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Progression-free survival, overall survival and quality of life: What is their medicoeconomic importance in oncology?☆

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Summary Medico-economic evaluations estimate, for a given health technology, the added cost and the clinical benefit compared to a reference strategy. The objective here is to analyze the criteria used to measure clinical benefit as the basis for market access and reimbursement decisions for drugs in oncology both in France and in Europe. Prolonged overall survival is the criterion of choice to demonstrate the benefit of an anticancer drug; a survival gain of 2 to 3 months or more would be considered as relevant for a new product versus the comparator. In the absence of survival benefit or mature data on survival, progression-free survival or symptom-free survival and the availability of alternative curative treatments, decrease in drug toxicity and quality of life improvement may be considered. Differences in clinical benefit assessment between regulatory agencies and payers are not specific to France. Case studies show that it is difficult to find a consistency in reimbursement and pricing decisions and to identify factors that may fully explain reimbursement decisions when survival benefit is not demonstrated.

Abbreviations

ASCO	American Society of Clinical Oncology
ASMR	added clinical benefit (*amélioration du service medical rendu*)
BIA	budget impact analysis
CEESP	Economic Evaluation and Public Health Committee (*Commission d'évaluation économique et de santé publique*)
CEPS	Economic Committee for Health Products (*Comité économique des produits de santé*)
CT	transparency committee
ESMO	European Society for Medical Oncology
EUnetHTA	European network for Health Technology Assessment
HAS	French health authority (*Haute Autorité de santé*)
HTA	European Health Technology Assessment Agencies
ICER	incremental cost-effectiveness ratio (RDCR ratio [*différentiel coût résultat*])
IQWIG	Institute for Quality and Efficiency in Healthcare (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*)
NICE	National Institute for Health and Care Excellence
NCCN	National Comprehensive Cancer Network
NHS	National Health Service
ONDAM	national health insurance spending objectives (*objectif national des dépenses d'Assurance maladie*)
OS	overall survival
PFS	progression-free survival
QALY	quality adjusted life years
QoL	quality of life
TC	transparency committee
WHO	World Health Organization

Introduction

Medico-economic evaluations estimate, for a given health technology, the added cost and the clinical benefit compared to a reference strategy. The result of this evaluation is a ratio, called incremental cost-effectiveness ratio (ICER), where the numerator is the cost difference between the strategy including an innovative technology and the reference strategy, and the denominator is the patient's clinical benefit. The ICER measures efficiency, which is the ratio between additional necessary resources and patients benefit of a new health technology compared to the reference. The role of medico-economic evaluations in the setting of drug pricing varies among European countries. In some countries like the United-Kingdom, the ICER is the main decision criterion for acceptation of financing by the national payer. The ratio associated to the new technology is compared to the threshold considered to be acceptable by the payer. According to the value of the ratio compared to the threshold, the new technology is recommended or rejected. In other countries, the result of the medico-economic evaluation is considered as a criterion to help decision-making, but it is not the sole criterion to grant reimbursement. In France, the efficiency opinion of the Economic Evaluation Committee for Health Care Product *(Commission d'évaluation économique et de santé publique* [*CEESP*]) is taken into account in pricing negotiation with the CEESP. In this evaluation, the CEESP of the French health authority (*Haute Autorité de santé* [HAS]) qualifies the results of the evaluation based on the quality of the method used. The pricing negotiation is also and primarily determined by the added clinical benefit (*amélioration du service médical rendu* [ASMR]): 1 to 3 = European price, 4 = negotiation, 5 = theoretically less than the comparator. When the comparator is an old drug, the price can be higher even in the absence of ASMR; when the comparator is in the public domain, prices are at the level of the generic drug, even if the pharmaceutical form is different.

We discuss here the mode of calculation of the ICER, the measure of cost and health gain (patient benefit), particularly for anticancer drugs because of the very number of new molecules in this therapeutic area. Criteria used to measure patient benefit in clinical trials, such as progression-free survival (PFS), overall survival (OS) and quality of life (QoL), have an impact on the ICER denominator, but also on the numerator through treatment duration and anticipated treatment cost.

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