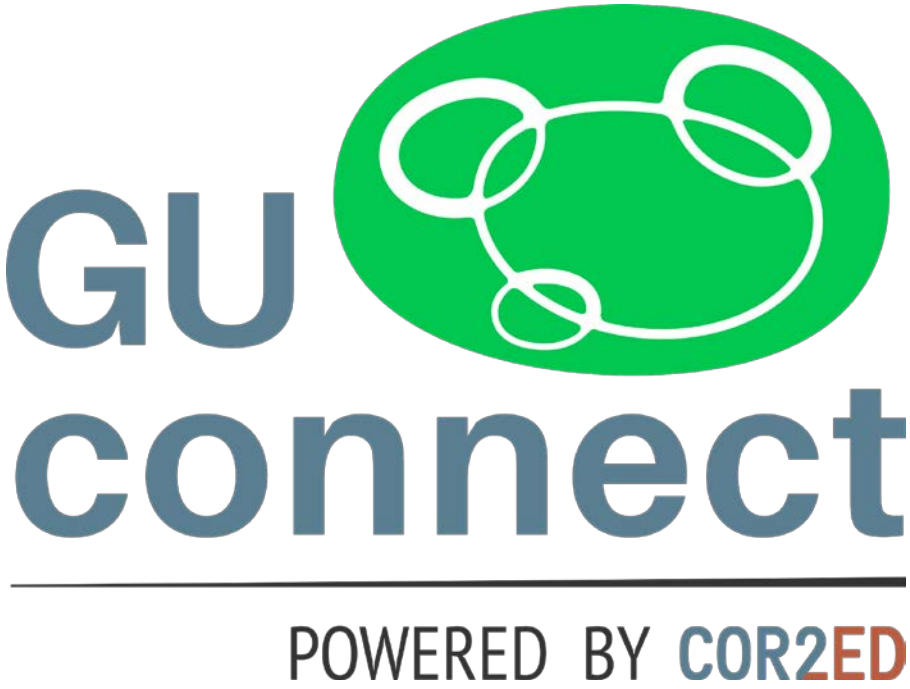
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UPDATE FROM ASCO GU
FEBRUARY 2018, SAN FRANCISCO, USA

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HIGH-RISK NON-METASTATIC (M0) CASTRATION-RESISTANT PROSTATE CANCER NEW THERAPEUTIC UPDATES

DISCLAIMER

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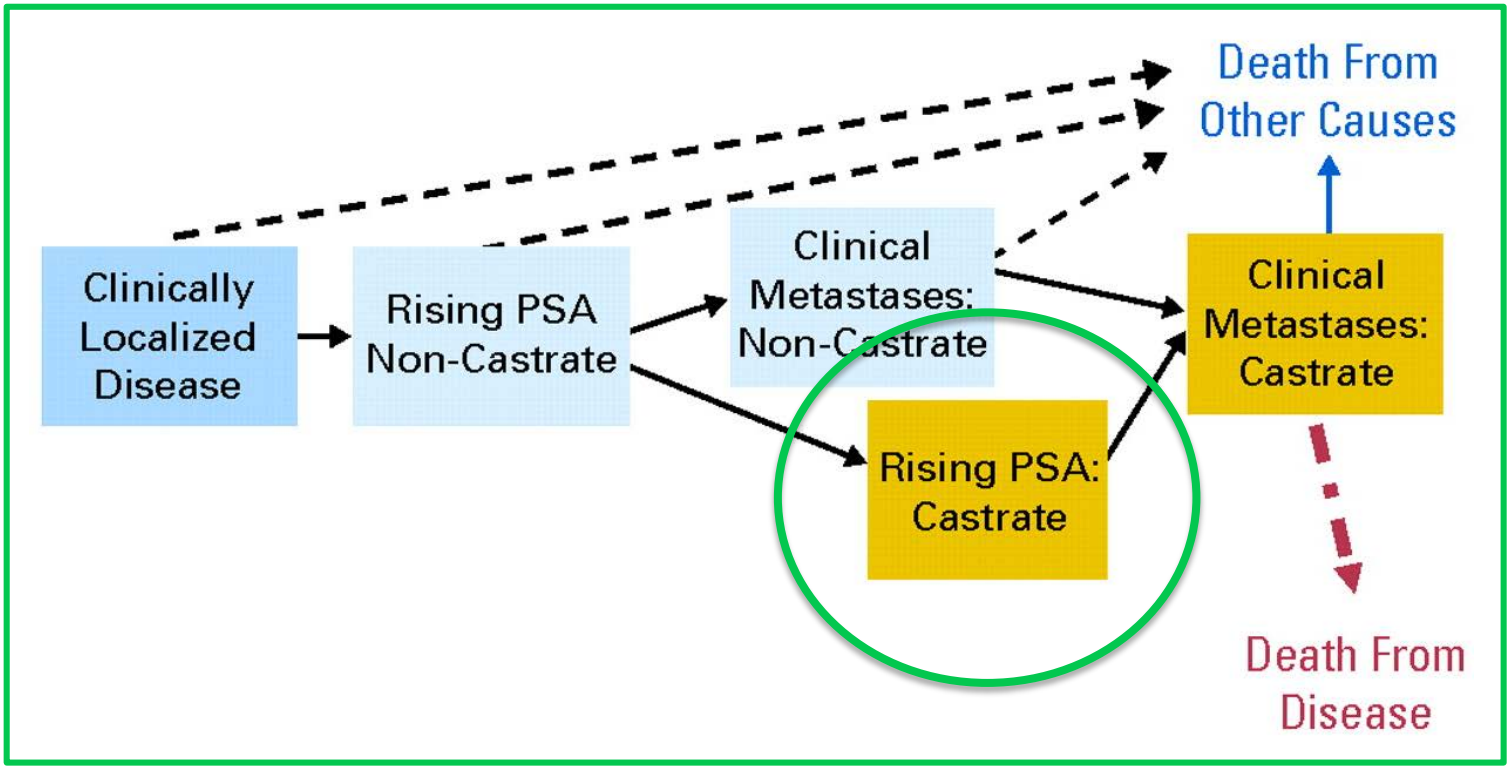
M0 CRPC AS PART OF THE CLINICAL STATES MODEL



