OBJECTIVES: To highlight the impact of tolerability profiles on HTA decision making in oncology. The impact of safety profiles and tolerability on HTA decision making for non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer from three European HTA agencies. METHODS: Safety 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 safety profile were more often recommended. 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 zotuzumab, 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 favorable 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 payers 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 extent to which individual lung cancer patients undergo guideline-recommended molecular testing in routine care prior to initiation of first-line erlotinib was 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 test ordering in a Cox proportional hazard model of receipt of first-line erlotinib therapy. RESULTS: Only 6.5% (500/7,678) were treated with first-line erlotinib and of those, only 8.6% underwent a molecular test. Testing and erlotinib therapy were independently associated with subsequent OS and QoL benefit. 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 educational mandates and payer mandates to submit test results before reimbursement for targeted therapies may encourage guideline-recommended implementation of these technologies.

OBJECTIVES: The Food and Drug Administration (FDA) grants breakthrough therapy designation (BTD) to facilitate faster approval of drug products are intended to treat a serious or life-threatening condition or provide substantial improvement over existing therapies. The purpose of this review is to compare time to approval, treatment cost and key clinical design characteristics of BTD to non-BTD drugs in oncology. METHODS: This narrative review used publicly reported data from drug manufacturers' and FDA websites to examine all oncology drugs approved between November 2013 and December 2014. Median time-to-approval was assessed for new molecular entities (NMEs) and monthly treatment cost was calculated for approved indications based on wholesale acquisition cost (WAC) from AnalySource. Approved oncology drugs were categorized as BTD and non-BTD drugs for comparison. RESULTS: A total of 25 FDA indications for oncology drugs were approved from November 2013 to December 2014. Nine indications were granted BTD, while 16 were granted fast track. For all indications, 1 trial initiation to indication approval was 2 times longer for non-BTD drugs (3414 days) compared to BTD drugs (1732 days). Pivotal trials had a median sample size for BTD drugs of 1095 patients, and 2157 patients for non-BTD drugs, respectively. For BTD drugs, pivotal trials were 44% phase 2, 44% single-arm, and 89% open-label studies. For non-BTD drugs, pivotal trials were 44% phase 2, 28% single-arm, and 69% open-label studies. Median treatment cost was $9,249 per month for BTD drugs and $7,369 per month for non-BTD drugs. CONCLUSIONS: The BTD approval pathway has offered a considerably shorter time-to-first approval for oncology drugs. Trials leading to approval for BTD drugs had a higher proportion of single-arm and open-label studies compared to non-BTD drugs. Our findings suggest that oncology drugs with BTD are not related to higher treatment costs.