BLINDED DIAGNOSTICS

SAME DAY LAB TEST RESULTS

for Pharmaceutical Clinical Trials

Presenters:
John Brennan
Blai Coll

Phase 2 Studies

RADAR and M12-812 (Japan)

- Type 2 diabetic patients with albuminuria on RAS inhibitors
- Doses: 0.75 mg and 1.25 mg x 12 weeks
- Subjects: 211
- Run-in: Maximize RAS inhibitor and optimize BP
- End-point: UACR reduction

M12-830 (Bioimpedance)

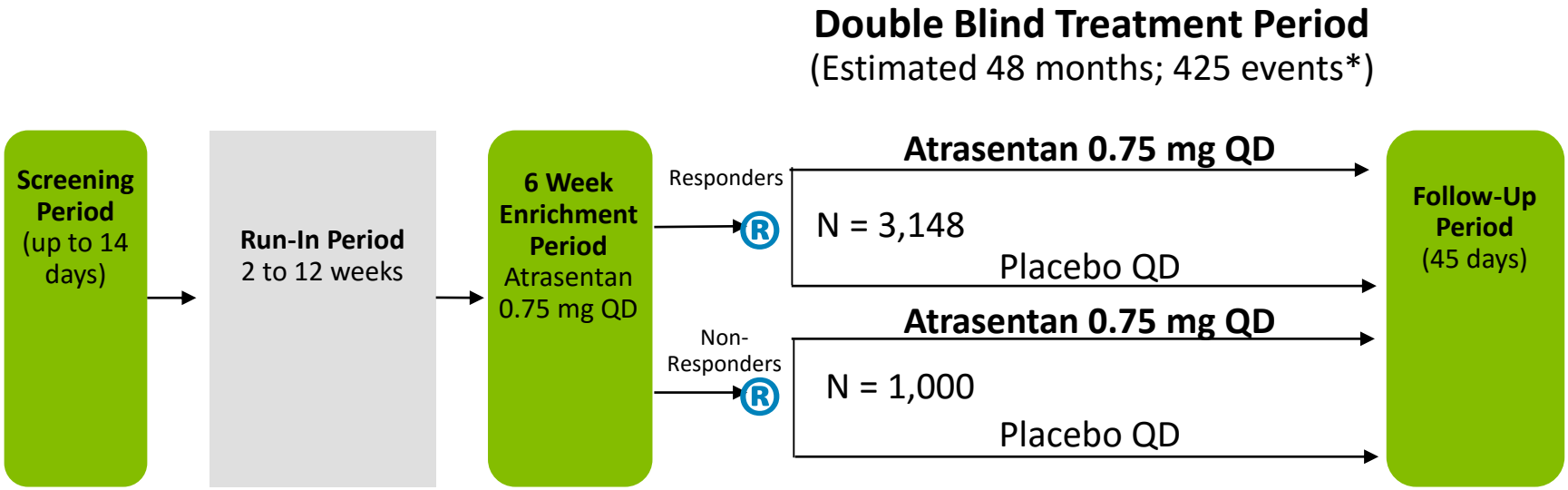
- Type 2 diabetic patients with albuminuria on RAS inhibitors
- Doses: 0.5 mg and 1.25 mg x 8 weeks
- Subjects: 45
- Run-in: Maximize RAS inhibitor and optimize BP
- End-points: UACR reduction; bioimpedance

- INCLUSION CRITERIA ***"NIGHTMARE"***
  - **Kidney Function**: estimated glomerular filtration rate (eGFR)
  - **Risk of kidney disease progression**:
    - Protein in urine (urinary albumin:creatinine ratio)

Challenge Faced

- High Screen Failure Rate in Phase II: >70%
- Larger number of sites planned for Phase III
- Anticipated high Central Lab cost for Phase III
- Large enrollment of patients on Global scale

