

Enrollment in protocol - biopsy

Initial Adaptive Randomization *Kras* mut

EML-ALK,
EGFR Mut
exclusion

Stage 1
N=200

Pre-specified markers
(mutations; IHC)

Discovery markers preclinical and
clinical (*BATTLE-1, 1st stage BATTLE-2*)

Statistical modeling and biomarker selection

Refined Adaptive Randomization:
“Best” Predictive Markers

Stage 2
N=200

Erlotinib (E)

E+AKTi MK-2206

MEKi AZD6244+ MK-2206

Sorafenib

1

2

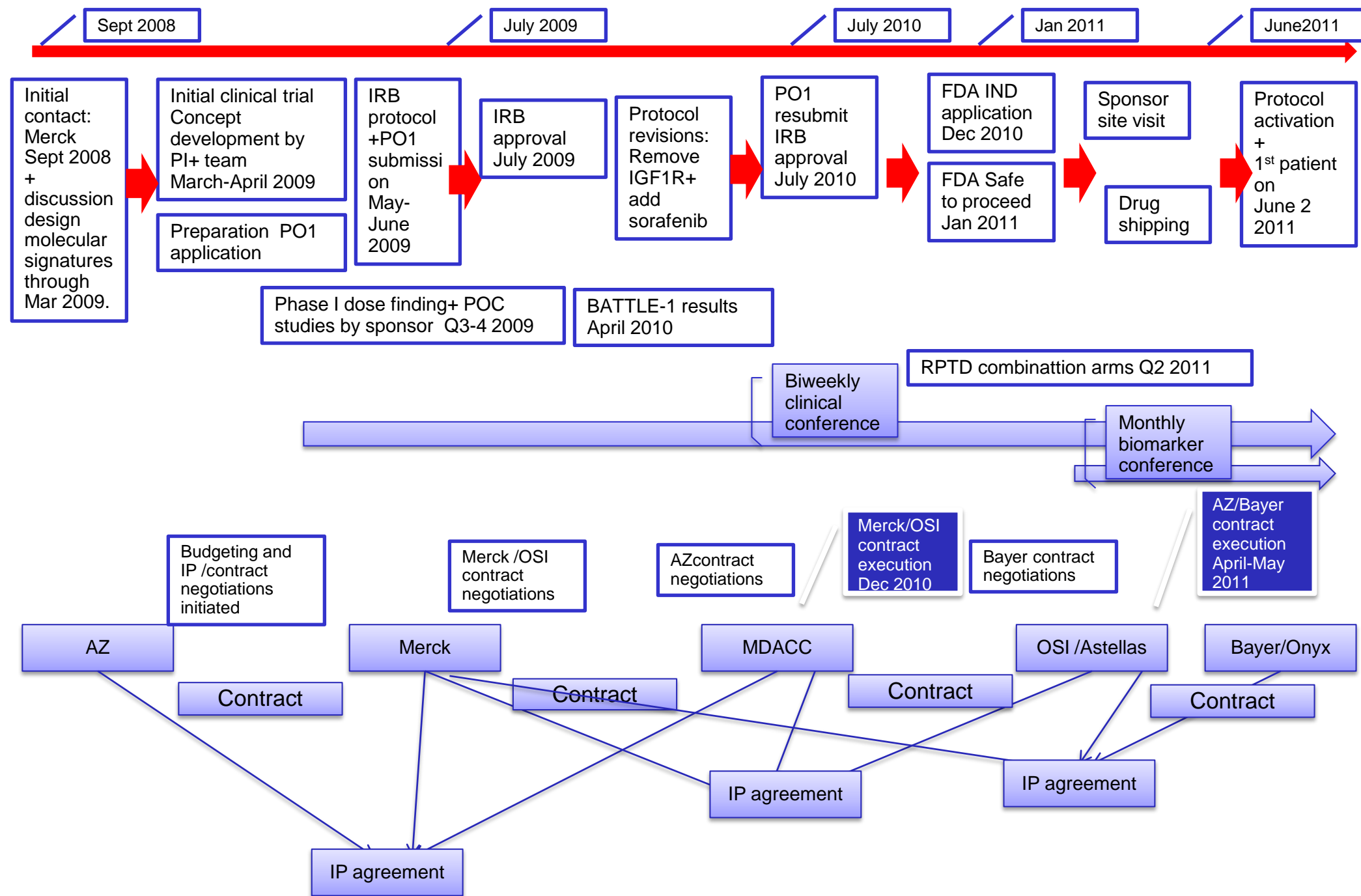
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BATTLE-2 Development of Study in Refractory NSCLC Patients

