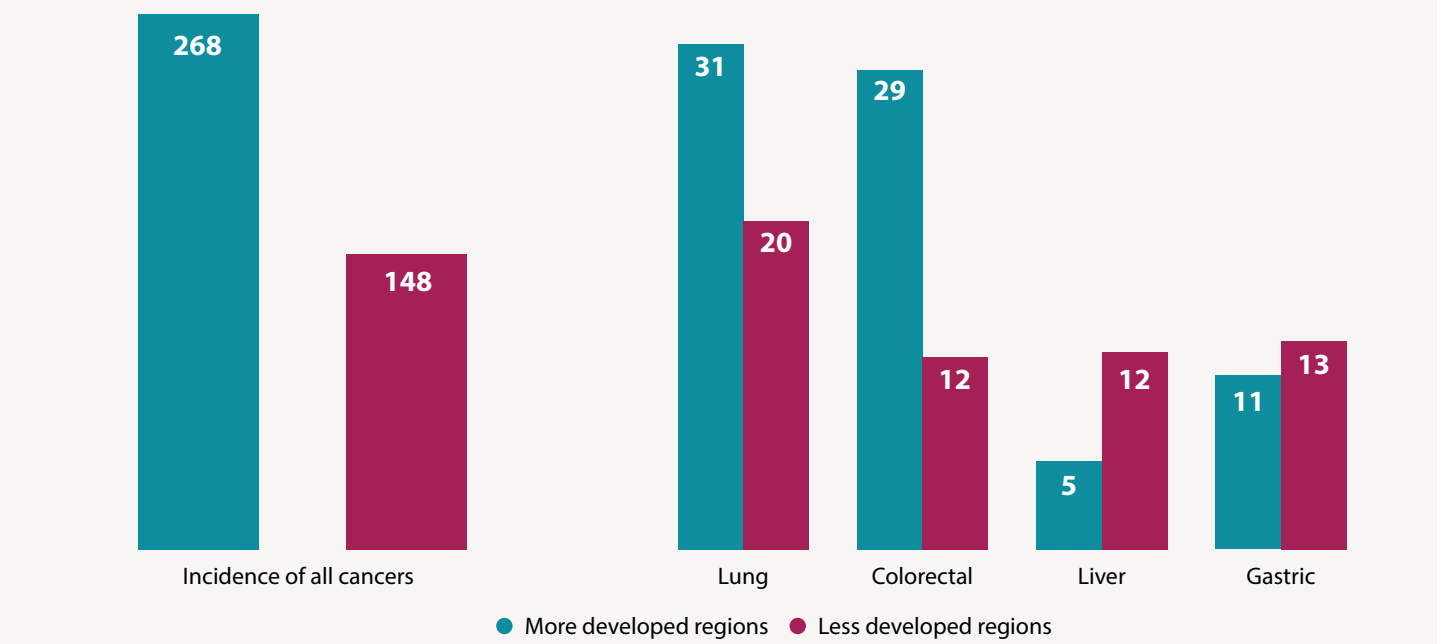
Global cancer incidence rates vary by regions and cancer types

2012 incidence rates (age-standardized incidence rate/100,000)



Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available at: http://globocan.iarc.fr. Accessed 12/13/2013.

