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1582O Developing a real-world outcomes forecast model using matched oncology clinical trials and real world evidence to inform policy-making and reimbursement approaches

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Background: Payers and pharmaceutical companies increasingly consider evidence-linked market access schemes or outcome-based pricing models, where access or payments depend on real-world outcomes and involve financial risk-sharing. A recognized barrier to implementation has been the uncertainty of basing policy or financial decisions on clinical trial results that may inadequately predict a product's performance in real-world settings or populations. To inform such models and policy decisions, stakeholders would ideally be able to forecast financial impact prior to implementation. Doing so also protects potential down-side financial risk—a key consideration in health systems reliant on public funds with responsibility for prudent budget management. We therefore sought to develop a methodology for forecasting a range of reasonably expected real-world clinical outcomes (RWCOs) using published data from recent oncology clinical trials and post-market studies.

Methods: Using a database of 40 follow-on, longitudinal outcomes studies from 2008-2019 in a large US community oncology network, we identified and matched phase 3 trials and cohorts to real-world studies to compile a dataset. To approach forecasting a range of reasonably expected RWCOs for the identified clinical trials in this dataset, we used nonlinear regression analysis and Monte Carlo simulation to fit and stress-test a curve across the matched cohorts and outcomes.

Results: Through a series of comparisons between phase 3 trial results and corresponding, matched long-term follow-on study results, future RWCOs can potentially be simulated in order to set upper and lower bounds with utility for outcomes-based or risk-sharing pharmaceutical pricing market access models. Next steps include expanding and refining the scope of algorithms tested for their predictive utility and validating these models against other matched sets of clinical trial and post-market studies.

Conclusions: Forecasting and modeling tools that predict RWCOs would allow policy and pricing stakeholders to better understand financial impacts of RWE-based policy decisions and could mitigate stakeholders' exposure to down-side financial risks.

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1583O Clinical benefit of cancer drugs approved in Switzerland during the last decade

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Background: It is unknown to what extent cancer drugs approved in Switzerland by Swissmedic fulfil criteria of clinical benefit according to ESMO, ASCO and the Swiss OLUtool criteria.

Methods: An electronic search of studies that led to new marketing authorisations in Switzerland between 2010 and 2019 was performed. Studies were evaluated according ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) v1.1, ASCO-Value Framework v2 (ASCO-VF) and OLUtool v2. Substantial benefit for ESMO-MCBS, was defined as a grade A or B for (neo)adjuvant intent and 4 or 5 for palliative intent. For ASCO-VF and OLUtool clinical benefit was defined as score >45 and A or B, respectively. Correlation between the frameworks was calculated with Cohen's Kappa (κ). Factors associated with clinical benefit were evaluated by logistic regression. All statistical tests were two-sided.

Results: In the study period, 48 cancer drugs were approved for 92 evaluable indications, based on 100 studies. Of all studies 93% were in the palliative setting and 81% were phase III studies. Ratings for ESMO-MCBS, ASCO-VF and OLUtool could be performed for 100, 86, and 97 studies, respectively. Overall, 39 (39%), 44 (51%), 45 (46%) of the studies showed substantial clinical benefit according to ESMO-MCBS, ASCO-VF, OLUtool criteria, respectively. There was fair concordance between ESMO-MCBS and ASCO-VF in the palliative setting ($\kappa = 0.31$, p=0.004) and moderate concordance between ESMO-MCBS and OLUtool ($\kappa = 0.41$, p<0.001). There was no concordance between ASCO-VF and OLUtool ($\kappa = 0.18$, p=0.12). Factors associated with clinical benefit in the palliative setting in multivariable analysis are shown in the table.

