Commonly used efficacy endpoints in oncology clinical trials

Endpoint	Definition	Pro	Cons
Overall Survival	Time from randomization until death for any cause	Universally accepted measure of direct benefit Easily and precisely measured	May require a larger trial population and longer follow-up to show statistical difference between groups May be affected by crossover or subsequent therapies Includes deaths unrelated to cancer
Progression Free Survival	Time from randomization until disease progression or death	Requires small sample size and shorter follow-up time compared with OS Includes measurement of stable disease (SD) Not affected by crossover or subsequent therapies Generally based on objective and quantitative assessment	Validation as a surrogate for survival can be difficult in some treatment settings Not precisely measured (ie, measurement may be subject to bias) Definition may vary among trials Requires frequent radiologic or other assessments Requires balanced timing of assessment among treatment arms
Time to progression	Time from randomization* until objective tumor progression; does not include deaths		
Time to treatment failure (TTF)	Time from randomization* to discontinuation of treatment for any reason, including disease progression, treatment toxicity, and death	Useful in settings in which toxicity is potentially as serious as disease progression (eg, allogeneic stem cell transplant)	Does not adequately distinguish efficacy from other variables, such as toxicity

Event-free survival (EFS)	Time from randomization* to disease progression, death, or discontinuation of treatment for any reason (eg, toxicity, patient preference, or initiation of a new treatment without documented progression)	Similar to PFS; may be useful in evaluation of highly toxic therapies	Initiation of next therapy is subjective. Generally not encouraged by regulatory agencies because it combines efficacy, toxicity, and patient withdrawal
Time to next treatment (TTNT)	Time from end of primary treatment to institution of next therapy	For incurable diseases, may provide an endpoint meaningful to patients	Not commonly used as a primary endpoint Subject to variability in practice patterns
Objective response rate (ORR)	Proportion of patients with reduction in tumor burden of a predefined amount	Can be assessed in single-arm trials Requires a smaller population and can be assessed earlier, compared with survival trials Effect is attributable directly to the drug, not the natural history of the disease	Not a comprehensive measure of drug activity
Duration of response (DoR)	Time from documentation of tumor response to disease progression		

Reference:

1. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Guidance for industry: clinical trial endpoints for the approval of cancer drugs and biologics. **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-endpoints-approval-cancer-drugs-and-biologics**. Published December 2018. Accessed August 21, 2019.