Regulating Bladder Cancer at the FDA's Oncology Center of Excellence: within FDA and beyond

Chana Weinstock, MD,
Team Leader, Genitourinary Cancers Team
U.S. Food and Drug Administration

Some of the questions I hope to answer today include-

- How are therapeutic products to treat bladder cancer regulated at FDA?
- How do Fast Track and Breakthrough Therapy Designations differ?
- How do Accelerated and Traditional Approval pathways differ?
- What opportunities exist for FDA to interact with sponsors developing products for bladder cancer?
- What sorts of outward-facing efforts have the GU teams at FDA been involved with in recent years?

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- FDA organizational structure
- Expediting drug approvals
- Interactions between FDA and Sponsors
- Bladder cancer at FDA in recent years

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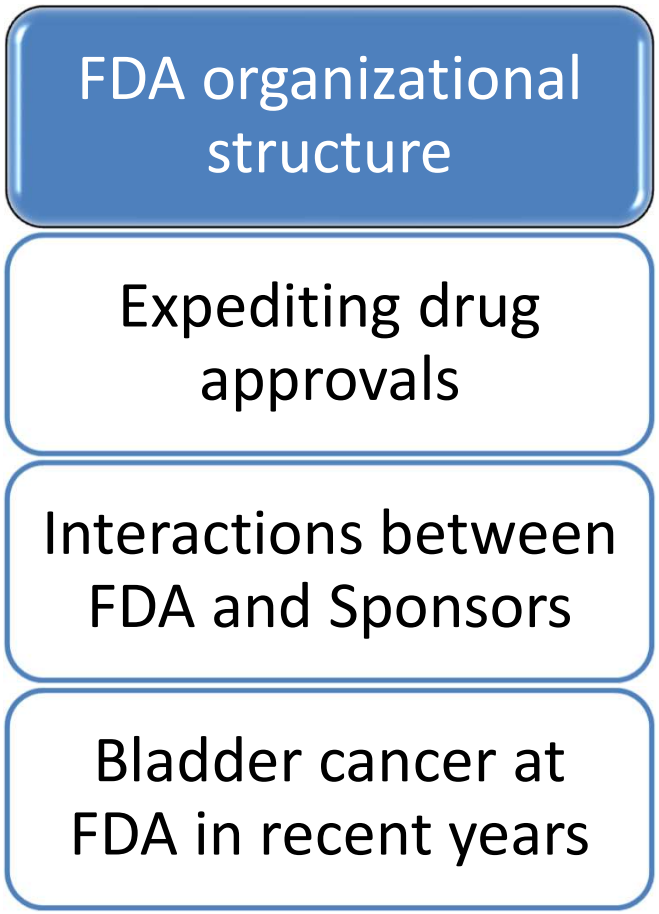


FDA's Oncology Center of Excellence brings together review of oncology products in different centers

Center for Drug Evaluation and Research (CDER)

- Drugs and Antibodies.
- Office of Hematology and Oncology Products

Center for Biologics Evaluation and Research (CBER)

