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Discrepancies in the therapeutic indications granted by the European Medicines Agency and the US Food and Drug Administration for new cancer drugs: An analysis of potential explanations

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ABSTRACT

Background: Studies have found notable differences between the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) in indications granted to new cancer drugs (e.g., different treatment lines). It is unknown why they occur; therefore, we aimed to analyse if maturity of data or characteristics of the pivotal trials might be explanations.

Methods: New cancer drugs approved by both EMA and the FDA in the study period between January 1, 2020, to December 31, 2022, and new cancer drugs that were approved by one agency in the study period and at the other agency outside the study period were included in the analysis. The drugs were identified by searching the FDA and EMA websites.

Results: A total of 36 new cancer drugs were included. Notable differences between EMA and the FDA in the granted indication were found in 15 (42 %) of the drugs. The proportion of cancer drugs with differences in maturity of data at time of assessment between EMA and the FDA was similar for drugs with and without notable differences in the indication. Furthermore, the results did not indicate that low level of evidence (e.g., early phase trial as the pivotal, single-arm design, or use of surrogate endpoints) was more common in the cancer drugs with notable differences in the indication.

Conclusion: The frequent discrepancies in the granted indications between EMA and the FDA for new cancer drugs during a three year period could not be explained by maturity of data at time of assessment or characteristics of the pivotal trials. Therefore, divergence in regulatory policies between the two agencies is considered a more likely explanation.

Policy summary: Discrepancies between regulatory agencies in the indications granted to new cancer drugs suggest a problematic extrapolation and thus uncertainty regarding the clinical benefit for the patients. The present study seeks to identify potential explanations for the discrepancies to reduce the misalignment in the future.

1. Introduction

A therapeutic indication for a given medicine describes what disease the medicine is intended to treat and the patient group that will benefit from it [1]. The therapeutic indication is decided by regulatory agencies (e.g., the European Medicines Agency and the US Food and Drug Administration) based on data from clinical trials submitted in the application for marketing authorisation. The clinical trials often investigate the medicine in a selective population constructed by pre-defined inclusion and exclusion criteria. Despite this, the therapeutic indications granted by the medicinal agencies are typically extrapolated to include a broader patient population (e.g., greater disease severity, older age groups, or patients with more comorbidities) that is expected to benefit from the trial [2]. This extrapolation is challenging and might lead to unpredictability about the benefit-risk balance for the patient group treated in the "real world".

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Previous studies have shown examples of new cancer drugs that underperform regarding overall survival in the real-world setting compared with the clinical trials [3–5]. The discrepancy can potentially be explained by several factors. First, the patients in clinical trials likely are monitored more closely regarding side-effects which reduces the risk of severe complications. Second, the patients included in the clinical trials do not necessarily represent the patients treated in the real-world setting, indicating that the medicinal agencies have extrapolated the clinical data to patient populations that do not benefit from the treatment [2]. Studies have found notable differences between EMA and the FDA in therapeutic indications granted to cancer drugs [6–8]. Discrepancies between the two agencies are of particular interest as it indicates a potentially problematic extrapolation for at least one of the two agencies and thus uncertainty regarding the clinical benefit for the given patient groups. It is unknown why these discrepancies occur. Recently, it has been suggested that the indications that differ might have greater uncertainty in data (e.g., low level of evidence) or that differences in maturity of data at time of assessment for the agencies might be an explanation [7]. However, these speculations have not been further investigated.

In this study, we aimed 1) to systematically compare the therapeutic indications granted by EMA and the FDA for new cancer drugs, 2) to analyse regulatory characteristics and pivotal trials for the included cancer drugs with notable differences in the therapeutic indications, 3) to compare maturity of data at time of assessment for the two agencies, and 4) to investigate if alignment in the approved indications have occurred post marketing for the drugs.

