

time gap from TFDA approval to reimbursement on mortality for advanced CRC patients. **METHODS:** The data was from 2 million sampling reimbursement data set of Taiwan's National Health Insurance Research Database (NHIRD) and diseased stage was derived from the Taiwan Cancer Registry (TCR) between 2007 and 2011. Diseased stage diagnosed for the first time ever of CRC patients was recorded in TCR. Patients' survival data and prescription time of target therapy were derived. Fisher exact test was used for the comparisons of frequencies; log rank was used survival comparisons; and hazard ratio was derived using both Cox regression with time and time independent analysis. **RESULTS:** 364 staged 4 CRC patients were derived and enrolled into the analysis. There were 11 patients diagnosed with CRC before the target therapy was approved for reimbursement, whereas 353 were diagnosed after. 70 of them were prescribed target therapy during the disease treatment period. Median survival years for those who were prescribed target therapy was 2.6 as compared to 1.2 without. There was a statistical significant survival difference between target therapy use after the reimbursement approval and non target therapy use before approval, HR = 0.073(0.031-0.176), $p < 0.0001$. The use of target therapy and non user was also significant with HR = 0.53(0.369-0.759), $p = 0.0005$. Multivariate Cox regression suggested that the effect of time gap in target therapy reimbursement approval was statistical significant with $p = 0.0019$. **CONCLUSIONS:** Time gap due to reimbursement process influences patient's mortality. Shortening the time gap to reimbursement approval is suggested.

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4+ YEARS OF AMNOG – CLINICAL DRIVERS FOR SUCCESSFUL DOSSIER SUBMISSIONS IN ONCOLOGY

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OBJECTIVES: 135 dossiers have been evaluated by G-BA since AMNOG was introduced. Looking at oncology products, 43 have started into AMNOG process and for 38 G-BA has finalized its decision. In 32 assessments an additional benefit was granted, leading to a success rate of 84% compared to only 36% in non-oncology products. Objective of this research is to identify drivers responsible for successful benefit assessment outcomes in oncology. **METHODS:** All oncology assessments were analysed to reveal key drivers responsible for positive assessments by IQWiG + G-BA. Next to comparator choice the analysis focused on submitted endpoints, where it is evaluated which endpoints contribute most in oncology indications to additional benefit. **RESULTS:** Additional benefit is assessed based on patient relevant endpoints (mortality, morbidity, quality of life & safety). More than 55% of submitted endpoints fall in the safety category, followed by morbidity (approx. 30%), mortality (approx. 10%) and quality of life (approx. 5%). OS has shown to be the most relevant endpoint, where the G-BA granted additional benefit in 23 out of 32 dossiers primarily based on OS data. In terms of morbidity, PFS, ORR and "Time to Pain Progression" are the top three submitted morbidity endpoints; however, only "Time to Pain Progression" led to additional benefit in 2 out of 3 cases and QoL led to additional benefit in 4 cases. **CONCLUSIONS:** OS will continue to be the most relevant endpoint for IQWiG + G-BA when determining the additional benefit in oncology. In the absence of OS, PFS will not help in the overall additional benefit decision by G-BA, unless the MNF can justify PFS to be patient relevant according to IQWiG methodology. Although QoL is an accepted endpoint by G-BA, due to the high methodological standards set by G-BA and IQWiG chances are low that a QoL improvement alone will lead to additional benefit.

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COMPARATIVE COST-EFFECTIVENESS OF DRUGS IN EARLY VERSUS LATE STAGES OF CANCER; REVIEW OF THE LITERATURE AND A CASE STUDY IN BREAST CANCER

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OBJECTIVES: Many oncological drugs that are being used in the adjuvant setting were first submitted for reimbursement in the metastatic stage, with differences in incremental cost-effectiveness ratios (ICERs) in both settings having potential implications for reimbursement and pricing. The aim of this study is to identify a possible trend in the cost-effectiveness for the early/adjuvant and late/metastatic stages of oncological drugs through review and case study. **METHODS:** We reviewed pairs of cost-effectiveness analyses of the same oncological drug in different stages for Scotland and the Netherlands. The case study in this report was directed at trastuzumab in the Dutch situation. Using a simplified Markov model, the cost-effectiveness in early and late stage of breast cancer was calculated and compared to the findings from the review. **RESULTS:** Comparable studies were found for cetuximab, bortezomib and bosutinib. Treatments in the late stage were found to be more expensive per QALY by a factor ranging from 1.5 to 12. The case study provided a similar result; late stage treatment was more expensive by a factor 10. Using, for example, a threshold of €80,000/QALY, the early stage of cetuximab, bosutinib and trastuzumab are deemed cost-effective, while their compared late stage is lifted over the threshold and potentially considered not cost-effective. **CONCLUSIONS:** ICERs of oncological drugs used in different stages are more unfavourable in the late stage than in the early stage. Applying a reasonable threshold may result in early stage treatment being deemed cost-effective while late stage potentially not. Authorities should be aware of this when assessing oncological drugs and interpreting the corresponding ICERs, in the situation where oncological drugs are generally most submitted for reimbursement in the late stage initially.

