

FDA Public Breast Cancer Workshop

Innovations in Breast Cancer Drug Development
NEOADJUVANT BREAST CANCER WORKSHOP



March 22, 2013

8:00 a.m. to 5:00 p.m.

Federal Research Center



American Society of Clinical Oncology



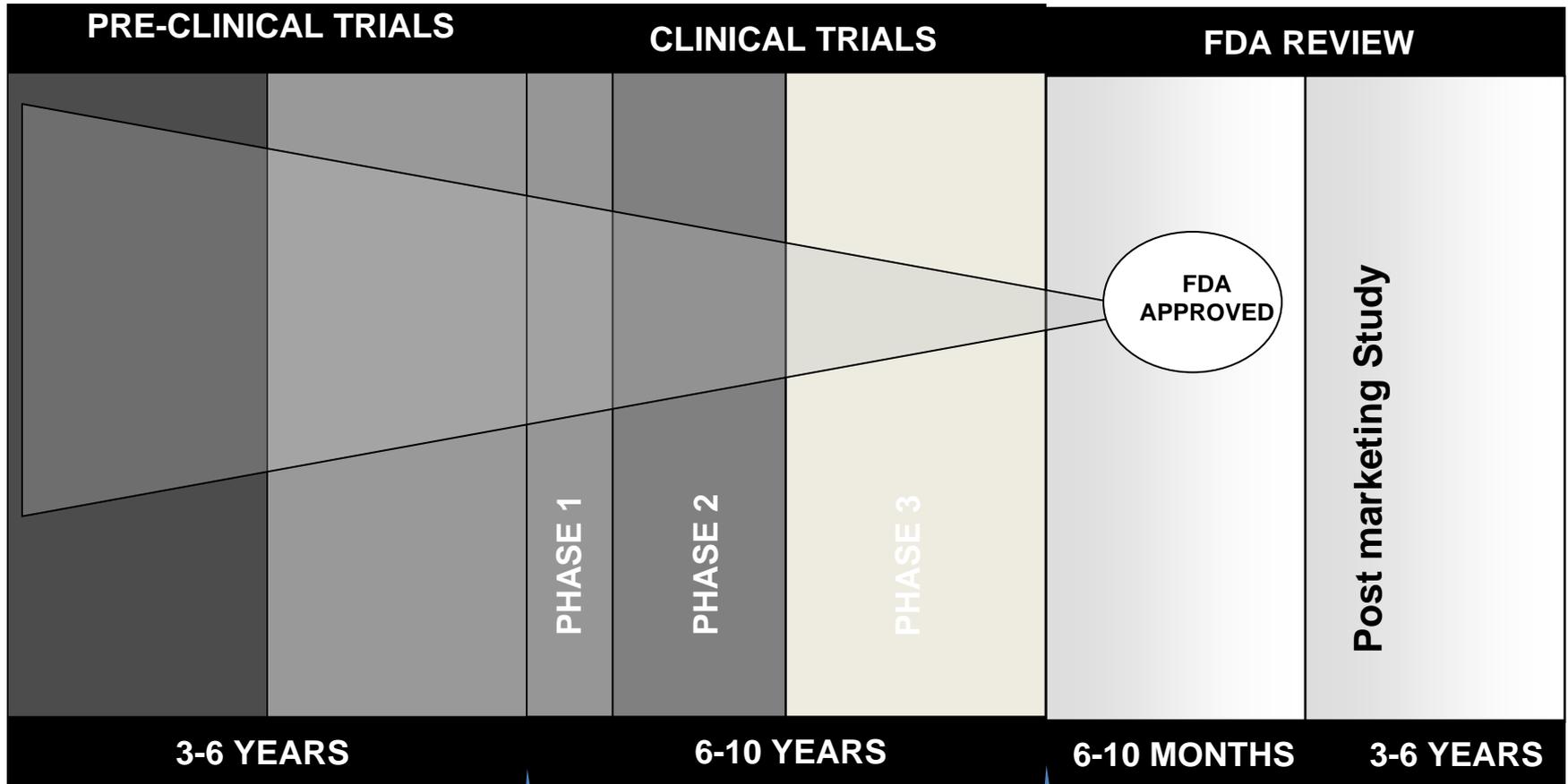
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U.S. Food & Drug Administration (FDA) &
American Society of Clinical Oncology (ASCO)

with support from the American Association for Cancer Research (AACR)

CO-CHAIRS: DR. SANDRA SWAIN AND DR. PATRICIA CORTAZAR

Drug Development Process



IND SUBMITTED TO FDA

NDA SUBMITTED TO FDA

Historical Breast Cancer Drug Development



Agents first developed in MBC:

- Tamoxifen 1977
- Docetaxel 1996
- Trastuzumab 1998
- Anastrozole 1995
- Letrozole 1997

Subsequently developed :

- Tamoxifen 1985
- Docetaxel 2004
- Trastuzumab 2006
- Anastrozole 2003
- Letrozole 2004

- Tamoxifen 1998

Current drug development paradigm needs improvement



What Is FDA Doing To Expedite Breast Cancer Drug Development?

