FOCUS Study: Physician's Choice Chemotherapy (PCC) Plus Bevacizumab and CA4P Versus PCC Plus Bevacizumab and Placebo in Platinum-Resistant Ovarian Cancer (prOC)

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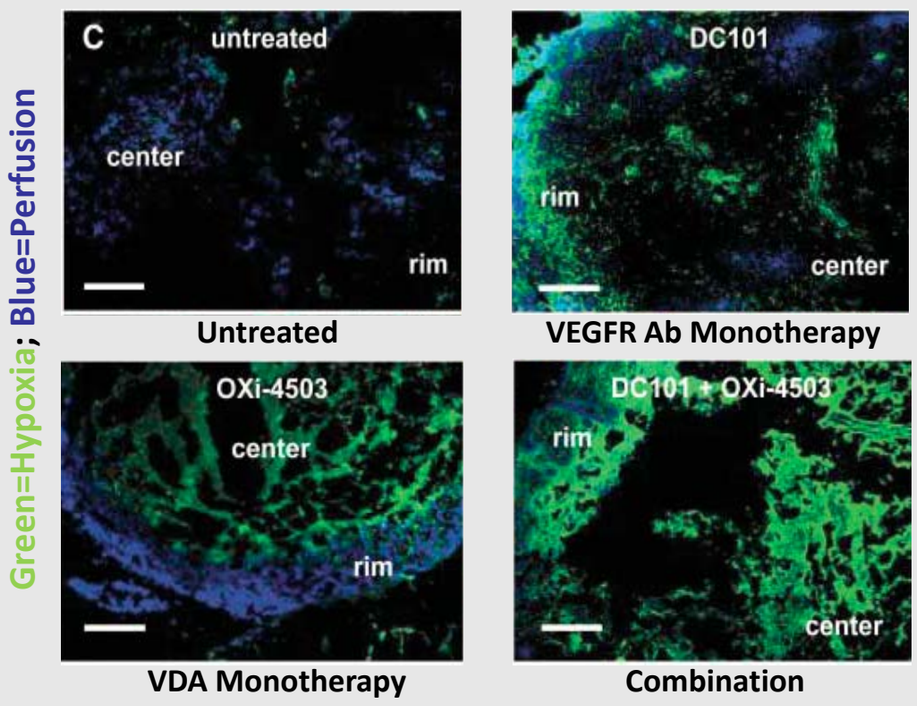
Background

- Vascular Targeted Therapies (VTTs) can be classified into 2 categories:
  - anti-angiogenics (AAs) – inhibit angiogenesis
  - vascular disrupting agents (VDAs) – directly interfere with tumor vasculature
- Combretastatin A4-phosphate (CA4P) is a tubulin-binding VDA that leads to endothelial cell shape changes that occlude tumor vasculature, resulting in ischemic necrosis of tumor cells[1, 2]
- Preclinical studies demonstrate that the activity of VTTs may be enhanced by combining a VDA with an AA (Figure 1)[3, 4]