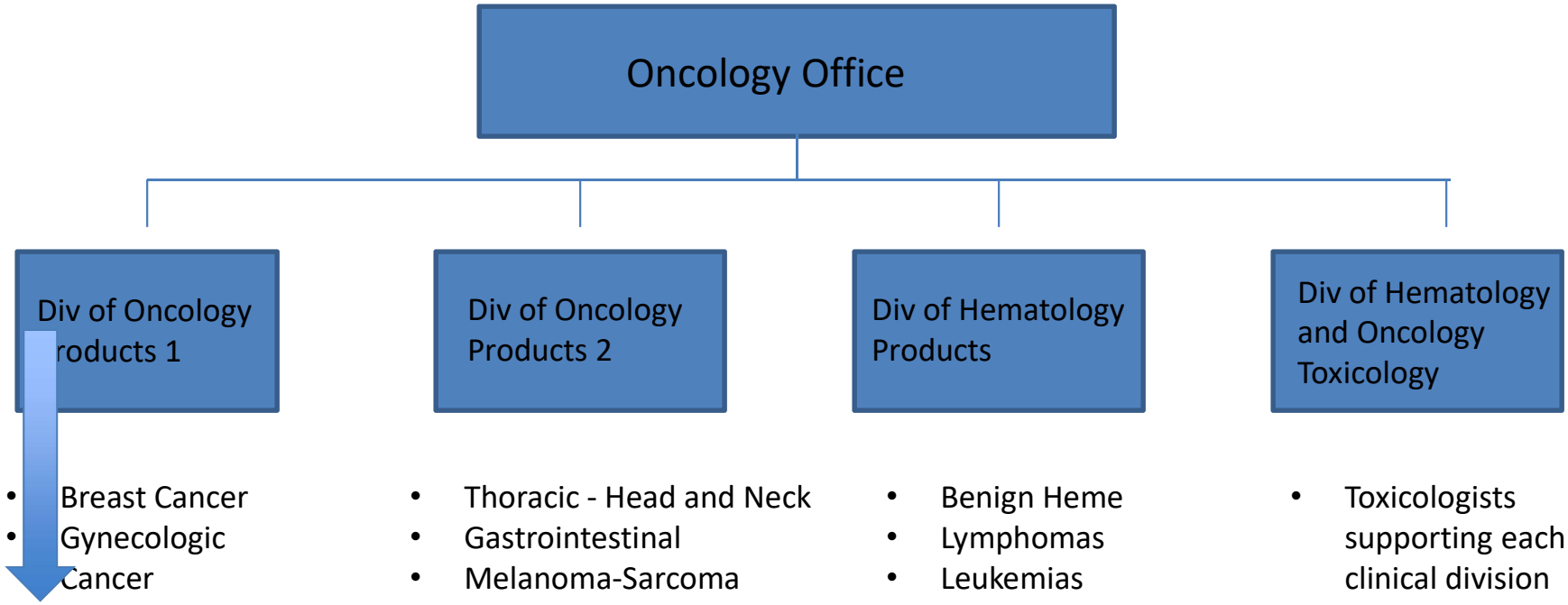
- Cellular and Gene Therapies, Vaccines.

Center for Devices and Radiologic Health (CDRH)

- Devices, In Vitro Diagnostics, Diagnostic and Therapeutic Radiologics.

Office of Hematology and Oncology

- Disease-specific structure akin to current academic models



>80 medical oncologists

GU TEAMS IN OHOP

- We are a group of medical oncologists and a radiation oncologist with expertise in GU malignancies
- We review all INDs (Investigational New Drugs), protocols, NDAs (New Drug Applications) and BLAs (Biological Licensing Applications) related to drugs developed for bladder, kidney, and prostate cancer
- Many of us maintain regular patient contact
  - JHU, VAMC, NCI, private practice

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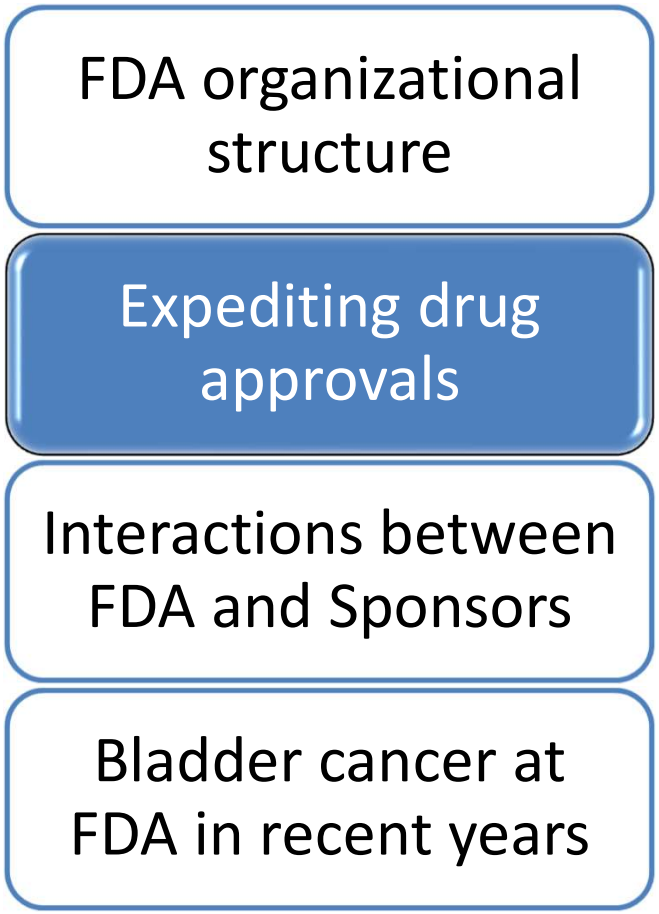

