OPTIMAL CANCER CARE ALLIANCE
Optimal Dosage. Best Outcome.

Introduction to the Optimal Cancer Care Alliance

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Chair of the Board of OCCA

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https://optimalcancercare.org/

Founded in 2016 as the Value in Cancer Care Consortium (Vic3) - Incorporated as a Michigan nonprofit

Initial focus on reducing prescribing costs, and improving access to treatment

Renamed OCCA in 2021

Revised focus is reducing toxicity to patients by using lower doses of modern (*i.e.*, expensive) drugs

Our mission is to ensure that each patient receives the optimal dose of the medications needed to effectively treat their cancer

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OCCA Objectives

- **Influence regulators (*e.g.*, FDA & EMA) to require companies to optimize doses of new drugs**
- Publicize evidence where drugs are used at higher than their optimal doses
- Influence guideline committees to recommend alternative (optimal) prescribing
- Convene and organize clinical trials of marketed drugs whose labeled dose is likely excessive

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OCCA is a strong supporter of FDA's Project Optimus

The Drug-Dosing Conundrum in Oncology — When Less Is More N Engl J Med 2021;385:1445-7

Mirat Shah, M.D., Atiqur Rahman, Ph.D., Marc R. Theoret, M.D., and Richard Pazdur, M.D.

Sotorasib was approved by FDA (5/28/2021), with a requirement to conduct a post-marketing study of 240 mg vs 960 mg

1. There was no relationship between dose (180-960 mg) and plasma concentrations
2. There was no relationship between dose and response rate
3. Diarrhea and nausea may be reduced at a lower dose
4. Animal data suggested that the optimal dose was 30-240 mg
5. It is difficult for patients to take 8 (120 mg) pills at a time

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Generating and publicizing evidence for dose optimization

VIEWPOINT

Interventional Pharmacoeconomics—A New Discipline for a Cost-Constrained Environment

Ratain MJ, Goldstein DA, Lichter AS. JAMA Oncol. 2019 Aug 1;5(8):1097-1098.

Near-Equivalence: Generating Evidence to Support Alternative Cost-Effective Treatments

Ian F. Tannock, MD, PhD[1]; Mark J. Ratain, MD[2]; Daniel A. Goldstein, MD[3]; Allen S. Lichter, MD[4]; Gary L. Rosner, ScD[5]; and Leonard B. Saltz, MD[6]

J Clin Oncol. 2021 Mar 20;39(9):950-955.

Pharmacokinetic Simulation Analysis of Less Frequent Nivolumab and Pembrolizumab Dosing: Pharmacoeconomic Rationale for Dose Deescalation

Cody J Peer [1], Brian L Heiss [2], Daniel A Goldstein [3 4], Jennifer C Goodell [1], William D Figg [1], Mark J Ratain [2]

J Clin Pharmacol. 2022 Apr;62(4):532-540.

EDITORIAL

Ann Oncol. 2022 Apr;33(4):360-361.

Improving access to immunotherapy in low- and middle-income countries

Patel A, Goldstein DA, Tannock IF.

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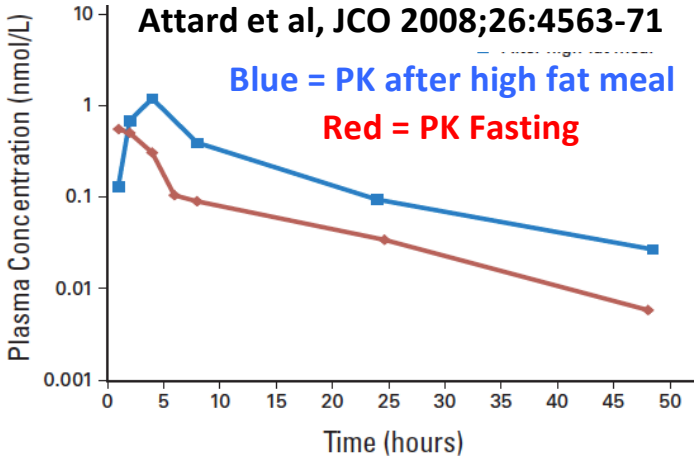
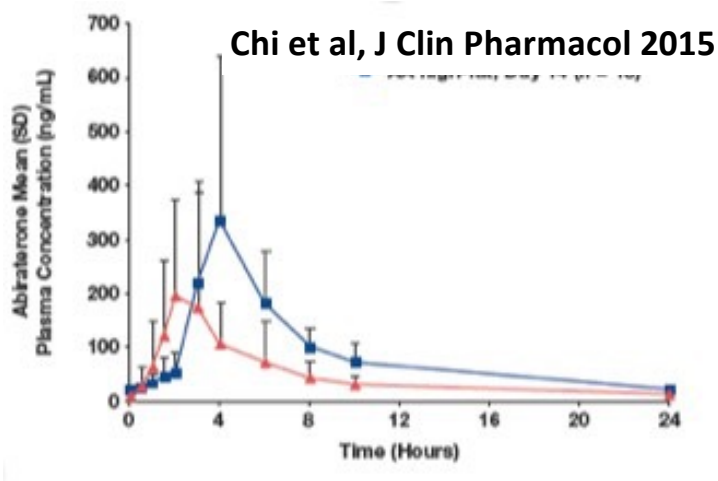
Abiraterone is an effective drug for men with prostate cancer