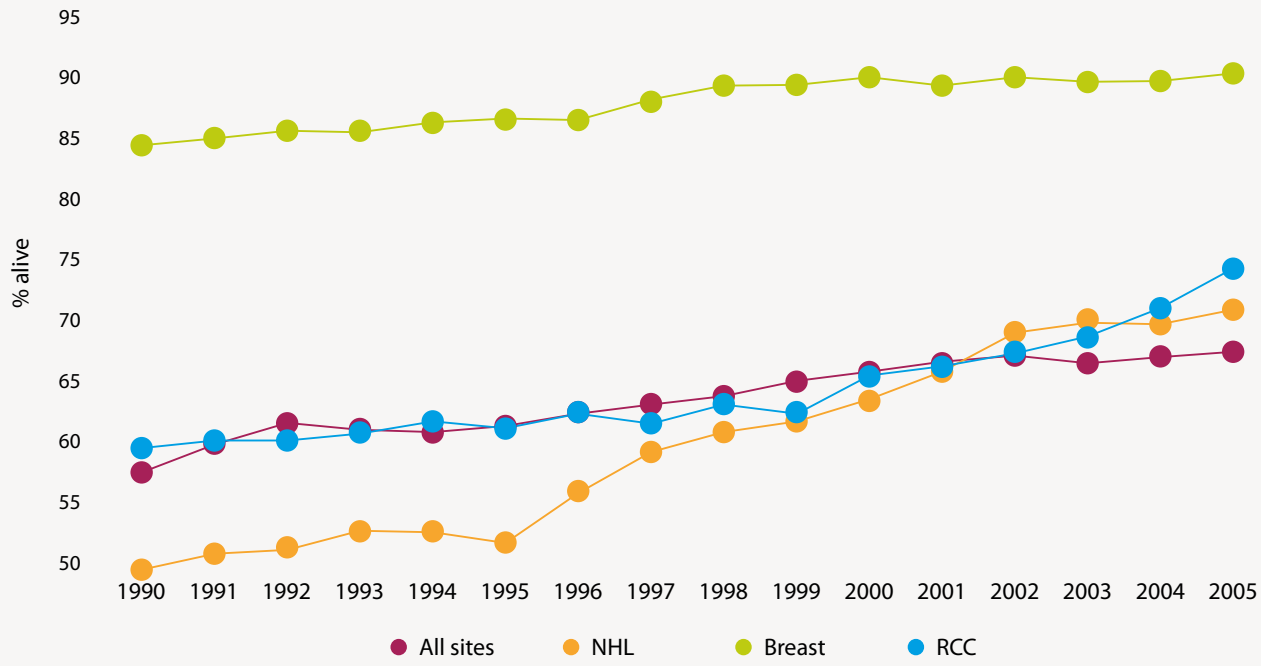
- The degree to which cancer incidence rates differ among countries can be quite substantial: differences arise from both disease trends and data availability.
- Overall, cancer incidence rates are lower in less developed regions; this may be the result of a number of factors.
- Populations in less-developed regions may have diminished access to health care services, and a higher probability of dying before being diagnosed with cancer.
- Public health organizations may be less likely to track and record case information for epidemiologic purposes, potentially resulting in lower perceived incidences.
- In terms of cancer type, lung and colorectal cancer incidence tends to be higher in more developed nations.
- Conversely, liver and gastric cancer incidence tends to be higher in less developed countries.
- A causal link between hepatitis C infection and liver cancer as well as higher likelihood of exposure to environmental toxins may offer some explanation of this phenomenon.
- In developed countries liver cancers will be on the rise due to life style. Obesity will take over as the main cause of hepatocellular carcinoma (HCC) in the U.S. (by 2030 forecasted) and in Europe shortly after.

Chart Notes:

More developed regions: all regions of Europe plus Northern America, Australia/New Zealand and Japan. Less developed regions: all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia.