	Fast Track	Breakthrough Therapy	Priority Review	Accelerated Approval
Program	Designation	Designation	Designation	Approval Pathway
Qualifying Criteria (all require condition to be serious)	Nonclinical or clinical data demonstrate potential address unmet need	Preliminary clinical evidence demonstrates substantial improvement over available therapies	If approved would provide significant improvement in safety or effectiveness	Demonstrates effect on endpoint reasonably likely to predict clinical benefit over available therapies
When to Submit	IND or after	Ideally no later than EOP2	With (s)BLA, (s)NDA	Discuss during development
Features	Expedite development and review Rolling review	Intensive guidance on drug development Organizational commitment Rolling review	6 month vs. 10 month review clock after filing	Approval based on effect on surrogate that is reasonably likely to predict clinical benefit

Accelerated Approval

- Requires Substantial Evidence of Safety and Efficacy
- "Provide meaningful therapeutic benefit… over existing therapies"
- *Can be based on a **"Surrogate endpoint… reasonably likely… to predict clinical benefit"***
- Post-Marketing Clinical Trials are Required
  - Should usually be underway at the time of accelerated approval
  - Applicant should carry out studies with due diligence

Traditional ("Regular") Approval

- **Traditional Approval** requires
  - Substantial evidence of safety and efficacy
  - Well-controlled clinical trials
  - based on **prolongation of life, a better life, or an established surrogate for either of the above**

- No comparative efficacy for Traditional Approval
  - As safe and effective as existing therapies, allowing for non-inferiority designs

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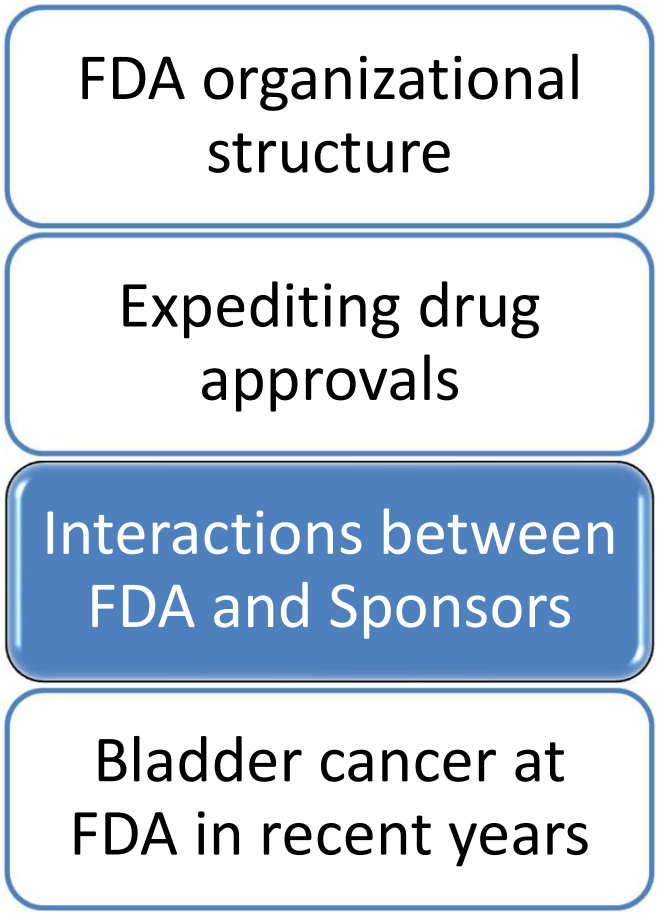
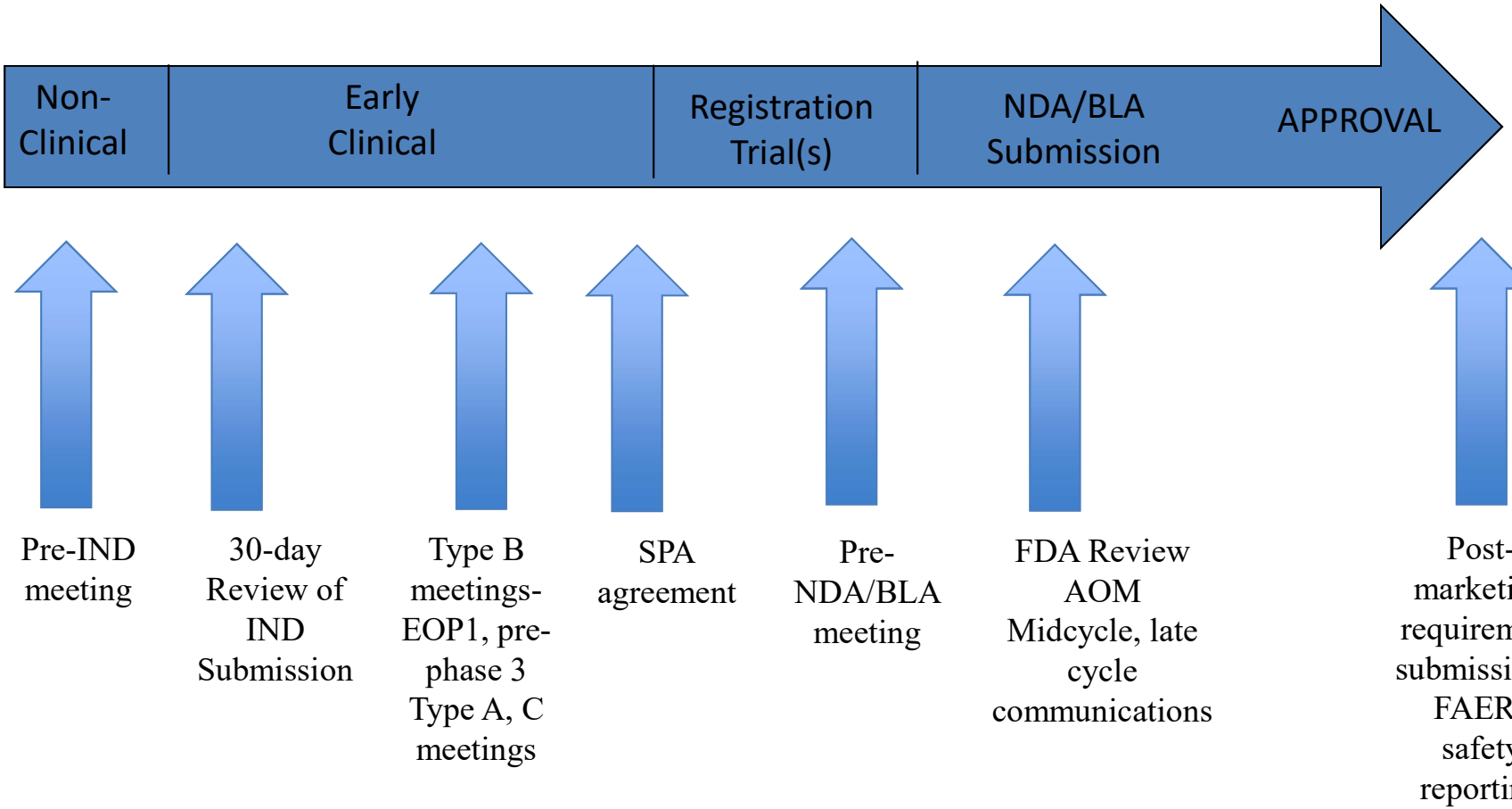


