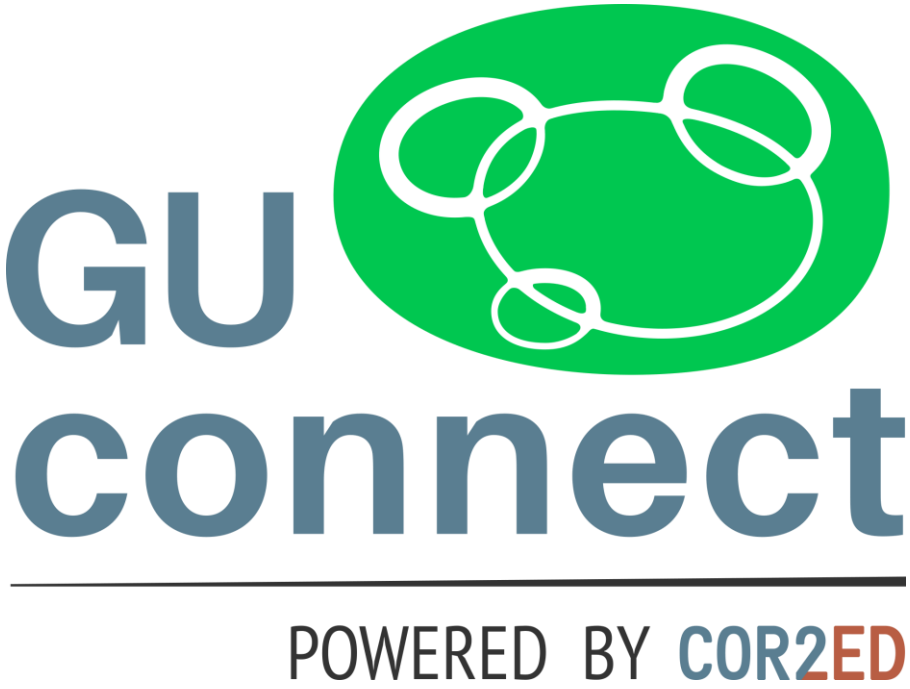
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MEETING SUMMARY

ASCO GU, FEBRUARY 16-18 2017, ORLANDO, USA

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CLINICAL, PATHOLOGIC AND MOLECULAR RISK PROFILING IN PROSTATE CANCER

OVERVIEW

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- Predicting response to treatment is a primary goal of practicing oncologists treating men with prostate cancer
  - Appropriately matches men with treatments that will benefit them
  - Prevents delay in time to effective therapy and exposure to treatments that will not confer benefit

- Several presentations suggest assessments that may enable prediction of treatment benefit in specific patient populations with prostate cancer

OVERVIEW

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- AR indifferent prostate cancer (PCa)
  - Aparacio
- Luminal and basal PCa subtypes
  - Feng
- Full-length androgen receptor (AR) in CTCs
  - Antonarakis

ADVANCES IN THE UNDERSTANDING AND TREATMENT OF AR-INDIFFERENT PROSTATE CANCER (PCa)

ANA APARACIO ET AL

AR INDIFFERENT PCa

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- Identified "AR indifferent PCa" as morphologically and biologically heterogeneous PCa that are not responsive to blocking AR signaling

- Clinical Features
  - Short lived response to AR-directed treatment
  - Respond to platinum-based chemotherapy
  - Histology may range from adenocarcinoma to small cell to poorly differentiated morphology
  - Visceral metastases, lytic bone metastases, or bulky nodes
  - Low PSA

MOLECULAR SIMILARITIES

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- Aggressive AR indifferent PCa molecular signature includes the ⩾ 2 alterations
  - Tp53, RB1, PTEN
  - Loss of these tumor suppressors reduces sensitivity to AR inhibition

- Molecular signature with ⩾ 2 alterations in Tp53, RB1, PTEN is associated with response to carboplatin
  - This signature is less sensitive to AR directed treatment

CONCLUSION

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Combining molecular signature (⩾ 3 Tp53, RB1, PTEN) with high risk clinical features (low PSA, visceral only metastases, lytic bone lesions, etc) may allow clinicians to recognize who will respond to platinum-based chemotherapy

LUMINAL AND BASAL SUBTYPES IN PCa

FELIX FENG ET AL

LUMINAL AND BASAL SUBTYPES IN PCa

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- Feng and colleagues applied the PAM50 assay to 3,782 PCa samples
  - PAM50 has been used in breast cancer to assess 50 classifier genes and 5 control genes and determine which subtype of cancer a patient had
- PAM50 identified luminal A and B, and basal subtypes of PCa
  - Heat maps of gene expression suggest a similar pattern to breast cancer

CLINICAL OUTCOMES

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- Luminal B histology had poorest outcomes, followed by Basal, then Luminal A with the best outcomes.
  - 10 yr BCR (29%, 39%, 41%)
  - Metastasis free survival (53%, 73%, 73%)
  - PCa specific survival (78%, 86%, 89%)
  - OS (69%, 80%, 82%)

- Subtypes predict response to ADT
  - Luminal B had significant benefit from ADT
    - 10 year metastasis = 33% with ADT vs 55% without ADT
  - Other subtypes did not significantly benefit from ADT

CONCLUSION

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- PAM50 identified histologic subtypes in prostate cancer
- Luminal B patients had poorer 10 yr BCR, PCa survival, MFS, and OS, followed by Basal and Luminal A subtypes
- Luminal B significantly benefited from ADT, while others did not
- PAM50 is not a clinically certified test for prediction of response to treatment in PCa.