Cancer survival is improving steadily as detection and treatment improve

Five-year U.S. relative survival by year of diagnosis



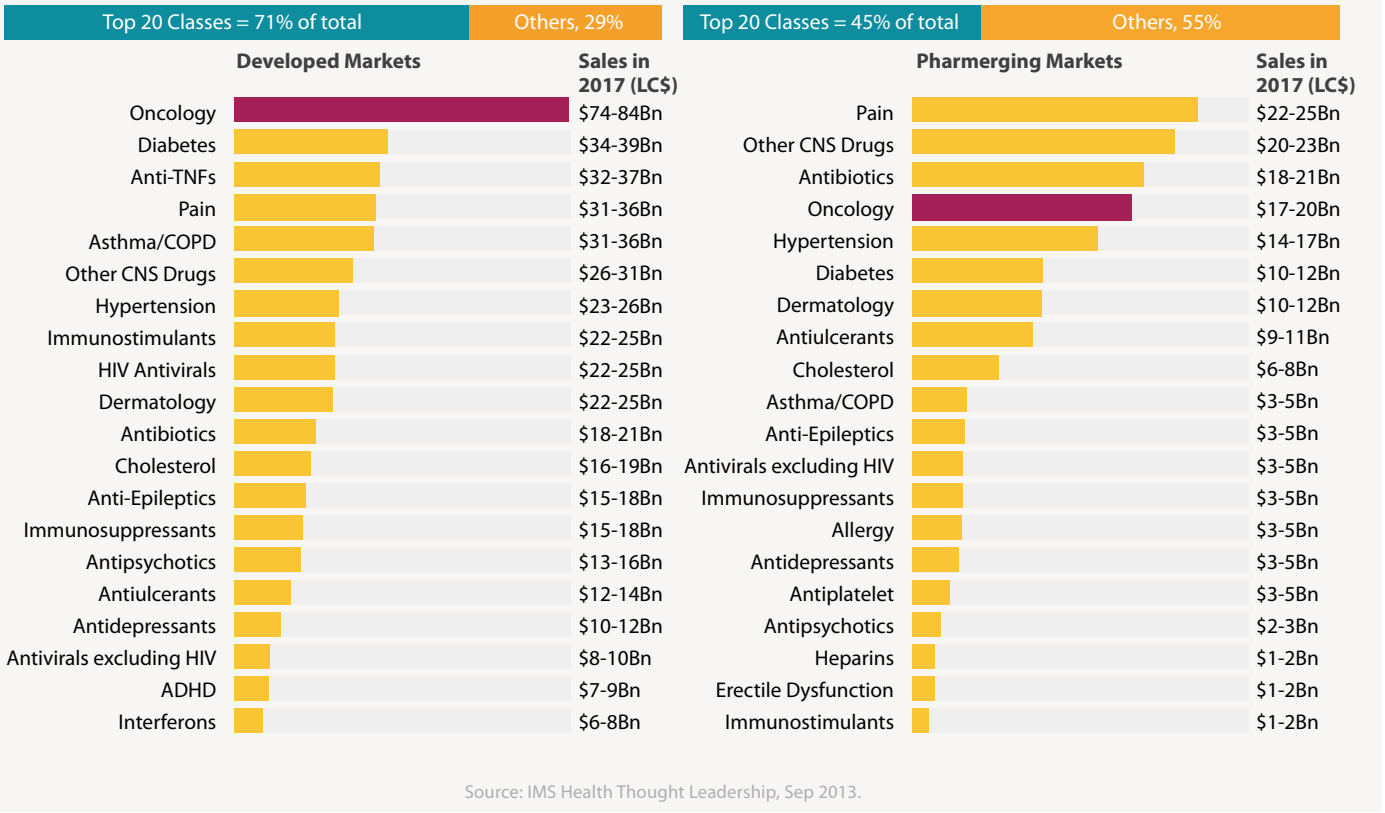
Source: National Cancer Institute. Surveillance, Epidemiology, and End Results Program.
Available at: http://www.seer.cancer.gov/csr/1975_2010/download_csr_datafile.php/. Accessed 3/11/2014

- Survival has improved significantly over the past two decades with published research suggesting that 23% of the improvement is due to behavioral changes, 35% is due to screening, 20% to advances in treatment, and the remaining 22% attributed to other factors.[1]
- Non-Hodgkin's lymphoma (NHL) provides an example of one group of cancers where improving survival is especially pronounced, due in part to the adoption of new targeted and cytotoxic therapies beginning in the 1990s.
- Improvements in survival vary substantially among cancers. Breast cancer, for example, has a historically high survival rate, and has seen only modest improvements despite new therapies being approved.

1. Cutler, David M. Are We Finally Winning the War on Cancer? Journal of Economic Perspectives. Volume 22, Number 4. 2008.

Oncology drives major medicines spend in developed and pharmerging markets

Spending by therapeutic area in 2017 (oncology does not include supportive care)



Source: IMS Health Thought Leadership, Sep 2013.