2. Methods

We performed a retrospective analysis of new cancer drugs approved by both EMA and the FDA in the study period between January 1, 2020, to December 31, 2022 (approval date by EMA was defined as the date the marketing authorisation was issued by the European Commission after a positive opinion from the Committee for Medicinal Products for Human Use (CHMP)) and new cancer drugs that were approved by one agency in the study period and at the other agency outside the study period. The study timeframe (2020–2022) was chosen to investigate the recent status of potential discrepancies in the granted indications by EMA and the FDA, and to allow a minimum of 2 years of follow-up to examine whether alignment of the indications has occurred after approval. The approved cancer drugs eligible for inclusion were identified in two steps. First, we searched the EMA website for annual reports with opinions from the Committee for Medicinal Products for Human Use (CHMP) [9]. From these reports, new active substances indicated for treatment of any cancer within the defined time period were included. Second, we searched the FDA lists of novel drug approvals and included new cancer drugs approved by the FDA within the time period but approved by EMA outside the time period [10]. We excluded new cancer drugs if they were advanced therapy medicinal products (ATMPs) e.g., cellular or gene therapy, or if the approved cancer indications were an extension of an already approved cancer drug in one of the two agencies [11,12]. Drugs that were withdrawn in one or more of the agencies post approval were not excluded from the analysis since the analysis focused on the initial approval.

For each of the included cancer drugs, we compared the indications granted by EMA and the FDA. Notable differences in the indications were defined as a different line of treatment, different requirements for pre-treatment, different subgroups of patients, or different treatment combinations; each indication could have more than one notable difference. The identified differences were characterized in terms of whether EMA or the FDA had given the broadest indication. The broadest indication was defined as the indication that includes the largest patient population e.g., if 1st line treatment was given by FDA and 2nd line treatment was given by EMA, the FDA indication was considered the broadest since 1st line treatment includes a larger patient population than 2nd line treatment. The data was coded by the first author (AC) and afterwards repeated by the last author (TSP). In case of disagreement, the evaluation was discussed between the two investigators, and, if the disagreement persisted, it was discussed in the full author group.

Furthermore, we divided the included cancer drugs into two groups based on whether there were notable differences between EMA and the FDA in the granted indication, or not. The two groups were descriptively compared regarding 1) type of approval (e.g., conditional marketing authorisation/exceptional circumstances/accelerated approval or regular approval, 2) difference in time of submission of application to EMA and the FDA, 3) difference in time of approval in EMA and the FDA, 4) difference between EMA and the FDA in available data at time of assessment defined as different data cutoff for efficacy analyses in the pivotal trial or different pivotal study (most data was defined as latest data cutoff or most recent pivotal study), and 5) characteristics of pivotal trial in terms of phase (I, II, or VII), study design (single-arm or RCT), confirmed effect on endpoint with highest clinical relevance (overall survival > progression-free survival > response rate). Additionally, the different parameters were tested for statistically signifi-cance between the two groups (Fisher's exact tests for binary outcomes and Mann-Whitney *U* test for continuous outcomes; significance level = 0.05). The data from the comparison was retrieved by searching the EMA website for assessment reports and by searching the Drugs@FDA database for FDA reviews for the included drugs [13,14]. Data were extracted in the period from October 13, 2023, to March 20, 2025.

Finally, the current status (as of March 20, 2025) of the approved indication for the same disease in EMA and the FDA were compared for changes since marketing authorisation. Extensions of indications to other diseases were not included in the comparison.

3. Results

We identified 44 new cancer drugs approved by both EMA and the FDA with a final decision in at least one of the agencies between January 1, 2020, to December 31, 2022. Of those, 8 were excluded resulting in a total of 36 new cancer drugs included in the analysis (Fig. 1; Appendix p 1–7).

3.1. Comparison of indications granted by EMA and the FDA for new cancer drugs

In 15 (42 %) out of the 36 included cancer drugs, a total of 21 notable differences between EMA and the FDA in the granted indication were found; 5 of the drugs had more than one notable difference (Fig. 2). Different lines of treatment were the most common difference identified (10 (28 %) drugs). Of the 15 indications with notable differences, the FDA granted the broadest indication in 11 (73 %), EMA granted the broadest indication in 2 (13 %), and in 2 (13 %) drugs it could not be determine whether EMA or FDA granted the broadest indication. The notable differences in the indications for the included cancer drugs are shown in Fig. 2 and Appendix p 1–7.