Two defining criteria

1. Rising PSA in the setting of castrate testosterone levels (<50 ng/dL)
2. No radiographically identifiable metastasis

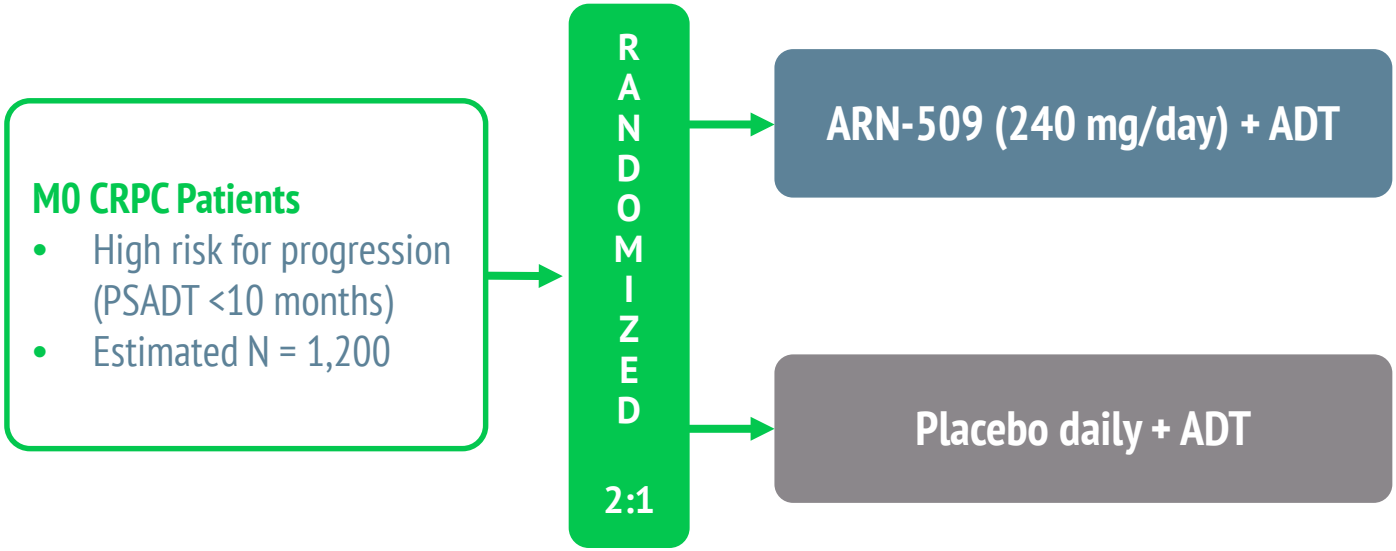
M0 CRPC: non-metastatic castration resistant prostate cancer; PSA: prostate specific antigen
Above diagram adapted from Scher HI et al. J Clin Oncol 2008; 26: 1148-59.

