be used for identifying new/ emerging anticancer drugs (Table 3.1-9).

internet information sources which provide cancer news from clinical trials and industry for health professionals on new treatment strategies

Cancer Consultants Professionals

Cancer Consultants, Inc. is a company that developed the oncology e-space. Cancer Consultants has been producing and distributing cancer information for patients and professionals since 1998. The purpose of Cancer News is to provide summaries of new treatment strategies as they are discovered and reported by cancer physicians around the world. Original news summaries from peer-reviewed journals and oncology meetings are provided daily.

PharmaLive – R&D News

gives insight in R&D strategies

PharmaLive provides broad coverage of pharmaceutical business, product marketing, and clinical research information. It is a product of the Canon Communications Pharmaceutical Media Group and since 1995 R&D Directions are published which provides extensive coverage of pharmaceutical product development and insight into successful R&D strategies.

Therapeutics daily - Oncology

on development, sales, and marketing

Therapeutics Daily – Oncology provides news and information focusing on the development, sales, and marketing of medicines that treat cancer. It is a product of the Canon Communications Pharmaceutical Media Group too and created by PharmaLive.

PhRMA – Medicines in Development Database

database of medicines in trials

PhRMA represents the leading Pharmaceutical Research and Manufacturers of America and provides a database with includes medicines currently in clinical trials or at the FDA for review.

Medscape Haematology-Oncology News

daily news on haematology-oncology

Medscape offers specialists, primary care physicians, and other health professionals timely comprehensive and relevant clinical information. One speciality site includes daily haematology-oncology news. Medscape is organized by medical specialty, with each supported specialty having its own customized website. Specialty content is evaluated, created, and presented under the guidance of a Medscape program director and a medical professional advisory board

Medknowledge

Germany only

Medknowledge-Germany provides information about medicine in Germany e.g., new drugs in pipeline.

Drug Information Online

independent

Drugs.com is a popular, comprehensive and up-to-date source of drug information online. It presents independent information in a clear and concise format for healthcare professionals and complies with the HONcode standard for trustworthy health information.

Pharmatrix

independent, Germany only

Pharmatrix provides independent information on drugs in development or newly approved in Germany and other countries for health professionals. Pharmatrix complies with the HONcode standard for trustworthy health information.

NeLM

medicines in Great Britain

The National electronic Library for Medicines (NeLM) (formerly known as DrugInfoZone) provides timely and relevant information on medicines and support prescribing to the NHS at the point of care. The NeLM is part of the National Library for Health (UK).

The Ones to Watch

drugs in pipeline

Thomson Reuters provides a quarterly review of the latest phase changes in the pharmaceutical pipeline in “The Ones to Watch”.

Table 3.1-9: Details of selected Newswires related to oncology

Name	URL	Information
CancerConsultants - Physician Resource Centre	http://professional.cancerconsultants.com/	See „conference coverage" and „cancer news" and Physician Resources – Drug Pipeline
PharmaLive	www.pharmalive.com	see „Today's News - R&D News" – information about Drug Approvals, Drug Discovery und Drugs in Development
Therapeutics daily – Oncology	http://www.therapeuticsdaily.com/	Choose channel "oncology" – a daily newsletter is available via email after free registration
PhRMA	http://www.phrma.org	See „Medicines in Development" -„search database" restrict indication to "cancer" and choose „any company" and "any stage"
Medscape Haematology – Oncology News	http://www.medscape.com/hematology-oncology/news	a daily newsletter is available via email after free registration
Medknowledge	http://www.medknowledge.de/	a weekly newsletter is available via email after free registration
Drug Information Online	http://www.drugs.com	See "Pharmaceutical News & Articles" - Pharma News, new drug approvals and clinical trials a monthly newsletter is available via email after free registration
Pharmatrix	www.pharmatrix.de	free registration with DocCheck Password via klinik-plus.de see „neue Arzneimittel"
NeLM – National electronic library for medicine	http://www.nelm.nhs.uk	See "latest news" and „categories – medicines information – Horizon Scanning" (licence extension) a daily newsletter is available via email after free registration
The Ones to watch	http://www.scientific.thomson.com/pharma/forms/matters/	A quarterly report about drugs in development is available via email after free registration

3.1.7 Medical Journals

11 different medical journals included

High quality medical journals are an important source for clinical experts to stay informed about medical progress. Based on clinical experts' suggestions, we therefore included 11 medical journals as potential information sources within our HSS (Table 3.1-10). We didn't subscribe to all journals but they offer a free email alerting service (eContent Alert service or Tables of Contents and Announcements – eTOC service). After subscribing, this free service sends out alerts by e-mail whenever new content in *the selected journal* is published. The table of contents of each journal can then be scanned easily.

Table 3.1-10: Details of selected Medical Journals

Name	URL	Information
American Journal of Clinical Oncology	http://www.amjclinicaloncology.com	eContent Alert available
Annals of Oncology	http://annonc.oxfordjournals.org/current.dtl	eContent Alert available
Cancer Treatment Reviews	http://intl.elsevierhealth.com/journals/ejca	eContent Alert available
European Journal of Cancer	http://www.sciencedirect.com/science/journal/09598049	eContent Alert available
Journal of Clinical Oncology	http://jco.ascopubs.org/content/vol25/issue7/	eTOC available
The Lancet Oncology	http://www.sciencedirect.com/science/journal/14702045	eContent Alert available
Blood	http://bloodjournal.hematologylibrary.org	eTOC available
Nature Medicine	http://www.nature.com/nm/index.html	eTOC available (topics: oncology / haematology / oncology medicine
The Lancet	http://www.thelancet.com/	eContent Alert available
NEJM	http://content.nejm.org/	eTOC available
Expert Opinion on Emerging Drugs	http://www.expertopin.com/toc/emd/12/2	eTOC available

3.1.8 Pharmaceutical Companies

information from 31 different pharmaceutical companies about their R&D activities in oncology

International pharmaceutical companies provide detailed information about their research and development activities concerning new drugs in their so-called R&D or pipeline section. We included homepages of 31 well-known manufacturers of anticancer drugs in our scanning process (Table 3.1-11.) although updates of the provided information are often poor.

Table 3.1-11: Details of included homepages of Pharmaceutical Companies

Name	URL	Information
Amgen	http://www.amgen.com/science/pipe.jsp	see Science - Pipeline
Antigenics	http://www.antigenics.com/products/pipeline/	see products & technologies - product pipeline
ArQule	http://www.arqule.com/res/pip/	see product R+D - pipeline
AstraZeneca	http://www.astrazeneca.com/article/511390.aspx	see research - pipeline summary
Bayer Schering	http://www.bayerscheringpharma.de/scripts/pages/de/forschung_und_entwicklung/entwicklungsprojekte/index.php	See Research and Development – Projects- - Pipeline Overview
Bioenvision	http://www.bioenvision.com/products_pipeline.php	see products - product pipeline
Boehringer-Ingelheim	http://www.boehringer-ingelheim.com/corporate/research/rd_areas_oncology.htm	see Research and Development - R&D areas - oncology
Bristol Myers Squibb	http://www.bms.com/research/content/data/pipeline.html	see R&D - pipeline
Cell Therapeutics	http://www.cticseattle.com/products.htm	see products - pipeline
Cephalon	http://www.cephalon.com/cephalon_science/pipeline.aspx	see Science - Pipeline
Celgene Corporation	http://www.celgene.com/research/drug-research-and-development-home.aspx	see research & development - pipeline
Cytogen Corporation	http://www.cytogen.com/products/index.php	see products - pipeline
Dendreon	http://www.dendreon.com/dndn/pipeline	see pipeline
Genentech	http://www.gene.com/gene/pipeline/status/	see development - pipeline

Genzyme	http://www.genzyme.com/research/pipeline/pipe_home.asp	see or research - research pipeline
GlaxoSmithKline	http://www.gsk.com/investors/pp_pipeline_standard.htm	see investors - product portfolio - pipeline
ImClone Systems Incorporated	http://www.imclone.com/clinical.php	see clinical development
Lilly Oncology	http://investor.lilly.com/pipeline.cfm	see investors - product pipeline
Merck KGaA	http://www.merck.com/	see Merck - pipeline
MGI Pharma	http://www.mgipharma.com/wt/page/pipeline	see pipeline
Millennium Pharmaceuticals	http://www.mlnm.com/rd/pipeline/index.asp	see R&D - pipeline
Novartis Oncology	http://www.novartisoncology.com/research-innovation/pipeline.jsp?usertrack.filter_applied=true&NovaId=11787617515438637 17	see research - research innovation - pipeline
Onyx Pharmaceuticals	http://www.onyx-pharm.com/wt/page/clinical_pipeline	see clinical development - clinical pipeline
Ortho Biotech	http://www.orthobiotech.com/products.html	see products & services
OSI Oncology	http://www.osip.com/products_oncology	see products & pipeline - oncology
Pfizer	http://www.pfizer.com/research/pipeline.jsp	see research & development - pipeline
Pharmacyclics	http://www.pharmacyclics.com/wt/page/programs	see therapeutic programs
Roche	http://www.roche.com/home/science/sci_prod/sci_prod_pharmap.htm	see R&D - product pipeline - pharmaceuticals
Sanofi-Aventis	http://en.sanofi-aventis.com/rd/portfolio/p_rd_portfolio_oncology.asp	see our research - R&D portfolio - oncology
Schering-Plough	http://www.schering-plough.com/schering_plough/research/spri/index.jsp	see R&D (products in development)
Ziopharm	http://www.ziopharm.com/clinical_dev.php	see clinical development

