G-TAC: A GCIG-wide targeted therapy umbrella study in cervical cancer

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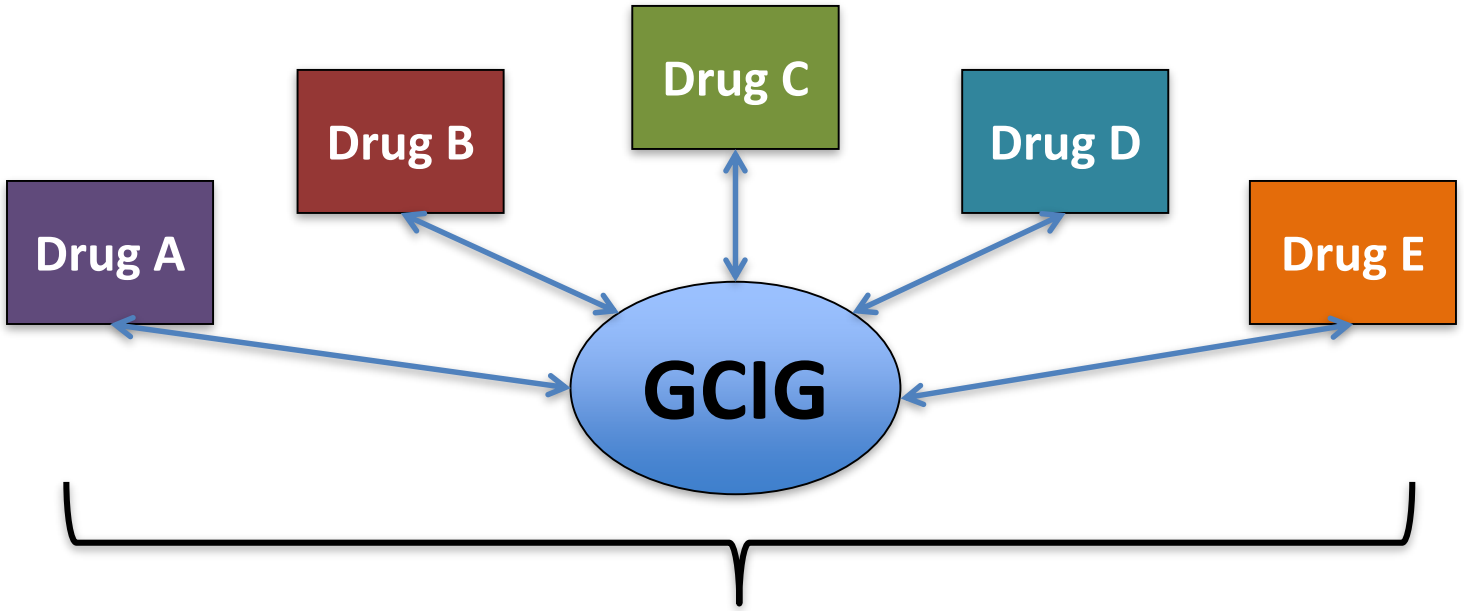
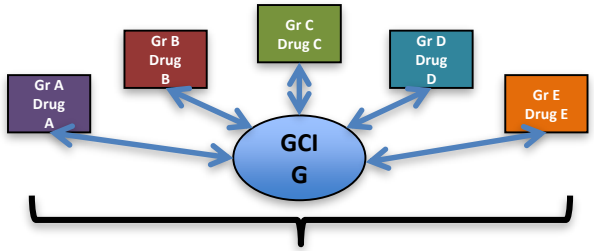
Group PIs: TBD by arm

