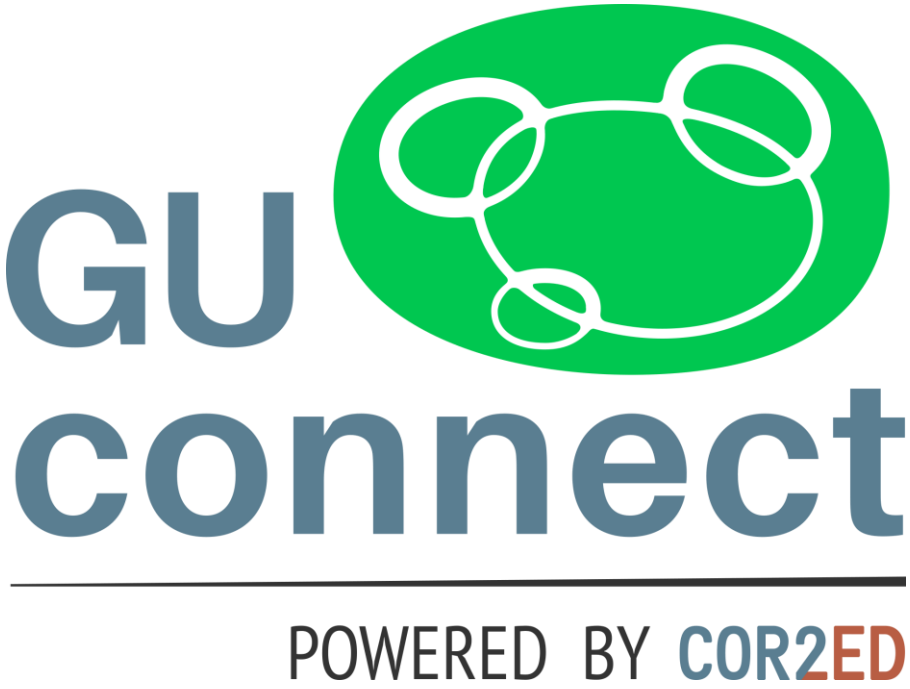
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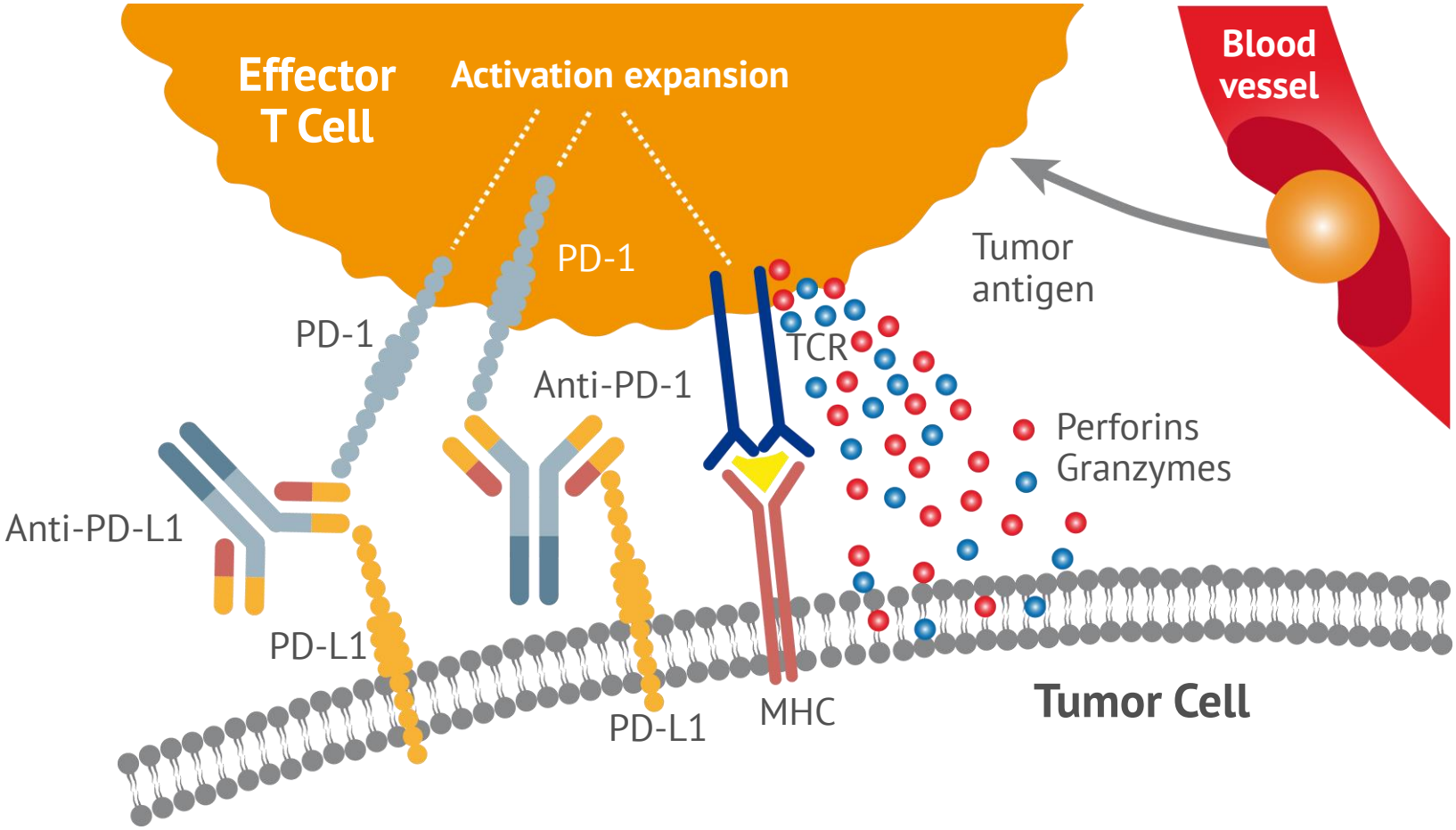
MEETING SUMMARY