Table: 1583O

	Factor	OR (p-value)
ESMO-MCBS 1.1	Breast cancer (vs. lung cancer) Melanoma (vs. lung cancer)	0.21 (0.093) 0.21 (0.073)
ASCO-VF v2*	**CPI combination tx (vs. small molecule)** Chemo mono tx (vs. small molecule) **CDK4/6 inhibitor plus endocrine tx (vs. small molecule)**	**0.08 (0.028)** 0.13 (0.093) **0.06 (0.017)**
OLUtool v2.0	**Blinded study (vs. open label)** Phase III study (vs. phase I or II)	**3.30 (0.012)** 3.47 (0.080)

CPI, checkpoint inhibitor; OR, odds ratio (adjusted); tx, therapy.
* no adjustments were made since no other covariates had a p-value <0.1 in univariable analysis.

Conclusions: Only around half of the trials supporting marketing authorisation of recently approved cancer drugs in Switzerland meet the criteria for substantial clinical benefit when evaluated with ESMO-MCBS, ASCO-VF or OLUtool. At best, there was only moderate concordance between the grading systems.

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1585MO Factors associated with change in overall survival and quality of life between time of approval and post-marketing among anti-cancer therapies

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Background: The US Food and Drug Administration (FDA) criteria for registration allow cancer drugs to be approved based on surrogate outcomes. Here, we explore factors associated with overall survival (OS) and quality of life (QoL) benefit both at the time of initial approval and in the post-marketing period (PMP).

Methods: For trials supporting FDA cancer drug approvals between January 2006 and December 2015, we performed a systematic search of Pubmed and ClinicalTrials.gov to identify updated OS and/or QoL data, with follow-up through to April 2019. We explored variables associated with improvement in OS or QoL in the palliative setting using logistic regression.

Results: Among 96 trials, approval was based on improved OS in 41%. Among 59 trials providing updated efficacy data in the PMP, 47% showed improved OS; 39% for the first time. Improved OS at any time was observed in 52% of all trials. Only 47% of trials reported patient-reported outcomes (PRO) initially. Of these, 58% demonstrated a significant improvement in at least one PRO. Among 50% of trials which reported updated PRO data, improved QoL was observed in 46%; 50% for the first time. Improved QoL was observed in 38% of all trials. There were statistically significant associations between improved OS at initial approval and regular approval (OR 21.38; p=0.004), orphan drug designation (OR 0.39; p=0.04), sample size (OR 1.70; p<0.001), most prevalent tumors (OR 2.40; p=0.041), and crossover (OR 0.16; p=0.001). There was a non-significant

association between improved QoL at initial approval and open-label studies (OR 3.85; p=0.053). Improved OS in the PMP was associated with immunotherapy (OR 8.20; p=0.026) and drugs with companion diagnostics (OR 11.67; p=0.006). Improved QoL in PMP was associated with sample size (OR 0.73; p=0.031), immunotherapy (OR 9.14; p=0.02) and open-label studies (OR 8.89; p=0.048).

Conclusions: Factors associated with OS and QoL benefit differs at the time of approval and in the PMP. Initially, drugs for prevalent tumors with regular approval are associated with OS benefit. In the PMP, immunotherapy and drugs with companion diagnostic tests are associated with improved OS.

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1587MO How much does it cost to research and develop a new medicine? A systematic review and evaluation of 40 years of literature

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Background: The biopharmaceutical industry faces challenges related to its research & development (R&D) productivity. At the same time, some pricing policies for new products, particularly those concerning anticancer and orphan medicinal products, have been perceived as non-transparent or even outrageous, resulting in increased resistance by policy makers to reimburse them. In this context, a controversial theme has been the cost of bringing a new molecular entity (NME) to market. We reviewed, and critically assessed, the studies providing estimates of the pre-launch research & development (R&D) cost per NME.

Methods: A full systematic literature review of publications estimating the (pre-launch) R&D costs was conducted. 22 articles with 45 cost estimates were included (three focus on oncology and 16 include cancer alongside other therapeutic areas). We appraised their quality by evaluating 16 factors covering three domains: (1) how the drug samples, success rates, and development times used for cost estimation were obtained; (2) potential sources attributing to the variation in R&D costs; and (3) the cost components.