GCIG/Pharma collaboration

G-TAC: GCIG - Targeted Agents in CxCa



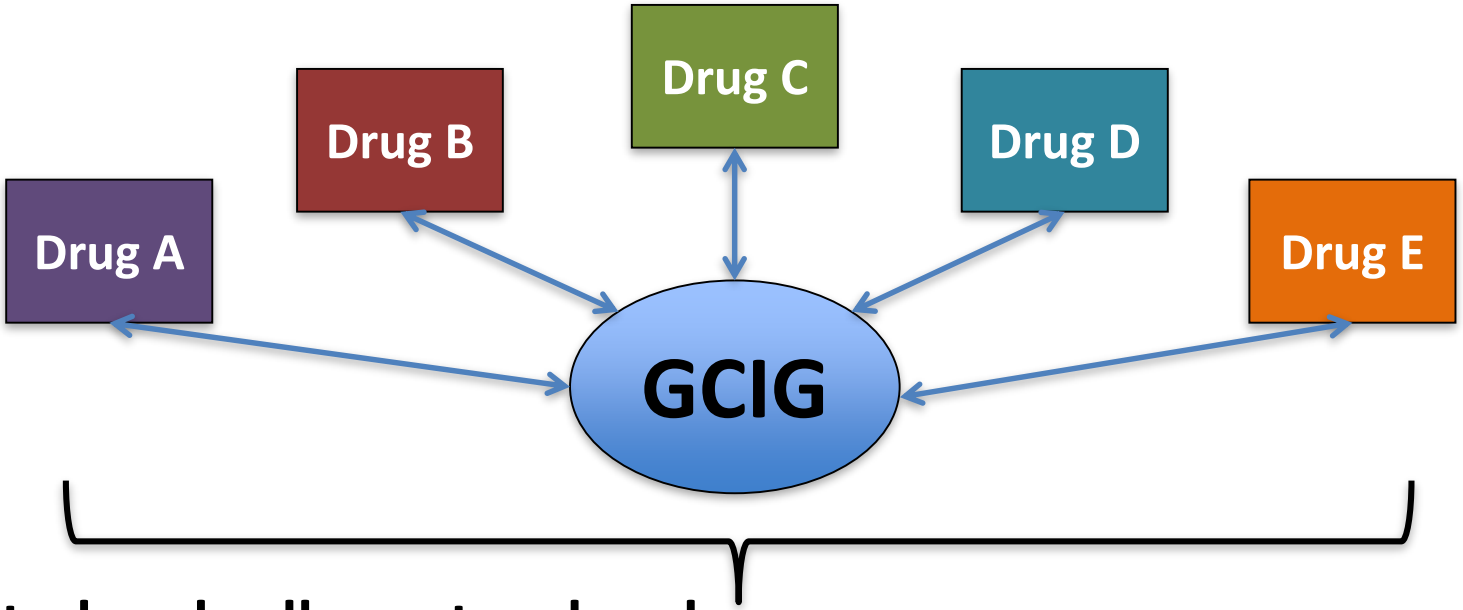
- creation of a "critical mass" of patient experience
- over numerous targeted agents
- more rapid potential accrual and maturation than single trial
- common data and laboratory elements



DESIGN:

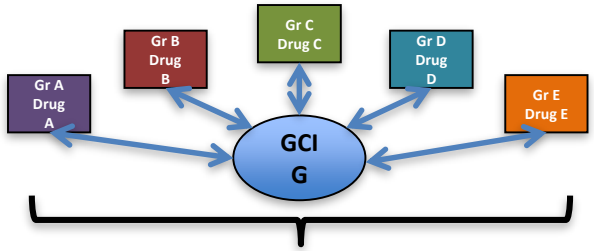
- core committee (subprotocol PIs)
- common core protocol (precis reviewed)
- common clinical data elements—harmonization planned, minimum CDEs to keep simple
- common biospecimen collection (for discussion*)
- common laboratory endpoints (for discussion)

Simple minimal collection (1 block/1 tube blood) can be attempted with later Introduction of laboratory endpoints pending investigators, collection, funding



- Central umbrella protocol such as:
  - high risk post CCRT pts (+12 wk CT), IIIB/IVA
  - tissue available from diagnosis
  - randomization v observation (SoC)
  - endpoint: TTP, with biopsy proven recurrence with tissue for molecular endpoints preferred
- Mandatory collection of tissue for uniform molecular analyses
  - WES across all arms will build large resource for mining
- Opportunity for per arm translational add-ons relative to their arm or across arms

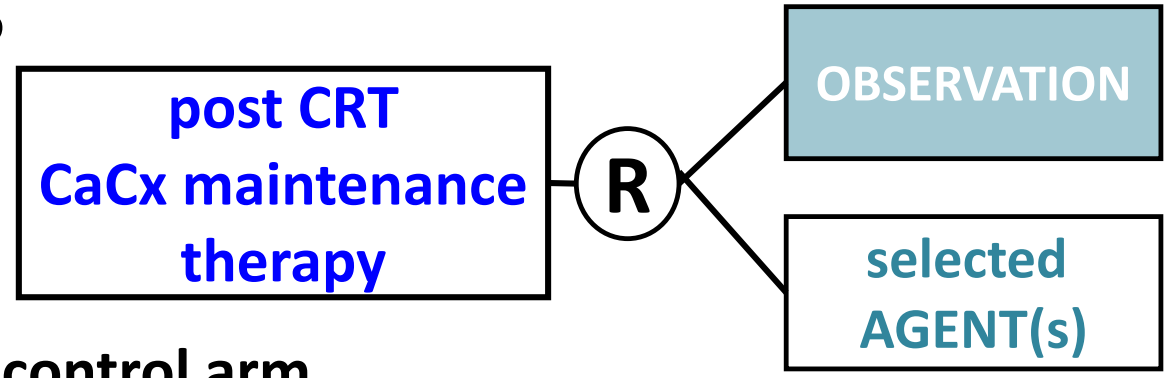
DESIGN ELEMENTS



OBJECTIVES

- 1^0: PFS
  - Median?
  - Landmark: options 2 or 3 years
- 2^0:
  - OS, sites of recurrence
  - Development of historical control dataset (meta analysis)
  - PRO?, could do meta of control pts to have baseline for future evaluation

