NSGO-CC1-MaRuC

A randomized double-blind placebo-controlled phase II trial of RUcaparib MAintenance therapy for patients with locally advanced Cervical cancer.

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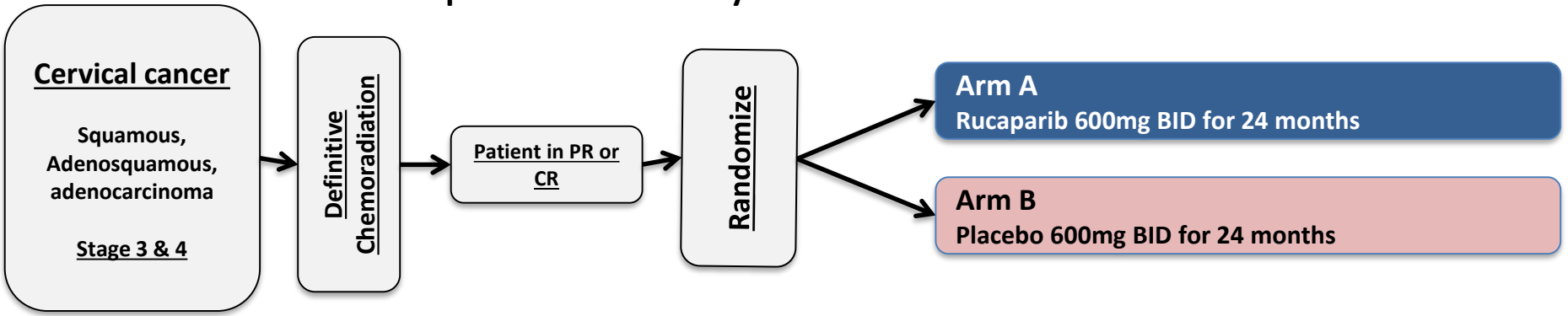

n = 162
Randomization: 2:1

Sponsor
NSGO

Stratification factors

- Histology (squamous vs adenosquamous, adenocarcinoma)
- FIGO stage (3 vs 4)
- Residual disease vs no residual disease

Enrolment of patients with squamous cell histology will be capped once 50% patients with this histo-type are enrolled

Rationale

- **DNA repair in cervical cancer is less established**
- **HPV infection and oncoviral proteins E6 & E7 causes inactivation of p53 & pRB tumour-suppressor genes leading to cell cycle dysfunction and impaired DNA repair**
- **Cells are therefore increasingly dependent on residual repair pathways**
- **A correlation between response to DNA repair pathways has been noted in the clinic:**
  - **Patients treated with chemoradiation have high expression of the nucleotide excision repair protein ERCC1 associated with decreased PFS & OS & activation of the BRCA pathway correlated with treatment failure**
  - **Impaired NHEJ repair was related to increased OS**
- **Early phase trials incorporating modulators of DNA repair such as PARP inhibitors are underway**

Duensing S et al. Cancer Res. 2002; 62:7075–7082
Balacescu O et al. BMC Cancer 2014; 14:246
NCT01281852

Design

- **This is a multicenter, phase 2, doubleblind, placebo-controlled trial of maintenance Rucaparib to obtain preliminary but not conclusive evidence of efficacy of rucaparib in locally advance cervical cancer:**

- **Randomization: 2:1**

- **Patients are stratified according to:**
  - **Histology (squamous vs adenosquamous, adenocarcinoma)**
  - **FIGO stage (3 vs 4)**
  - **Residual disease vs no residual disease**

- **Squamous cell carcinoma patients will be capped to 50% of patient population**

Study arms

- **Arm A:** **rucaparib 600mg BID for 24 months**
- **Arm B:** **placebo BID for 24 months**

Study population

- **Histologically confirmed squamous cell, adenocarcinoma or adenosquamous carcinoma of the cervix.**
- **Subject must have completed definitive chemoradiation for curative intend and is evaluated to be in partial or complete remission post chemoradiation**
- **Initial FIGO stage IIIA, IIIB, IVA (biopsy proven); or any stage with para-aortic metastases.**
- **Toxicities resulting from chemoradiation must resolve to ≤Grade 1 prior to randomization.**

Study Statistics

- The study is designed to detect a difference in PFS at 24 months corresponding to a hazard ratio of 0.66 (PFS at 24 months to be increased from 46% to 60%) with a power of 80%; one-sided alpha of 15%;

- The randomization is 2:1 (2 rucaparib; 1 placebo).

- The number of needed events is 83 corresponding to 144 patients.

- With an expected dropout rate of 10%, and matching the randomization ratio, we shall recruit a total of 162 patients (108 patients in the rucaparib arm, and 54 patients in the placebo arm) within 18 months.

- PFS data should be mature after a minimum follow-up of 24 months.

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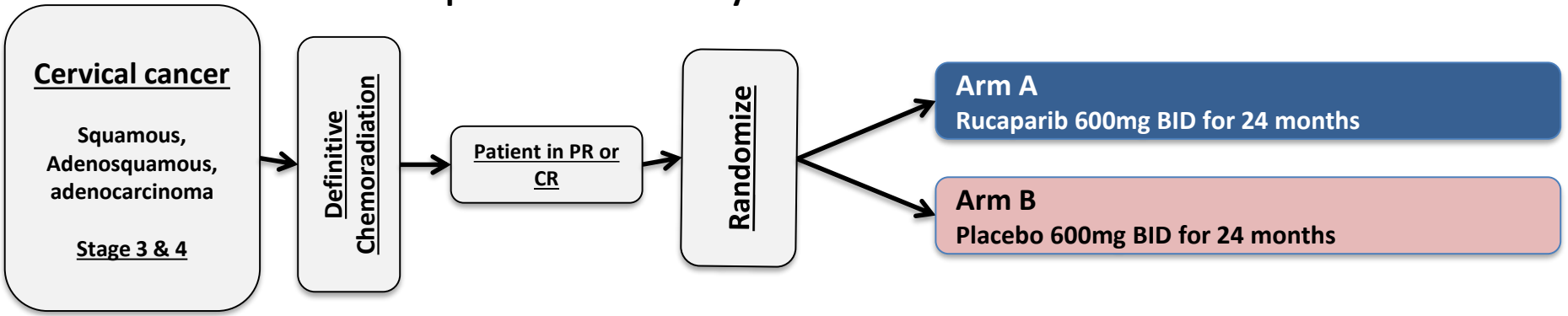

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