3.2. Differences in regulatory characteristics of drugs with notable differences in the indication

Eleven (31 %) of the 36 included drugs were both granted standard marketing authorisation by EMA and the FDA, 14 (39 %) were granted conditional approval (conditional marketing authorisation or accelerated approval) by both agencies, whereas discrepancies in the approval type were found in the remaining 11 (31 %); in 8 out of these remaining 11 (73 %) the FDA granted accelerated approval (AA) whereas EMA granted standard marketing authorisation. The application for marketing authorisation was submitted median (IQR) 58 (17;278) days later to EMA than the FDA. The approval date was median (IQR) 347 (218;559) days later in EMA than in the FDA. EMA had more mature data for the

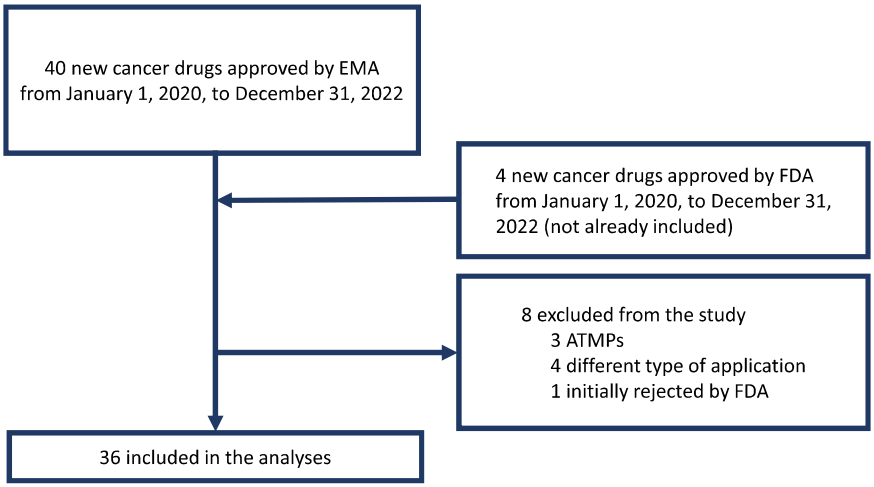

Fig. 1. Flow-chart of included drugs.

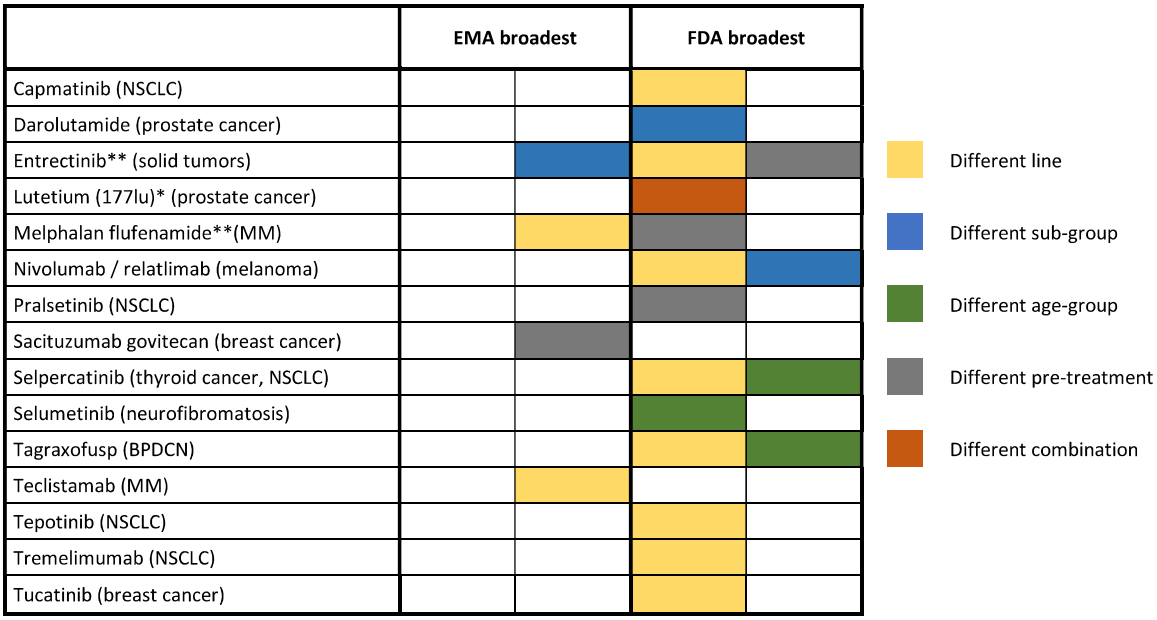

Fig. 2. Drugs with notable differences between the indications granted by EMA and the FDA. The specific differences are divided based on whether EMA or the FDA includes the broadest population. Drugs without notable differences in the indications are not included in the figure. NSCLC=non-small cell lung cancer, MM=multiple myeloma, BPDCN=blastic plasmacytoid dendritic cell neoplasm. *Lutetium (177lu) vipivotide tetraxetan **For Entrectinib and Melphalan flufenamide it could not be determined whether EMA or the FDA granted the broadest indication.

efficacy assessment in 23 (64 %) of the drugs, whereas for the remaining 13 (36 %) the available data for EMA and the FDA were identical. The efficacy assessment by EMA and the FDA was based on the same pivotal trial for 92 % of the drugs.