SONAR Study Design



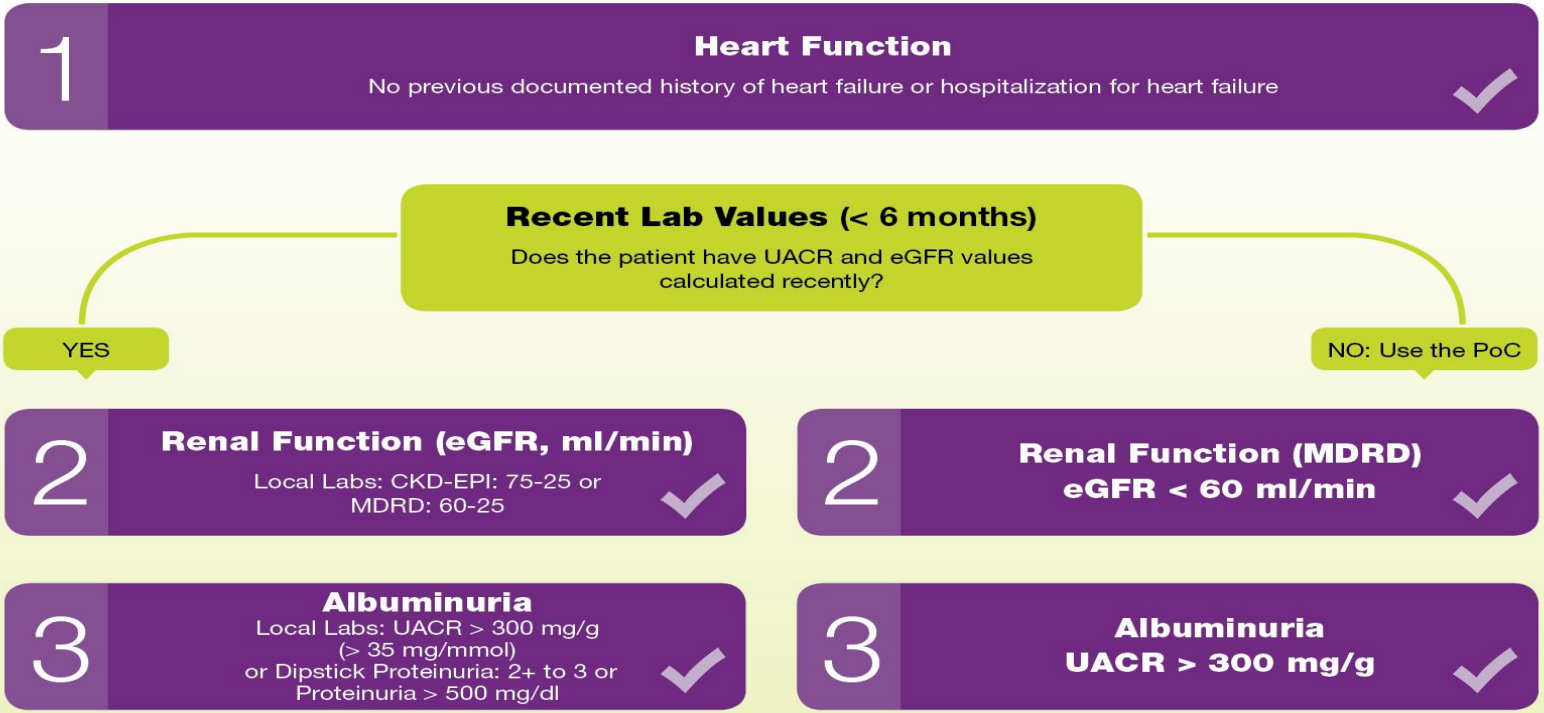
Importance of the enrichment period:

- **Identify patients with the greatest likelihood of benefiting from treatment**
- **Reduce the risk of tolerability issues during the double blind treatment period**

