

AAADV-ASCO-CDDF Joint Workshop

Global collaboration and cancer prevention

H. Kim Lyerly
(AAADV, US)

Disclaimer

- H. Kim Lyerly is Director of the AAADV Workshop

Scope

- AAADV held annual conference until 2019, interrupted by COVID19 pandemic.
- Recent meetings held virtually
- Focus remains on evidence/critical data generation for regulatory decision makers by academic and commercial drug and device developers.
- Complements FDA and non-US regulatory educational activities
- Creates an open forum to support patient oriented/patient focused anti-cancer agent development in US and world

Global Cancer Drug Development—A Report From the 2022 Accelerating Anticancer Agent Development and Validation Meeting

Brooke E. Wilson, MD^{1,2} ; Richard Sullivan, MD^{3,4} ; Richard Peto, FRS⁵; Bello Abubakar, MD⁶ ; Christopher Booth, MD^{1,2} ; Gustavo Werutsky, MD⁷ ; Cary Adams, MSc⁸; Agnes Saint-Raymond, MD⁹ ; Thomas R. Fleming, PhD¹⁰; Kim Lyerly, MD¹¹ ; and Julie R. Gralow, MD¹² 

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ABSTRACT

Rapidly expanding systemic treatment options, combined with improved screening, diagnostic, surgical, and radiotherapy techniques, have led to improved survival outcomes for many cancers over time. However, these overall survival gains have disproportionately benefited patients in high-income countries, whereas patients in low- and middle-income countries (LMICs) continue to experience challenges in accessing timely and guideline concordant care. In September 2022, the Accelerating Anticancer Agent Development and Validation workshop was held, focusing on global cancer drug development. Panelists discussed key barriers such as the lack of diagnostic services and human resources, drug accessibility and affordability, lack of research infrastructure, and regulatory and authorization challenges, with a particular focus on Africa and Latin America. Potential opportunities to improve access and affordability were reviewed, such as the importance of prioritizing investments in diagnostics, investing health infrastructure and work force planning, coordinated drug procurement efforts and streamlined regulatory processing, incentivized pricing through regulatory change, and the importance of developing and promoting clinical trials that can answer relevant clinical questions for patients in LMICs. As a cancer community, we must continue to advocate for and work toward equitable access to high-quality interventions for patients, regardless of their geographical location.

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By Sanket S. Dhruva, Aaron S. Kesselheim, Steven Woloshin, Robin Z. Ji, Zhigang Lu, Jonathan J. Darrow, and Rita F. Redberg

Physicians' Perspectives On FDA Regulation Of Drugs And Medical Devices: A National Survey

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ABSTRACT Physicians' knowledge of Food and Drug Administration (FDA) approval processes is important in informing clinical decisions and patient discussions. Among a randomly selected national sample of 509 internists, cardiologists, and oncologists, 41 percent reported moderate or better understanding of the FDA's drug approval process, and 17 percent reported moderate or better understanding of the FDA's medical device approval process. Nearly all physicians thought that randomized, blinded trials that met primary endpoints should be very important factors required to secure regulatory approval. Also, nearly all physicians thought that the FDA should revoke approval for accelerated-approval drugs or breakthrough devices that did not show benefit in postapproval studies. Our findings suggest that physicians commonly lack familiarity with drug and medical device regulatory practices and are under the impression that the data supporting FDA drug and high-risk device approvals are more rigorous than they often are. Physicians would value more rigorous premarket evidence, as well as regulatory action for drugs and devices that do not demonstrate safety and effectiveness in the postmarket setting.

Sanket S. Dhruva (sanket.dhruva@ucsf.edu), University of California San Francisco and San Francisco Veterans Affairs Medical Center, San Francisco, California.

Aaron S. Kesselheim, Brigham and Women's Hospital and Harvard University, Boston, Massachusetts.

Steven Woloshin, Dartmouth College, Lebanon, New Hampshire.

Robin Z. Ji, University of California San Francisco.

Zhigang Lu, Brigham and Women's Hospital and Harvard University.

Jonathan J. Darrow, Brigham and Women's Hospital and Harvard University.

Rita F. Redberg, University of California San Francisco.