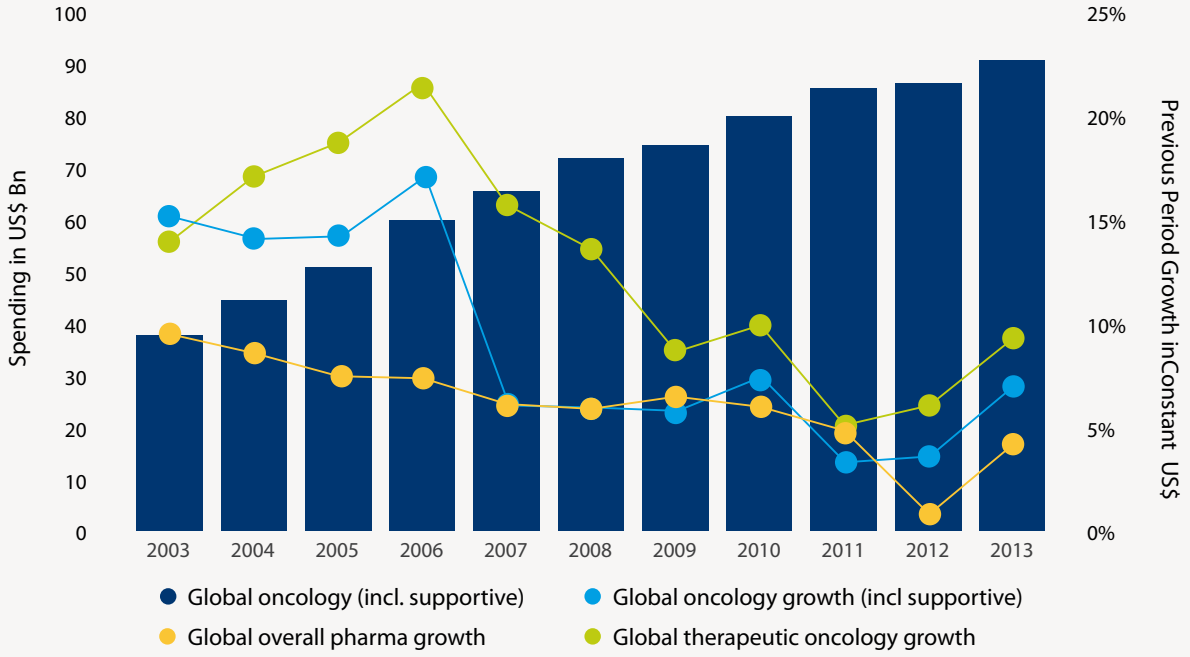
- Oncology is forecasted to be the number one therapeutic area for developed nations in terms of 2017 spending leading all other therapeutic areas, even those associated with primary care.
- Among pharmerging nations, oncology is anticipated to be the fourth-largest therapeutic area in terms of spending in 2017 and the largest specialty area, only falling behind certain primary care therapeutic areas.

Chart notes:

Pharmerging: China, Brazil, Russia, India, Mexico, Turkey, Venezuela, Poland, Argentina, Saudi Arabia, Indonesia, Colombia, Thailand, Ukraine, South Africa, Egypt, Romania, Algeria, Vietnam, Pakistan and Nigeria.

Global spending on oncology drugs has grown to $91Bn in 2013, including supportive care