3.2 Scanning Process

weekly scanning of information sources on the Internet, eAlerts and eNewsletters

Within the selection process (see chapter 2.3) of information sources we concurrently determined the frequency of information update carried out by each website. In preparation of the later arranged feasibility study we installed a separate email account for our project called **'hss-onko@hta.lbg.ac.at'** which could be used for subscriptions to eContent Alerts and listservs and where all emails from our information sources could be collected for the scanning process. Afterwards, over a period of two weeks we concentrated on making ourselves familiar with each website by scanning the sources daily and collecting data on new/ emerging anticancer drugs. Due to our experiences from this testing phase and the availability of eContent Alerts and listservs via email from several providers we preliminarily decided to scan the above mentioned information sources from the categories Regulatory Authorities, Societies of Oncology, Clinical Trial Registries, HTA Agencies with existing HSS, Newswires (medical and/ or oncology news) and medical Journals once a week. Homepages of pharmaceutical companies are scanned only once a month because of rare updates. The duration of the whole process depends on the amount of emails received and the amount of data on new/ emerging anticancer drugs which should be extracted (see below).

3.3 Data Extraction

collection of detailed information about identified anticancer drugs

During the scanning process any data on new/ emerging anticancer drugs according to the defined inclusion criteria (see chapter 2.1.) were collected and tabulated in a previously prepared Excel spreadsheet. We collected data concerning the following parameters:

- Drug name (brand name, if available)
- Company/developer
- Short drug description (drug class, mode of action)
- Patient indications
- Approximate number of patients with disease in Austria (Source: Statistics Austria [1])
- Stage of development
- Has the technology already been approved in the EU for other indications (incl. orphan drug status) or by the FDA?
- Costs in Euro € (if available)

permanent scanning, identification and extraction of data: 6-10 hours per week

The aim of data extraction is to gather basic information of sufficient quality on new/ emerging anticancer drugs and their applications. Finally, the extraction sheet should comprise a detailed description of all identified anticancer drugs and should be appropriate for our expert panel to apply the defined prioritisation criteria (i.e. to enable subsequent priority setting).

The scanning and data extraction process can be summarized as follows: the optimal and necessary scanning frequency is set at once a week and once a month for the companies' websites. The time which is needed to scan the 63

sources and to extract data on identified anticancer drugs fulfilling the inclusion criteria spans from 6 to 10 hours a week.

3.4 Priority Setting Criteria

seven criteria with an underlying score were included in our priority setting instrument

Based on four predefined categories (i.e., phase of development, indication, drug description, clinical/ economic impact), the criteria collected from literature [10-13] and after consultation with our clinical experts, we determined a final priority setting instrument of seven criteria (Table 3.4-1). Each criterion has several answer options with a deposited score ranging from 0 to 2 (3). We did not weight our criteria (each criterion was defined as equivalent to the others and none of the criteria was more important than the others).

Table 3.4-1: Criteria for Priority Setting

criterion	answer options	score
1) When does the technology appear likely to be launched in Austria/in the EU?	it is already available/adopted	0
	in 0-2 years	2
	in 2-4 years	1
	in 4 or more years	0
2) Burden (severity) of disease (mortality, morbidity, quality of life)	high	2
	moderate	1
	low	0
	unknown	0
3) Estimated number of patients with disease in Austria (per year)	more than 1000	3
	500-1000	2
	100-500	1
	0-100	0
4) Is this an innovative drug for a disease with no satisfactory standard treatment?	yes	2
	no	0
	don't know	1
5) Is there potential for a significant health benefit to the patient group (high clinical impact)?	major	2
	moderate	1
	minor	0
	unknown	0
6) Is there potential for a significant impact on hospital drug budgets if the technology diffuses widely (because of expected moderate to high unit costs and/or because of high patient numbers)?	major	2
	moderate	1
	minor	0
	unknown	0
7) Is there potential for inappropriate diffusion (too fast or too slow) or use (off-label) of the technology?	major	2
	moderate	1
	minor	0
	unknown	0

The maximum score which could be obtained is 15 and the following cut-off points were chosen to define high relevant anticancer drugs:

drugs with a score of 10 to15 are considered for early assessment

- Score 10-15: highly relevant drugs which should be considered for early assessment
- Score 5-9: drugs which should be monitored
- Score 0-4: drugs which should be dropped

3.5 Feasibility Study

3.5.1 Procedure

identification of 116 different anticancer drugs within a scanning period of 3 months

From January 1, 2008 to March 31, 2008 one person scanned the selected information sources and the information received via email (eNewsletters, eTOCs) weekly. Data on new and emerging anticancer drugs were collected and entered into the prepared Excel spreadsheet. The weekly scanning and data extraction process took approximately 8 hours. Subsequent to the 3-month scanning period, the extracted data were revised and adapted to the experts' needs for the prioritisation process. Finally, after removal of duplicates (overlap in results from different information sources) we obtained a list of 140 hits comprising 116 different anticancer drugs. This difference indicates that some drugs are in development for various indications. About 90 out of the 140 hits are in development stage clinical trial phase II. The preparation of this final extraction sheet took an additional 8 hours.

3.5.2 Results

prioritisation by 3 experts revealed 5 highly relevant anticancer drugs

From April to the beginning of May the prioritisation step was carried out, with the aim to narrow down the original list to a manageable amount of anticancer drugs to be subjected to further evaluation. The whole list (Excel Spreadsheet) in alphabetical order was sent to our expert panel who applied individually the predefined prioritisation criteria to the 140 hits and who commented on the feasibility of the instrument and the HSS in general. The completed lists from our 3 experts were then analysed separately by translating and quantifying their answers into the corresponding achieved scores (see Table 3.4-1): Each item received a score from each expert depending on the respective selected answer options. The results were compared to each other. Then a mean score was calculated for each anticancer drug to achieve a final ranking. The analysis resulted in a narrowed list comprising the 5 highest scoring drugs which should be considered for further evaluation. Figure 3.5-1 shows the results from the prioritisation process.

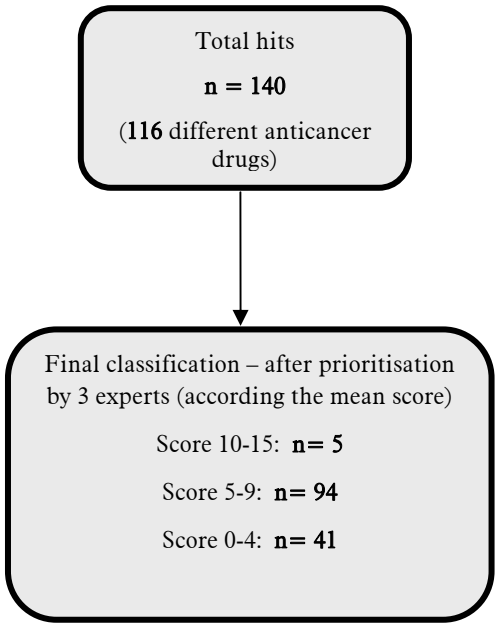

Figure 3.5-1: Results of the prioritisation process

usefulness of results is limited by clear differences in prioritisation by experts:

consensus proposed

The detailed results (single and mean score for the 140 hits respectively 116 different anticancer drugs) from the prioritisation process by the 3 clinical experts is provided in the appendix (see chapter 7). The results have to be interpreted carefully because there was to some extent great variability in the prioritisation by the individual experts and they reported several unexpected difficulties while working hands-on with the provided data and the priority setting instrument (see chapter 3.5.3). The calculation of a mean score for each anticancer drug was not leading to useful results and therefore was an insufficient method. According to Douw and Vondeling [11] in most HSS the final decision on which anticancer drugs to assess is based on agreement by consensus, this could therefore be an additional step in our priority setting process .