Results: Estimates of the total average capitalized R&D costs vary widely, from $161million to $4,539 million (2019 USD), with cancer drugs marking the top. We found evidence that the magnitude of these estimates has increased over time, but it is not related to study quality. In addition, average costs mask important differences, e.g. estimations suggested positive skewness for oncological drugs, with an average capitalized R&D cost between $944 and $4,539 million, while a median between $788 and $2,818 million (2019 USD). "Potential sources of variation" was the domain that shows the lowest quality scores.

Conclusions: Due to the heterogeneity of the methodologies and the variability (e.g., by therapeutic area) of the results, caution must be exercised when applying the estimated R&D cost averages. Given the variability of pre-launch drug R&D cost estimates, a standardized framework specifying the factors that ought to be considered in cost estimation seems warranted, and we propose one such here.

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1589MO Opposition to a patent covering tisagenlecleucel: Using intellectual property (IP) legislation to defend sustainable access to cancer therapies

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Background: Since 2013, cancer care professionals have raised concerns about cancer treatment high prices. As prices on cell therapies have skyrocketed over $350,000, there is now a consensus that cancer drugs' high prices may become a barrier to universal access to new cancer therapy, and to the sustainability of public health systems. High prices on new cancer drugs are linked to monopolies, misuse of patents and lack of public scrutiny regarding the quality of patents. This situation has hindered rational policy making. Patent oppositions have been recognized as one effective way to contest abusive monopolies. Used since 2005 by NGOs from the Global South in their fight against HIV/aids, this legal procedure has allowed for public scrutiny of patents, raised awareness on the weakness of health inventions patents, and strengthened patentability analysis standards. Following this path, in July 2019, Médecins du Monde and Public Eye questioned a Car-t treatment tisagenlecleucel patent at the European Patent Office (EPO) based on its lack of inventive step.

Methods: We have filed a patent opposition to the patent EP3214091. A patent opposition is a legal procedure for challenging the validity of a granted patent based on lack of novelty, inventive step and/or industrial application. As a result, the patent may be maintained, amended or revoked. When revoked, the legal effects associated with the patent are suspended, including monopoly rights.

Results: In November 2019, in response to our patent opposition, Novartis and the University of Pennsylvania requested revocation of the patent. In December 2019, the EPO revoked patent EP3214091. Our patent opposition was effective to scrutinize patent EP3214091. This result weakened tisagenlecteucel monopoly and produced a strong argument for public officers to demand fairer prices. Other patents are in force that still do not allow the production of biosimilar versions of tisagenlecleucel.

Conclusions: We have showed a method through which monopoly abuses on new cancer treatments can be regulated. A stronger mobilization of oncologists is necessary to prevent abusive monopolies in order to safeguard sustainable access to cancer treatments.

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1590MO Income loss after a cancer diagnosis from the patient perspective: An analysis based upon the German Socio-Economic Panel (SOEP) survey

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Background: Cancer treatments often require intensive use of healthcare services and limit patients' ability to work, potentially causing them to become financially vulnerable. In Europe, research on this topic has been largely neglected, arguably due to the belief that financial hardship for cancer patients is not a major concern in European social welfare states. The present study is the first attempt to measure, on the German national level, the magnitude of income loss after a cancer diagnosis.

Methods: This study analyzes data from the German Socio-Economic Panel (SOEP) survey, one of the largest and most comprehensive household surveys in Germany, consisting of approximately 20,000 individuals, who are traced annually. The empirical strategy consists of OLS and multinomial logistic estimators to measure changes in job income, work status, working hours, and pension as a result of reporting a cancer diagnosis for the period between 2009 and 2015. Sample consistency checks were conducted to limit measurement error biases.

Results: Our empirical results show that job incomes dropped between 21% and 28% within the year a cancer diagnosis was reported. The effect persisted for two years after the diagnosis and was no longer observable in our data set after four years. The finding was linked to an increased likelihood of unemployment and a reduction of working hours by 24%. Pension levels, on the other hand, were not affected by a cancer diagnosis.

Conclusions: Our analysis suggests that many cancer patients are exposed to financial hardship in Germany, particularly when the cancer diagnosis occurs during their active life and before requirements to obtain a pension are met. Further research seems warranted to identify particularly vulnerable patient groups.

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