Figure 1. VDA + AA Enhances Antivascular Activity

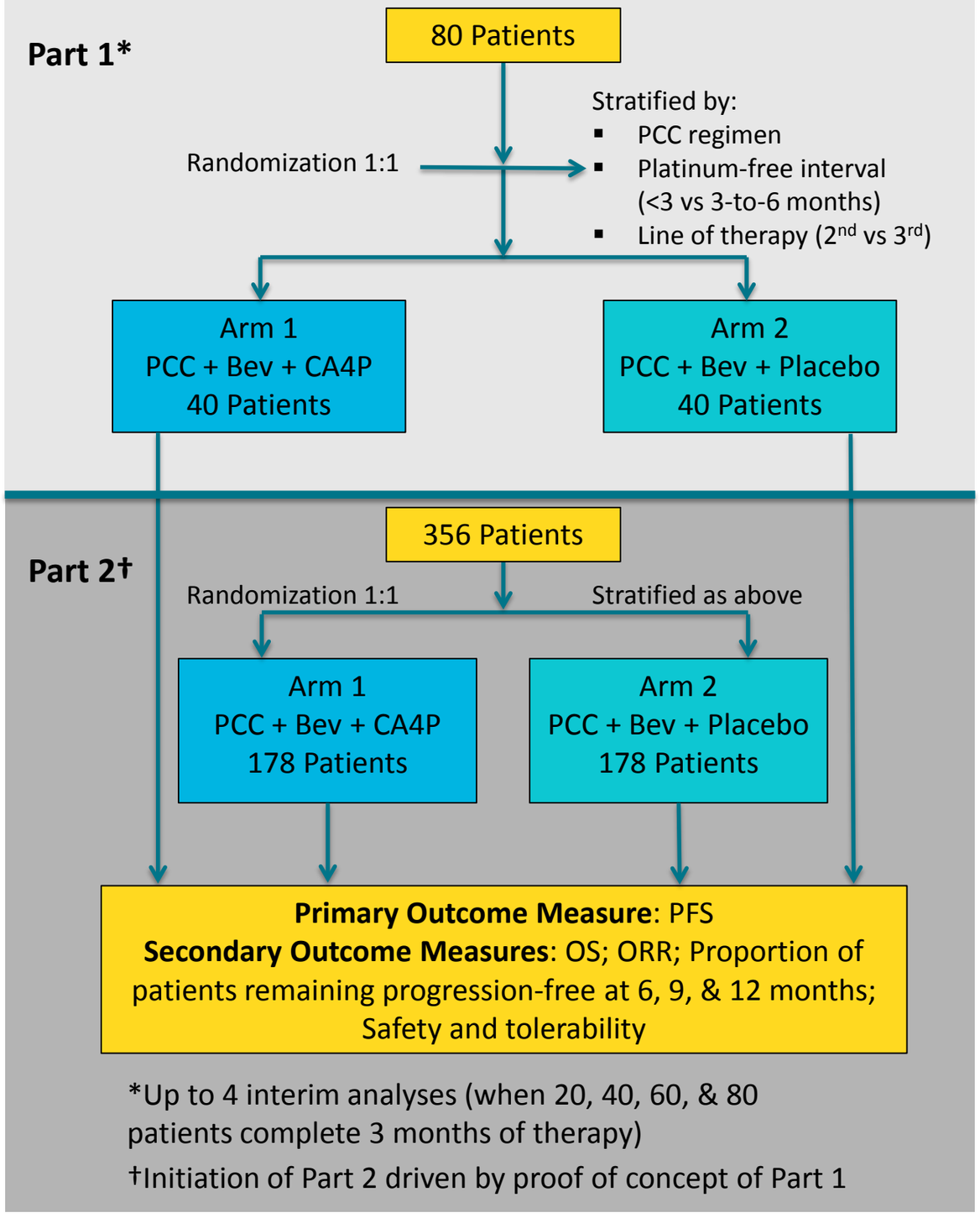


- Early-phase clinical results support combination VTT[5, 6]
- GOG-0186I: A Phase 2 study of Bev +/- CA4P in recurrent OC[6]
  - Median PFS was 7.3 months for CA4P + Bev vs. 4.8 months for Bev alone (HR, 0.69, 90%CI [0.47 to 1.00]; 1-sided *P*=.049)

FOCUS Study: Design and Methodology

- Multicenter, randomized, double-blind, Phase 2/3 study using a 2-stage design (Figure 2):
  - Part 1: Phase 2 exploratory study enrolling up to 80 patients
  - Part 2: Phase 3 pivotal study enrolling ~356 patients
- Treatment Regimens:
  - ***Arm 1***: PCC + Bev + CA4P
    - PCC: EITHER paclitaxel 80 mg/m^2 IV Days 1, 8, 15, 22 q4wks; OR paclitaxel 80 mg/m^2 Days 1, 8, 15 q4wks; OR pegylated liposomal doxorubicin [PLD] 40 mg/m^2 IV Day 1 q4wks
    - Bev: 10 mg/kg IV on Days 1 and 15 q4wks
    - CA4P: 60 mg/m^2 on Days 1 and 15 q4wks
  - ***Arm 2***: PCC (as above) + Bev (as above) + Placebo (q4wks)
- Patients continue treatment until progression, unacceptable toxicity, investigator decision, consent withdrawal, or study discontinuation
- **Key Inclusion Criteria:**
  - Women ≥18 years with ECOG PS 0-1
  - Platinum resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer
  - Received ≥1 prior platinum-based regimen
  - Measurable disease
  - LVEF ≥45% at baseline assessment if subject is receiving PLD
- **Key Exclusion Criteria:**
  - Prior treatment with CA4P therapy
  - Previously failed treatment with Bev + intended PCC
  - Previous treatment with >2 PCC treatments
  - Platinum-refractory disease
  - >Grade 2 peripheral neuropathy
  - Any history of thrombotic or hemorrhagic disorder or event
  - History of fistula, GI perforation, or intra-abdominal abscess
  - Uncontrolled hypertension or proteinuria

Figure 2: FOCUS Study Schema



*Up to 4 interim analyses (when 20, 40, 60, & 80 patients complete 3 months of therapy)

†Initiation of Part 2 driven by proof of concept of Part 1

Assessments

- ***Efficacy***: Radiologic evaluation (CT or MRI) performed at baseline and repeated every 8 weeks until disease progression; CA-125 assessed at baseline and every 4 weeks
- ***Safety***: Safety and tolerability measured by physical exams, vital signs, laboratory measures, ECOG PS, and incidence of AEs using the NCI CTCAE version 4.03

Statistical Analyses

- Primary Endpoint: PFS based on ITT population, using a stratified 2-sided log-rank test to test the hypothesis of equality of survival curves between groups (0.05 significance level)
- Secondary Endpoints/Safety: ORR analyzed using Cochran-Mantel-Haenszel test; Adverse event incidence rates for each treatment arm and for overall patients summarized using frequency and percentage

Study Status

- Study enrollment began in June 2016; it is anticipated that approximately 30 sites will be activated in the U.S. and Europe
- Part 1 of the FOCUS study is currently ongoing with results expected mid-2017

References

1.) Galbraith SM et al. *Anticancer Res.* 2001;21:93-102. 2.) Vincent L et al. *J Clin Invest.* 2005;115:2992-3006. 3.) Shaked Y et al. *Science.* 2006;313:1785-1787. 4.) Siemann DW, Shi W. *Anticancer Res.* 2008;28:2027-31. 5.) Nathan P et al. *Clin Cancer Res.* 2012;18:3428-39. 6.) Monk BJ et al. *J Clin Oncol.* 2016;34:2279-86.

FOCUS CLINICAL STUDY MATEON THERAPEUTICS