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**Clinical versus surrogate outcome measures in pivotal supporting studies for medicines granted conditional or accelerated marketing authorisation by the European Medicines Agency**

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**Introduction:** In situations of unmet medical need, conditional marketing authorisation (CMA) and accelerated approval (AA) pathways introduced by the European Medicines Agency (EMA) permit new drugs to be marketed more quickly than through the standard approval process. CMAs allow marketing before comprehensive data are available but marketing authorisation holders are obliged to undertake specified post-marketing studies.(1) AA reduces the approval timeframe but not the evidence requirements. In both cases, the pivotal studies supporting approval applications may report surrogate outcomes because they are cheaper, easier and faster to evaluate than waiting for clinical outcomes.(2) Some surrogates are not validated as accurately reflecting the intended clinical outcomes. Our aim was to determine how commonly CMAs and AAs were based on surrogate rather than clinical outcome studies, if surrogates were validated, and to assess CMA-imposed post-authorisation study completion.

**Methods:** Using European Public Assessment Reports (EPARs), we assessed CMAs and AAs issued between January 2011 and March 2016.(3) Ethics approval was not required.

**Results:** Of fifteen CMAs identified, the pivotal studies in six (40%) reported clinical outcomes. Nine (60%) reported surrogate outcomes of which seven, mainly for malignancies, were validated. Three post-marketing studies, including two for CMAs without validated surrogates, imposed clinical outcomes. Of nine CMAs for which the post-marketing study due-date had passed by 1-3 years, the EPARs reported the results for two studies (22%). The EPARs did not confirm completion, explain delays, or report results for seven post-marketing studies (78%). Nineteen AAs were identified. The pivotal studies were based on clinical outcomes in ten (53%) and on surrogate outcomes in nine (47%) AAs of which two surrogates were validated. Seven AAs were issued for hepatitis C treatments but the surrogate outcome, sustained virological response, has not been shown to predict the clinical outcome, reduced risk of hepatocellular carcinoma.(4)

**Conclusion:** Both CMAs and AAs are issued on the basis of surrogate outcomes alone, some of which are not validated. According to the EPARs, results of many CMA-imposed post-authorisation studies appear considerably delayed without explanation.

**References:**

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