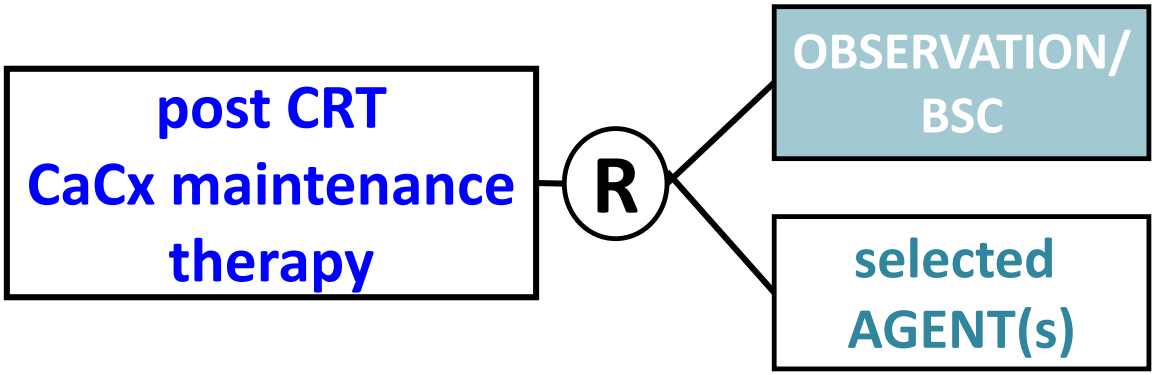
DESIGN ELEMENTS



DESIGN

- Common observation control arm
- Eligibility:
  - newly diagnosed untreated (no surgery)
  - Entry at any time during CCRT or within XX months of completion to start therapy within 3 months of completion of treatment (can include any type chemoradiotherapy +/- brachy
  - Intermediate to high risk IB2 – IVA
    - Any +ve LN on exam, path, imaging, PET/CT
    - Any IIIA, B, IVA
  - Squamous, adeno, adenosquamous
  - ECOG 0-2, informed consent

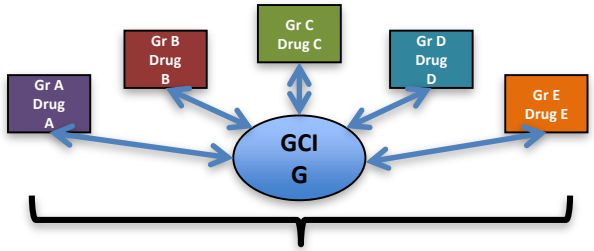
DESIGN ELEMENTS



DESIGN

- **Each randomization is independent within the umbrella with overarching collaborative agreement for meta analysis and template for harmonized CRFs**
- **Each randomization includes the same observation/BSC arm**
- **Each "subprotocol" includes the preplanned meta-analysis of controls**
- **Registration can be early. Nonresponders do not randomize.**
  (useful because gives some sense of early failures)
- **Randomization to be determined when? 3 months post tx?**

DATA COLLECTION

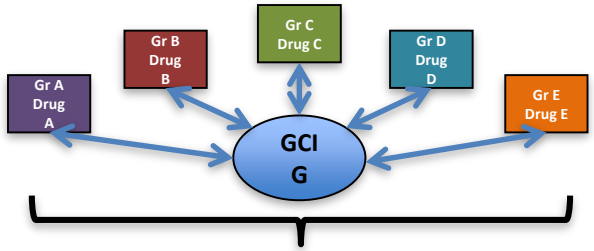


HARMONIZATION

Required across all participating groups for

- **minimum data required**
- **common data elements**
- **eCRFs**
- **translational targets minimum harmonized**