3.5.3 Experts' Comments on the Procedure

An additional task of our expert group was to comment on the feasibility of the proposed procedure regarding the following important parts of a HSS:

Sources and provided information on anticancer drugs

Although the time period of scanning the selected information sources was only three months, the specified information sources seem to be suitable for an HSS in oncology. Some information from different sources about anticancer drugs was still overlapping so that in the context of a continuous scanning process the sources for identification should be monitored and if necessary, supplemented by others or reduced by redundant ones.

The parameter for data extraction (see chapter 3.3) were chosen adequately but extracted data sometimes were not detailed enough to apply the priority setting criteria. Especially the parameters "drug description" and "patients' indication" should be filled out in more detail and short information on preliminary efficacy results from clinical trials should be mentioned. All experts had to use additional sources (e.g. publications, meeting abstracts) to get an idea about the efficacy of the described anticancer drugs. In addition, more precise incidence or prevalence data regarding Austria for the described diseases would be helpful.

more detailed description of patients' indication and information about efficacy necessary

Identified anticancer drugs

A lot of drugs for cancer treatment appear on the horizon but never reach market entry. Especially in oncology many drugs which are tested in clinical phase II trials fail to enter the more important phase III trials because they are lacking positive efficacy results. Identifying and selecting all drugs in development stage phase II is not necessary because only results from completed clinical trials phase II determine the drugs' future. Experts suggested as a kind of filtering instrument prior to the real prioritisation process to concentrate on anticancer drugs with positive phase II results from completed clinical trials, on drugs with FDA fast track designation or with FDA/ EMEA Orphan drug designation and on drugs currently in clinical trials phase III or in the phase of adoption.

focus on FDA fast track designations, orphan drug status and anticancer drugs in phase III

Comments on prioritisation criteria

In general, the defined priority setting instrument was applicable and useful, but criteria 4, 6 and 7 (see chapter 3.4) should be specified more precisely to ensure a consistent prioritisation by different experts:

more precise definition of criterion 4, 6 and 7

- Criterion 4 "innovative drug for a disease with no satisfactory standard treatment": A suggestion was made to divide the question into one for "innovative drug" and one for "disease with no satisfactory treatment", because these two features are not necessarily linked
- Criterion 6 "impact on hospital drug budgets": this should be discussed further because some new anticancer drugs also affect social insurance budgets due to their using oral applications and requiring prescriptions for outpatients; for most drugs no cost information was available. Therefore, the expert panel should discuss how to deal with missing cost data
- Criterion 7 "potential for inappropriate diffusion": the experts should elaborate on what inappropriate diffusion could be concerning anticancer drugs e.g. reasons for off-label use

Furthermore, all comments mentioned that positive efficacy results from preliminary clinical trials should be the most important criterion for selection and further considerations. Therefore, the use of weighted criteria must be discussed.

Comments on the prioritisation process and the size of the expert panel

multistage process and more experts with expertise in specific tumour entities

On average the experts needed about 4 hours to apply the priority setting criteria to the 140 identified items, but could have needed longer if more information had been available. Due to the high number of drugs in development phase II, the lacking efficacy information and the imprecise definition of some criteria, experts could not do an unambiguous prioritisation. The exchange of information on the identified drugs in the context of periodical joint meetings or by using the Delphi technique would be necessary to reach a consensus on the most relevant new/ emerging anticancer drugs which should be considered for early assessment and finally for decision making and prospective budget planning. In addition, they mentioned that three experts might not be able to cover the wide field of developments in haematology and oncology and they suggested constituting a more specific expert panel (e.g. separate experts for solid tumours, haematological neoplasm and for the large cancer entities like e.g. breast cancer, lung cancer, colorectal cancer) to improve the prioritisation process.

3.6 Early Assessment

method of early assessment will be explored as one of the next steps

The step of early assessment was not part of our feasibility study, but we compared different formats from three well-known agencies with HSS and propose a method which has to be explored and discussed within the next steps of our HSS concept (see chapter 4.3).

3.6.1 Format

We compared the formats from Danish Health Technology Alerts (Danish Centre for Evaluation and HTA), from NHSC's Technology briefings and Canadian Emerging Drug Lists (CADTH) to get an idea about a suitable approach for our HSS in oncology (Table 3.6-1).

Table 3.6-1: Comparison of different formats (selection, not exhaustive)

	Danish Health Technology Alert	Technology briefings (NHSC)	Emerging Drug List (CADTH)
Content structure	Summary Disease Current treatment New treatment Use in Denmark Evidence (efficacy, safety) Ongoing trials Costs Implementation References	Target group Technology description Innovation Place of use Availability Relevant guidance Clinical need/ burden of disease Existing treatments Efficacy/ safety Estimated costs Potential impact References	Indication Current regulatory status Description Current treatment Cost Evidence (efficacy, safety) Commentary References
Length	4 pages	6 pages	4 pages

An early assessment should summarize the best available evidence to estimate in particular clinical and financial consequences of the new/ emerging drug. In view of the above mentioned formats of early assessments, we suggest the following structure and a length of 4 to 6 pages depending on the amount of available information:

- Technology description
- Indication
- Burden of disease in Austria
- Current treatment
- Current regulatory status/ Availability
- Evidence (efficacy, safety)
- Ongoing trials
- Estimated costs
- Commentary/ recommendation
- References

The structure of early assessments should be consistent with the LBI-HTA's internal manual for systematic reviews [26]. One of the challenges of early assessment in HSS is the lack of evidence and the limited access to information on new technologies. Therefore, the involvement of pharmaceutical companies to provide information should be considered to ensure the inclusion of comprehensive data on the selected new/ emerging anticancer drug for early assessment.

3.6.2 Process and Dissemination

target groups of the HSS in oncology are health professionals, hospital administrators, drug commissions and social insurance organisations

Early assessments will be performed by the LBI-HTA. The number of assessments produced will depend on the resources available and the number of relevant anticancer drugs considered for early assessment per year. Peer review is already a standard process at the LBI-HTA and should also be performed for early assessments to guarantee high quality output. The detailed process has to be discussed further and explored by applying the method to concrete examples of relevant anticancer drugs. The aim should be to generate a standardized, transparent and systematic method for conducting early assessments in accordance with already existing methods at the LBI-HTA [26].

The dissemination of reports is the final step of our HSS. Potential target groups of our Horizon Scanning reports are health professionals, hospital administrators, drug commissions and social insurance organisations. The final dissemination strategy yet to be defined but could include individual communication with decision makers, announcements within our monthly HTA newsletter, presentations in the context of our quarterly 'HTA in hospital-meetings and online availability at the LBI-HTA's publication index.

4 Discussion

4.1 Concept of Horizon Scanning in Oncology

concept provides a basis for implementation of a HSS at the LBI-HTA

This concept provides a basis for discussion on the implementation of an Austrian Horizon Scanning System in oncology. Based on a literature search and advice from experts, we developed a concept of a HSS which focuses on anticancer drugs and tested the feasibility of its two main steps: identifying new/ emerging anticancer drugs and determining their priority rating.

The principle structure of the Horizon Scanning System is well defined but the feasibility study showed that further improvements are necessary to ensure an effective HSS. In particular, revisions could be made in the procedures for collecting data for new/ emerging anticancer drugs and for prioritising medicines by clinical experts. For the latter, two important aspects have to be considered: first, the size and composition of the expert panel, and second, the priority setting instrument itself, because the priority setting process is highly dependent on the individuals involved in the process [12]. A review of Noorani et al.'s comparison of various priority setting approaches can be used for optimizing our prioritisation method [27].