Regulatory characteristics between the cancer drugs with and without notable differences in the indication granted by EMA and the FDA can be found in Table 1. The percentage of drugs with discrepancy in approval decision was higher for drugs with notable differences (40 % vs. 24 %). Nine of the drugs with notable differences in the indication had the same approval type, whereas 6 of the of the drugs with notable differences in the indication had different approval type. Of the 6 drugs with notable differences in the indication that also have discrepancies in the approval decisions, the FDA granted AA in 4 of them (67 %), whereas EMA granted standard marketing authorisation. In the remaining 2, EMA granted conditional marketing authorisation (CMA) and marketing authorisation under exceptional circumstances, whereas the FDA granted standard marketing authorisation. Differences in time of submission and approval between the two agencies were similar for drugs with or without notable differences in the indication. It was slightly more common that EMA had more mature efficacy data than the FDA in drugs without notable differences in the indication (67 % vs. 60 %); in 40 % of the drugs with notable differences in the indication, the efficacy assessments were based on identical pivotal trial data, and in all of them, the FDA granted the broadest indication. The efficacy assessment in EMA and the FDA was based on the same pivotal trial in 87 % of the drugs with notable differences and 95 % without notable differences. Pivotal phase II trials were more common in drugs with notable differences (60 % vs. 43 %). Drugs with notable differences in the indication had a confirmed effect on overall survival in 30 % vs. 20 % for drugs without notable differences. Randomised controlled trial with a comparator as the pivotal trial was similar for drugs with and without notable differences in the indication (57 % vs. 53 %). No statistically significant differences for each parameter were found between the two groups.

Table 1
Regulatory characteristics of all included cancer drugs, cancer drugs without notable differences in the indication granted by EMA and the FDA, and cancer drugs with notable differences in the indication granted by EMA and the FDA.

	Indications without a notable difference (n = 21)	Indications with notable difference (n = 15)	P-value
Approval type: n (%)			
Standard	6 (29)	5 (33)	1.00
Conditional[a]	10 (48)	4 (27)	0.30
Discrepancy between EMA and the FDA	5 (24)	6 (40)	0.47
Difference in time of submission between EMA and the FDA: Median days [IQR][b]	78 [13;322]	53 [20;188]	0.87
Difference in time of approval between EMA and the FDA:Median days [IQR][c]	343 [202;583]	351 [251;489]	0.98
Most recent data available in efficacy assessment: n (%)			
EMA	14 (67)	9 (60)	0.74
FDA	0 (0)	0 (0)	1.00
Identical	7 (33)	6 (40)	0.73
Application to EMA and the FDA based on the same pivotal trial: n (%)			
Yes	20 (95)	13 (87)	0.56
No	1 (5)	2 (13)	0.56
Phase of pivotal trial: n (%)			
III	8 (38)	4 (27)	0.72
II	9 (43)	9 (60)	0.49
I	3 (14)	0 (0)	0.25
Different pivotal trials[d]	1 (5)	2 (13)	0.56
Design of pivotal trial: n (%)			
Randomised with Comparator	12 (57)	8 (53)	1.00
Single-arm	8 (38)	5 (33)	1.00
Different study design[d]	1 (5)	2 (13)	0.56
Confirmed effect on endpoint with highest clinical relevance: n (%)			
Overall Survival	2 (10)	3 (20)	0.63
Progression-free survival	4 (19)	2 (13)	1.00
Response rate	12 (57)	8 (53)	1.00
Other	2 (10)	0 (0)	0.48
Different endpoint	1 (5)	2 (13)	0.56

*****Testosterone suppression for futibatinib and major molecular response for asciminib.

[a] Conditional marketing authorisation by EMA and accelerated approval by the FDA.

[b] A positive number indicates that the application has been submitted to FDA first.