FULL LENGTH ANDROGEN RECEPTOR (AR-FL) IN CTCs

EMMANUEL S. ANTONARAKIS ET AL

FULL LENGTH AR (AR-FL) in CTCs

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- Prospectively assessed prognostic value of the presence of AR-FL in CTCs in 202 men starting abiraterone or enzalutamide
  - AR-FL negative in 48%
  - AR-FL level was less than median in 26%
  - AF-FL level was more than median in 26%
  - Presence of AR-FL correlated with presence of AR-V7

AR-FL CORRELATED WITH OUTCOMES

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- AR-FL correlated with PSA decline >50%
  - 55.4 copies of AR-FL in patients with PSA decline >50%
  - 6.7 copies in patients without PSA decline >50%

- PFS and OS correlated with AR-FL
  - AR-FL negative PFS 11.1 mo, OS 33.3 mo
  - AR-FL < median PFS 8.7 mo, OS 18 mo
  - AR-FL > median PFS 3.2 mo, OS 11.3 mo

- In MVA, AR-FL prognostic for PSA-PFS, and trend to being prognostic for PFS and OS

CONCLUSION

- AR-FL in CTCs may be prognostic for patient outcomes during treatment with enzalutamide or abiraterone

- AF-FL assessments are not yet used in clinical practice for treatment decision making

CONCLUSION

CONCLUSION

- Predicting response to treatment is a primary goal of practicing oncologists treating men with prostate cancer

- Several presentations at GU ASCO 2017 suggest potential options for the development of clinically useful predictive tests

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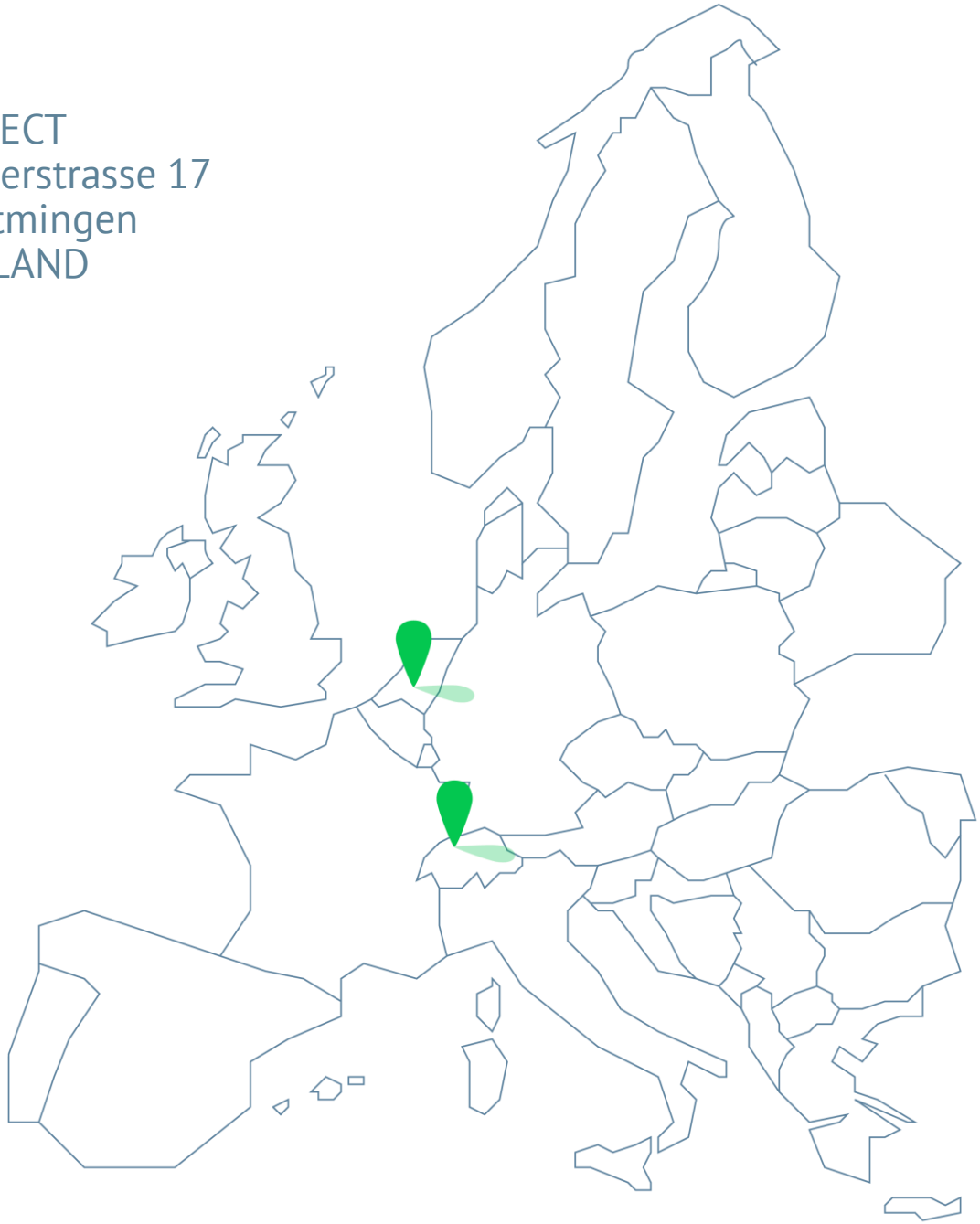

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