OBJECTIVES: To highlight the impact of tolerability profiles on HTA decision making in oncology. The study evaluated on-treatment tolerability of lung cancer and prostate cancer from three European HTA agencies. METHODS: Tolerability assessments on NSCLC, ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. RESULTS: In the UK, safety profiles of the investigated drugs did not seem to have major impact on the recommendation. It was however seen that drugs with a good tolerability profile were more often recommended for clinical outcomes; on the final decision from NICE was, for example, seen in the assessment of afatinib, where a significant increase in serious adverse events did not negatively impact the recommendation because clinical benefits outweighed safety concerns. Safety data and patient-relevance of endpoints is of high importance in Germany. A beneficial safety profile resulted in a higher benefit rating, whereas a negative safety profile lowered the G-BA rating. Case examples are evaluations of afatinib and crizotinib, where a negative safety profile lowered the benefit rating. Efficacy outcomes were weighted against safety outcomes in all assessments in France. An unfavourable safety profile appeared to have a negative impact on the ASMR rating from HAS, while a favourable profile did not have a positive impact. An example is the assessment of cabazitaxel, where the safety data presented at the initial submission was unfavorable, resulting in a lower ASMR rating (IV), however a resubmission with additional safety data resulted in a higher rating (III). CONCLUSIONS: Different EU countries seem to have a different view on safety profiles, with the highest impact seen in Germany and the lowest impact seen in the UK.

OBJECTIVES: The extent to which individual lung cancer patients undergo guideline-recommended molecular testing in routine care prior to initiation of first-line erlotinib is not known. Prevalence and factors associated with testing and erlotinib therapy were determined in Stage IV non-small cell lung cancer (NSCLC). METHODS: We identified incident cases diagnosed between 2007-2009 using SEER-Medicare data. Multivariable models were used to identify factors independently associated with undergoing molecular testing and first-line erlotinib therapy. RESULTS: Only 6.5% (5007/76,678) were treated with first-line erlotinib and of those, only 8.6% underwent a molecular test. Testing and erlotinib therapy were independently associated with phenotypic enrichment using correlates of epidermal growth factor receptor (EGFR) mutations (female gender, Asian ethnicity, non-squamous-cell histology). Older age, Medicare enrollment, and admission to hospice decreased likelihood of testing but increased probability of erlotinib therapy. CONCLUSIONS: Vast majority of high-risk NSCLC patients are not undergoing clinical molecular testing. Clinical enrichment criteria were influential in patient selection for erlotinib therapy and testing, but these attributes do not adequately discriminate between EGFR mutant and wild-type tumors. Provider education and payer mandates to submit test results before reimbursement for targeted therapies may encourage guideline-recommended implementation of these technologies.

OBJECTIVES: To evaluate whether the orphan designation has an impact on the reimbursement and pricing for drugs in oncology between 2006 and 2013 and appraised by four agencies (HAS, France; G-BA, Germany; PCN180 AstraZeneca, Cheshire, The Netherlands; NICE, UK). METHODS: HTA assessments on non-small cell lung cancer (NSCLC), ovarian cancer and prostate products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. In addition ASCO and ESMO guidelines were reviewed for recommendations. RESULTS: In the UK, safety profiles of the investigated drugs did not seem to have major impact on the recommendation. It was however seen that drugs with a good tolerability profile were more often recommended for clinical outcomes; on the final decision from NICE was, for example, seen in the assessment of afatinib, where a significant increase in serious adverse events did not negatively impact the recommendation because clinical benefits outweighed safety concerns. Safety data and patient-relevance of endpoints is of high importance in Germany. A beneficial safety profile resulted in a higher benefit rating, whereas a negative safety profile lowered the G-BA rating. Case examples are evaluations of afatinib and crizotinib, where a negative safety profile lowered the benefit rating. Efficacy outcomes were weighted against safety outcomes in all assessments in France. An unfavourable safety profile appeared to have a negative impact on the ASMR rating from HAS, while a favourable profile did not have a positive impact. An example is the assessment of cabazitaxel, where the safety data presented at the initial submission was unfavorable, resulting in a lower ASMR rating (IV), however a resubmission with additional safety data resulted in a higher rating (III). CONCLUSIONS: Different EU countries seem to have a different view on safety profiles, with the highest impact seen in Germany and the lowest impact seen in the UK.

OBJECTIVES: To highlight the hierarchy of clinical endpoints in Health Technology Assessment (HTA) decision making in oncology. The study evaluated on-treatment tolerability of lung cancer and prostate cancer from three European HTA agencies. METHODS: Tolerability assessments on non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. In addition ASCO and ESMO guidelines were reviewed for recommendations around endpoints. RESULTS: HTA agencies base their decisions on the significance of the presented outcomes, but an analysis of NSCLC assessments showed that when the effect sizes in overall survival (OS) and progression-free survival (PFS) were deemed to be clinically irrelevant, recommendations were less positive. Significant improvements in OS and PFS can still be rejected in the UK because of unacceptable cost-effectiveness. Assessments demonstrating improvements only in PFS were most of the time rejected. Significant improvements in OS were associated with a higher ASMR rating in France. Assessments with improvements in surrogate outcomes, including PFS and overall response rate, were also accepted. OS and PFS are the main surrogates for clinical benefit in guideline-recommended treatment in Germany. A combination of OS and QoL improvements was associated with a higher G-BA benefit rating. When OS or QoL data were absent, the benefit rating was lower. CONCLUSIONS: The quality of data is considered the gold standard for clinical benefit in oncology, but surrogate outcomes and QoL benefits were also accepted when non-significant OS results were seen. In addition, it seems that statistical significance in itself is not enough, as payers want to see a clinically meaningful difference. Further research on tolerability, cost and clinical endpoints for which thresholds for clinical-relevance have been published recently, could validate these results.