The drug development process-timeline

The drug development process- Examples of FDA-Sponsor interactions

The drug development process- Examples of FDA-Sponsor interactions



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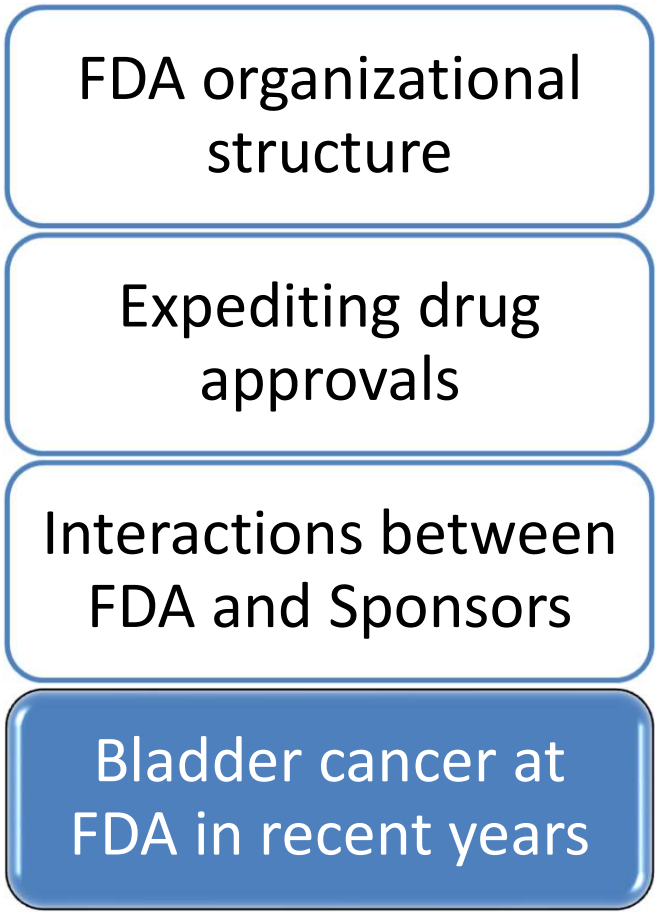

