Observation-enriched Randomized Controlled Trial (ORCT)
a hybrid allocation study design
to consider when the gold-standard RCT is not feasible to get done

Consent: includes option to choose randomization
or to choose the preferred study arm
(education is provided during consent
to explain why the best approach is not yet known)

Patient chooses randomization

Patient chooses study arm

Registration (n=)

Registration (n=)

Random assignment (1:1)

Decision per
treating physician and patient*

Study Arm 1

Study Arm 2

Study Arm 1

Study Arm 2

Propensity scoring can help correct for bias in observation arms
Study arms can be closed to achieve minimum random allocations or balance in observation arms
* Referring centers can be randomized - or selected to correct for known institutional preferences

Consider when comparing approaches with very different risks
Consider when either or both treatments can be used off study
Consider when biomarker discovery is primary endpoint
... and heterogenous disease biology predicting outcomes is not known

Will foster efficient accrual in large trials - consent decisions can be captured and evaluated
Mitigates selection bias associated with "volunteering to be randomized"
Observation arms having same eligibility and response assessment - thus are superior to historical controls
ORCT is superior to single-arm study or RCT that's not feasible to get done
Comparison of Observation and Randomized cohorts tests the validity of Observation data
ORCT design maximizes respect for persons