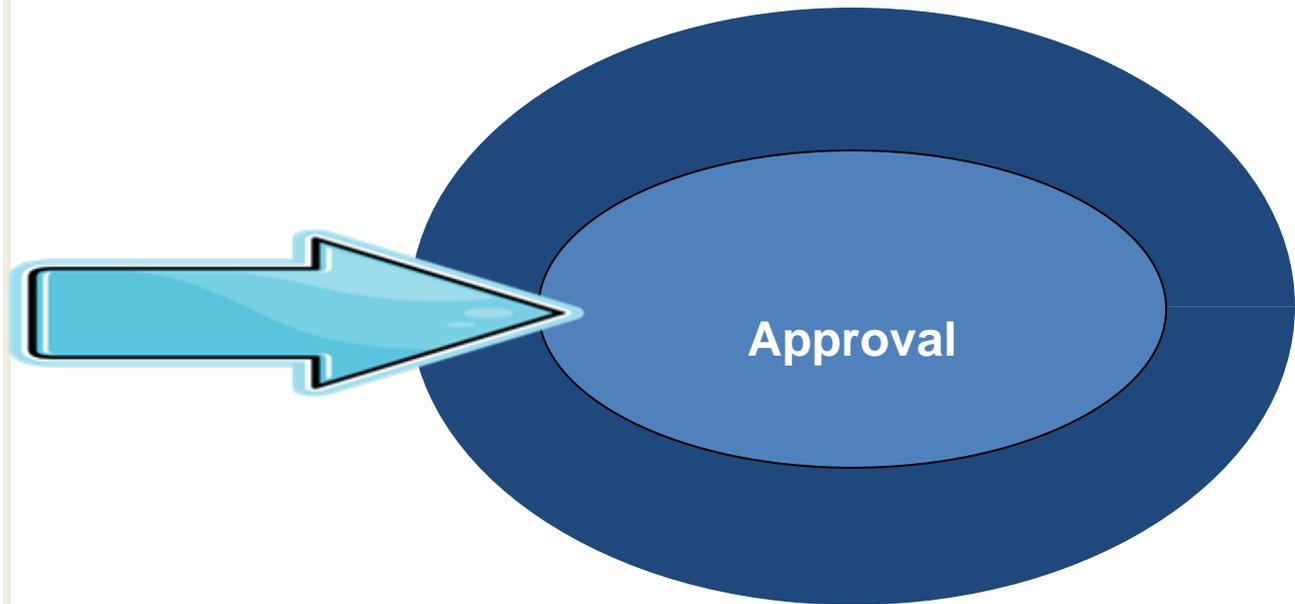


- Opening path forward to neoadjuvant trials to support Drug Approval
 - ▶ CTNeoBC Meta-analysis to learn about neoadjuvant trials
 - ▶ Writing a Guidance for neoadjuvant trials
- Looking at other alternatives to accelerate approval in breast cancer

