LUNG-MAP

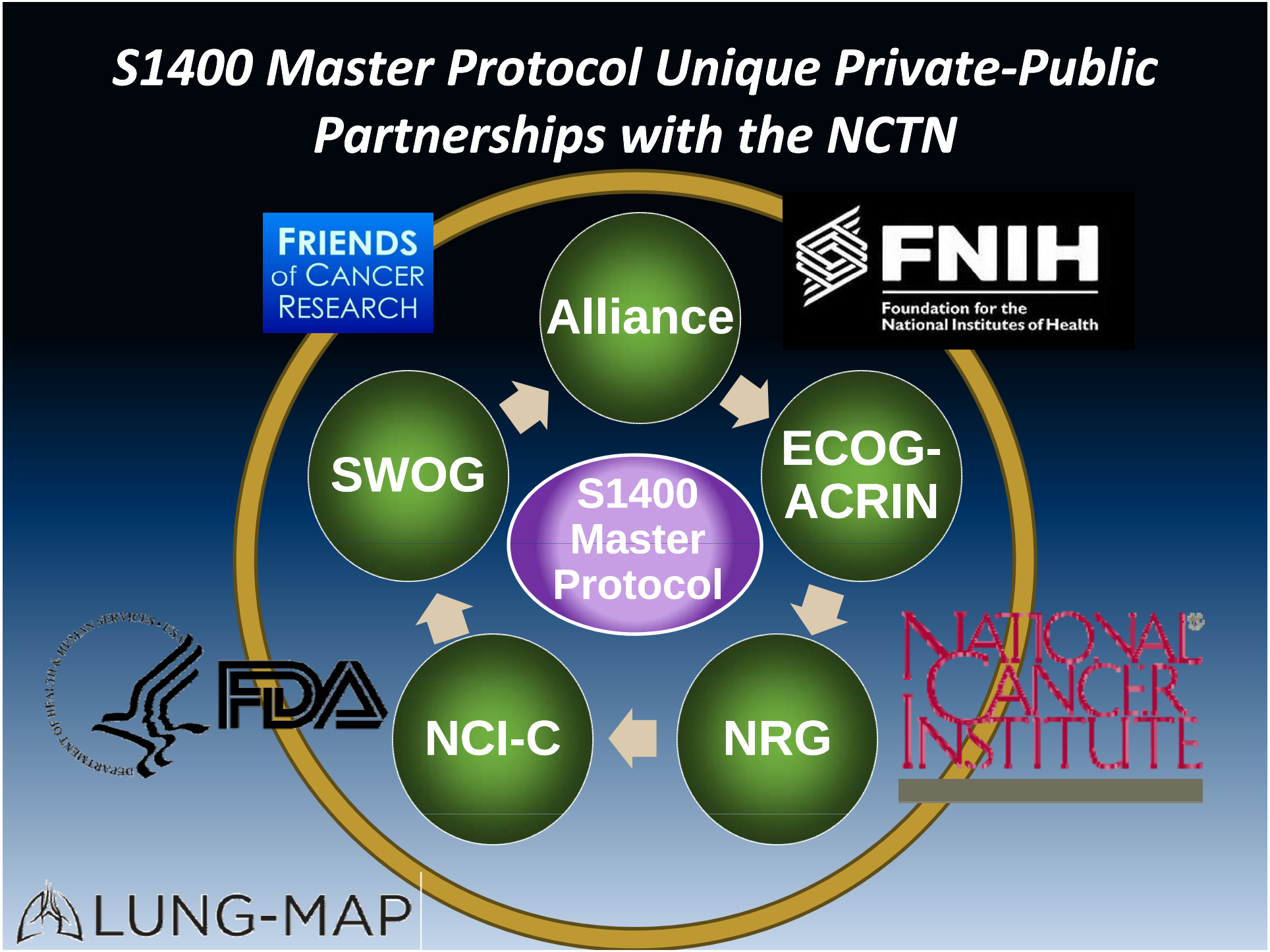
S1400 Lung Master Protocol Update

SWOG Fall Meeting

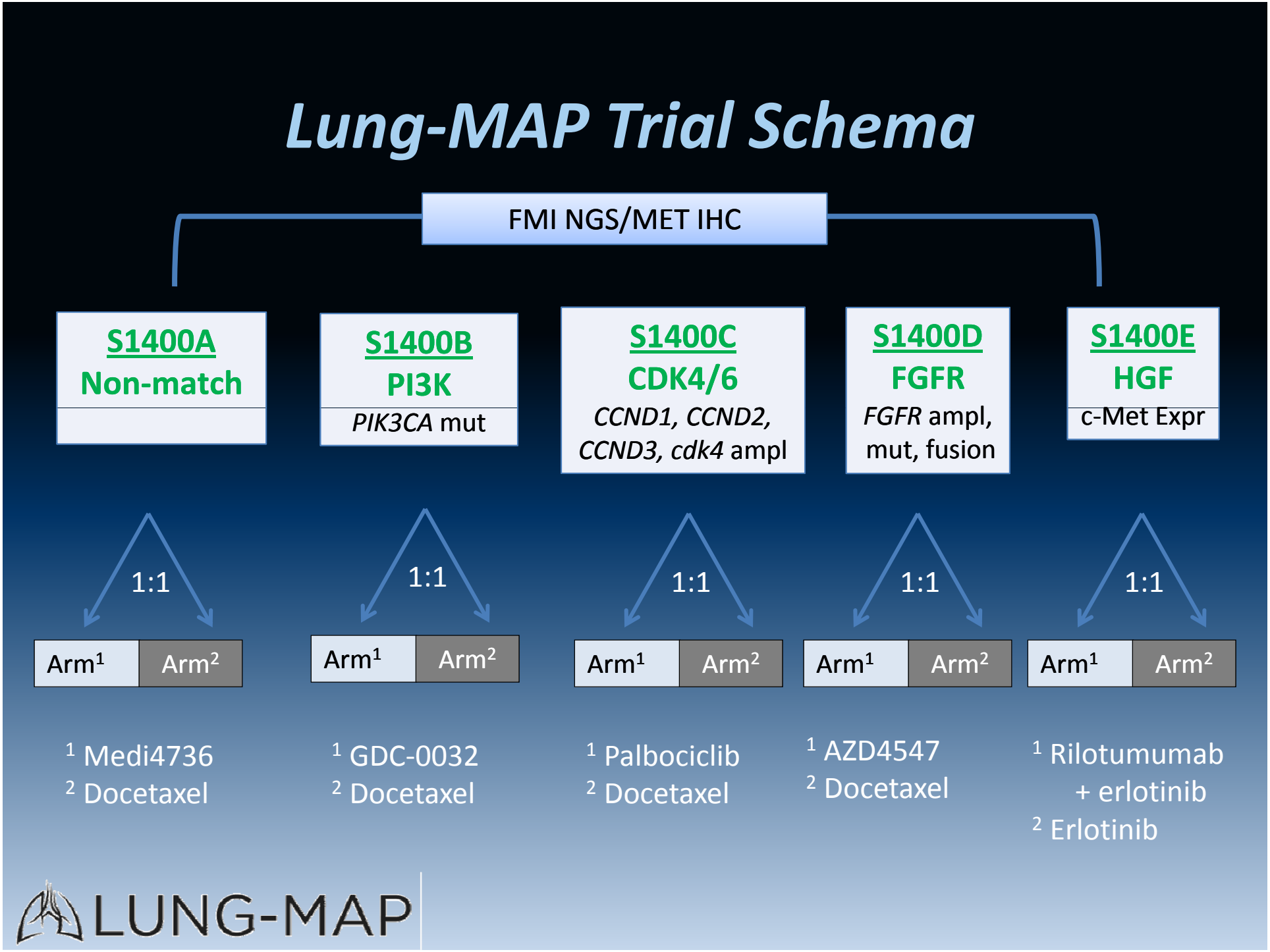
October 24, 2014

“Phase II/III Biomarker-Driven Master Protocol for Second Line Therapy of Squamous Cell Lung Cancer.”