Clinical experts are a key element of the HSS but their ability to predict an anticancer drug's impact remains unclear. A recent study concluded that information from experts may be valuable as part of a process aimed at efficiently selecting technologies for evaluation [28]. For the expert panel responsible for the selection of anticancer drugs for further evaluation, we suggest involving several clinical experts with specific expertise in one single clinical speciality of oncology (e.g., lung cancer, breast cancer) to ensure a more certain and valid selection of relevant anticancer drugs. Due to the fact that priority setting is the most critical step within the HSS (i.e. to miss an important drug or to select unimportant ones) we have to re-adapt our criteria (e.g., using weighted criteria), to introduce a multistage process and to provide clinical expert training and time to adapt to the priority setting instrument [11].

characteristics and components of an effective early warning system are described in literature

Murphy et al. investigated the important characteristics and components of an effective early warning system and the results can be used as a guide for setting up such a system [29]. Our HSS should be designed to comply with the following five characteristics that were identified as fundamental (i.e. highly important) and crucial:

- The information in the early warning system output should be relevant to the customer in terms of the finally assessed anticancer drugs having an impact on Austrian hospitals (clinical and financial consequences)
- The system should be independent of industrial or commercial influences: this structural component is already fulfilled by the LBI-HTA and will also apply to the HSS which will be part of the agency
- There should be sufficient funding and staffing of the early warning system to enable its aims: that is an important point which must be considered before the final implementation of the HSS

- A clearly defined route for the system outputs to reach decision makers must exist: this will be part of the definition of a final dissemination strategy
- Defined customers for the system outputs are needed: our project was initiated by hospital decision makers who need specific and timely information about new anticancer drugs which will have effects on hospital drug budgets; so they are one potential target group for our HSS outputs

4.2 Limitations of the Proposed Concept

strengths and weaknesses, revisions

Given the very short amount of time we had to complete our feasibility study, we believe our method explored the strengths and limitations of a proposed Horizon Scanning System in the best way possible. The main limitations of the proposed concept can be summarized as follows:

- Information Sources: First, we did not examine overlap between the sources. Second, company websites providing limited information on emerging anticancer drugs were used as sole source of information from the industry on product pipelines instead of direct contact with drug companies.
- Data collection on identified anticancer drugs: First, we did not collect efficacy data from clinical trials which would be necessary for the subsequent prioritisation process. Second, in a large part no cost information for drugs was available.
- Filtering step: We did not include a filtering step leading to the identification of a lot of anticancer drugs which are in a very early development stage and for which a prioritisation is not feasible.
- Size of expert panel: First, three clinical experts are unlikely to be able to provide appropriate comment on the possible place in therapy of all new drugs in oncology. Second, we involved only oncologist. It may be of benefit to engage representatives of drug commissions (e.g., pharmacologists) in the process.
- Prioritisation criteria and process: The prioritisation process has not turned out satisfactory. The usefulness and its value should be studied further.

Shortcomings could be eliminated by conducting a follow-up feasibility study that includes modifications like: a more specific expert panel, a revised priority setting process, inclusion of an early assessment step and involvement by target groups (e.g. hospital managers, drug commissions) in the assessment and dissemination process to ensure useful outputs for decision making (e.g. budget planning, changes in clinical practice).

4.3 Approach to Implementation

next steps: public presentations, resource planning, setting up organizational structure etc.

A plan to implement an effective HSS at the LBI-HTA should comprise the following steps:

- Setting up of an organizational structure (financial and human resource needs and resource planning)
- Presenting the present concept to experts in HSSs (at HTAi Conference 2008 in Montreal, Canada)
- Assembling an extended prioritisation panel comprising clinical experts with expertise in specific tumours and representatives of drug commissions
- Definition of a filtering step prior to the real prioritisation process (e.g., concentration on anticancer drugs with positive phase II results from completed clinical trials, discussion of the optimum time horizon)
- Determining a multistage priority setting process, the definition of decision rules/ cut-off points to arrive at an overall judgment on the relevance of emerging anticancer drugs, and provision of expert training in the application of prioritisation criteria
- Preparing a final concept which includes proposed modifications (e.g. inclusion criteria for drugs, more detailed data collection, definition, scoring, weighting of prioritisation criteria)
- Giving presentations to target groups/ customers (e.g. drug commissions) and discussing the format of early assessment and dissemination strategy
- Planning and organising a more extensive follow-up feasibility study and subsequent evaluation of the HSS and its outputs
- Starting the regular scanning of the selected information sources
- Joining EuroScan and exchanging information on new/ emerging anticancer drugs with other agencies

5 Conclusion

establishment of the HSS in oncology and monitoring of its value for decision makers

The HSS, established at a national level, should provide decision makers in hospitals with essential information to reduce a premature introduction of new anticancer drugs into clinical practice across Austria which can lead to patient harms and inadequate use of resources and thereby advance good quality and innovative cancer therapy in Austria and elsewhere.

The establishment of such a HSS should be based on the concept proposed as well as considerations arising from the feasibility study results. The operation and output of a HSS will need to be monitored and evaluated to judge its value for decision makers. Factors to be weighed include the timeliness and quality of information on new/ emerging anticancer drugs and their potential consequences.

In any case, each round of scanning is likely to result in the identification of fewer new/ emerging anticancer drugs and more often the same drugs will be monitored moving through the different stages before market introduction. We therefore estimate only 20-30 new entries each year and about five qualifying for early assessment.

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7 Appendix

Table 7-1: Detailed results from the feasibility study (identified anticancer drugs and their prioritisation by 3 experts