EXHIBIT 1

Physicians' perceptions of the Food and Drug Administration (FDA) process for approval of new drugs and medical devices, survey of internists, oncologists, and cardiologists, 2021-22

	Drugs (n = 489)		Medical devices (n = 479)		p value
	Number	Percent	Number	Percent	
Understands FDA approval process					<0.001
Extremely well	34	7	17	4	
Moderately well	166	34	64	13	
Somewhat well	169	35	115	24	
Slightly well	63	13	95	20	
Not at all well	57	12	188	39	
Perception of newly FDA-approved products (multiple responses allowed)					
More effective than other available treatments for same condition	190	39	208	43	<0.001
More effective than placebo	446	91	314	66	<0.001
Safer than other available treatments for same condition	153	31	177	37	<0.001
Perceived evidence requirement for FDA approval					<0.001
2 or more randomized controlled trials	156	32	169	35	
A single randomized controlled trial	319	65	252	53	
Registries or other nonrandomized studies	14	3	58	12	
What should be the evidence requirement for approval? ^a					0.32
2 or more randomized controlled trials	276	57	285	60	
A single randomized controlled trial	209	43	186	39	
Only data from registries	1	0.2	4	0.8	
Only case reports and expert opinion	1	0.2	2	0.4	
Perception of current bar for FDA approval					0.05
Too high or much too high	57	12	38	8	
About right	289	59	316	66	
Too low or much too low	143	29	125	26	
5-year change in perception of FDA approval threshold					<0.001
Has risen/become more stringent	54	11	40	8	
Has stayed the same	206	42	338	71	
Has fallen/become more lenient	229	47	101	21	

SOURCE Authors' analysis of data from their survey of internists, oncologists, and cardiologists conducted during October 2021–September 2022. **NOTES** N = 509 respondents. Survey questions are in appendix exhibit A3 (see note 14 in text). p values were calculated for the difference between responses for drugs and for medical devices. ^aNumber of respondents for this question decreased from 489 to 487 for responses about drugs and from 479 to 477 for responses about medical devices.

Educational Session I



Martin Stockler, MBBS



Elizabeth Eisenhauer



Ian Tannock



Ludovic Trinquart



Max Parmar



Bishal Gyawali

9:00 AM^(EST)

Plenary Session A: Overcoming the hazards of survival analysis - PFS, RFS, HR, RMST, and CSO

Session Chairperson: Martin Stockler (University of Sydney)

- **Martin Stockler (University of Sydney)** Time to event analysis in oncology
- **Elizabeth Eisenhauer (Queens University)** Progression-free survival in advanced cancer
- **Ian Tannock (University of Toronto)** Relapse-free survival and adjuvant therapy
- **Ludovic Trinquart (Tufts University)** Use and abuse of hazard ratios in oncology
- **Mahesh (Max) Parmar, (MRC CTU UCL)** Restricted mean survival time in oncology
- **Bishal Gyawali (Queens, Kingston, ON)** Time for Common Sense in Oncology
- **Panel Discussion**

Educational Session II

12:30 PM^(EST)

Plenary Session B: STATISTICAL DESIGN AND ANALYSIS

Session Chairpersons: Thomas Fleming (University of Washington, Seattle) and Lisa McShane (National Cancer Institute)

- **Thomas Fleming (University of Washington, Seattle)** Subset analysis
- **John H. Powers (George Washington University)** Surrogate biomarkers/endpoints
- **Amylou C. Dueck (Mayo Clinic)** Patient reported outcomes for assessing benefits & harms in cancer treatment and prevention trials.
- **Panel Discussion**



Thomas Fleming, PhD



Lisa McShane



John H. Powers, III



Amylou Dueck

Study design/analysis



Lisa McShane



Marco Bonetti



Bernard Cole



Richard Gelber



John Simes

9:00am (EST)

Satellite #4: Clinical trial design/analysis for global drug development

Session Chairperson: Lisa McShane (National Cancer Institute)

- **Lisa McShane (National Cancer Institute):** Clinical trial designs to evaluate liquid biopsy-guided therapy
- **Marco Bonetti, Bernard Cole, Richard Gelber:** Exploring treatment-effect heterogeneity using continuous biomarkers: the STEPP approach
- **John Simes (University of Sydney)** Design and analysis issues evaluating biomarkers in cancer clinical trials
- **Panel Discussion**

Global drug development



Richard Schilsky



Emile E. Voest



Janet Dancey



Scott Patterson



Tania Szado



Deo Ruhangaza, MD, MMed.