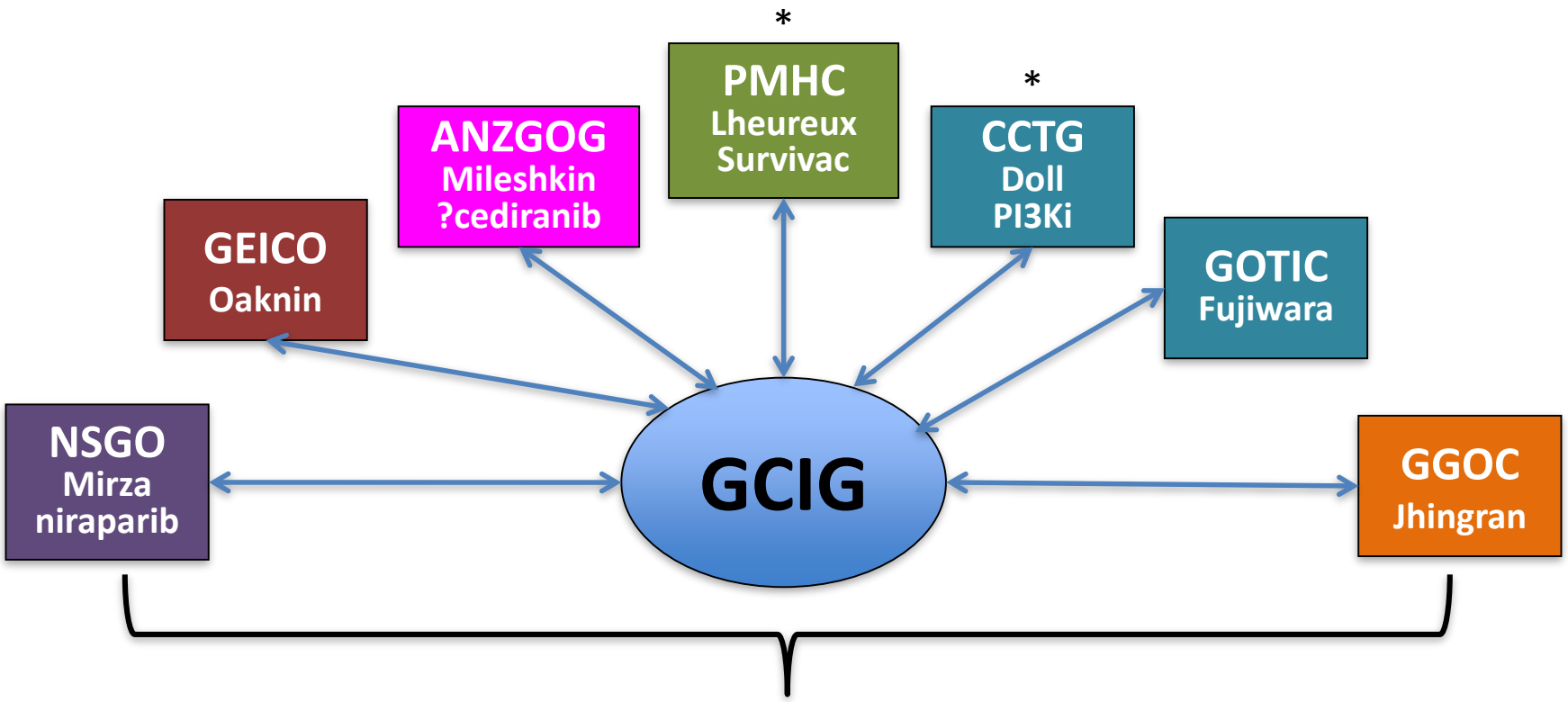
STATISTICAL ELEMENTS



Points to consider:

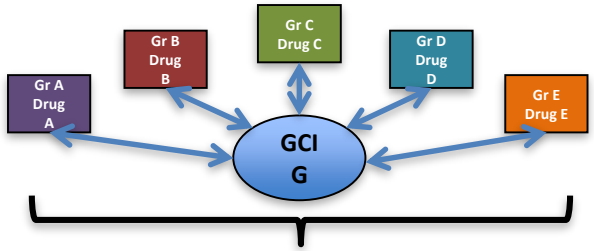
- Unbalanced randomization based on number of starting randomizations (eg 2:1 or 3:1)
- Stratification factors:
  - Pelvic v paraAo LN v none
  - Brachy or not
  - NED v any residual at XX months

PROGRESS TO DATE



* Study discussions initiated

STATISTICAL ELEMENTS



"…assumption… a reasonable proportion of stage III patients with adverse prognostic and features and including stage IVa patients that would give an overall 2 year PFS rate of around 40% in maybe around 20% of all patients." Thanks to Dr. Paul

<u>SAMPLE SIZE CONSIDERATIONS</u>:

2 yr PFS H_0= 40% → H_a= 55%, HR 0.65

Requires 99 PFS events observed for 90% power, α = 20% 1-sided

if 2.2 pt accrued/month→5 yr recruitment with another 20 mo for maturation

if went 2:1 randomization→ reduces recruitment to 3.3 yr, 28 mo for maturation