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
1	ABT-869	Genentech	small molecule vascular endothelial growth factor (VEGF) receptor-based kinase inhibitor; tablets (oral)	hepatocellular carcinoma (HCC)	872 (liver cancer)	Phase II	No	NA				0	7	3	**3**
	ABT-869	Genentech	small molecule vascular endothelial growth factor (VEGF) receptor-based kinase inhibitor; tablets (oral)	in combination with paclitaxel, for disease progression in metastatic breast cancer	4832 (breast cancer in women)	Phase II	No	NA		maybe an oral alternative to bevacizumab		0	12	3	**5**
2	Acadesine (Acadra)	Protherics	novel nucleoside analogue, activates adenosine monophosphate-activated protein kinase (AMPK) and induces apoptosis	B-CLL	964 (leukaemia, all forms)	Phase I/II	EMEA orphan designation since 2005	NA		multiple new drugs in CLL coming		0	4	1	**2**
3	ADH-1	Adherex Technologies	Targets N-cadherin, a protein present on certain tumor cells and established tumor blood vessels.	in combination with melphalan for melanoma	1.169 (malignant melanoma)	Phase IIb	FDA orphan drug designation for the treatment of Stage IIB/C, III, and IV malignant melanoma, in Feb 2008	NA		new good treatment for melanoma existing		0	12	3	**5**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
4	AEZS-108 (AN-152)	Aetrena Zentaris	a hybrid molecule composed of a synthetic peptide carrier and doxorubicin, LHRH agonist	LHRH receptor-positive ovarian and endometrial cancer	783 (ovarian cancer) 951 (endometrial carcinoma)	Phase II	No	NA				0	7	2	**3**
5	Aflibercept (VEGF-Trap)	Sanofi-Aventis	unique fusion protein that binds all forms of Vascular Endothelial Growth Factor-A, Angiogenesis-inhibitor	advanced ovarian cancer, third line	783 (ovarian cancer)	Phase II	No	NA		multiple VGEF based therapies under way		0	8	3	**4**
6	Alpharadin	Algeta	radiopharmaceutical based on the alpha particle emitter radium-223	treatment for bone metastases in hormone-refractory prostate cancer (HRPC)	5.416 (prostate cancer, malignant)	Phase II	No	NA		technically difficult only in major centres possible		0	5	4	**3**
7	Alvespimycin	Kosan Biosciences	Hsp90-inhibitor (second generation)	HER-2 positive metastatic breast cancer	4832 (breast cancer in women)	Phase II	No	NA				0	13	4	**6**
8	Alvocidib (Flavopiridol)	Sanofi-Aventis	cyclin-depending Kinase-Inhibitor (CDK)	refractory chronic lymphatic leukaemia (CLL)	964 (leukaemia, all forms)	Phase II/III	No	NA		multiple new drugs in CLL coming		0	9	3	**4**
9	AMG-479	Amgen	human monoclonal antibody that binds to insulin-like growth factor-1 receptor	confirmed HR-positive, locally advanced or metastatic breast cancer	4832 (breast cancer in women)	Phase II	No	NA				0	14	3	**6**
10	Amrubicin	Pharmion, Celgene	third-generation synthetic anthracycline	small-cell lung cancer (SCLC)	3.864 (lung cancer, all forms)	Phase III	EMEA orphan drug status; FDA orphan drug in March 2008 for SCLC	NA				8	9	4	**7**
11	ARC 197	ArQule	C-Met Inhibitor, orally administered drug	pancreatic cancer	1.388 (pancreatic cancer)	Phase II	No	NA				0	10	5	**5**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
12	ARC 501	ArQule	E2F1 Pathway Activator	monotherapy in head and neck cancer	1.029 (head and neck cancer)	Phase II	No	NA				0	1	3	**1**
13	Aroplatin	Antigenics	third-generation platinum chemotherapeutic, liposomal formulation	colorectal cancer	4.849 (colorectal cancer)	Phase II	FDA orphan drug designation for malignant mesothelioma	NA				0	4	5	**3**
14	Asentar (DN 101)	Schering Plough	high-dose oral formulation of calcitriol, a potent hormone that exerts its effects through the vitamin D receptor (VDR)	in combination with Taxotere for Prostate cancer	5.416 (prostate cancer, malignant)	Phase III	No	NA				0	10	5	**5**
15	Axitinib	Pfizer	VEGF-Tyrosinkinase-Inhibitor, angiogenesis- inhibitor	second-line treatment of patients with metastatic colorectal cancer	4.849 (colorectal cancer)	Phase II	FDA orphan drug designation for pancreatic cancer in July 2007	NA				0	13	4	**6**
	Axitinib	Pfizer	VEGF-Tyrosinkinase-Inhibitor, angiogenesis- inhibitor	advanced pancreatic cancer	1.388 (pancreatic cancer)	Phase II/III	FDA orphan drug designation for pancreatic cancer in July 2007	NA				0	14	5	**6**
	Axitinib	Pfizer	VEGF-Tyrosinkinase-Inhibitor, angiogenesis- inhibitor	Refractory Metastatic Renal Cell Cancer	1.224 (kidney cancer)	Phase II	FDA orphan drug designation for pancreatic cancer in July 2007	NA		bevacizumab already registered		0	5	3	**3**
	Axitinib	Pfizer	VEGF-Tyrosinkinase-Inhibitor, angiogenesis- inhibitor	Advanced thyroid cancer	686 (thyroid cancer)	Phase II	FDA orphan drug designation for pancreatic cancer in July 2007	NA				0	4	4	**3**
16	AZD0530	Astra Zeneca	orally available, dual-specific, Src/Abl kinase inhibitor	advanced ovarian cancer	783 (ovarian cancer)	Phase II	No	NA				0	8	2	**3**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
17	AZD2281	Astra Zeneca	PARP inhibitor	breast cancer	4832 (breast cancer in women)	Phase II	EMEA orphan drug status for ovarian cancer in Dec 2007	NA				0	15	3	**6**
18	AZD6244 (ARRY-142886)	Astra Zeneca	MEK inhibitor	Unresectable AJCC Stage 3 or 4 Malignant Melanoma	1.169 (malignant melanoma)	Phase II	No	NA				0	11	4	**5**
19	Bavituximab	Peregrine Pharmaceuticals	monoclonal antibody	advanced breast cancer, combination with docetaxel	4832 (breast cancer in women)	Phase II	No	NA				0	1	3	**1**
20	bendamustine (Treanda)	Cephalon	alkylating drug	relapsed indolent Non-Hodgkin's Lymphoma - progress after/during rituximab regime	979 (Non-Hodgkin lymphoma)	Phase II	Extension of indication; FDA approval for CLL in March 2008; approved in Germany	Ribomustin 25mg: 50€		Bendamustine works in multiple indications CLL, Myeloma already available	data presented on ASH 07	5	5	4	**5**
21	Bevacizumab (Avastin)	Genentech	anti-VEGF antibody	ovarian cancer	783 (ovarian cancer)	Phase II	Extension of indication; EMEA approval for breast cancer, CRC, NSCLC, RCC	Avastin 400mg: 1300€				11	11	4	**9**
	Bevacizumab (Avastin)	Genentech	anti-VEGF antibody	in combination with erlotinib in advanced or metastatic liver cancer	872 (liver cancer)	Phase II	Extension of indication	Avastin 400mg: 1300€				9	5	5	**6**
	Bevacizumab (Avastin)	Genentech	anti-VEGF antibody	relapsed glioblastoma multiforme (GBM)	638 (all brain and CNS tumours)	Phase II/III	Extension of indication	Avastin 400mg: 1300€				8	11	6	**8**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
22	Bexarotene (Targretin)	Cephalon	inhibition of Retinoid-X-Receptors, synthetic retinoid, orally	in Chemotherapy-Naive Patients With Advanced or Metastatic Non-Small-Cell Lung Cancer, in combination with cisplatin and vinorelbine	3.864 (lung cancer, all forms)	Phase III	EMEA approval for cutanous T-cell lymphoma since 2001	Targretin 75mg 100 Kps: 1780€				8	3	6	**6**
23	BIBW 2992*	Boehringer Ingelheim	dual EGFR/HER2 (ErbB2) tyrosine kinase inhibitor, second generation	NSCLC (late stage)	3.864 (lung cancer, all forms)	Phase III	Fast Track Designation status by the FDA in Feb 2008	NA				10	14	5	**10**
24	Brivanib (BMS-582664	Bristol-Meyers-Squibb	vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor	metastatic colorectal cancer	4.849 (colorectal cancer)	Phase II/III	No	NA		multiple alternatives		12	6	4	**7**
25	Brostallicin	Cell Therapeutics	a synthetic DNA minor groove binding agent	first-line single-agent chemotherapy in patients with advanced or metastatic soft tissue sarcoma	NA	Phase II	No	NA				0	1	4	**2**
26	CC-4047 (pomalidomide / actimid)	Celegene	thalidomide analogue	metastatic hormone refractory prostate cancer (HRPC)	5.416 (prostate cancer, malignant)	Phase II	No	NA				10	10	3	**8**
27	CDX-110	Celldex Therapeutics	a EGFRvIII Vaccine, Immunotherapy	Radiation and Temozolomide in Patients with Newly Diagnosed Glioblastoma Multiforme	638 (all brain and CNS tumours)	Phase II/III	FDA orphan drug status for glioblastoma multiforme in Dec 2007	NA				7	9	4	**7**
28	Cediranib (Recentin)	Astra Zeneca	oral VEGFR-Tyrosinkinase-Inhibitor	metastatic colorectal cancer	4.849 (colorectal cancer)	Phase III	No	NA				9	8	4	**7**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
29	Lestaurtinib (CEP-701)	Cephalon	receptor tyrosine kinase inhibitor	AML	964 (leukaemia, all forms)	Phase II	FDA orphan drug status for AML in April 2006 and EMEA orphan drug in 2006	NA				0	8	3	**4**
30	Cetuximab (Erbitux)	Merck	in combination with gemcitabine and cisplatin	advanced pancreatic cancer	1.388 (pancreatic cancer)	Phase II	Extension of indication; approved for colorectal cancer and head and neck cancer by EMEA	Erbitux 100mg: 220€				11	10	6	**9**
	Cetuximab* (Erbitux)	Merck	in combination with cisplatin/vinorelbine	first-line therapy in EGFR-expressing advanced non-small-cell lung cancer	3.864 (lung cancer, all forms)	Phase II	Extension of indication; approved for colorectal cancer and head and neck cancer by EMEA	Erbitux 100mg: 220€				12	11	6	**10**
31	Cloretazine	Vion Pharmaceuticals	alkylating drug	relapsed AML, in combination with cytarabine	964 (leukaemia, all forms)	Phase III	FDA orphan drug status since 2005	NA				4	3	4	**4**
32	Tremelimumab (CP-675206)	Pfizer	CTLA4-rezeptor Antagonist	Melanoma	1.169 (malignant melanoma)	Phase III	No	NA				7	10	3	**7**
33	Darinaparsin	Ziopharma	a new class of organic arsenicals	advanced myeloma	NA	Phase II	No	NA				0	3	3	**2**
34	DCVax	Northwest Biotherapeutics	brain cancer vaccine	Glioblastoma multiforme	638 (all brain and CNS tumours)	Phase II	approved in Switzerland since Sept 2007	NA				0	9	5	**5**
35	Deforolimus	Merck	Inhibitor of mTOR(mammalian Target of Rapamycin)-Kinase	metastatic soft-tissue and bone sarcomas	NA	Phase III	No	NA				8	6	7	**7**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
36	Degarelix (Firmagon)	Ferring	GnRH blocker, androgen deprivation therapy	advanced prostate cancer	5.416 (prostate cancer, malignant)	Phase III	No	NA		me too drug		9	7	5	**7**
37	Denosumab	Amgen	human monoclonal antibody, targets the receptor activator of nuclear factor kappa B ligand ("RANKL"),	multiple myeloma	NA	Phase II	No	NA		drug is in phase 3 -> supportive therapy alternative to bisphosphonates		0	11	5	**5**