S1400 Master Protocol Unique Private-Public Partnerships with the NCTN



Lung-MAP Trial Schema



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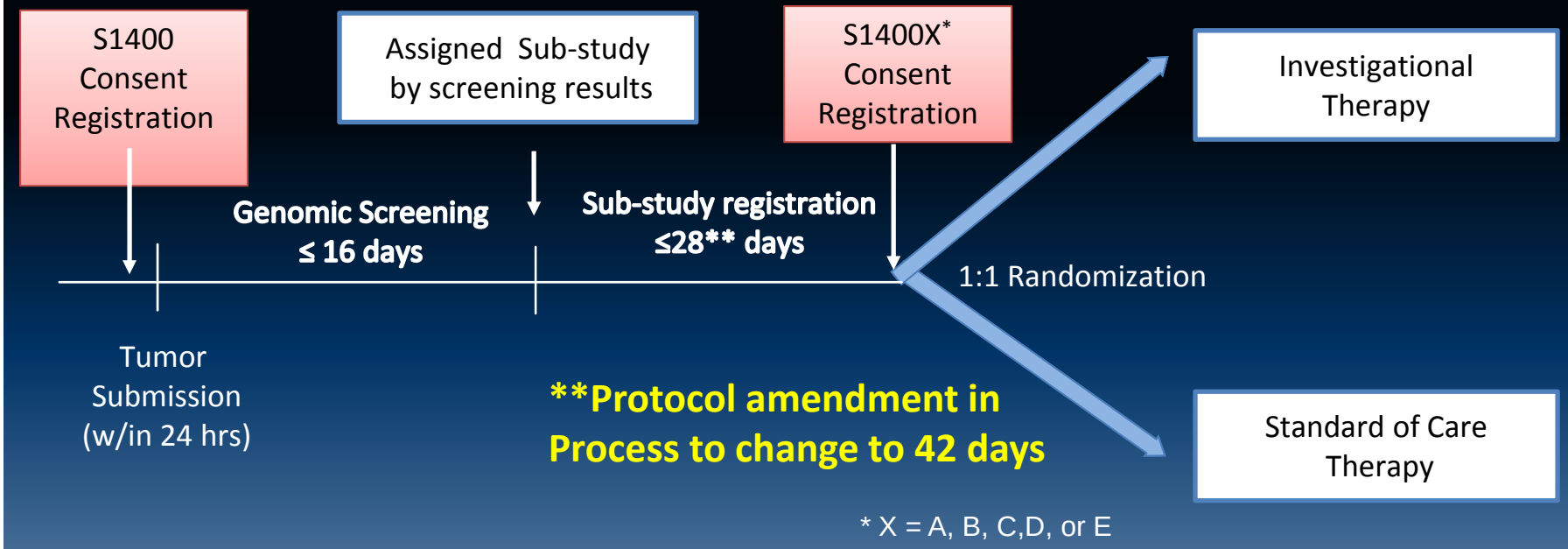
Eligibility Updates

Original	Revised
Disease setting	
Incurable stage IIIB or Stage IV	Only Stage IV
Mixed Histology ≥50% allowed	Mixed histology not allowed
Prior Treatment	
No restrictions on prior radiation	Prior radiation within 28 days before S1400 registration not allowed
Exactly one platinum-containing chemotherapy regimen	Platinum-based chemotherapy required. • Can be regimen for Stage I-IIIB • 2nd for Stage IV allowed after progression of Stage I-IIIB.
	• If initial chemo given for Stage IV, exactly one allowed
Other	
Register to assigned sub-study within **28** days	Register to assigned sub-study within **42** days
SGOT/SGPT <= 2.5	ALT/AST <= 2.0

Reiterating Previous Treatment Criterion

- Patients must have progressed after receiving a platinum-based chemotherapy regimen.
- Patients who received platinum-based chemotherapy for Stage I-IIIB disease may have received at most one additional chemotherapy regimen for Stage IV disease and must have progressed after receiving this regimen for Stage IV disease.
- Patients who progressed after chemotherapy for Stage IV disease must not have received any additional chemotherapy.