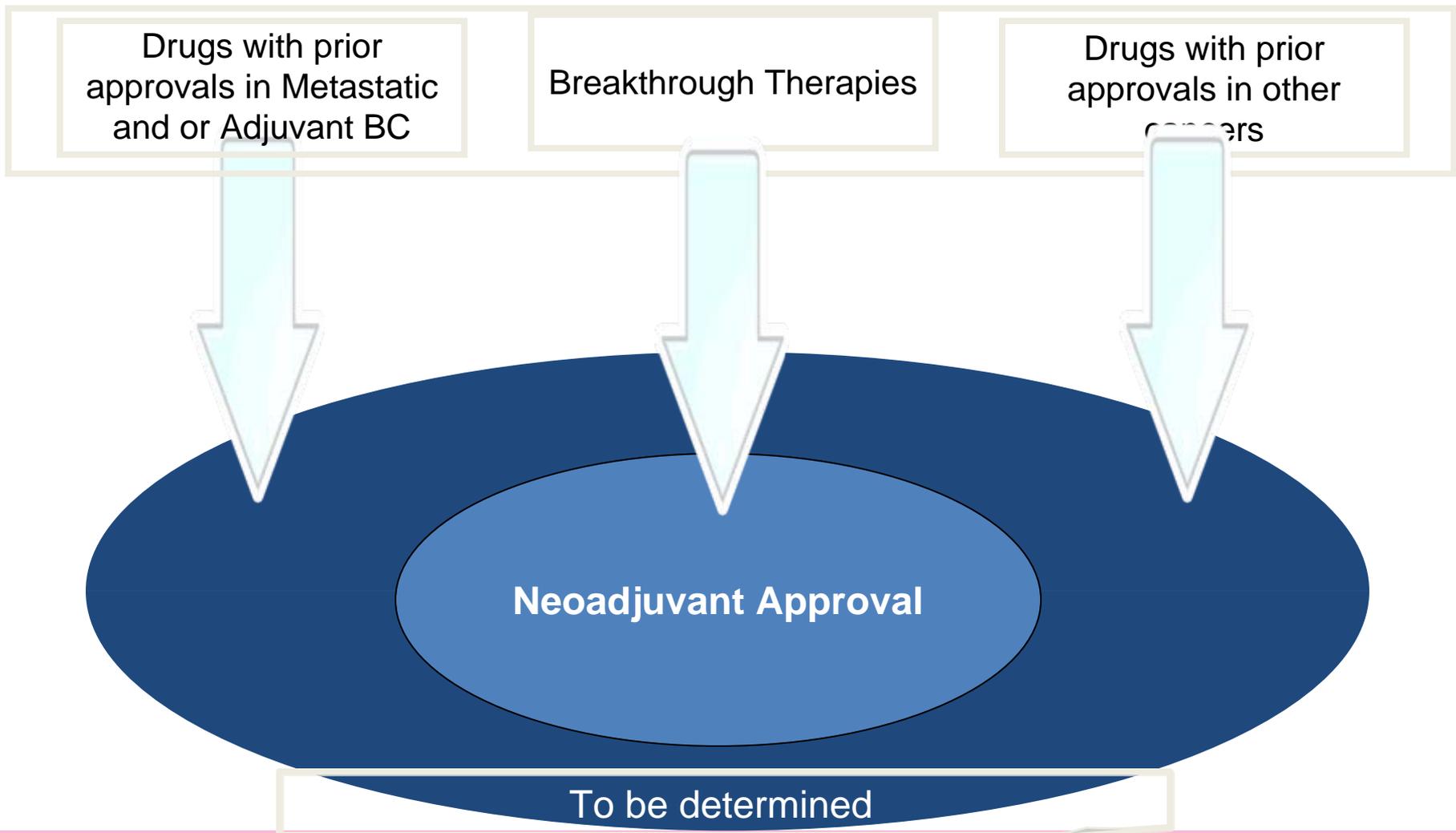
Neoadjuvant Drug Approval Pathway for New Drugs With No Prior Approval



- High risk early breast cancer
- RCT powered for EFS and OS
- Accelerated approval based on pCR
- Regular approval based on EFS, DFS or OS
- If postop therapy is required (e.g. anti HER2), should be the same in both arms.



Potential Neoadjuvant Drug Approval Pathways



Workshop Goal



The discussions at this workshop will be taken into consideration as the FDA moves to finalize the Draft Guidance for Industry - Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval

Pros and Cons of Neoadjuvant Trials to Support Drug Approval



Panel Discussion:

- Do we believe the advantages of granting accelerated approval based on a Neoadjuvant trial outweighs the concerns?
- How much safety data is needed to adequately assess the benefit risk ratio of a new drug for patients with a curable disease?
- Can the clinical benefit results (Event-Free Survival (EFS) or Overall Survival (OS)) obtained from neoadjuvant trials be extrapolated to the adjuvant and metastatic setting? Why or why not?

Implications of the CTNeoBC Meta-analysis



- Should pCR be considered reasonably likely to predict for clinical benefit?
- How should “high-risk” be defined for regulatory purposes in designing neoadjuvant trials intending to use pathologic complete response (pCR) to support an accelerated approval?
- What absolute risk of relapse should be considered “high-risk” for regulatory purposes?
- What magnitude of improvement in EFS should be considered clinically meaningful?
- What is the feasibility of improving EFS in HER 2-positive breast cancer, where the EFS improvement is already high?

Neoadjuvant Therapy & Loco-Regional Management of Breast Cancer



- How should the surgical management of the axilla be standardized?
- Need to standardize management of surgical specimen and preliminary recommendations

Considerations for Neoadjuvant Breast Cancer Trials to Support Accelerated Approval



- Discuss advantages/disadvantages of a single-trial versus a multi-trial approach. Is one approach preferable to the other and why?
- How can we address the feasibility issues of conducting a confirmatory adjuvant randomized trial once a drug is approved for a neoadjuvant indication?
- Are there other clinical trial strategies that should be considered?
- How do we avoid negatively impacting drug development in metastatic breast cancer?

Thank you