Global oncology market dynamics 2003-2013

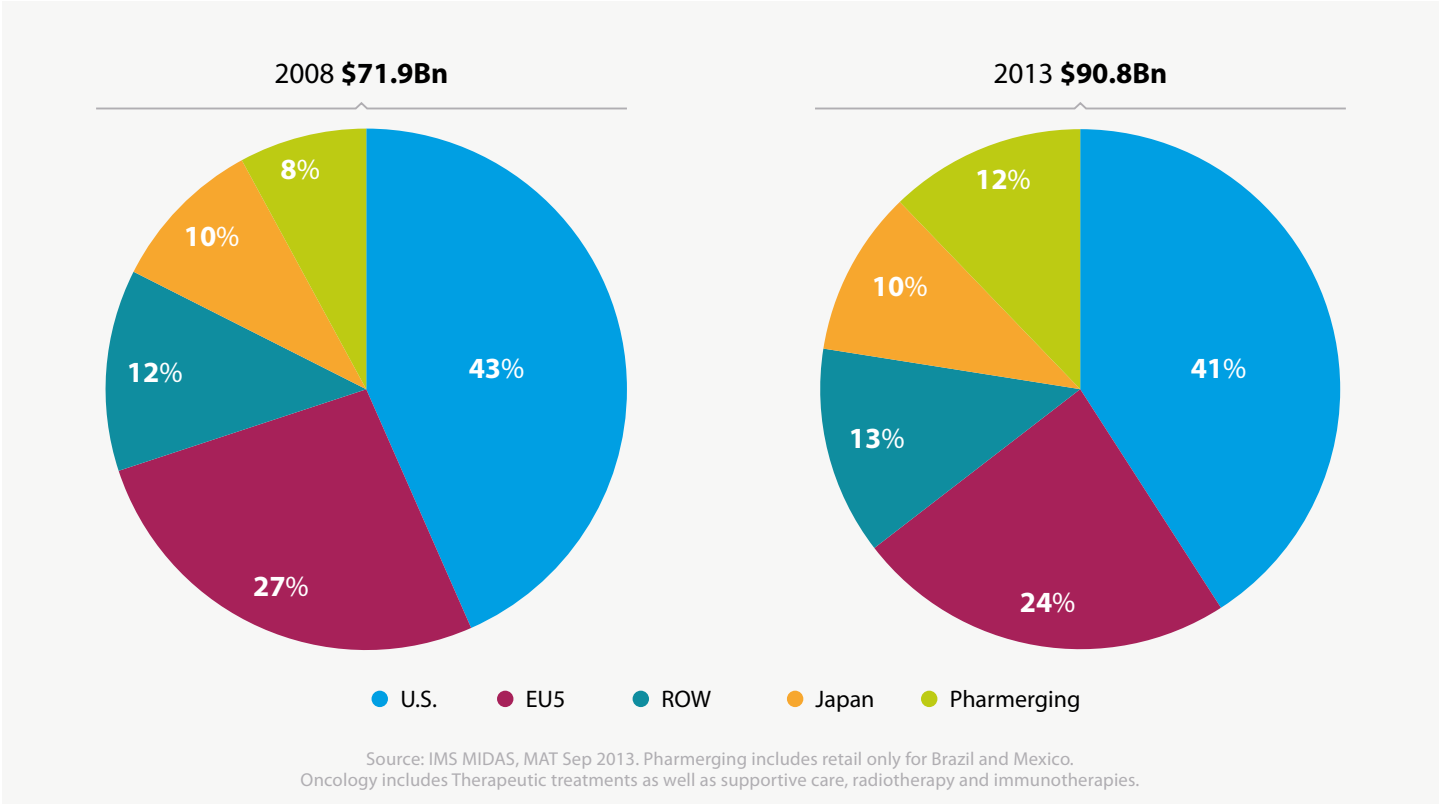


Source: IMS MIDAS, Dec 2013. Oncology includes therapeutic treatments as well as supportive care, radiotherapy, and immunotherapies.

- From 2003 to 2008, growth was consistently above 15% for therapeutic agents, reflecting the launch of bevacizumab (Avastin) and expansion of trastuzumab (Herceptin) into adjuvant breast cancer.
- Safety issues regarding the use of the erythropoietin stimulating agents (ESA) in 2007 resulted in a dramatic drop in their use, particularly in the U.S.
- Most launches between 2005 and 2009 addressed smaller patient populations and saw lower adoption rates than earlier products.
- 2012 featured a record number of FDA approvals, particularly in oncology.
- Meanwhile, the growth of Herceptin and rituximab (MabThera/Rituxan) sales slowed in 2013.
- Recent approvals for lymphomas, immunotherapy agents for melanoma, PD-1 modulators, and anti-PD-L1 therapies represent the next phase of targeted agents in oncology.

