Cancer Care Ontario

Guidance to Disease Site Leads and Others Involved in Recommending New Drugs and Regimens for Funding Through Cancer Care Ontario's Systemic Treatment – Quality-Based Program

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One important goal of Cancer Care Ontario's new Systemic Treatment – Quality-Based Program (ST-QBP) is to ensure that all drugs/regimens that are funded through ST-QBP are evidence-based. Drugs covered by CCO's New Drug Funding Program undergo a rigorous review through the pan-Canadian and provincial review mechanisms and are not the subject of this guidance document. This document provides advice to those involved in making recommendations on which drugs/regimens (IV and oral) should be added to the current list of evidence-informed drugs/regimens. Generally, these recommendations will relate to older drugs used in new combinations, the broadening of indications for "new" drugs beyond their initially approved indication, or new drugs not yet approved for provincial funding. It is not meant to cover all drugs/regimens for every clinical circumstance, especially when treatment is required for patients with complex medical conditions.

Recently, the American Society of Clinical Oncology and the European Society of Medical Oncology have published frameworks for the evaluation of new drugs (1,2). Both of these frameworks attempt to define the value of a new drug or regimen based on a combination of survival improvement (overall survival and/or progression free survival), degree of treatment-related toxicity and impact on quality of life in the adjuvant and palliative situation. A scoring system based on the magnitude of benefit in these categories, which is disease context specific provides a measure of relative value but without consideration of cost or cost-effectiveness. The authors of both publications acknowledge that their frameworks represent an initial attempt to define value and will likely evolve with input from providers, patients and payers. Both of these scoring systems are complex and as yet have not been demonstrated to be useful to decision makers in funding drug/regimens in a publicly funded healthcare system.

The approach that has been selected for CCO ST-QBP parallels, in most respects, the decision making process used by the pan- Canadian Oncology Drug Review but without the evaluation of cost-effectiveness, as most regimens that will be evaluated through this process will be older and less expensive drugs.

Therefore, for the purposes of the ST-QBP, a decision to fund a regimen or drug will be considered to be "evidence-informed" when the criteria for benefit and evidence outlined below are met.

Criteria for Benefit:

- The regimen or drug meets an unmet clinical need, and
    - The benefit represents an improvement with respect to survival and/or toxicity and/or quality of life and/or symptom management when compared to currently funded clinical alternatives, and
    - The benefit is judged to be clinically meaningful and not solely statistically significant by those who are experts in the management of the particular cancer;
    - Appropriate statistical analyses have been conducted and the results are determined to be statistically significant and clinically meaningful for the given tumor type. In assessing survival benefits in the palliative setting, generally, the hazard ratio (HR) for overall survival (OS) or progression free survival (PFS) should be less than 0.8.

- From a patient perspective, the drug/regimen offers a meaningful benefit:
    - The magnitude and type of benefit are, or would be judged by patients or their families, to be of value.
    - The toxicities of the treatment regimen are manageable and harms are acceptable to patients.
- If a drug/regimen is demonstrated to be clinically equivalent in effectiveness and safety to an existing evidence-informed therapy, the benefit may be a reduction in the cost of treatment, or an increase in the efficiency of administration.

Criteria for Evidence:

- The evidence of benefit should be derived from one or more prospective clinical trials with a comparison group. If from more than one trial, the benefit(s) should ideally be reported in a meta-analysis or systematic review.
- If the evidence is from a single prospective clinical trial, it should meet the following criteria:
    - The patients in the trial should be randomized using a method to avoid bias, including features such as generation of an allocation sequence, allocation concealment and blinding (3);
    - The trial should have sufficient power to detect a clinically meaningful benefit in survival, progression free survival and/or quality of life;
    - Other features of quality clinical trials to be considered include intention-to-treat analysis documentation of withdrawals and lost to follow-up patients, differences in baseline patient characteristics, length of follow-up and reasons for early termination;
- Where there are insufficient patients to mount a randomized trial, the results of Phase II/single arm studies will be considered. Although the number of patients in the trial will be dependent on how uncommon the tumour type is, ideally 50 patients or more should be included in these single arm trials;
- Phase I trial results will not be considered as demonstrating sufficient evidence of clinical benefit
- The trial was conducted in an ethically sound manner;
- The source of trial funding is documented;
- The population entered in the trial is relevant in the Canadian context.

Publications:

The results of clinical trials must be peer-reviewed and fully published. Abstracts, editorials, case reports, notes, commentaries or letters to the editor will not be considered to provide sufficient information to be used as evidence in support of funding.

***Disclaimer**: Although all regimens funded through the ST-QBP will be evidence-informed, all evidence-informed systemic therapy regimens will not necessarily be funded in the face of budgetary restrictions.*

References:

1. Schnipper LE, Davidson NE, Wollins DS., et al. American Society of Clinical Oncology statement: conceptual framework to assess the value of cancer treatment options. Available at: http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2015.61.6706
2. Cherny NI, Sullivan R, Dafni U et al. A standardized, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: European Society for Medical Oncology magnitude of clinical benefit scale (ESMO-MCBS). Annals of Oncology advance access published May 30, 2015. Available at: http://annonc.oxfordjournals.org/
3. The Cochrane Collaboration's tool for assessing risk of bias. Available at http://handbook.cochrane.org/chapter_8/table_8_5_a_the_cochrane_collaborations_tool_for_assessing.htm

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