- Standard dose is 1000mg/day (4 pills) on an empty stomach. Cost in USA/Canada is ~$10,000/month
- 250mg after a fatty meal gives similar drug concentration





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Prospective International Randomized Phase II Study of Low-Dose Abiraterone With Food Versus Standard Dose Abiraterone In Castration-Resistant Prostate Cancer

Russell Z. Szmulewitz, Cody J. Peer, Abiola Ibraheem, Elia Martinez, Mark F. Kozloff, Bradley Carthon, R. Donald Harvey, Paul Fishkin, Wei Peng Yong, Edmund Chiong, Chadi Nabhan, Theodore Karrison, William D. Figg, Walter M. Stadler, and Mark J. Ratain

J Clin Oncol. 2018 May 10;36(14):1389-1395.

- 72 men randomized to abiraterone 1000mg/d on empty stomach (STANDARD) or 250mg/d after low fat breakfast (LOW)
- Primary endpoint: change in PSA at 12 weeks
  - No sig diff. with a trend to greater fall in PSA in LOW arm
  - Time to PSA progression ~14 months in both arms (p=0.56)
- Similar pharmacokinetics with less variability in LOW arm
- Similar effects to decrease target adrenal androgen

On the basis of this study we applied successfully for NCCN to include low dose Abiraterone with food in their guidelines

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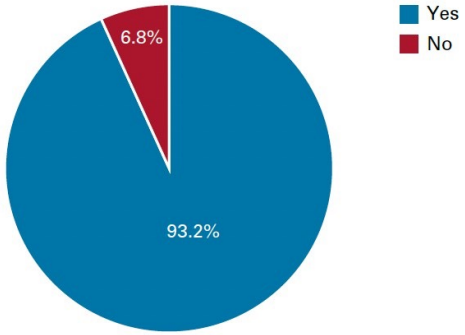
JCO® Global Oncology

Low-Dose Abiraterone in Metastatic Prostate Cancer: Is It Practice Changing? Facts and Facets

Amol Patel, MBBS, MD, DM[1]; Ian F. Tannock, MD, PhD[2]; Priyanka Srivastava, MD, DNB[3]; Bivas Biswas, MD, DM[4]; Vineet Govinda Gupta, MD, DM[5]; Atul Batra, MD, DM[6]; Sainath Bhethanabhotla, MD, DM[7]; Raja Pramanik, MD, DM[6]; Shubh Mahindru, MBBS, DNB[8]; TVSVGK Tilak, DM[9]; Chandan Krishna Das, MD, DM[10]; and Prashant Mehta, MD, DM[11]

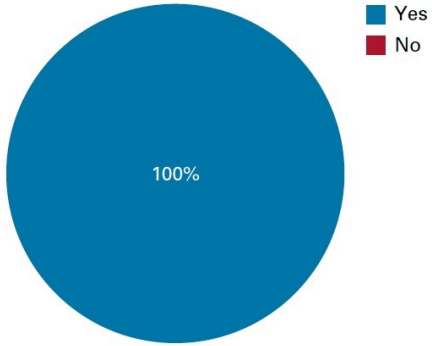
Do you feel that abiraterone 250 mg will improve patients' compliance?

118 responses



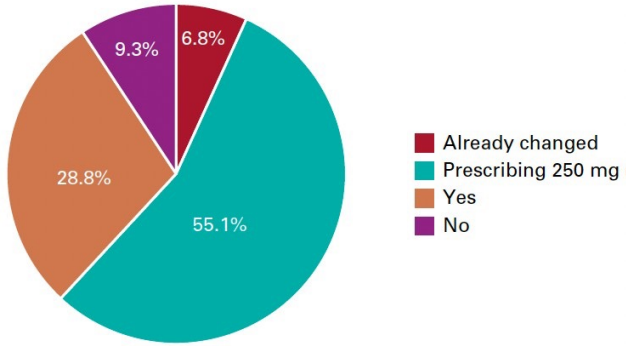
Do you feel that abiraterone 250 mg will reduce cost for patients?

118 responses



Will you change your practice from abiraterone 1,000 mg to abiraterone 250 mg?

118 responses



Average Indian patient would save INR 260,000
Annual saving to Indian Health Service ~US$182million (INR 13.5billion)

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Ongoing

A Randomized Study Investigating the Pharmacokinetics of Standard Interval Dosing Compared to Extended Interval Dosing of Nivolumab or Pembrolizumab in Locally Advanced or Metastatic Cancers
NCT04295863; Sponsor: University of Chicago; Sample size: 264

Proposed

The DILUTAMIDE Trial:
A comparison of the registered daily dose with 50% of that dose for treatment of metastatic hormone-sensitive (mHSPC) prostate cancer with enzalutamide, apalutamide or darolutamide.

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Our Limitations & Problems

- Lack of funding to support dose-finding studies
  - Trials that evaluate reduced dosing save more money than they cost, but challenge is to persuade payers to finance them
- Persuading patients that reduced dosing will not decrease benefit from treatment – and may increase it
- Limited implementation of lower-dose strategies