reviewers. To determine the association between biases related to attrition, missing data, and the use of intention to treat and effect sizes, a two-level analysis was conducted using a meta-meta-analytic approach.

Results. Three-hundred and ninety-three trials included in 43 meta-analyses, analyzing 44,622 patients contributed to this study. From these, 134 trials (34.1%) used ITT and 218 (55.5%) did not use ITT. Trials which did not use the ITT principle, or which were assessed as having an inappropriate control of incomplete outcome data (based on the Cochrane risk of bias tool) tended to underestimate the treatment effect when compared with trials with adequate use of ITT (ES= -0.13; 95%CI -0.26, -0.01) or trials which were assessed as having an appropriate control of incomplete outcome (ES= -0.18; 95%CI -0.29, -0.08).

Conclusions. Our results suggest that when evaluating risk of bias of primary RCTs, systematic reviewers should pay attention to these biases since they could underestimate treatment effects. Systematic reviewers should perform sensitivity analysis including trials with low risk of bias in these domains.

OP53 Health Technology Assessment Acceptability Of Innovative Survival Metrics In Oncology

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Introduction. Most new oncology therapies are studied in the advanced/metastatic setting. However, there is an increasing focus on earlier stage disease. Nevertheless, measuring Overall Survival (OS) in neo-/adjuvant therapy trials can be very challenging due to the increased life expectancy and the confounding effects of subsequent treatments. Thus, their primary endpoints tend to be surrogate survival metrics (e.g. metastases-free survival). This research aims evaluates the health technology assessment (HTA) acceptability of such endpoints through recent neo-/adjuvant HTA assessments.

Methods. The European Medicines Agency (EMA) website was screened for any neo-/adjuvant oncology therapies approved (1 January 2013-22 October 2018) and any corresponding publicly-available assessments by HTA bodies (NICE, SMC, IQWiG, G-BA, CADTH, PBAC, HAS) were identified and key data extracted.

Results. Six neo-/adjuvant therapies have received marketing authorization by the European Commission (EC). These six have been on the market for an average of 8.9 months (range: 0.9-39.3 months, median: 3.3 months). In four of the six, the pivotal trial primary endpoints were measures of relapse-/disease-free survival, (others: pathological complete response and PFS/OS co-primary). Only one had mature OS data available at EC-approval. Four of the six therapies had received at least draft guidance by an HTA body, encompassing 11 HTA assessments in total (4: NICE, 2: IQWiG, HAS; 1: SMC, CADTH, G-BA). Only two of 11 (18%) were positive outcomes (both NICE), the remaining nine were negative.

Conclusions. Oncology therapies are increasingly receiving regulatory approval in the neo-/adjuvant setting. However, their pivotal trials are frequently powered to show benefits in disease-/metastases-free survival. Whilst sufficient for regulatory approval, translating this to favorable HTA decisions has been more challenging. Clearly establishing linkages between surrogate survival metrics and OS alongside measuring metrics that clearly portray patient benefits (e.g. time to symptomatic progression) could improve HTA-acceptability. Further, some payers allow for temporary reimbursement whilst additional evidence is generated (e.g. Cancer Drugs Fund in England).

OP54 Monitoring Evidence On Overall Survival Benefits Of Anti-Cancer Drugs

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Introduction. The introduction of fast-track licensing strategies increases the approval of anti-cancer drugs with ambiguous benefit-risk profiles. Thus, in many instances there is lacking evidence about overall survival (OS) at the time of marketing authorisation. Our objective was to monitor and characterise therapies with ambiguous benefit-risk profiles and identify any post-approval updates on median OS after at least three years of approval by the European Medicines Agency (EMA).

Methods. We included all originator anti-cancer drugs with initially ambiguous benefit-risk profiles that received marketing authorization from the EMA between 1 Jan 2009 and 31 May 2015. Our monitoring timeframe was at least three years after EMA-approval. To identify study updates, the following three sources were included: clinicaltrials.gov, European Public Assessment Reports (EPARs), and PubMed.

Results. In total, we identified 102 eligible approval studies. Out of these, a negative difference in median OS or no information was available in forty-three (42.2%) instances. During monitoring, eleven updates with accessible information on median OS could be identified. Including monitoring results, there are still thirty-two remaining therapies (31.4%) where no or negative information (n = 27 [26.5%] and n = 5 [4.9%], respectively) regarding median OS was present at least three years after EMA approval.

Conclusions. One-third of oncology drugs with ambiguous benefit-risk profiles failed to demonstrate a survival benefit even several years following marketing authorization. Systematic and transparent post-approval monitoring mechanisms will be of high relevance to assure a clinically relevant patient benefit, since the trend towards faster access to medicines with uncertain benefit is increasing rather than declining.

OP56 Are Therapeutic Positioning Reports Driving Pharmaceutical Reimbursement Outcomes In Spain?

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