Appropriate Chemotherapy Dosing for Obese Adult Patients With Cancer: American Society of Clinical Oncology (ASCO)’s Clinical Practice Guideline

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This practice tool for physicians is derived from an ASCO® practice guideline. The practice guideline and this tool are not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients. This tool does not recommend any particular product or course of medical treatment. Use of the practice guidelines and this tool are voluntary. The practice guidelines and additional information are available at http://www.asco.org/guidelines/wbd. Copyright © 2012 by the American Society of Clinical Oncology. All rights reserved.
Introduction:
This is a tool derived from ASCO’s guideline on Appropriate Chemotherapy Dosing for Obese Adult Patients with Cancer. The guideline was developed by an Expert Panel. The goal of this tool is to address frequently asked questions. In addition to abundant preclinical studies, this guideline is supported by clinical evidence from several randomized controlled trials (RCTs) comparing delivered dose intensity, retrospective analyses of RCTs and cohort studies, as well as pharmacokinetic studies.

5 Things to Remember About Patients with Cancer Who Are Obese
1. Many obese patients are under-dosed, which compromises the efficacy of cytotoxic chemotherapy and the chance for cure.
2. Obese patients should receive weight-based doses.
3. There is no evidence that toxicity will increase with weight-based dosing for patients who are obese.
4. It is ok to talk to patients about obesity and appropriate dosing. It is possible to reassure patients about careful monitoring and managing toxicities.
5. There are a few select agents* that are given in a capped dose and some therapeutic agents, e.g., targeted agents, where the data are insufficient to recommend weight-based doses.

Frequently Asked Questions
Q. I've always capped the dose, perhaps because of toxicity concerns. Really – you want me to write for that large a dose now?

A. Many clinicians are reluctant to prescribe weight-based doses, in fact, studies show that appropriate dosing leads to better overall survival. Patients may need extra time and reassurance if they question the “increased” dose. Randomized controlled trials (RCTs), observational studies, and pharmacokinetic studies do not support dose capping.

Clinicians are often reluctant to discuss obesity with cancer patients. It can be difficult to reassure patients that increased doses of cytotoxic chemotherapy (IV or oral) do not usually mean increased toxicity.


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Empiric decreases from pharmacokinetic findings in drug dose for obese patients do not support dose capping for any agent.

*It is acceptable to cap the dose for some agents, e.g., a maximum dose of 2.0 mg of vincristine when used as part of the CHOP [cyclophosphamide, hydroxydoxorubicin (doxorubicin), vincristine, prednisone] and CVP [cyclophosphamide, vincristine, prednisone] regimens.

There are insufficient data for addressing dosing for overweight and obese patients receiving targeted therapies.

Q. Are obese patients with cancer concerned about toxicity from increased weight-based doses?
A. There is not any evidence that obese patients are more concerned about increased toxicity. Most patients with cancer want the highest tolerable dose and cure.

Q. My patient has a BSA of 3.0 $m^2$, should I really calculate a weight-based dose for her?
A. Yes – clinicians should calculate weight-based doses for cytotoxic chemotherapy regardless of a patient’s obesity status. While there are not enough high quality studies about morbidly obese, the Panel recommends full weight-based dosing, if other comorbidities are not a contraindication.

Q. Is there an exception to the recommendation for full weight-based dosing?
A. Clinicians must always consider comorbidities when choosing a cytotoxic chemotherapy regimen.

Q. My patient has experienced increased toxicity, e.g. Grade 3 or Grade 4 toxicity. Should the dose be adjusted and by how much and can I return to the weight-based dose?
A. The Panel recognizes the need for clinicians to exercise judgment when providing care for patients who have experienced Grade 3 or 4 chemotherapy toxicity. When the symptoms and tests indicate that the toxicity has been resolved, consider resuming full weight-based doses.

Q. How should I dose for the patient with metastatic disease?
A. Most of the data in support of full weight-based dosing come from the treatment of early stage disease. Data supporting the use of full weight-based doses in the advanced disease setting are limited. However, in the absence of these data, it may be prudent to provide full weight-based chemotherapy dosing to obese cancer patients, especially in those receiving treatment for curative intent.

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Q. Am I going to run into issues with the CMS and third party payers for potentially writing for such a large dose?

A. The use of full weight-based dosing may have cost implications for payers, particularly if full weight-based doses of chemotherapy lead to more frequent use of white blood cell growth factors as prophylaxis to reduce the incidence of febrile neutropenia. *This guideline may be useful when communicating with payers.*

Q. What’s the future of pharmacokinetics in determining appropriate dosing for obese patients with cancer?

A. In the future, pharmacokinetic and pharmacogenetic principles in dosing may provide a more personalized approach to treatment for patients who are obese. However, large prospective studies are required to support this practice.

Q. Does this guideline address pediatric patients?

A. There are special considerations in this population and a separate guideline for appropriate dosing for children with cancer who are obese is needed.

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**Case Study**
O.N. is a 57 year old post-menopausal woman diagnosed with a T2, N1, M0, stage IIB infiltrating ductal carcinoma of the left breast. The patient has a medical history that includes obesity (BMI=53), hypertension, elevated cholesterol, diabetes, and depression. Her BSA was 2.52 m$^2$. The patient underwent left partial mastectomy and pathology revealed a 2.5 cm infiltrating ductal carcinoma, grade 3, estrogen 71-100% positive, progesterone negative. There was no vascular invasion, perineural invasion, or tumor necrosis identified. Surgical margins were negative and 4 out of 18 axillary lymph nodes were positive. Chemotherapy with 4 cycles of doxorubicin at 60 mg/m$^2$ and cyclophosphamide at 600 mg/m$^2$ followed by paclitaxel at 175 mg/m$^2$ for 4 additional cycles was recommended. This was to be followed by adjuvant radiation therapy and a 5 year course of anastrozole. The patient received all her chemotherapy at full dose. She tolerated her treatment well overall.