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

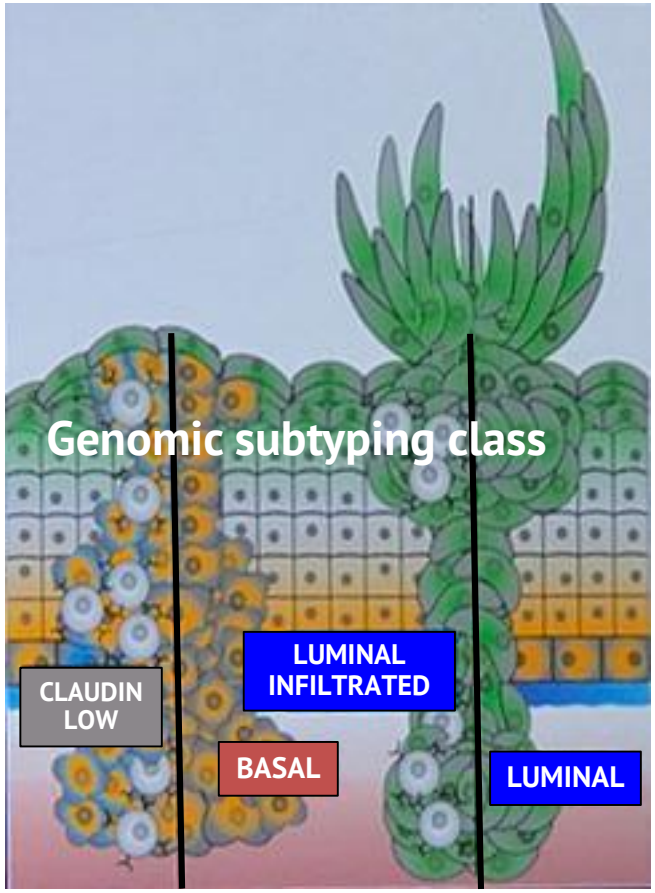
STEVEN JONIAU, MD, PHD
ASSOCIATE PROFESSOR IN THE DIVISION OF UROLOGY,
DEPARTMENT OF DEVELOPMENT AND REGENERATION,
UNIVERSITY HOSPITALS LEUVEN, BELGIUM

NOVELTIES ON BLADDER CANCER FROM ASCO-GU

PD-L1


Effector
T Cell
Activation expansion
Blood
vessel
Tumor
antigen
PD-1
PD-1
Anti-PD-1
TCR
Perforins
Granzymes
Anti-PD-L1
PD-L1
PD-L1
MHC
Tumor Cell

CLASSES IN SINGLE SAMPLE CLASSIFIER (GSC)



