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134 novel anti-cancer therapies were approved between January 2009 and April 2016: What do we actually know about oncological therapies at the time of approval?

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Background and project aim

All (western) health care systems are challenged by high expenditures for oncological therapies which use a large proportion of hospital drug budgets—with an increasing tendency of the amount spent on high priced anti-cancer drugs [1]. Moreover, international debate about the actual clinical value and patient benefit of many anti-cancer therapies as well as criticism about the methodology of approval studies is on the rise [2].

In May 2016, an agreement between the countries of Belgium, the Netherlands, Luxemburg and Austria (Benelux-A) was signed that will implement a shared Horizon Scanning System (HSS) forecasting all expensive drugs and the according early shared price negotiations [3]. Therefore, we conducted a systematic investigation on all anti-cancer drugs approved by the European Medicines Agency (EMA) between January 2009 and April 2016 [4]. The objective of this study was to extract and quantify the knowledge of the clinical benefit, in regard to overall survival (OS) and progression-free survival (PFS), of oncological therapies at the time of approval.

Methods

We included all new anti-cancer therapies and expanded indications of already approved drugs that received marketing authorisation between January 1, 2009 and April 15, 2016. Our sources of information were the EPARs (European Public Assessment Reports) published by the EMA, and the LBI-HTA HSO documents. To examine the clinical benefit of novel oncological therapies we documented the difference of the median OS and PFS compared to the control arm of the respective approval study. To ensure comparability, we assigned all approved indications into the International Classification of Diseases (ICD, 10th revision) defined by the World Health Organisation (WHO). We analysed the data using Microsoft Office Excel 2010.

Results

ICD–10 categories

We identified 134 different new anti-cancer therapies and expanded indications that received marketing authorisation between 2009 (Jan 1) and 2016 (April 15). The assignment of the investigated therapies resulted into 15 different ICD groups (Table 1). The majority (N=34) of the approved therapies pertain to the ICD–10 category C81–C96 (blood tissue cancer). The second most commonly approved drugs belong to the C15–C26 (N=22, malignant neoplasms of digestive organs) as well as the C30–C39 (N=20, lung cancer) category. The categories with sparse novel approvals were C45–C49, C40–C41, C69–C72, D37–D48 and C81–C96.

Table 1: Anti-cancer therapies that received marketing authorisation between 2009 and April 15th 2016 classified in ICD–10 categories – Sequenced according to their frequency

International Classification of Diseases 10th Revision (ICD 10) (N = 134)	N
C81–C96 MN, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	34
C15–C26 MN of digestive organs	22
C30–C39 MN of respiratory and intrathoracic organs	20
C50–C50 MN of breast	16
C43–C44 Melanoma and other MN of skin	13
C60–C63 MN of male genital organs	8
C51–C58 MN of female genital organs	4
C64–C68 MN of urinary tract	4
C51–C58 & C45–C49 MN of mesothelial and soft tissue[A]	4
C73–C75 MN of thyroid and other endocrine glands	3
D37–D48 Neoplasms of uncertain or unknown behaviour	2
C45–C49 MN of mesothelial and soft tissue	1
C40–C41 MN of bone and articular cartilage	1
C69–C72 MN of eye, brain and central nervous system	1
D37–D48 & C81–C96[A]	1

[A] *Oncological therapies which received marketing authorisation for an indication that includes diseases which do not belong to the same ICD–10 category were allocated into one combined group of two ICD–10 categories; MN, malignant neoplasm.*

Overall median OS gain

22 (16%) therapies achieved a median OS gain of over three months. The maximum survival prolongation was 15.7 months obtained by one compound for the first-line treatment of metastatic HER2 positive breast cancer. In the majority of the approved therapies (N=54, 39%), an OS gain between 0 and 3 months could be achieved. Six (5%) therapies shortened OS compared to the control arm. The study endpoint OS was not reached by 15 therapies (11%); in addition, three therapies showed no estimable OS data (2%). Data for median OS was not available in 37 interventions (27%) (Figure 1).

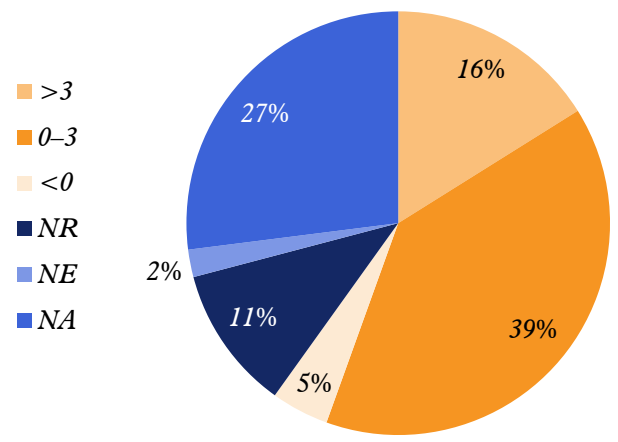

Figure 1: Overall median OS gain in months (N=137). >3, median OS gain over 3 months compared to the control arm. 0–3, median OS gain between 0–3 months compared to the control arm. <0 shorten median OS compared to the control arm. NA, no data for median OS was available. NE, median OS was not estimable. NR, median OS was not reached.

Conclusion

In total, cancer drugs for 134 new indications were approved between January 2009 and April 2016, of which one-fourth (N=34, 25%) are indicated for blood tissue cancer. For 37 indications (27%) no data was available for PFS and OS at time of approval. A gain in median OS was reached by 76 licensed indications (55.5%); 22 (16%) of them achieved a gain of more than three months. Our findings indicate that in a large number of therapies no valid knowledge about the survival benefit is available at the time of approval. These results in combination with recent studies emphasise the need for a systematic tool to evaluate the benefit of novel drugs in a standardised and transparent way, as well as the importance of the systematic assessments of follow-up trials 1–2 years after approval of all anti-cancer drugs.

References

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