11:00am (EST)

Plenary Session #2: The utility and success of multi-center basket trials in cancer drug development:

Session Chairperson: Richard Schilsky (University of Chicago)

- **Rich Schilsky (University of Chicago):** Targeted Agent and Profiling Utilization Registry (TAPUR)
- **Emile E. Voest (Netherlands Cancer Institute):** Netherlands Drug Rediscovery Protocol (DRUP)
- **Janet Dancey (Canadian Clinical Trials Group):** Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR)
- **Panel Discussion**
 - **Scott Patterson (Gilead)** Invited Discussant
 - **Tania Szado (Genetech)** Invited Discussant
 - **Deo Ruhangaza (Butaro Cancer Center, Rwanda)** Invited Discussant

Global drug development



Bob T. Li



Katherine Van Loon



Aminu Umar-Sadiq



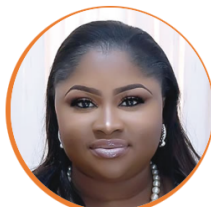
Jennifer Dent



Abasi Ene-Obong



Chitkala Kalidas, Ph.D.



Adedayo Joseph

1:30pm (EST)

Plenary Session #3: The development of precision medicine in LMIC:

Session Chairpersons: Bob Li, (Memorial Sloan Kettering Cancer Center), Katherine Van Loon (UCSF)

- **Aminu Umar-Sadiq (Nigeria Sovereign Investment Authority)** Investing in Cancer Centers of Excellence in Nigeria (NLCC)
- **Jennifer Dent (BioVentures)** The Cancer Clinical Trial Landscape in Africa and through AC3T
- **Abasi Ene-Obong (Syndicate Bio)** Genomic testing in LMIC
- **Panel Discussion**
 - **Chitkala Kalidas (Bayer)** Invited Discussant
 - **Adedayo Joseph (NLCC)** Invited Discussant

Cancer prevention



Philip E. Castle, Ph.D.,
M.P.H

9:25am (EST)

Discussion- Cancer Prevention Opportunities in 2023

Speaker: *Philip E. Castle (National Cancer Institute, Division of Cancer Prevention (DCP-NCI))*



Philip E. Castle, Ph.D., M.P.H



Ludmil Alexandrov

10:00am (EST)

Plenary Session #3: Carcinogenesis and the emerging science of precision prevention

Session Chairperson: *Philip E. Castle (Division of Cancer Prevention, National Cancer Institute (DCP-NCI))*



Sudhir Srivastava, Ph.D., M.P.H.



Mary "Nora" Disis

- **Ludmil Alexandrov (University of California, San Diego):** The genomic landscape of human precancer
- **Sudhir Srivastava (National Cancer Institute):** The Biology of Precancer
- **Mary "Nora" Disis (University of Washington, Seattle):** Immunoprevention
- **Panel Discussion**



Renzo Canetta, MD



John T. Schiller, Ph.D.



David M. Miller MD, PhD



Seema A Khan, MD



ANDREW T. CHAN, MD, MPH



Ian Thompson, M.D.

12:30pm (EST)

Plenary Session #5: Case studies in cancer prevention Successes and pitfalls

Session Chairperson: Renzo Canetta (Independent Consultant)

- **John Schiller (National Cancer Institute):** HPV vaccines for cervical and other cancers
- **David M. Miller (Harvard University):** Nicotinamide for skin cancer after transplant
- **Seema Khan (Northwestern University):** Tamoxifen for breast cancer
- **Andrew Chan (Harvard University):** Celecoxib and Aspirin For colorectal adenomatous polyps
- **Ian Thompson (National Cancer Institute):** Dutasteride/finasteride for prostate cancer prevention
- **Panel Discussion**



Robert H. Shoemaker



Steven Reed



Zelanna Goldberg, MD



Brian Cholewa



Shizuko Sei, M.D.