Oncology spending is still dominated by the U.S. and EU5

Proportion of oncology spending by global market share, 2008-2013

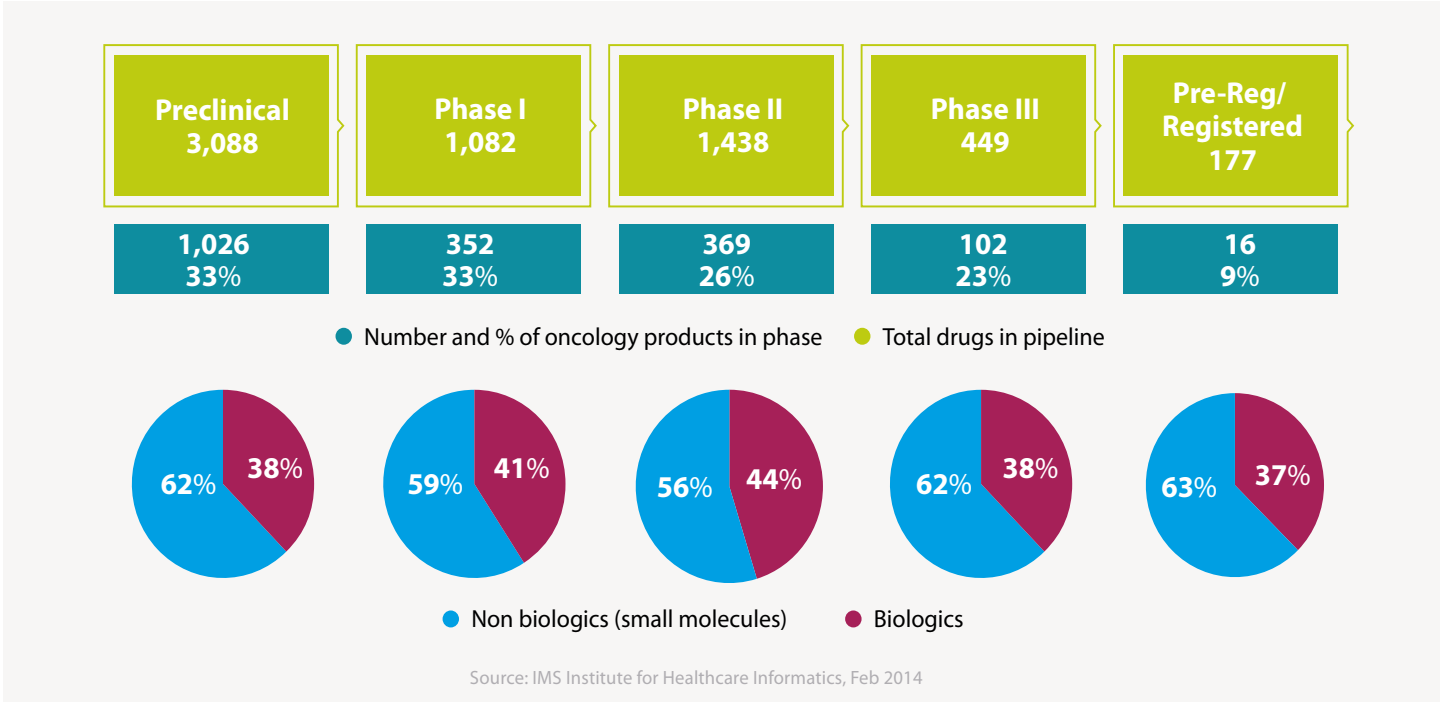


Source: IMS MIDAS, MAT Sep 2013. Pharmerging includes retail only for Brazil and Mexico.
Oncology includes Therapeutic treatments as well as supportive care, radiotherapy and immunotherapies.

- U.S. share of total spending declined by 2% but remains the largest oncology market.
- The five largest European markets also reduced their share of the global spending by 3%.
- While the pharmerging share of total spending has grown by 12%, 75% of total sales are represented by the U.S., EU5, and Japan alone.
- The U.S. relevance in global oncology extends beyond its size but also because the access and pricing associated with the U.S. health care system have encouraged use of innovative treatments.

Oncology is the largest area of focus in R&D, with almost 2000 products in the pipeline