SPARTAN: A PHASE III DOUBLE-BLIND, RANDOMIZED STUDY OF APALUTAMIDE VERSUS PLACEBO IN PATIENTS WITH NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Small EJ et al. Abstract #161

PHASE III SPARTAN TRIAL DESIGN

- Multicenter, double-blind, placebo-controlled study



- **Primary endpoint:** MFS

ADT: androgen deprivation therapy; MFS: metastasis-free survival; M0 CRPC: non-metastatic castration resistant prostate cancer; PSADT: PSA doubling time
https://clinicaltrials.gov/ct2/show/NCT01946204.
Small EJ et al. GU ASCO 2018. Abstract #161

PHASE III SPARTAN DATA

- **Median MFS** 40.5 vs. 16.2 months (HR 0.28; p<0.0001)
- 55% risk reduction in time to symptomatic progression
- OS interim analysis data not mature with HR 0.70 with just 24% of required events but trend with p=0.07
- **PFS2** with 51% risk reduction of progression for combination endpoint assessed by investigator
- PROs show QOL with no decrement but not sure tools sensitive enough to detect decrement or improvement
- Adverse events of interest with apalutamide
  - 2x grade 3/4 falls
  - 3x grade 3/4 fractures
  - 3x grade 3/4 fatigue (0.9 vs. 0.3%)

HR: hazard ratio; MFS: metastasis-free survival; OS: overall survival; PFS2: progression free survival 2; PROs: patient-reported outcomes; QOL: quality of life
Small EJ et al. GU ASCO 2018. Abstract #161

PROSPER: A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ENZALUTAMIDE IN MEN WITH NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Hussain M et al. Abstract #3

PHASE III PROSPER TRIAL DESIGN

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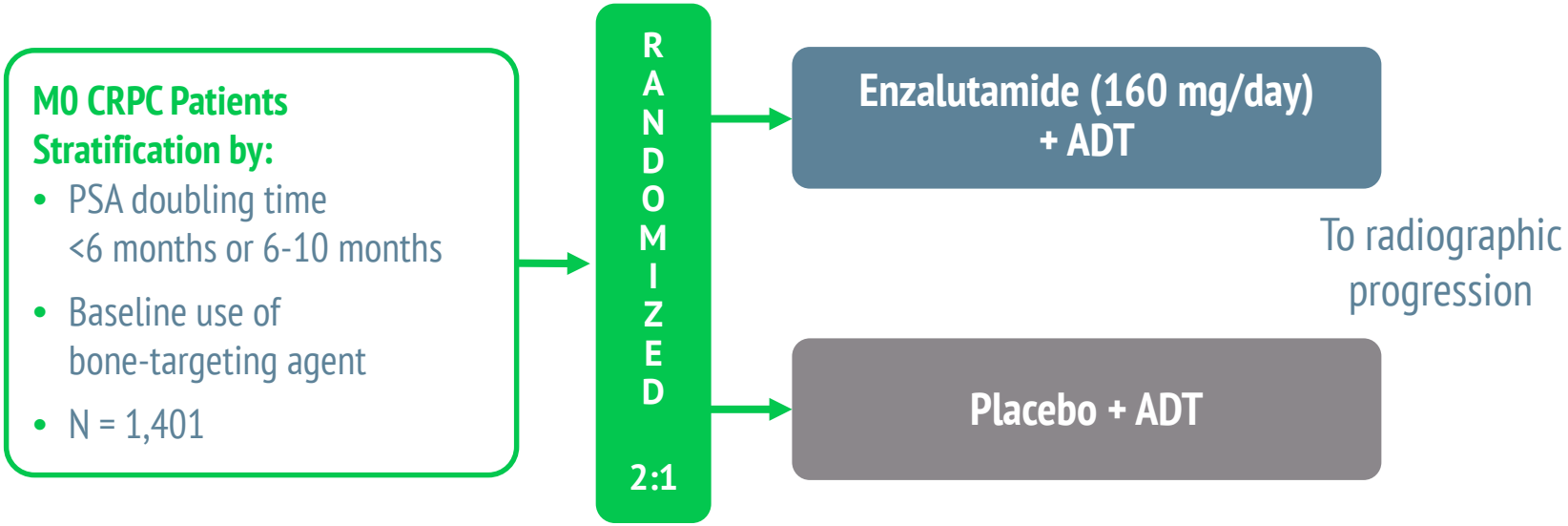
- Randomized, double-blind, placebo-controlled international study



- **Primary endpoint:** MFS = time to radiographic progression or death on study

ADT: androgen depravation therapy; M0 CRPC: non-metastatic castration resistant prostate cancer; MFS: metastasis free survival; PSA: prostate specific antigen
https://clinicaltrials.gov/ct2/show/NCT02003924.
Hussain M et al. GU ASCO 2018. Abstract #3

PHASE III PROSPER DATA

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- **Median MFS** 36.6 vs. 14.7 months (HR 0.29; p<0.0001)
- Time to use of new antineoplastic therapy median 39.6 vs. 17.7 months
- OS interim analysis data not mature with HR 0.80 with p=0.1519
- Adverse events of interest with enzalutamide
  - grade ⩾3 Hypertension 5% vs. 2%
  - 3x grade 3/4 fatigue (3 vs. 1%)