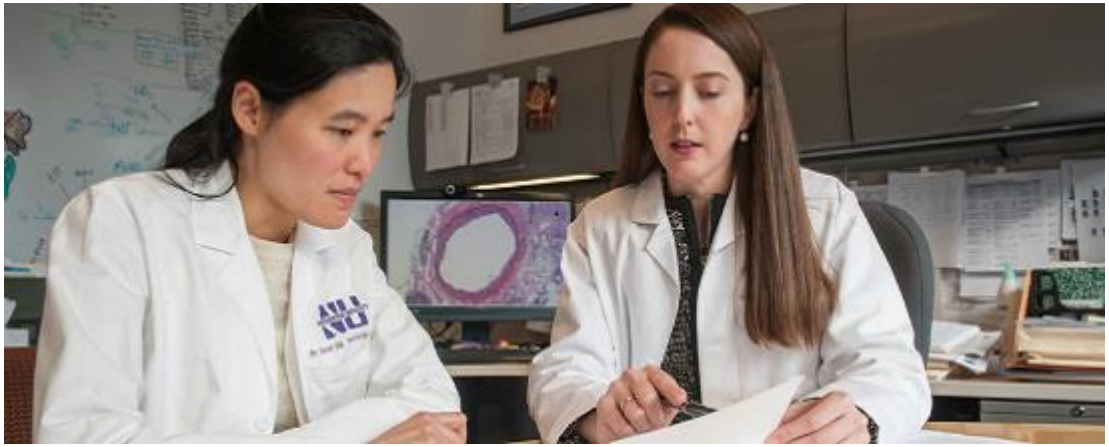
Pre-Screening Period

- Objective – Decrease Screen Failure rate by obtaining current eGFR and albuminuria data using POC (point of care) devices from patients who do not have recent lab data
- Screen Failure:
  - Screen Fail Rate in SONAR: 53%
  - Similar trials with SF Rate > 70%
- If recent Local Labs available, may proceed directly to Screening Visit 1 (S1) without Pre-Screening

Check List for Sites/Pre-Screening



Strategy to reduce Central Lab Screen Failures



Provide guidance and tools to Investigator Sites to improve patient selection for the study prior to Central Lab Screening step.

Pre-Screening with Point of Care at Sites

- Two Tests: UACR and Creatine eGFR
- Pre-Screen Consent
- Selection of point of care devices
- CRO support
- POCT deployment and support
- Training Investigators and Site Staff
- Regulatory Issues

Pre-Screening Period - Procedures

- Sign Pre-Screening Informed Consent (or Main ICF if pre-screening included)
- Obtain
  - Blood sample (eGFR) by finger-stick
  - Urine sample (albuminuria)
- Inform patient during the visit of their eligibility for the Initial Screening Visit
- May perform Screening visit (S1) on same day
- Pre-screening data will **NOT** be collected in EDC

Implementation

- Devices, Consumables and Quality Control materials sent to each site
- Didactic presentation and hands on training at investigator meetings
- Webinar Refresher sessions
- Phone and email support for sites
- POCT Project Manager on weekly calls
- CRO reorder point
- Monitoring screen failure rates by site

Ongoing Observations

- Screen Failure Rate ~50%
- Majority of study sites are using the POCT pre-screening
- Study sites using POCT appear to have lower screen failure rates
- Greater than 95% Satisfaction of Sites with POCT devices and support
- Cost savings from reducing screen failures were achieved and resulted in better study management

Correlation of the combined eGFR and UACR criteria for screening based on the use of the POC pre-screen had a 79% Agreement

POCT and Central Lab Screen (Includes correlation on patients excluded and included for both tests with both methods)	**79%**	Agreement
POCT out / CL Screened in	6%	False negative
POCT in / CL Screen out	15%	False positive

Conclusions

- By using a two test criteria as a pre-screen with POCT, 41% of subjects were ruled out of the higher cost screening period.

- Since the POCT correlated well with Central Lab, 79% of the time, the study enrollment rates increased as the screen failures declined.

- Cost savings from reducing screen failures were achieved and resulted in better study management

Thank You!