Number of active products in the pipeline to date = 6,234



Source: IMS Institute for Healthcare Informatics, Feb 2014

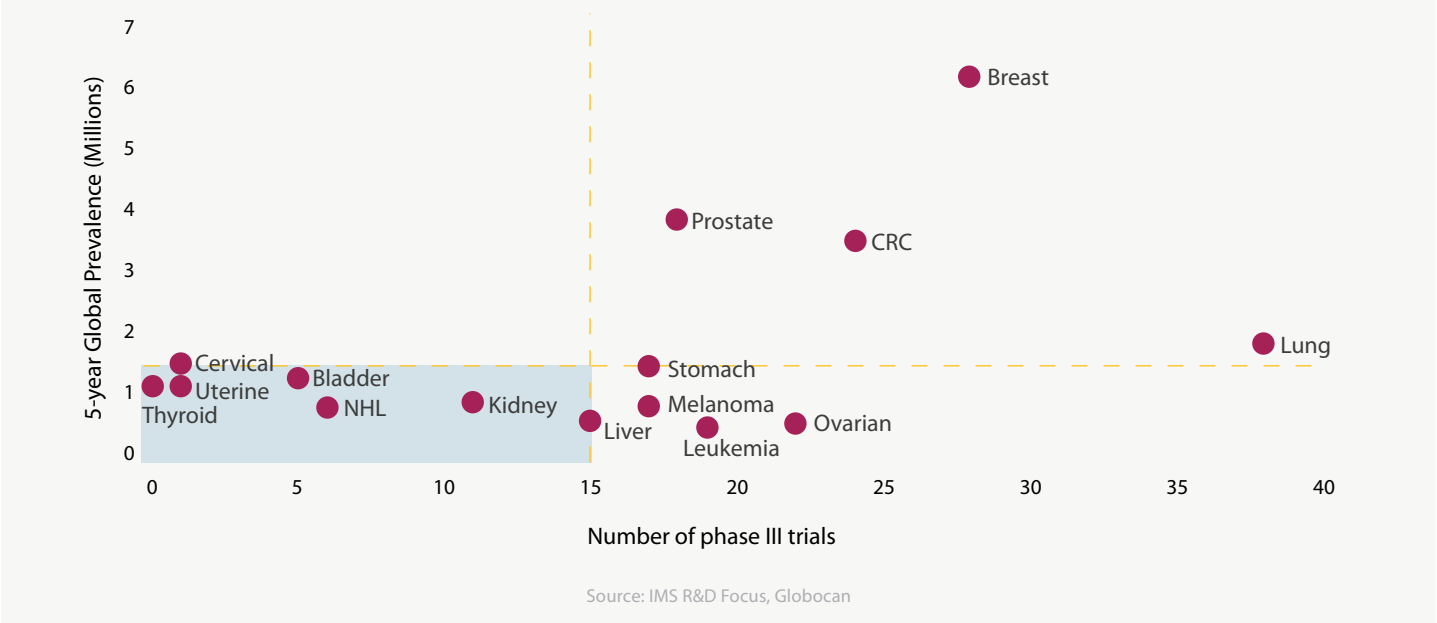
- Oncology represents the largest cluster of R&D activity, with over 30% of preclinical and phase I activity.
- Fewer cancer drugs are progressing to phase II and III which indicates both the high levels of early phase activity and the difficulties in generating successful results in the clinic.
- While only 9% of drugs pending with regulators were for cancer, over a quarter of NME launches in the past three years in the U.S. were cancer medicines, and cancer medicines are more likely to be fast-tracked by regulators and progress rapidly from phase III to approval.
- The first drug launched with an FDA breakthrough designation was a cancer drug (obinutuzumab; Gazyva), and many of the others pending with FDA with this designation are also cancer treatments.
- In 2013, 17 new drugs were launched to treat orphan diseases, rare conditions affecting less than 200,000 people and for which few therapies are effective. Eight of the new orphan drugs were for the treatment of cancer, and many were fast-tracked by the FDA.

Chart notes:

Chart notes: Chart counts the number of unique products in R&D for the most-advanced phase they are being researched for. Many cancer drugs are investigated for multiple indications and counting only unique products may understate late-stage cancer research.

R&D focus appears to be based on factors other than disease prevalence or potential treatment populations