[c] A positive number indicates that the application has been approved by FDA first. Approval date by EMA was defined as the date the marketing authorisation was issued by the European Commission after positive opinion from the Committee for Medicinal Products for Human Use (CHMP).

[d] The applications to EMA and the FDA were based on different pivotal trials.

3.3. The current status of the included indications

As of March 20, 2025, changes in the indication for the same disease since marketing authorisations have occurred in 5 (33 %) out of the 15 drugs with notable differences between EMA and the FDA in the initially granted indication. In one of the drugs (sacituzumab govitecan) the difference in the indications was aligned post approval due to updated data from confirmatory trials. In two of the drugs (entrectinib and selpercatinib) there are still notable differences in the indications. In the remaining two drugs (melphalan flufenamide, and pralsetinib), the indications were withdrawn in either the EU or the US. The regulatory histories of the indication of the five drugs are described in appendix p8.

4. Discussion

We found that 42 % of new cancer drugs at the time of marketing authorisation have notable differences in the therapeutic indication between EMA and the FDA. The discrepancies could not be explained by differences in maturity of data at time of assessment for the two agencies. Furthermore, the results did not indicate that low level of evidence (e.g., early phase trial as the pivotal, single-arm design, or use of surrogate endpoints) were more common for the drugs with notable differences in the indication. Based on these findings, it is considered most likely that the discrepancies between EMA and the FDA primarily are explained by divergence in regulatory policies between the two agencies.

The largest observed regulatory difference between the two groups was that 40 % of the drugs with notable differences in the indication had a disagreement between EMA and FDA in the type of approval (e.g., standard approval or AA/CMA) compared to 24 % of the drugs without. This finding indicates divergent opinions between EMA and the FDA on whether a clinical benefit has been confirmed, which also might explain the differences in the granted therapeutic indication. Discrepancies in the type of approval for cancer drugs granted by the two agencies have previously been shown and might partly be explained by differences in the requirements for the conditional approvals (e.g. AA and CMA) and how the agencies use them [15–17].

Studies comparing differences in the therapeutic indications given by EMA and the FDA is sparse. A study found that 21 % of new drug approvals from 2014 to 2016 in EMA and the FDA had differences in the indications within all therapeutic areas [18]. Specifically for oncology, a recently published study found notable differences in 52 % of the therapeutic indications which was similar to the results of the present study [7]. Additionally, a study showed differences in the indications given by the two agencies for new gene therapies [19].

The most common notable difference among the therapeutic indications was differences in the line of treatment (28 % of the included cancer drugs). Granting therapeutic indication in an earlier line of treatment can have a major impact on the potential revenue for the marketing authorisation holder as it will include a substantially larger number of patients that potentially can be treated with the drug [20,21]. In 11 (73 %) out of the 15 therapeutic indications with notable differences, the FDA granted a broader indication than EMA (i.e. an earlier line of treatment), whereas EMA granted the broadest indication in 2 (13 %). The results suggest that EMA is more restrictive in extrapolating data from the clinical trials, which is supported by other studies [7,19]. After marketing authorisation, we found that only one (sacituzumab govitecan in metastatic breast cancer) out of the 15 therapeutic indications with disagreements was changed resulting in an agreement between the two agencies. This indicates that the discrepancies between the two agencies generally are not affected by post-approval evidence and remain years after initial approval.

It has been demonstrated that a large proportion of new cancer drugs have limited therapeutic value based on data from pivotal trials [22]. Extrapolation of the clinical data to a broader indication might further reduce the clinical benefit of the treatment potentially changing the benefit-risk balance from positive to negative, which can have severe consequences. First, the treatment might end up harming patients. Second, due to the very high prices of new cancer drugs, it might also have a large health-economic impact without any gained health benefits [23–25].

Research on extrapolation from clinical trials to a therapeutic indication is scarce. EMA has published guidelines for its regulatory assessors to enhance the consistency in the extrapolation of clinical data to therapeutic indications and to investigate clinical benefits for subgroups in confirmatory clinical trials [26,27]. The result from the present study underlines the need for more studies that compare clinical benefits in the real-world setting with the clinical trials to identify patient characteristics that drive a potential discrepancy. Increasing evidence-based extrapolation will hopefully minimize the risk of influencing the benefit-risk balance and likely improve the agreement in decisions across regulatory agencies.