	Denosumab*	Amgen	human monoclonal antibody, targets the receptor activator of nuclear factor kappa B ligand ("RANKL"),	Prostate cancer	5.416 (prostate cancer, malignant)	Phase III	No	NA		drug is in phase 3 -> supportive therapy alternative to bisphosphonates		13	13	5	**10**
38	E10A	Double Bioproduct Inc	Adenovirus-Mediated Endostatin **Gene** (E10A)	head and neck cancer	1.029 (head and neck cancer)	Phase II	No	NA				0	4	3	**2**
39	Eribulin (E7389)	Eisai	synthetic analogue of halichondrin B (HB),	third-line treatment of advanced breast cancer in patients who were pre-treated with anthracycline, taxane and capecitabine	4.832 (breast cancer in women)	Phase III	No	NA				12	4	2	**6**
40	Edotecarin	Pfizer	topoisomerase inhibitor	Glioblastoma multiforme	638 (all brain and CNS tumours)	Phase III	No	NA				6	8	6	**7**
41	Elacyt	Clavis	elaidic acid ester of the antimetabolite cytarabine	first line, single agent therapy in metastatic malignant melanoma	1.169 (malignant melanoma)	Phase II	No	NA				0	5	3	**3**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
42	Elesclomol	Synta Pharmaceuticals and GSK	increase in oxidative stress – the level of reactive oxygen species (ROS), novel mechanism	stage IV metastatic melanoma	1.169 (malignant melanoma)	Phase III	FDA orphan drug status for melanoma in Jan 2008	NA				7	11	3	**7**
43	EndoTAG-1	Medigene	in combination with gemcitabine	in pancreatic cancer	1.388 (pancreatic cancer)	Phase II	No	NA				0	6	3	**3**
44	Enzastaurin	Lilly	oral serine/threonine kinase inhibitor	Second or Third line Therapy of NSCLC	3.864 (lung cancer, all forms)	Phase II	No	NA				1	8	3	**4**
45	Everolimus	Novartis	serine/threonine kinase inhibitor	advanced kidney cancer	1.224 (kidney cancer)	Phase III	EMEA orphan drug status for kidney cancer in June 2007	NA				6	10	5	**7**
46	Forodesine	BioCryst Pharmaceuticals	purine nucleoside phosphorylase (PNP) inhibitor	CLL	964 (leukaemia, all forms)	Phase II	No	NA				0	3	1	**1**
47	GDC-0449	Genentech	Hedgehog antagonist	First-line therapy for metastatic colorectal cancer	4.849 (colorectal cancer)	Phase II	No	NA				0	10	3	**4**
48	Gefitinib (Iressa)	Astra Zeneca	tyrosinkinase inhibitor, orally	first-line in advanced colorectal cancer (combination with FOLFOX-4)	4.849 (colorectal cancer)	Phase II	FDA approval for NSCLC since 2003	NA			data presented on ASCO 08	10	5	4	**6**
	Gefitinib (Iressa)	Astra Zeneca	tyrosinkinase inhibitor, orally	first-line therapy followed by chemotherapy in advanced non-small-cell lung cancer	3.864 (lung cancer, all forms)	Phase II	FDA approval for NSCLC since 2004	NA				10	5	3	**6**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
49	gemtuzumab ozogamicin (Mylotarg)	Wyeth	CD33 monoclonal antibody	added to fludarabine, melphalan and allergenic haematopoietic stem cell transplantation for high-risk CD33 positive myeloid leukaemia and myelodysplastic syndrome	964 (leukaemia, all forms)	Phase I/II	EMEA recommended refusal of marketing authorisation for AML in Jan 2008	NA		only in very specialized centres used		0	6	1	**2**
50	GI-4000 Tarmogen	GlobeImmune	causes the targeted elimination of any cell containing mutations in the *ras* oncogene	NSCLC	3.864 (lung cancer, all forms)	Phase IIa	No	NA				0	10	2	**4**
51	Glufosfamide	Treshold Pharmaceuticals	alkylating drug	soft tissue sarcoma	NA	Phase II	FDA orphan drug status for pancreatic cancer in Sept 2006	NA				0	4	4	**3**
	Glufosfamide	Treshold Pharmaceuticals	alkylating drug	platinum-resistant ovarian cancer	783 (ovarian cancer)	Phase II	FDA orphan drug status for pancreatic cancer in Sept 2007	NA				0	6	2	**3**
52	GVAX	Cell Genesys	Immunotherapy	Prostate cancer	5.416 (prostate cancer, malignant)	Phase III	FDA Fast track status	NA				0	8	4	**4**
53	Hu3S193	NA	Y90 - monoclonal antibody	ovarian epithelial cancer, fallopian tube cancer, or peritoneal cavity cancer	783 (ovarian cancer)	Phase II	No	NA				0	4	3	**2**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
54	huC242-DM4	ImmunoGen	immunotoxin of a humanized monoclonal antibody C242 (MoAb HuC242) conjugated with a derivative of cytotoxic agent maytansine, DM4	metastatic or locally advanced gastric or gastroesophageal junction cancer	1.442 (gastric cancer)	Phase II	No	NA				0	4	3	**2**
55	Imatinib (Glivec)	Novartis	protein-tyrosine kinase inhibitor, orally	Unresectable Hepatocellular Carcinoma	872 (liver cancer)	Phase II	Extension of indication; EMEA approval for other indications	NA		alternatives	negative results known	7	4	1	**4**
56	IMC-1121B	ImClone	an anti-vascular endothelial growth factor receptor-2 (VEGFR-2) monoclonal antibody	liver cancer	872 (liver cancer)	Phase II	No	NA		alternatives		0	4	2	**2**
57	IMC-11F8	ImClone	against EGFR	advanced colorectal cancer	4.849 (colorectal cancer)	Phase II	No	NA		alternatives		0	6	2	**3**
58	IMC-A12	ImClone	anti-IGF-1R recombinant monoclonal antibody	metastatic pancreatic cancer	1.388 (pancreatic cancer)	Phase II	No	NA				0	10	3	**4**
	IMC-A12	ImClone	anti-IGF-1R recombinant monoclonal antibody	advanced liver cancer	872 (liver cancer)	Phase II	No	NA				0	9	3	**4**
59	IPI-504	Medimmune	A small-molecule inhibitor of heat shock protein 90 (HSP90) with antiproliferative and antineoplastic activities, IPI-504 binds to and inhibits the cytosolic chaperone functions of HSP90	advanced breast cancer	4.832 (breast cancer in women)	Phase II	FDA granted orphan drug designation for the treatment of gastrointestinal stromal tumors (GISTs) in August 2007	NA				0	9	1	**3**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
60	Ipilimumab	Bristol-Meyers-Squibb	monoclonal antibody directed against cytotoxic T-lymphocyte-associated antigen-4 (CTLA4	with dacarbazine as a first-line therapy for metastatic melanoma or as monotherapy for second-line therapy for metastatic melanoma	1.169 (malignant melanoma)	Phase II	Fast Track Designation status by the FDA in Feb 2007	NA				0	12	3	**5**
61	Ispinesib (SB-715992)	Cytokines	a novel kinesin spindle protein inhibitor	metastatic breast cancer	4.832 (breast cancer in women)	Phase II	No	NA				0	12	2	**5**
62	Ixabepilone (Ixempra)	Bristol-Meyers-Squibb	a microtubule inhibitor belonging to a class of antineoplastic agents, the epothilones	in combination with capecitabine for the treatment of patients with metastatic or locally advanced breast cancer resistant to treatment with an anthracycline, and a taxane	4.832 (breast cancer in women)	Phase II	FDA approval for breast cancer in Oct 2007	NA				10	11	2	**8**
63	Karenitecin	BioNumerik Pharmaceuticals	member of the camptothecin class, camptothecin related	advanced ovarian cancer, resistant to platinum and taxane chemotherapy drugs	783 (ovarian cancer)	Phase III	No	NA				10	9	4	**8**
64	larotaxel (XRP9881)	Sanofi-Aventis	in combination with cisplatin	first line treatment of locally advanced/metastatic urothelial tract or bladder cancer	1.705 (bladder cancer)	Phase III	No	NA				4	10	4	**6**
65	Lumiliximab	Biogen	a monoclonal antibody targeted against the CD23 antigen	CLL	964 (leukaemia, all forms)	Phase II/III	Orphan drug - EMEA positive opinion - Jan 2008, FDA orphan drug status	NA		might be effective in lot of lymphomas		7	12	3	**7**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
66	Volociximab (M200)	Biogen	anti-angiogenic α5β1 integrin inhibitor	ovarian cancer or primary peritoneal cancer, in combination with doxorubicin	783 (ovarian cancer)	Phase II	No	NA				0	10	2	**4**
67	MGCD0103	Pharmion	histone deacetylase inhibitor, orally-administered, isotype-selective HDAC inhibitor	AML	964 (leukaemia, all forms)	Phase II	EMEA orphan drug status for the treatment of Hodgkin lymphoma and for AML 2008,FDA orphan drug status in Sept 2007	NA		might work in MDS		0	11	2	**4**
68	mifamurtide (L-MTP-PE)	IDM Pharma	a lipophilic derivative of the muramyl dipeptide	non-metastatic, resectable osteosarcoma	NA	Phase III	EMEA orphan drug status in 2004, FDA orphan drug	NA				7	7	6	**7**
69	Milatuzumab	Immunomedicines	humanized anti-CD74 antibody	multiple myeloma	NA	Phase II	FDA orphan drug designation in March 2008	NA				7	11	5	**8**
70	MK0646	Merck	Insulin-Like Growth Factor Receptor Inhibitor	metastatic colorectal cancer, in combination with cetuximab and irinotecan	4.849 (colorectal cancer)	Phase II	No	NA				12	6	3	**7**
71	Motesanib*	Amgen	Multikinase-Inhibitor	First-line for NSCLC	3.864 (lung cancer, all forms)	Phase III	No	NA				11	14	5	**10**
	Motesanib	Amgen	Multikinase-Inhibitor	Thyroid cancer	686 (thyroid cancer)	Phase II	No	NA				9	10	5	**8**
	Motesanib	Amgen	Multikinase-Inhibitor	first-line breast cancer	4.832 (breast cancer in women)	Phase II	No	NA				11	14	3	**9**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
72	Naptumomab estafenatox	Active Biotech Research	a fusion protein consisting of one antigen binding fragment (Fab) from a cancer cell binding antibody and a bacterial superantigen	renal cell carcinoma	1.224 (kidney cancer)	Phase II	Orphan drug - EMEA positive opinion in Dec 2007	NA				7	7	2	**5**
73	NKTR-102 (PEG-Irinotecan)	Nektar Therapeutics	PEGylated form of irinotecan	colorectal cancer	4.849 (colorectal cancer)	Phase II	new formulation of irinotecan	NA				11	7	1	**6**
74	Oblimersen (Genasense)	Genta	bcl-2 Antisense Oligonucleotide Oblimersen	initial therapy for extensive-stage small-cell lung cancer (ES-SCLC	3.864 (lung cancer, all forms)	Phase II	No	NA				10	13	5	**9**
	Oblimersen (Genasense)	Genta	bcl-2 Antisense Oligonucleotide Oblimersen	relapsed or refractory CLL	964 (leukaemia, all forms)	Phase II	No	NA		might be effective in lot of lymphomas		9	12	1	**7**
75	Ofatumumab	Genmab	human monoclonal anti-CD20 antibody	relapsed or refractory CLL	964 (leukaemia, all forms)	Phase I/II	No	NA		might be effective in lot of lymphomas		4	12	2	**6**
76	OGX-011 (custirsen)	OncoGenex	is designed to block production of clusterin, a cell survival protein that is overproduced in several cancer indications	second-line chemotherapy in patients with hormone refractory prostate cancer	5.416 (prostate cancer, malignant)	Phase II	No	NA				9	12	3	**8**
77	Vitespen (Oncophage)	Antigenics	autologous, tumour-derived heat shock protein gp96 peptide complexes, cancer vaccine	kidney cancer	1.224 (kidney cancer)	Phase II/III	EMEA orphan drug status	NA				8	10	3	**7**