Umbrella cells

Intermediate cells

Basal cells
Basal memebrane
Submuscosal layer

Muscle tissue

CLINICAL SIGNIFICANCE: OVERALL SURVIVAL

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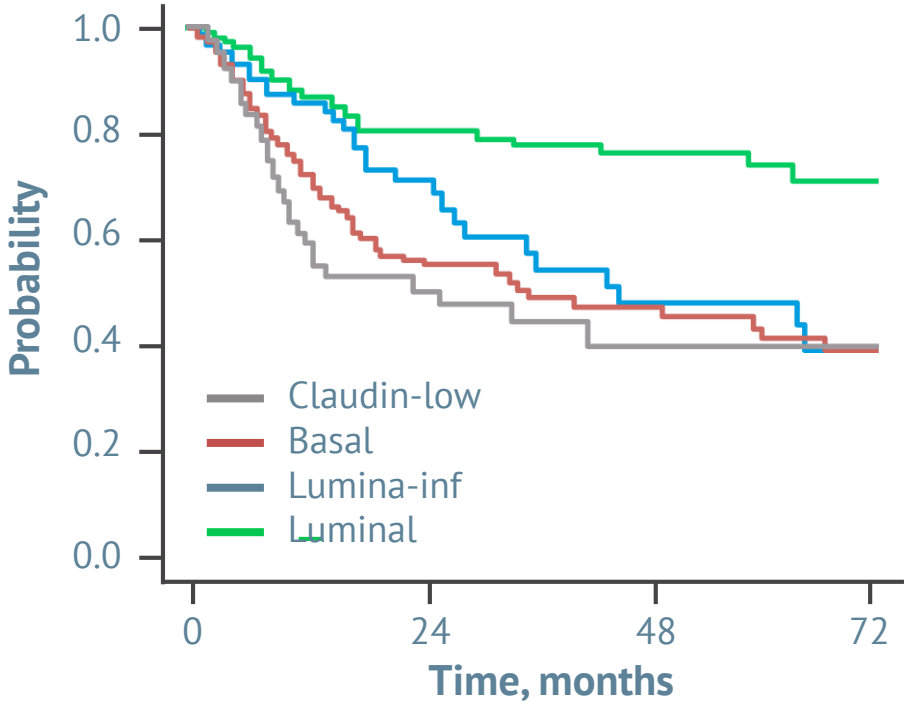
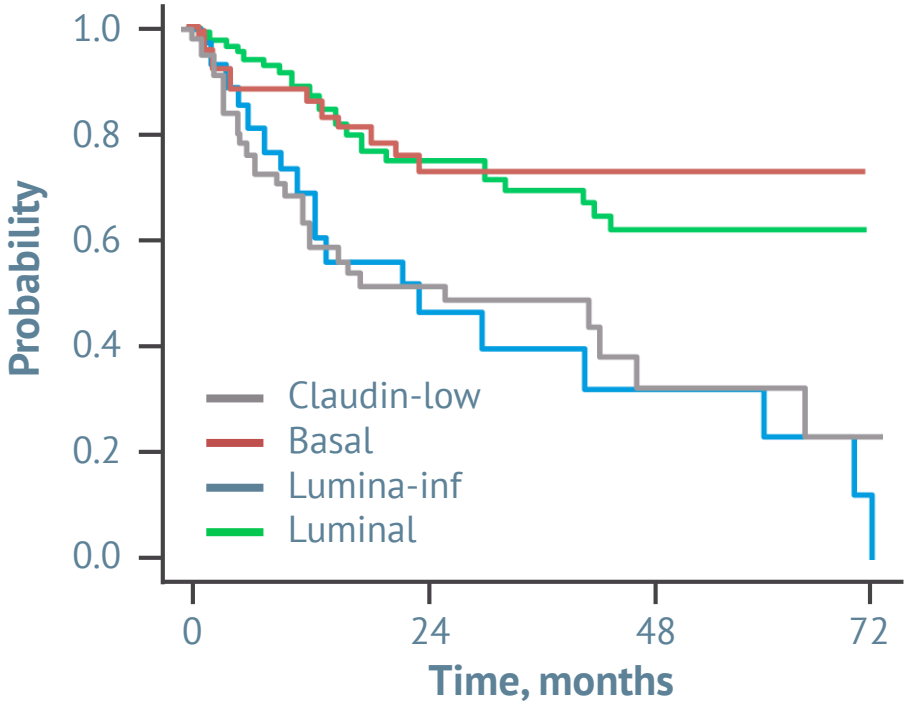
without chemotherapy



with neoadjuvant chemotherapy



Presented at ASCO GU 2017 by: Roland Seiler

CONCLUSIONS

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- Confirms finding that basal tumors appear to benefit significantly from platinum-based chemotherapy
    - Benefit to basal subtype appears to be regardless of down-staging
    - Does not automatically follow that other subtypes do not benefit from neoadjuvant chemotherapy
- Findings require prospective validation before implementation in clinical practice

BACKGROUND: NMIBC AFTER BCG

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- Optimal management for patients with BCG- unresponsive NMIBC remains to be established
  - Valrubicin (FDA approved for CIS) – 10% 1 yr DFS
  - Intravesical gemcitabine, gemcitabine/mitomycin, and various taxane preparations investigated
  - Overall, studies limited by relatively small number of patients included, modest efficacy