Phase III trials by cancer type and 5-year disease prevalence



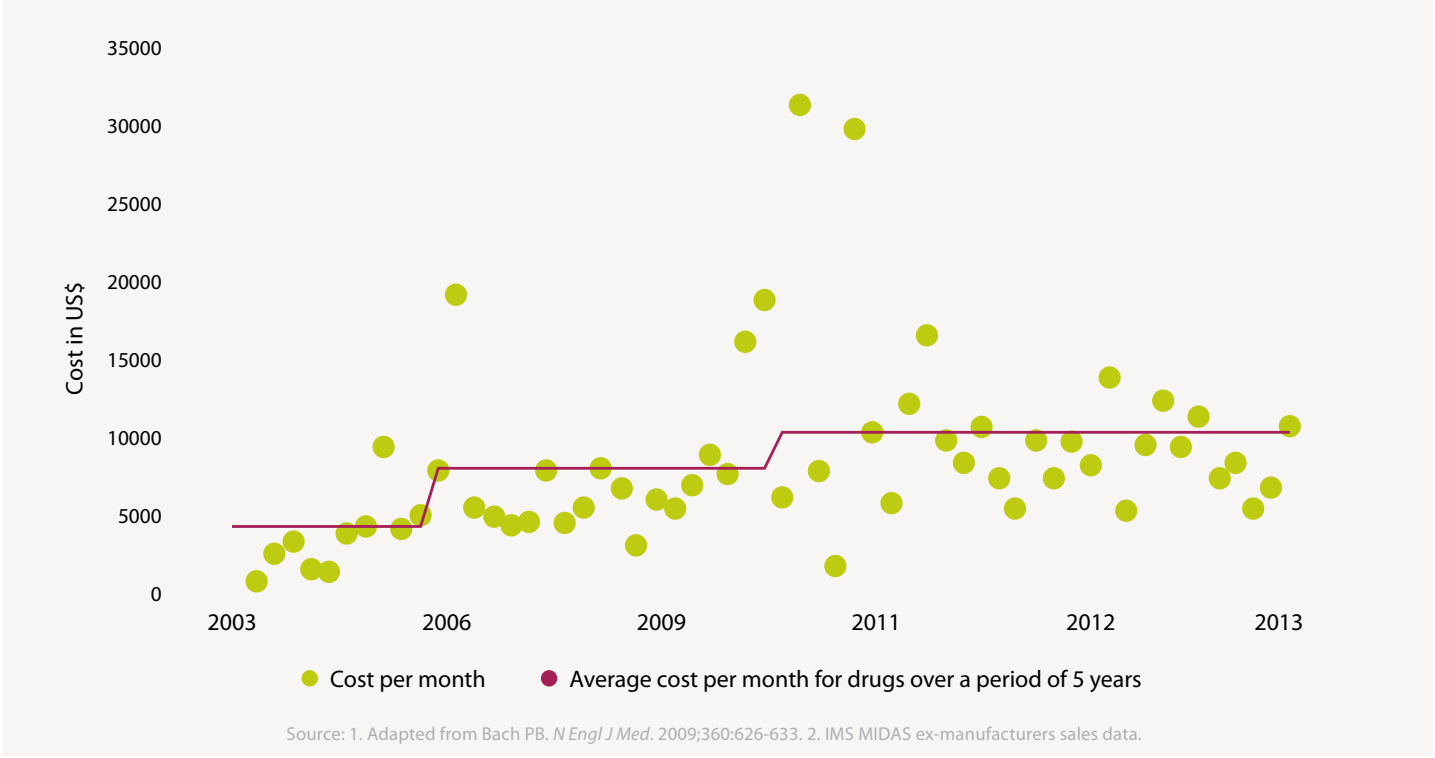
Source: IMS R&D Focus, Globocan

- While it is not surprising that higher prevalence tumors have more late-stage pipeline development, another key driver of innovation is unmet needs, which are not always tied to prevalence.
- Although prostate cancer has approximately twice the 5-year global prevalence, the number of trials investigating agents for the treatment of lung cancer is more than twice that for prostate cancer.
- This is presumably due to the fact that molecular targets in non-small cell lung cancer—particularly epidermal growth factor receptor (EGFR)—have been long-since identified and extensively studied.
- Similar phenomena likely play a role in the relatively high number of agents being investigated for colorectal, breast, and ovarian cancer, specifically those targeting KRAS, BRAF, and ALK mutations and human epidermal growth factor receptor 2 (HER-2).
- So in a pipeline overwhelmingly populated by targeted therapies, agents with well characterized molecular targets and accompanying biomarkers appear to be high potential investments.
- Conversely, six key tumor types (thyroid, uterine, cervical, bladder, NHL, and kidney) with lower prevalence and corresponding lower numbers of clinical trials evaluating investigational therapies, represent an opportunity for R&D efforts in the future.
- It is also important to note the impact of immune therapy and recent success in clinical trials. This is expected to enhance focus in lung cancer and melanoma, and has already impacted gastrointestinal cancers.

Chart notes:
Phase III numbers refers to counts of drugs in clinical trials

The average monthly cost of branded oncology drugs has doubled over the past decade

U.S. cost per month of branded oncology drugs (2003-2013)



Source: 1. Adapted from Bach PB. *N Engl J Med*. 2009;360:626-633. 2. IMS MIDAS ex-manufacturers sales data.

- The average monthly cost of branded oncology drugs was ~$5,000 in 2003 compared with ~$10,000 in 2013.
- Certain individual branded oncology agents cost upwards of $30,000 per month.
- These costs do not include discounts, or patient payment shares.