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OPPORTUNITIES WITH ACCELERATED APPROVAL TIMES, BUT STUMBLER AT HTA? THE IMPACT OF A LIMITED EVIDENCE PACKAGE

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OBJECTIVES: Accelerated approval pathways can shorten time to market for therapies treating diseases, particularly those with significant morbidity and mortality and few effective alternatives. However, little is known about payers' reactions to submissions based on a Phase 2, single-arm trial. This study aimed to identify market access challenges for products with accelerated marketing authorization based on this limited data package. **METHODS:** Oncology products receiving European marketing authorization since 2012 based on a Phase 2, single-arm study were identified and the associated EPARs and HTA submissions in France, Germany and the UK (NICE) reviewed. **RESULTS:** Six products were identified (Adcetris, Bosulif, Erivedge, Iclusig, Imbruvica, and Zydelig); four had orphan designation. No pivotal trials included survival as the primary endpoint, none reported HRQL and no comparative data were cited in the regulatory packages. Only one product was reviewed by NICE (England) and was not recommended (another did not submit). All six G-BA (Germany) reviews resulted in either additional benefit not proven, not quantifiable (or minor in one subgroup). In France, the ASMR ratings ranged from III to V (moderate, to no improvement compared with existing treatments). Common themes identified which could be addressed by additional evidence generation included: (1) clarity on the target patient population and unmet need; (2) establishing the current standard of care and positioning within the treatment pathway; (3) determining relative efficacy given the focus on survival benefit and the increasing weight of additional value drivers. **CONCLUSIONS:** Although marketing authorization is granted, products supported by Phase 2, single-arm trial data face significant HTA challenges; payers are being asked to make decisions based on limited data. Some evidence gaps can be addressed with additional evidence generated alongside the pivotal trial. However, uncertainty about a product's value may result in poor HTA outcomes, and a poor position from which to negotiate price.

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DOES BUDGET IMPACT AFFECT REIMBURSEMENT DECISIONS MADE BY THE CANCER DRUGS FUND IN ENGLAND?

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OBJECTIVES: The Cancer Drugs Fund (CDF) in England has an annual budget of £280 million to fund cancer drugs on the NHS that were not assessed by or were rejected by NICE. In 2014, drugs on the CDF were re-assessed based on criteria including cost per patient and 16 were removed from the list. Previous analysis on a sub-set of the drugs that were re-assessed indicated that drugs with a higher budget impact might be more likely to be rejected by the CDF (presented at HTAi 2015). We aimed to expand the analysis to all those re-appraised by the CDF, to investigate whether this trends holds when a larger sample size is used. **METHODS:** Using the cost per cycle, cycle length and median duration of treatment extracted from the CDF decision summaries, the cost per patient was calculated for every drug assessed in 2014. The budget impact of those drugs that had previously been reimbursed by the CDF was calculated based on the number of notifications that the CDF received in 2014. A point-biserial correlation coefficient (rpb) was used to assess whether cost per patient and total budget impact were correlated with the CDF reimbursement decision. **RESULTS:** Investigation of the larger sample set confirmed the initial results of the previous analysis and determined that there was a positive correlation for cancer drugs with a higher cost per patient to be included in the CDF (rpb=0.643); this is most likely due to the superior clinical evidence. The budget impact was found to have little influence on the CDF reimbursement decision in this larger sample size (rpb=0.105). **CONCLUSIONS:** Although the CDF's new criteria for reimbursement do involve an evaluation of the cost of each drug, it seems that neither the cost per patient nor the overall budget impact greatly influences their decisions.

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PATIENT REPORTED OUTCOMES (PRO) IN POSTPROGRESSION ONCOLOGY: IMPLICATIONS IN HEALTH TECHNOLOGY ASSESSMENTS (HTA) & PAYER DECISION MAKING

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OBJECTIVES: To assess the impact of PRO data collected after clinical progression (i.e., postprogression) on payer decision making in oncology. **METHODS:** One-on-one interviews were conducted with 16 payers and payer advisors from 14 countries in 2014. An online assessment was conducted (December 8, 2014, to March 4, 2015) with 20 completed surveys (China, France, Germany, Spain, Taiwan, the UK, the US) and 7 partially completed surveys (Australia, South Korea, the US) by payers from the RTI Health Solutions Global Payer Advisory Panel. **RESULTS:** PRO data are commonly collected during trials; however, collection of PRO data postprogression is less common. When asked about the value of collecting PRO data postprogression, payers indicated that they consider this particularly important in cancer types with relatively long survival and those that involve palliative and/or long-term care. All payers in the one-on-one interviews advised collecting postprogression PRO data in both the control and comparator arms. Eleven of the 16 respondents in the one-on-one interviews indicated that it is worthwhile to collect PRO data postprogression and that positive PRO data may support continued therapy, even if the tumor is progressing. Results from the online assessment indicated that payers outside the US considered postprogression PRO data more useful than US payers did. When queried about specific types of postprogression data, payers generally thought that all types of PRO data examined (stability of disease, improvement in health-related quality of life, improvement in symptom severity or frequency, improvement in functional status, slower rate of functional deterioration compared to control/comparator arm) were important to decision making. Payers generally deferred to clinical experts on the length and frequency of postprogression PRO data collection. **CONCLUSIONS:** PRO data provide compelling evidence even after tumors have progressed clinically and may help differentiate products, especially in situations where therapies do not provide significant survival benefits.