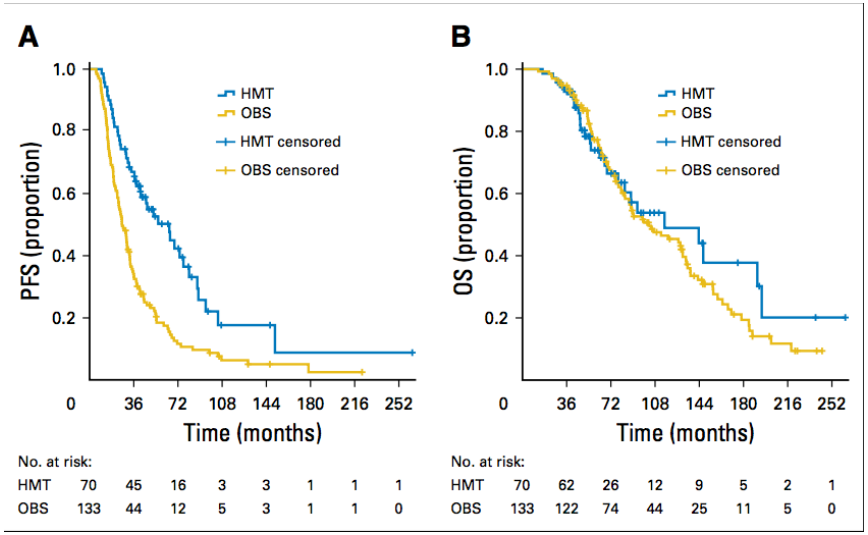
A randomized, 3-arm phase III trial of paclitaxel/carboplatin versus paclitaxel/carboplatin/maintenance letrozole versus letrozole monotherapy in patients with stage II-IV, primary low-grade serous carcinoma of the ovary or peritoneum

Pis: Amanda Nickles Fader & David Gershenson

Background
Both retrospective studies

MD Anderson Study

- **203 pts (133 OBS, 70 HMT)**



Gershenson et al.
J Clin Oncol 2017
HMT hormone therapy

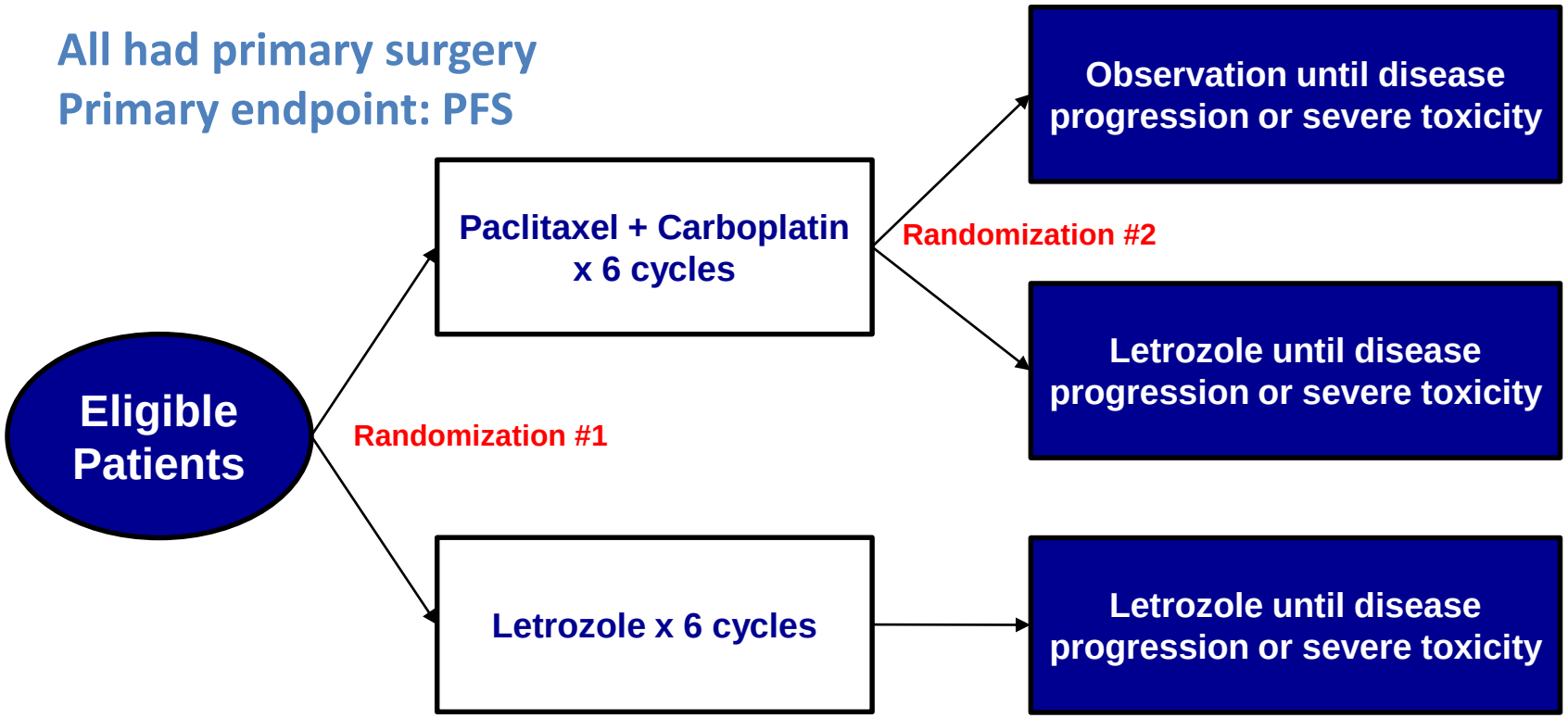
Johns Hopkins Study

- **27 pts with stage II-IV LGSC**
- **Primary CRS + HT**
- **Median duration HT = 18 mo**
- **After median FU = 38 mo (range 15-147), 5 (18.5%) pts relapsed**
- **Median PFS and OS not reached**
- **2-yr PFS = 82.8%**
- **2-yr OS = 100%**
- **Not yet presented**

Nickles Fader et al

Study Design/Schema

All had primary surgery
Primary endpoint: PFS



Randomization #1 will be done in a 5:2 ratio (250 to CT, and 100 to L)
Stratified by residual disease (≤ 1 cm vs > 1 cm)

Randomization #2 will be done in a 1:1 ratio
Stratified by no persistent vs persistent disease

Statistical Design

- 350 pts (250 to chemo; 100 to letrozole)
- Primary endpoint: PFS
- Secondary endpoints: Toxicity & response (MD)
- Exploratory endpoints, OS, QoL
- Lab correlates: NGS, ER, PR, Ki-67, ESR1 mutation
- With 100 pts per arm and assuming 24-mo PFS of 0.60 for the CT→O arm, have power of 80% to detect HR = 0.59 for either experimental arm vs control arm
- Assuming 24-mo PFS of 0.7 for CT→L arm, have 80% power to detect HR = 0.59 for L→L arm vs CT→L arm
- Futility analysis planned

Outstanding Issues

- Letrozole drug supply
- Letrozole placebo not feasible
- Is CT→O arm acceptable?
- Is letrozole monotherapy arm acceptable?
- Duration of Letrozole?
- Use of bevacizumab?
- Feasibility of parallel trials with single data center
- TR biomarkers