	vitespen (Oncophage)	Antigenics	autologous, tumour-derived heat shock protein gp96 peptide complexes, cancer vaccine	stage IV melanoma	1.169 (malignant melanoma)	Phase II/III	EMEA orphan drug status	NA				8	10	3	**7**
78	Ortataxel	Indena	a novel second-generation taxane	taxane-resistant NSCLC	3.864 (lung cancer, all forms)	Phase II	No	NA				8	8	5	**7**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
79	Paclitaxel poliglumex, CT-2103 (Xyotax)	Cell Therapeutics	large macromolecule conjugate of paclitaxel	first-line therapy in NSCLC	3.864 (lung cancer, all forms)	Phase III	new formulation of paclitaxel, in approval by EMEA	NA				11	8	5	**8**
80	Palifosfamide	Ziopharma	stabilized metabolite of ifosfamide	in combination with doxorubicin in the treatment of patients with sarcoma	NA	Phase II	No	NA				7	3	4	**5**
81	Panitumumab (vectibix)	Amgen	EGFR monoclonal antibody	head and neck cancer	1.029 (head and neck cancer)	Phase II/III	EMEA approval for colorectal cancer in 2007	NA	Initially for patients with recurrent cancer, extension of indication possible (see Cetuximab)	me too for cetuximab		9	10	7	**9**
82	panobinostat	Novartis	a member of the hydroxamic acid group of histone deacetylase (HDAC) inhibitors	cutanes T-cell lymphoma, topical treatment	NA	Phase II/III	Orphan drug - EMEA positive opinion in August 2007, FDA orphan drug in Sept 2007	NA				1	3	5	**3**
83	Panzem NCD	EntreMed Inc.	blocking the VEGF receptor and by inhibiting HIF-1alpha,	advanced or metastatic carcinoid tumours, in combination with bevacizumab	NA	Phase II	No	NA		me too		6	2	1	**3**
84	pazopanib (Armala)	GSK	multi kinase angiogenesis inhibitor	renal cell cancer	1.224 (kidney cancer)	Phase III	EMEA orphan drug status 2006	NA		several alternatives		10	8	2	**7**
85	pralatrexate	Allos Therapeutics	novel, next-generation small molecule chemotherapeutic agent that inhibits dihydrofolate reductase	relapsed or refractory peripheral T-cell lymphoma	1.130 (lymphoma, all forms)	Phase II (PROPEL Trial)	No	NA				8	5	5	**6**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
	pralatrexate	Allos Therapeutics	novel, next-generation small molecule chemotherapeutic agent that inhibits dihydrofolate reductase	stage IIIB/IV NSCLC (failed prior platinum-based regime); comparison to erlotinib (tarceva)	3.864 (lung cancer, all forms)	Phase IIb	No	NA				8	12	1	**7**
86	Perifosine	Aetrena Zentaris	An orally active alkyl-phosphocholine compound, inhibits the anti-apoptotic mitogen-activated protein kinase (MAPK) pathway	NSCLC	3.864 (lung cancer, all forms)	Phase II	No	NA				11	10	1	**7**
87	Pertuzumab (Omnitarg)	Roche	blocks the human epidermal growth factor (HER) receptor family,	advanced HER2-positive breast cancer, in combination with Trastuzumab	4.832 (breast cancer in women)	Phase II/III	No	NA		might replace Herceptin		11	11	4	**9**
88	Phenoxodiol	Marshall Edwards, Inc	regulates signal transduction pathways in cancer cells resulting in the break down of the intracellular proteins -- XIAP (X-linked Inhibitor of Apoptosis Protein) and FLIP (Fas Ligand Inhibitory Protein)	platinum resistant ovarian cancer	783 (ovarian cancer)	Phase III	FDA Fast track status	NA				11	11	2	**8**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
89	PI-88	PROGEN Pharmaceuticals	Heparanase inhibitor PI-88 inhibits the endo-beta-D-glucuronidase heparanase, which may interfere with the heparanase-mediated degradation of heparan-sulfate proteoglycans in extracellular matrices, an important step in the metastatic process	hepatocellular carcinoma	872 (liver cancer)	Phase II/III	No	NA				6	4	2	**4**
	PI-88	PROGEN Pharmaceuticals	Heparanase inhibitor PI-88 inhibits the endo-beta-D-glucuronidase heparanase, which may interfere with the heparanase-mediated degradation of heparan-sulfate proteoglycans in extracellular matrices, an important step in the metastatic process	combination with docetaxel in prostate cancer	5.416 (prostate cancer, malignant)	Phase II	No	NA				9	6	3	**6**
90	picoplatin	Poniard Pharmaceuticals	new generation organic platinum analogue	small-cell lung cancer (SCLC)	3.864 (lung cancer, all forms)	Phase II/III	Orphan drug - EMEA positive opinion 2007 for SCLC	NA				8	11	4	**8**
91	pixantrone	Cell Therapeutics	novel anthracycline derivate	non-Hodgkin Lymphoma (NHL)	979 (Non-Hodgkin lymphoma)	Phase III	FDA Fast track status	NA				5	8	2	**5**
92	Provenge (Sipuleucel-T)	Dendreon	cellular immunotherapy	advanced prostate cancer	5.416 (prostate cancer, malignant)	Phase III	FDA approval 2007	NA	no FDA approval 2007 – was withdrawn			11	13	3	**9**
93	RAV12	Raven Biotech-	monoclonal antibody	metastatic pancre-	1.388	Phase II	No	NA				12	10	4	**9**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
		nology		atic cancer, in combination with gemcitabine	(pancreatic cancer)										
94	Reolysin	Oncolytics Biotech	a novel treatment for Ras activated tumour cells	metastatic ovarian, peritoneal or fallopian tube cancer	783 (ovarian cancer)	Phase I/II	No	NA				6	5	3	**5**
95	RP101	SciClone	nucleoside analogue	adjunct treatment of pancreatic cancer, in combination with gemcitabine	1.388 (pancreatic cancer)	Phase II	FDA orphan drug designation in Feb 2008	NA				7	7	3	**6**
96	S-1	Taiho Pharmaceuticals	orally active combination of tegafur, gimeracil (an inhibitor of dihydropyrimidine dehydrogenase, which degrades fluorouracil), and oteracil (which inhibits the phosphorylation of fluorouracil in the GI tract)	first-line treatment of advanced gastric cancer	1.442 (gastric cancer)	Phase III	No	NA				9	5	3	**6**
97	Sarasar	Schering Plough	Farnesyl transferase inhibitor	breast cancer	4.832 (breast cancer in women)	Phase II/III	No	NA				4	9	2	**5**
98	SNDX-275	Syndax	HDAC inhibitor SNDX-275 binds to and inhibits histone deacetylase, an enzyme that regulates chromatin structure and gene transcription	in combination with erlotinib in the treatment of Advanced Non-Small Cell Lung Cancer	3.864 (lung cancer, all forms)	Phase II	No	NA				7	13	1	**7**
99	SNS-595	Sunesis Pharmaceuticals	topoisomerase II inhibitor	in platinum-resistant ovarian cancer patients	783 (ovarian cancer)	Phase II	No	NA				4	4	2	**3**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
100	Sorafenib (Nexavar)	Bayer Schering	tyrosinkinase inhibitor, orally	AML	964 (leukaemia, all forms)	Phase II	Extension of indication; EMEA approval for HCC and RCC	Nexavar 200mg Tabl 112 St: 3800€				7	7	7	**7**
	Sorafenib (Nexavar)	Bayer Schering	tyrosinkinase inhibitor, orally	breast cancer	4.832 (breast cancer in women)	Phase II	Extension of indication EMEA approval for HCC and RCC	Nexavar 200mg Tabl 112 St: 3800€				10	12	5	**9**
	Sorafenib (Nexavar)	Bayer Schering	tyrosinkinase inhibitor, orally	first line for melanoma	1.169 (malignant melanoma)	Phase III	Extension of indication, EMEA approval for HCC and RCC	Nexavar 200mg Tabl 112 St: 3800€			negative results Phase III known	10	8	3	**7**
	Sorafenib (Nexavar)	Bayer Schering	tyrosinkinase inhibitor, orally	First-line for NSCLC	3.864 (lung cancer, all forms)	Phase III	Extension of indication, EMEA approval for HCC and RCC	Nexavar 200mg Tabl 112 St: 3800€				12	12	4	**9**
	Sorafenib (Nexavar)	Bayer Schering	tyrosinkinase inhibitor, orally	chemo-naive castration-resistant prostate cancer	5.416 (prostate cancer, malignant)	Phase II	Extension of indication, EMEA approval for HCC and RCC	Nexavar 200mg Tabl 112 St: 3800€				12	12	2	**9**
101	Sunitinib (Sutent)	Pfizer	tyrosinkinase inhibitor, orally	previously treated advanced NSCLC	3.864 (lung cancer, all forms)	Phase II	Extension of indication, EMEA approval for GIST and RCC	Sutent 25 mg Kps 30 St: 2600€				12	12	4	**9**
	Sunitinib (Sutent)	Pfizer	tyrosinkinase inhibitor, orally	Metastatic Breast Cancer Previously Treated With an Anthracycline and a Taxane	4.832 (breast cancer in women)	Phase II	Extension of indication, EMEA approval for GIST and RCC	Sutent 25 mg Kps 30 St: 2600€				10	12	4	**9**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
102	Tanespimycin	Kosan Biosciences	binds to and inhibits the cytosolic chaperone functions of heat shock protein 90 (HSP90)	multiple myeloma (after first relapse, in combination with bortezomib - Velcade)	NA	Phase III (TIME-1 trial)	No	NA				10	12	6	**9**
103	Tesetaxel	Genta	oral formulation, semisynthetic taxane	NSCLC	3.864 (lung cancer, all forms)	Phase II	No	NA				13	7	4	**8**
104	TG4010 Vaccine	Transgene	cancer vaccine	as adjunct in first-line chemotherapy of NSCLC (combination with cisplatin + gemcitabine)	3.864 (lung cancer, all forms)	Phase IIb	No	NA				9	7	1	**6**
105	Thalidomide	Pharmion	in combination with topotecan	recurrent ovarian cancer	783 (ovarian cancer)	Phase II	EMEA orphan drug status for multiple myeloma	NA				7	4	4	**5**
106	Trilostane (Modrenal)	Bioenvision	A synthetic derivative of androstane with adrenocortical suppressive properties. Trilostane reversibly inhibits 3 beta-hydroxysteroid dehydrogenase delta 5-4 isomerase in the adrenal cortex, resulting in the decreased synthesis of mineralocorticoids	post-menopausal advanced breast cancer following relapse to initial hormone therapy	4.832 (breast cancer in women)	Phase II	No	NA				10	6	4	**7**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
107	Triphendiol	BioSpace	down regulation of the expression of X-linked inhibitor of apoptosis, oral second-generation derivative of phenoxodiol	Stage IIB through Stage IV malignant melanoma	1.169 (malignant melanoma)	Phase II/III	FDA orphan drug status in Feb 2008; FDA Orphan Drug status for the treatment of pancreatic cancer and for the treatment of cholangio-carcinoma	NA				6	10	1	**6**
108	TroVax	Biomedica	cancer immunotherapy	renal cancer	1.224 (kidney cancer)	Phase III	No	NA	Studies on colorectal cancer exist, possible high costs due to high number of patients with disease			10	6	3	**6**
	TroVax	Biomedica	cancer immunotherapy	metastatic hormone-refractory prostate cancer	5.416 (prostate cancer, malignant)	Phase II	No	NA				13	8	1	**7**
109	Urocidin	Bioniche	Mycobacterial Cell Wall-DNA Complex (MCC) is formulated from Mycobacterium phlei, a non-pathogenic strain of mycobacteria. MCC has been shown to have immune stimulatory and apoptosis (programmed cell death) activity against cancer cells	first-line non-muscle-invasive bladder cancer	1.705 (bladder cancer)	Phase III	FDA Fast track status	NA				3	10	4	**6**