We acknowledge that our work is limited by several factors. First, we did not investigate extensions of therapeutic indications for already approved cancer drugs, which now account for most of the new applications for cancer indications [28]. Second, the evaluation of whether EMA or the FDA had the most data available at the time of assessment was based on the data cutoff for the efficacy analyses in the pivotal trial. This definition is simplified and does not account for differences in safety analyses as well as differences in the availability of data from other trials than the pivotal. Third, due to a relatively small study sample, the statistical comparisons of the regulatory characteristics between the drugs with and without differences have some level of uncertainty. However, no convincing differences were observed descriptively between the groups, which supports the conclusions of the study. Finally, in this study we used a strict definition of a "notable" difference based on objective discrepancies in the granted indication. Due to the strict definition, some of the indications defined as having "notable" differences between the agencies might subjectively not feel like that since it potentially only affects few patients. For example, a small age difference between the indications granted by EMA and the FDA (e.g., selumetinib) might only affect few patients, whereas a difference in line of treatment might affect many more. Another example is lutetium (177Lu) vipivotide tetraxetan where the discrepancy between the two agencies is because requirement of concomitant treatment with androgen deprivation therapy only is mentioned in the EMA indication. Since the vast majority of these patients are receiving androgen deprivation therapy, this discrepancy might only affect few patients. Using other definitions of a "notable" difference in the indications such as defining it based on the number of patients affected of the difference in the indications might yield other results.

5. Conclusions

We found notable differences between EMA and the FDA in 42 % of the therapeutic indications granted at time of marketing authorisation for new cancer drugs. Overall, the cancer drugs with and without notable differences showed similar regulatory characteristics. Therefore, it is considered most likely that the discrepancies between EMA and the FDA primarily are explained by divergence in regulatory policies between the two agencies. The findings from the present study warrant more research focusing on extrapolation of clinical data as well as more collaboration between EMA and the FDA which may improve the regulatory decisions and reduce the misalignment in the future.

Contributors

All authors conceptualized and designed the study. AC performed data collection and analysis. AC wrote the first draft of the manuscript, which was supported by TSP. All authors revised the manuscript critically for important intellectual content and approved the final version for submission.

Ethics statements

Ethical approval not required.

Transparency

The authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jcpo.2025.100660.

Data availability

All data used in the study are provided in the tables and the supplemental material.

References

[1] The European Medicines Agency. Enhancing consistency in wording of therapeutic indications to support healthcare decision-making. 2019. ⟨https://www.ema.europa.eu/en/news/enhancing-consistency-wording-therapeutic-indications-support-healthcare-decision-making⟩.
[2] D. Feldman, J. Avorn, A.S. Kesselheim, Use of extrapolation in new drug approvals by the US food and drug administration, JAMA Netw. Open 5 (2022) E227958.
[3] S. Mailankody, V. Prasad, Overall survival in cancer drug trials as a new surrogate end point for overall survival in the real world, JAMA Oncol. 3 (2017) 889–890.
[4] S. Khozin, K.R. Carson, J. Zhi, et al., Real-world outcomes of patients with metastatic non-small cell lung cancer treated with programmed cell death protein 1 inhibitors in the year following U.S. regulatory approval, Oncologist 24 (2019) 648–656.
[5] H.K. Sanoff, Y. Chang, J.L. Lund, B.H. O'Neil, S.B. Dusetzina, Sorafenib effectiveness in advanced hepatocellular carcinoma, Oncologist 21 (2016) 1113–1120.
[6] A. Cramer, F.K.H. Sørup, H.R. Christensen, T.S. Petersen, K. Karstoft, Withdrawn accelerated approvals for cancer indications in the USA: what is the marketing authorisation status in the EU? Lancet Oncol. 24 (2023) e385–e394.
[7] M. Perini, B. Castiglioni, E. Galai, D. Trapani, A.A. Genazzani, G. Miglio, Differences in the on-label cancer indications of medicinal products between Europe and the USA, Lancet Oncol. 26 (2025) e103–e110.
[8] F. Trotta, H.G.M. Leufkens, J.H.M. Schellens, R. Laing, G. Tafuri, Evaluation of oncology drugs at the European Medicines Agency and US Food and Drug Administration: when differences have an impact on clinical practice, J. Clin. Oncol. 29 (2011) 2266–2272.
[9] Annual reports and work programmes. The European Medicines Agency (EMA). ⟨https://www.ema.europa.eu/en/about-us/annual-reports-work-programmes⟩ (accessed May 30, 2024).
[10] Novel Drug Approvals at FDA. FDA. ⟨https://www.fda.gov/drugs/development-approval-process-drugs/novel-drug-approvals-fda⟩ (accessed Nov 1, 2023).
[11] Advanced therapy medicinal products: Overview. European Medicines Agency (EMA). ⟨https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview⟩ (accessed Oct 13, 2024).
[12] Approved Cellular and Gene Therapy Products. U.S. Food & Drug Administration. ⟨https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products⟩ (accessed Oct 13, 2024).
[13] European Medicines Agency. Search the website. ⟨https://www.ema.europa.eu/en/search/search⟩ (accessed May 30, 2024).
[14] U.S. Food & Drug Administration. Drugs@FDA: FDA-Approved Drugs. ⟨https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm⟩ (accessed May 30, 2024).
[15] Lythgoe M., Krell J., Warner J.L., Desai A., Khaki A.R. Time intervals between U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) new cancer therapy approvals. https://doi.org/101200/JCO20213915_suppl1575 2021; 39: 1575–1575.
[16] A. Cramer, F.K.H. Sørup, H.R. Christensen, T.S. Petersen, K. Karstoft, Cancer drug applications to the EMA and the FDA: a comparison of new drugs and extension of indication in terms of approval decisions and time in review, Br. J. Clin. Pharmacol. (2025), https://doi.org/10.1111/BCP.16391.