Recent activity in bladder cancer

- 5 checkpoint inhibitors approved in 2nd line metastatic setting;
  - 4 accelerated approval
  - 1 traditional approval
- Cisplatin ineligible- 2 approvals of checkpoint inhibitors in the up-front metastatic setting
  - Both accelerated approval
- First FGFR-targeted therapy approved in bladder cancer (2nd line)
  - Accelerated approval
- 2 ODACs (NMIBC)

FDA-AUA Public Workshop May 2013-NMIBC

Urology. 2014 Feb;83(2):262-4. doi: 10.1016/j.urology.2013.10.030. Epub 2013 Dec 12.

Clinical trial design for the development of new therapies for nonmuscle-invasive bladder cancer: report of a Food and Drug Administration and American Urological Association public workshop.

Jarow JP[1], Lerner SP[2], Kluetz PG[3], Liu K[4], Sridhara R[5], Bajorin D[6], Chang S[7], Dinney CP[8], Groshen S[9], Morton RA[10], O'Donnell M[11], Quale DZ[12], Schoenberg M[13], Seigne J[14], Vikram B[15].

Author information

Abstract

OBJECTIVE: To summarize the discussion at a public workshop, cosponsored by the U.S. Food and Drug Administration (FDA) and the American Urological Association, reviewing potential trial designs for the development of new therapies for non-muscle-invasive bladder cancer (NMIBC). There have been only 3 drug approvals for NMIBC in the last 30 years, and product development for this disease has been stymied by difficulties in trial design and patient accrual.

METHODS: A workshop evaluating potential trial design for the development of therapies for NMIBC was held in San Diego, CA, in May 2013. Invited experts representing all stakeholders, including urology, medical oncology, radiation oncology, industry, and patient advocates, discussed development of products for all risk strata of NMIBC.

BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment

Guidance for Industry

FDA-NCI Adjuvant Bladder Cancer Workshop November 2017

FDA-NCI Public Workshop: Defining Disease Recurrence and Harmonizing Conduct in Adjuvant Bladder and Kidney Cancer Trials

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Organized by the:
U.S. Food & Drug Administration (FDA) and National Cancer Institute (NCI)
with support from the Society of Urologic Oncology (SUO)
Twitter #OCEGU17

Co-Chairs: Sundeep Agrawal, MD, FDA/CDER
Harpreet Singh, MD, FDA/CDER and
Andrea Apolo, MD, NIH/NCI

Date: November 28, 2017

FDA-BCAN Neoadjuvant Bladder Cancer Endpoints Workshop

BCAN – FDA WORKSHOP: AUGUST 8, 2019. 12-4PM EDT

AUGUST 2, 2019 UNCATEGORIZED

Endpoints for the Development of Neoadjuvant Systemic Therapy Regimens for Muscle Invasive Bladder Cancer

BCAN – FDA WORKSHOP AGENDA FINAL

Follow the Workshop: @BladderCancerUS, @FDAOncology, #pCRMIBC2019

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ONCOLOGY CENTER OF EXCELLENCE

PROJECT FACILITATE

Assisting healthcare providers with requests for access to investigational oncology products

DO YOU NEED HELP SUBMITTING A SINGLE PATIENT IND EXPANDED ACCESS (EA) REQUEST (ALSO KNOWN AS COMPASSIONATE USE) FOR A PATIENT WITH CANCER?

...FDA's Oncology Center of Excellence (OCE) can help:

- Locate IRB resources
- Find an EA contact for a drug/biotech company
- Complete Form FDA 3926

Phone: (240) 402-0004

Email: OncProjectFacilitate@fda.hhs.gov

www.fda.gov/oce

Patients: Talk to your healthcare provider to discuss whether expanded access is an appropriate option.

Conclusions

- FDA's Oncology Center of Excellence brings together reviewers for drugs, biological products, and medical devices for the treatment of cancer
- Several programs are in place to expedite the drug development and approval process
- There are many opportunities to interact with FDA during drug development
- Numerous drug approvals and collaborative workshops in bladder cancer have occurred in recent years @FDAOncology

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