2:30pm (EST)

Plenary Session #6: Regulatory pathways for next generation prevention agents:

Session Chairperson: Robert H. Shoemaker (National Cancer Institute, Division of Cancer Prevention)

- **Steven Reed (HDT Bio):** mRNA vaccines in cancer prevention
- **Zelanna Goldberg (Replicate Bioscience):** Self replicating mRNA vaccines preventing resistance
- **Brian Cholewa (National Cancer Institute, Division of Cancer Prevention):** Regulatory pathways
- **Shizuko Sei (National Cancer Institute, Division of Cancer Prevention):** NCI-DCP activities in cancer prevention
- **Panel Discussion**

Track A



Jian Wang



Max Diehn



Laura van't Veer



Jeanine Tie



Takayuki Yoshino



Soma Ghosh

11:00am (EST)

Satellite #2: Advancements in ctDNA: Prognostication & MRD assessment for early-stage solid tumor drug development

Session Chairperson: Jian Wang (AstraZeneca)

- **Max Diehn (Stanford University):** Non-small cell lung cancer
- **Jeannie Tie (Peter MacCallum Cancer Center):** Colon Cancer
- **Takayuki Yoshino (National Cancer Institute Japan):** Colorectal Cancer
- **Laura van't Veer (UCSF):** Breast Cancer
- **Soma Ghosh (FDA):** FDA perspective
- **Panel Discussion / QA**



David Arons



Chitkala Kalidas, Ph.D.



Kristin Schroeder



Parvati Dev



Kenneth Buetow



Gregory Reaman

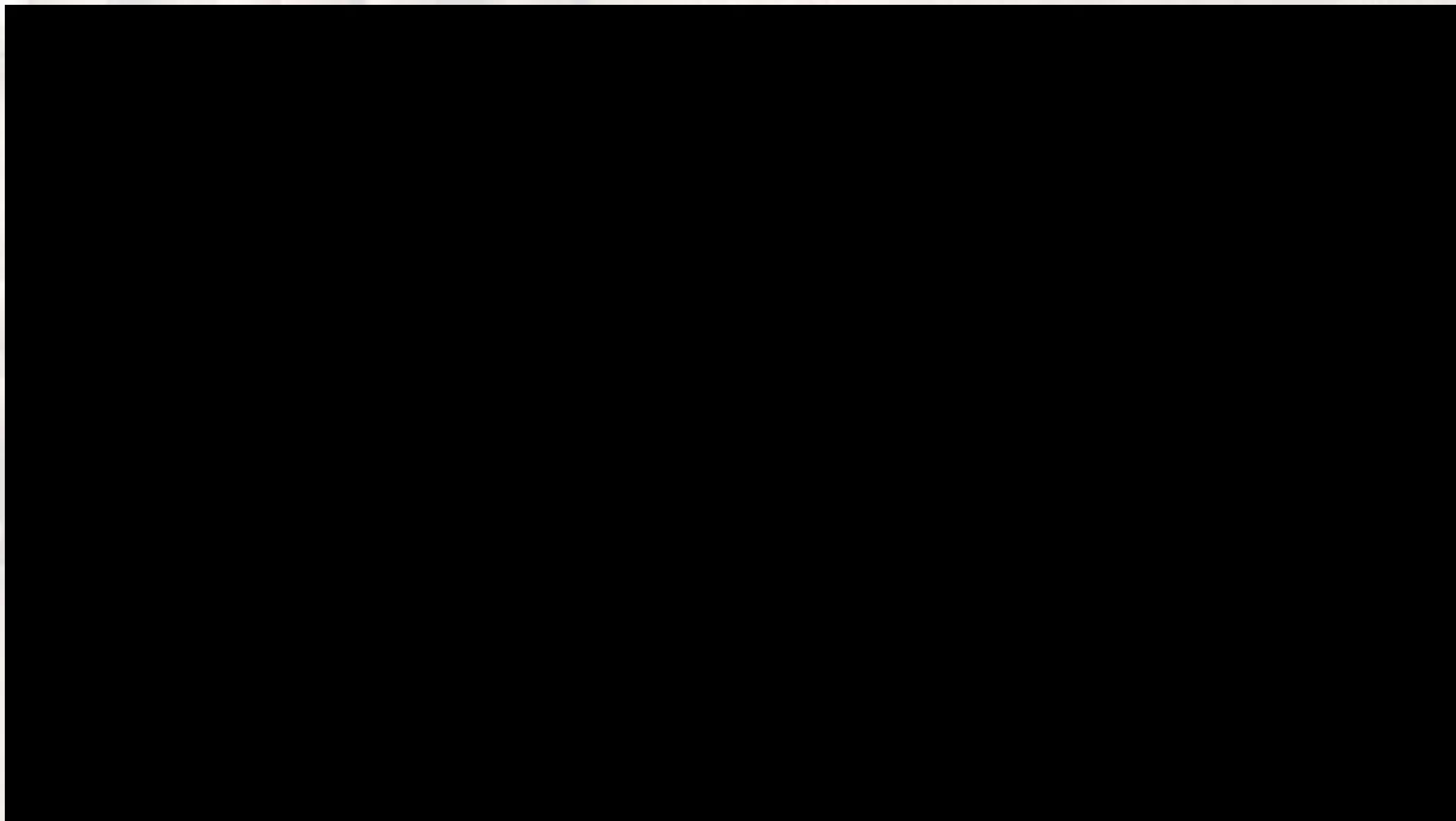
1:30am (EST)