- AUA NMIBC guidelines include clinical trial enrollment as option

Lerner SP et al. *Bl Cancer* 2015; Dinney CPN et al. *Urol Oncol* 2013; Chang SS et al. *J Urol* 2016
Presented at ASCO GU 2017 by: S. A. Boorjian

DEVELOPMENT AND PRECLINICAL ACTIVITY OF rAd-IFNα/Syn3

- rAd-IFNα = recombinant adenovirus
- Syn3 = excipient (enhances adenoviral transduction of NMIBC cells)
- Ad-IFNα/Syn3 induced the regression of human bladder cancer growing in athymic nude mice
- Sustained, high urinary IFNα levels noted
- No major toxicity in preclinical studies

Yamashita M et al. *Cancer Gene Ther* 2002; Tao Z et al. *Cancer Gene Ther* 2006; Connor RJ et al. *Urology* 2005
Presented at ASCO GU 2017 by: S. A. Boorjian

PHASE II TRIAL DESIGN

- Open-label, parallel-arm US multicenter trial
  - 13 centers
  - Trial conducted from 2012-2015

- Eligible patients = HG NMIBC after BCG

  - BCG refractory – failure to achieve disease-free state 6 months after induction + maintenance or re-induction at 3 months
  - BCG relapse – recurrence within 1 year after CR

PHASE II TRIAL DESIGN

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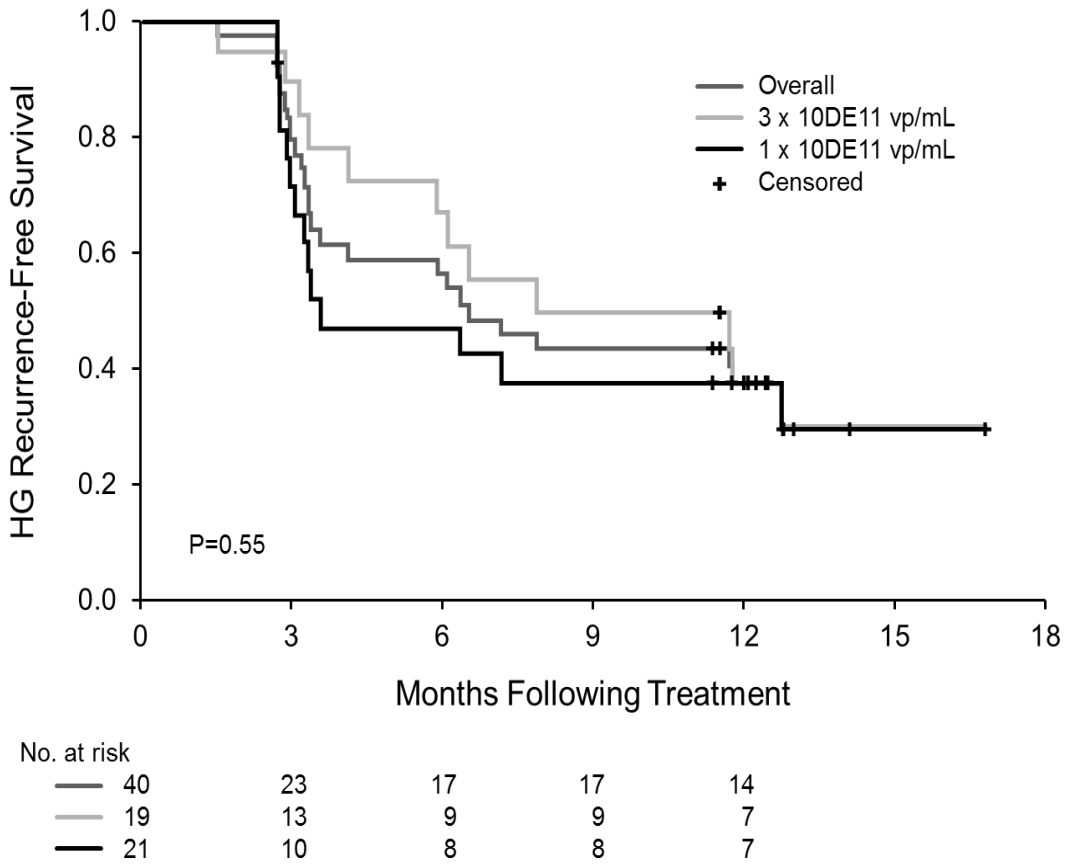
- Patients randomized 1:1 to receive intravesical rAd-IFNα/Syn3 at dose of 1 vs 3 x 10^{11} vp/mL
- Patients maintaining CR could be re-treated every 3 months, up to month 12
- **Primary endpoint = 12 month high-grade recurrence-free survival**
  - Defined by biopsy
  - Goal = 25% 12 month HG RFS