No.	Drug name (brand name)	Company / Developer	Short Drug description	Patients' indications	Number of patients with disease in Austria (Source: Statistics Austria, 2004)	stage of development	Is the technology already approved for other indications (incl. Orphan drug status) or by the FDA?	costs in € NA = not available	COMMENTS Expert 1	COMMENTS Expert 2	COMMENTS Expert 3	Score E1	Score E2	Score E3	Mean Score
110	Vandetanib* (Zactima)	Astra Zeneca	VEGF/EGF TK inhibitor with RET kinase activity	for non-small cell lung cancer – locally advanced or metastatic, second line therapy	3.864 (lung cancer, all forms)	Phase III	FDA and EMEA orphan drug status	NA				10	15	5	**10**
	Vandetanib (Zactima)	Astra Zeneca	VEGF/EGF TK inhibitor with RET kinase activity	Medullary thyroid cancer – locally advanced or metastatic	686 (thyroid cancer)	Phase II	FDA and EMEA orphan drug status	NA				9	10	4	**8**
111	VDQ-002	VioQuest	inhibits protein kinase B	multiple myeloma	NA	Phase II	FDA orphan drug designation in Feb 2008	NA				9	12	1	**7**
112	Veltuzumab	Immunomedics	humanised IgG1 monoclonal anti-CD22 antibody	non-Hodgkin Lymphoma (NHL)	979 (Non-Hodgkin lymphoma)	Phase III	No	NA		several alternatives		8	7	6	**7**
113	Vorinostat (Zolinza)	Merck	A synthetic hydroxamic acid derivative with antineoplastic activity. Vorinostat, a second generation polar-planar compound, binds to the catalytic domain of the histone deacetylases (HDACs).	AML	964 (leukaemia, all forms)	Phase II/III	No	NA	Out-patient, FDA approval for cutanous T-cell Lymphoma			7	8	4	**6**
114	WX-671	Wilex AG	an oral second generation serine protease inhibitor	HER2-receptor negative metastatic breast cancer, in combination with capecitabine	4.832 (breast cancer in women)	Phase II	No	NA	Oral = no impact on hospital budget			11	6	2	**6**
115	XL-184	Exelixis	multi-tyrosine kinase inhibitor	NSCLC (progressive disease while on erlotinib therapy)	3.864 (lung cancer, all forms)	Phase I/II	No	NA				13	11	1	**8**
116	ZD4054	Astra Zeneca	Endothelin A Antagonist	hormone resistant prostate cancer (HRPC	5.416 (prostate cancer, malignant)	Phase III	No	NA				13	11	4	**9**

*Red marks: Five highest scored anticancer drugs