Satellite #3: Pediatric Neuroncology and Childhood Cancer Data Initiative

Session Chairperson: David Arons (National Brain Tumor Society)

- **Chitkala Kalidas (Bayer):** A global pediatric neuro oncology network
- **Kristin Schroeder (Duke University):** Tanzania and Duke pilot in global pediatric neuro-oncology
- **Parvati Dev (Open Health Systems Laboratories):** Information systems supporting a pediatric neuro-oncology
- **Ken Buetow (Arizona State University):** Digital Twin
- **Greg Reaman (National Cancer Institute):** Childhood Cancer Data Initiative
- **Panel Discussion / QA**

Video session archive





Terrell Baptiste

11:00am (EST)

Satellite #5 Panel: Use of Regulatory Headwinds to Manage Towards Properly Enrolled Clinical Trials

Session Chairperson: Terrel Baptiste (Gilead)



Stacey Bledsoe



Barbara Bierer



Binita Patel



Shaalan Beg



Chitkala Kalidas, Ph.D.

- **Stacey Bledsoe (Gilead):** Head of Clinical Trial Diversity, Gilead
- **Binita Patel (Bayer):** Clinical Operations, Diversity Lead, Bayer
- **Barbara Bierer (MRCT Center):** Center Director
- **Shaalan Beg (Science37):** Vice-President
- **Panel Discussion**
 - **Chitkala Kalidas (Bayer)**– Invited Discussant
 - **Patricia Keegan (TopAllianceBio)**– Invited Discussant



Michelle Treagar

1:30pm (EST)

Satellite #6: Access to care following screening and prevention trials

Session Chairperson: Michelle Treagar (National Breast Cancer Coalition)



Derek Raghavan



Eduardo Vilar-Sanchez



Philip E. Castle



Jeffrey Levi



Jennifer Berzok

- **Derek Raghavan (Levine Cancer Center):** Screening for lung cancer
- **Eduardo Vilar-Sanchez (MD Anderson):** Lynch Syndrome Vaccines
- **Panel Discussion**
 - **Philip E. Castle (National Cancer Institute)**- Invited Discussant
 - **Jeffrey Levi (George Washington University)**– Invited Discussant
 - **Jennifer Berzock**- Invited Discussant
 - **Christine Carpenter**- Invited Discussant

Highlights of the Discussion

- Global drug development process remains of high interest, and there are opportunities for clarification and optimization.
- Delivering the promise of precision oncology will require education and capacity building.
- Cancer prevention has great potential, and remains a priority for governments. Regulatory pathways for development are emerging for novel, non-toxic prevention strategies.

Take-home Message

- Virtual meeting format enabled participation and speakers from US and non-US sites.
- Limited networking opportunities during meeting highlights the benefit of in person meetings.
- Future meetings to be in person, with streaming access, and video archives available.

Next Steps

- Return to in-person AAADV meetings in 2025
- Coordinate sessions to compliment other educational activities of regulatory agencies
- Delivery of live streaming and recorded sessions for those unable to attend (currently have archived 100+ AAADV video sessions since 2020)
- Publication of session proceedings in peer reviewed journal