HR: hazard ration; MFS: metastasis-free survival; OS: overall survival
Hussain M et al. GU ASCO 2018. Abstract #3

SUMMARY POINTS

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- Both apalutamide and enzalutamide offer an impressive **approximate median 2 year improvement in MFS** and may represent a new standard of care
- Cannot determine if one agent is superior over the other
- Overall survival data is not mature but trends are in the right direction
- Adverse events well tolerated but probably more fatigue, hypertension, falls and fractures
- M0 CRPC is likely rare in many countries given presence of next generation imaging; however, this disease state may increase in the United States as these new agents become available

M0 CRPC: non-metastatic castration resistant prostate cancer; MFS: metastasis-free survival

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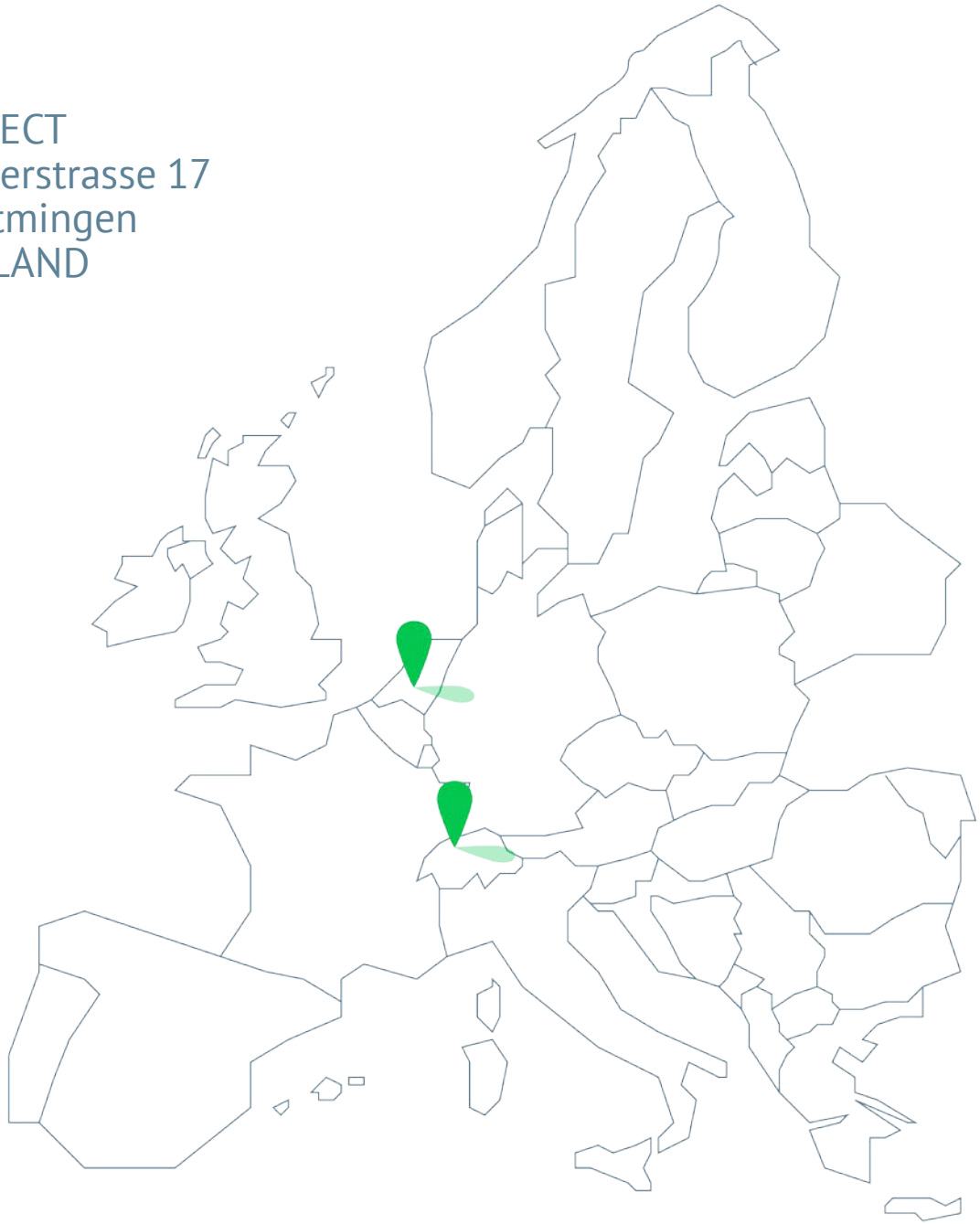

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