[17] T.S. Petersen, K. Karstoft, F.K.H. Sørup, M. Lund, A. Cramer, Regulatory fate of cancer indications in the European Union after accelerated approval in the US, JAMA Oncol. 11 (2025), https://doi.org/10.1001/JAMAONCOL.2024.5145.
[18] M. Kashoki, Z. Hanaizi, S. Yordanova, et al., A comparison of EMA and FDA decisions for new drug marketing applications 2014–2016: concordance, discordance, and why, Clin. Pharm. Ther. 107 (2020) 195–202.
[19] K.N. Vokinger, C.E.G. Glaus, A.S. Kesselheim, Approval and therapeutic value of gene therapies in the US and Europe, Gene Ther. 30 (2023) 756–760.
[20] V. Mathew Thomas, Y. Jo, N. Tripathi, et al., Treatment patterns and attrition with lines of therapy for advanced urothelial carcinoma in the US, JAMA Netw. Open 7 (2024) E249417.
[21] C.C. Steffens, C. Elender, U. Hutzschenreuter, et al., Treatment and outcome of 432 patients with extensive-stage small cell lung cancer in first, second and third line - results from the prospective German TLK cohort study, Lung Cancer 130 (2019) 216–225.
[22] K.N. Vokinger, A.S. Kesselheim, C.E.G. Glaus, T.J. Hwang, Therapeutic value of drugs granted accelerated approval or conditional marketing authorization in the US and Europe from 2007 to 2021, JAMA Heal Forum 3 (2022) e222685.
[23] M.D. Miljković, J. Tuia, T. Olivier, A. Haslam, V. Prasad, Cancer drug price and novelty in mechanism of action, JAMA Netw. Open 6 (2023) E2347006.
[24] D.T. Michaeli, T. Michaeli, Cancer drug prices in the United States: efficacy, innovation, clinical trial evidence, and epidemiology, Value Heal 26 (2023) 1590–1600.
[25] K.N. Vokinger, T.J. Hwang, T. Grischott, et al., Prices and clinical benefit of cancer drugs in the USA and Europe: a cost–benefit analysis, Lancet Oncol. 21 (2020) 664–670.
[26] CHMP). Wording of therapeutic indication - A Guide for Assessors of Centralised Application. 2019. ⟨https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/wording-therapeutic-indication-guide-assessors-centralised-applications_en.pdf⟩ (accessed Oct 13, 2024).
[27] Guideline on the investigation of subgroups in confirmatory clinical trials. The European Medicines Agency. 2019. ⟨https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-investigation-subgroups-confirmatory-clinical-trials_en.pdf⟩ (accessed Oct 19, 2024).
[28] E.C. Scott, A.C. Baines, Y. Gong, et al., Trends in the approval of cancer therapies by the FDA in the twenty-first century, Nat. Rev. Drug Discov. 22 (2023) 625–640.