Patient-level Schema



* X = A, B, C,D, or E

Central genomic and IHC screening:
Foundation Medicine: NGS test platform (CLIA/CAP).
Clarient: c-MET IHC

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Tissue Requirements

1. Tissue block (preferred) or at least 12 five-micron unstained slides (20 slides are strongly recommended).
   - Tissue must contain at least 20% viable tumor cells
2. Hematoxilyn-eosin (H&E)-stained slide or Aperio H&E-stained slide
3. Local pathology report from initial diagnosis
4. **S1400** Local Pathology Review Form:

   Tumor material must be reviewed by a local pathologist to ensure sufficient tumor cells are present in the sample. The local pathologist must review and sign off on the **S1400** Local Pathology Review form noting that the tumor tissue contains at least 20% viable tumor cells.

S1400 Registration and Sub-study Assignment

Screen for eligibility, consent patient and confirm that required amount of tissue is available for submission
(pathologist to complete the *Local Pathology Review Form*)

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Register to S1400 in OPEN

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Submit tissue specimen within 1 day after registration
(Ship to FMI and and log shipment using the Specimen Tracking System)

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Within 16 days after S1400 registration

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Site staff receives email from SWOG with sub-study assignment
(Assignment will also display in the *Sub-study Assignment* form in Rave®)

Post Sub-study Assignment

Evaluate common eligibility and sub-study specific eligibility criteria

If patient IS eligible for assigned sub-study

Register to sub-study in OPEN within 42days of receiving sub-study assignment email to receive randomized sub-study treatment assignment

Administer protocol treatment within 7 working days of sub-study registration, conduct follow-up, obtain and submit specimens and forms per sub-study protocol

Post Sub-study Assignment

Evaluate common eligibility and sub-study specific eligibility criteria

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If patient is assigned to S1400B,C,D, or E, meets common eligibility but does NOT meet study-specific eligibility criteria

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Submit *Request for Sub-study Reassignment* Form in Rave®

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Site staff receives email with new sub-study assignment
(Timing and process same)

Post Sub-study Assignment

Evaluate common eligibility and sub-study specific eligibility criteria

If patient is NOT eligible for the common sub-study criteria OR assigned to S1400A and does NOT meet S1400A eligibility criteria

Submit *Notice of Intention not to Register* Form in Rave®

Follow and submit required forms until 3 years from registration or death (whichever comes first) per S1400 protocol

QA/Monitoring Status

- Monitoring visits began October 2014
- Any site with patients registered to a sub-study will be audited on site
- If no patients have been registered to a sub-study, we have the option of conducting the audit off site

Funding Highlights

- **Sites will receive up to $5,869 ($1,079 screening/$4,790 registration) for each patient on trial**
- **If biopsies are needed, sites will receive $3,000/$6,000 for the biopsies performed at screening and/or progression after initial response on Arm 1**
- **Sites will be reimbursed for additional research based procedures**
- **Sites will be reimbursed $1,333 for extra audit visits outside regular schedule**

Funding Changes

FDA has requested tests/procedures to be performed on the investigational and standard of care arms. Sites will be reimbursed for the following additional procedures on both arms.

Sub-study	Additional Funding for Procedure/Test
S1400A	TSH T3/T4*
S1400B	HbA1c, Lipase, Amylase
S1400C	EKG, HbA1c*
S1400D	OCT Scan, Ophthalmological Assessment, MUGA, Phosphate, Urinalysis, Troponin
S1400E	No changes

*This is an added test requested by the Company as part of the amendment

Where are we now?

- IRB Approvals:
  - 337 sites
  - 29 sites with at least 1 patient accrual (19 SWOG sites)
- Accruals:
  - 56 patients registered to S1400
  - 40 patients notified of their sub-study assignment
  - 18 patients registered to a sub-study

S1400A: 8
S1400B: 0
S1400C: 2
S1400D: 2
S1400E: 6

Questions?