HIGH-GRADE RECURRENCE-FREE SURVIVAL



INTRAVESICAL rAD-IFNα/Syn3 PHASE II TRIAL: CONCLUSIONS

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- 35% 12 month high-grade recurrence-free survival
  - In heavily pre-treated population
- 50% 12 month high-grade recurrence-free survival in patients with papillary-only (Ta/T1) disease
- Tolerable treatment schedule
- Acceptable toxicity

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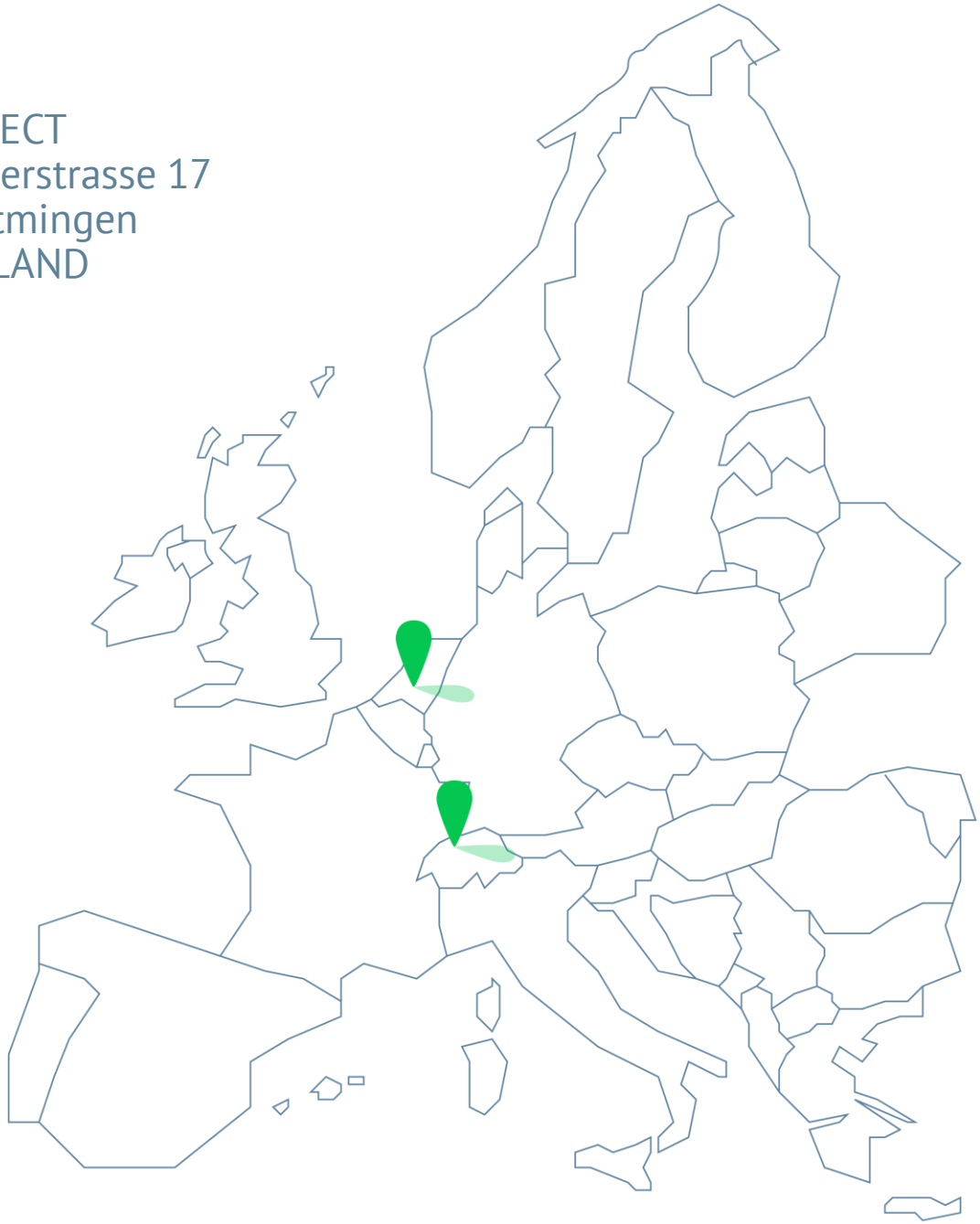

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