- Meetings and Conference Calls with Thoracic Group and Merck
Initial contact: September 2008, reviewed Merck's molecular signatures and potential targeted agents; discussed possible validation in BATTLE tissue, reviewed pipeline and identified novel agents for ph II trial in NSCLC refractory setting based on 2009 science and clinical landscape.
- Protocol development and first IRB approval July 2009, 10 protocol revisions and approved amendments, based on POC clinical trial results (Merck, BATTLE-1) and evolution of scientific knowledge.
- Three 3way IP agreements and 4 contracts between MDACC and pharmaceutical sponsors
- 4 NCI Grant applications (initial PO1 and resubmission, initial RO1 and resubmission)
- Three oral presentations of preliminary results developed in preparation for grant and protocol submission (molecular signatures and impact of different KRAS mutations in NSCLC) and three manuscripts submitted.

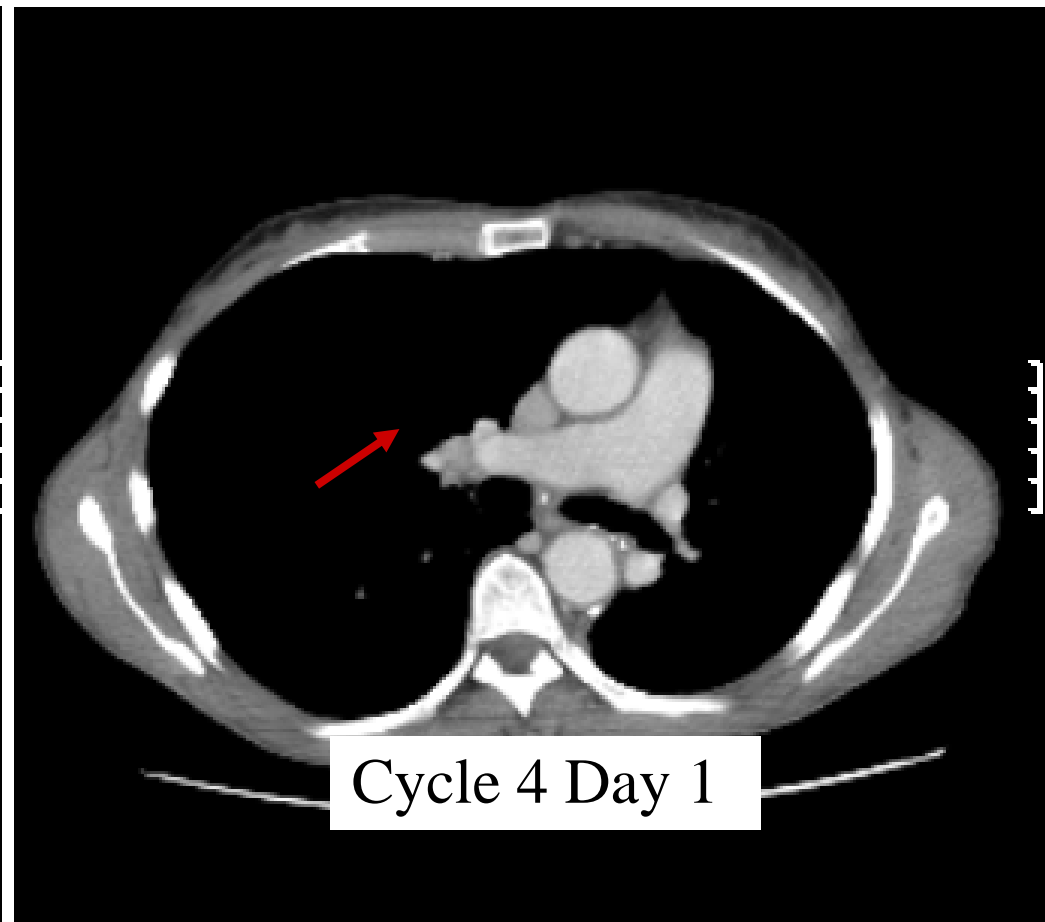
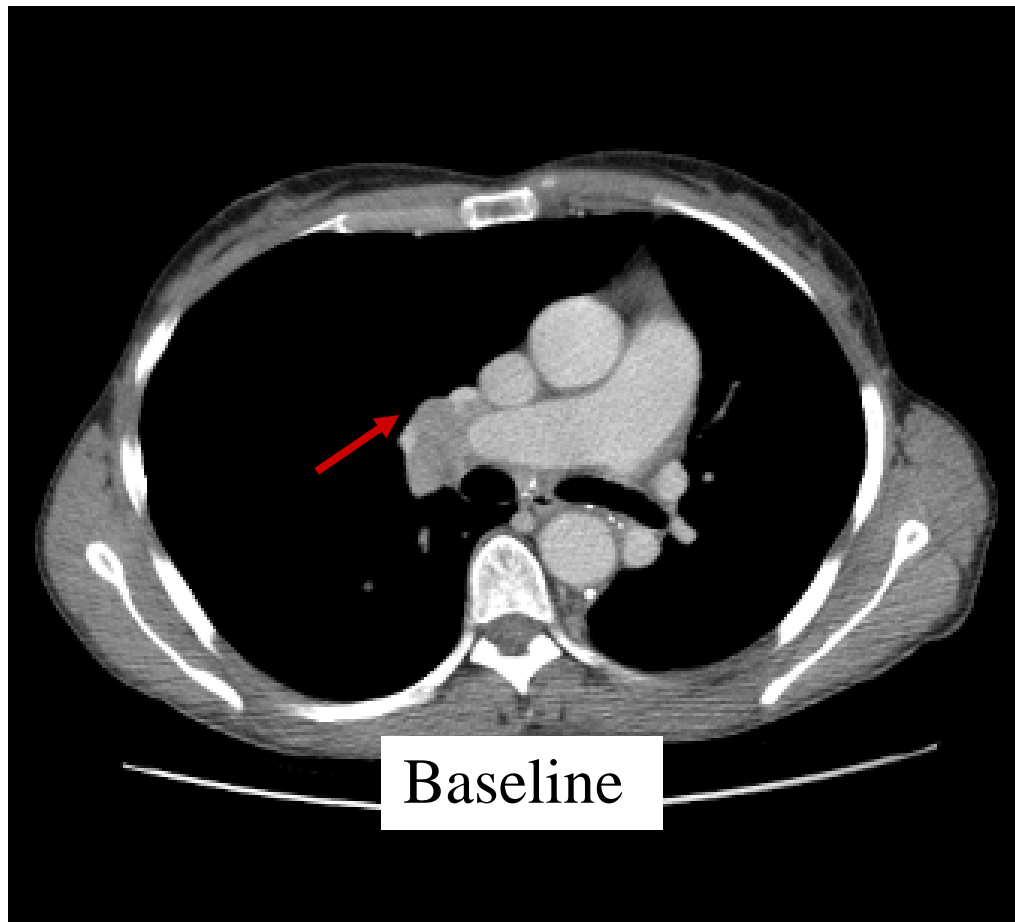
BATTLE-2 PREPARATION AND ACTIVATION STEPS



Entities and Partners

- Principal Investigator
- 4 pharmaceutical sponsors
- Academic collaborations (MDACC, Yale)
- Molecular pathologist and 2 teams of scientists (academic and pharma)
- 4 basic science and translational academic collaborators for grant development.
- 2 teams of statisticians (academic and pharma)
- Division chair and Department head
- Regulatory staff
- Thoracic Team
- CRC +IRB
- Grants and contracts office
- Office of protocol research/IND office/FDA
- 5 legal departments (1 academic, 4 pharma)
- Study coordinators
- Institutional collaborators (interventional radiology, pathology, molecular pathology, ophthalmology, cardiology, dermatology)
- Pharmacy

A phase I dose escalation study of
oral MK-2206 (allosteric AKT inhibitor)
with oral selumetinib (AZD6244; ARRY-142866) (MEK inhibitor) in patients
with advanced or metastatic solid tumors . Tolcher AW et al, ASCO 2011, abstr#77652, NCT01021748



NSCLC KRAS Mutant, PR after Course 2