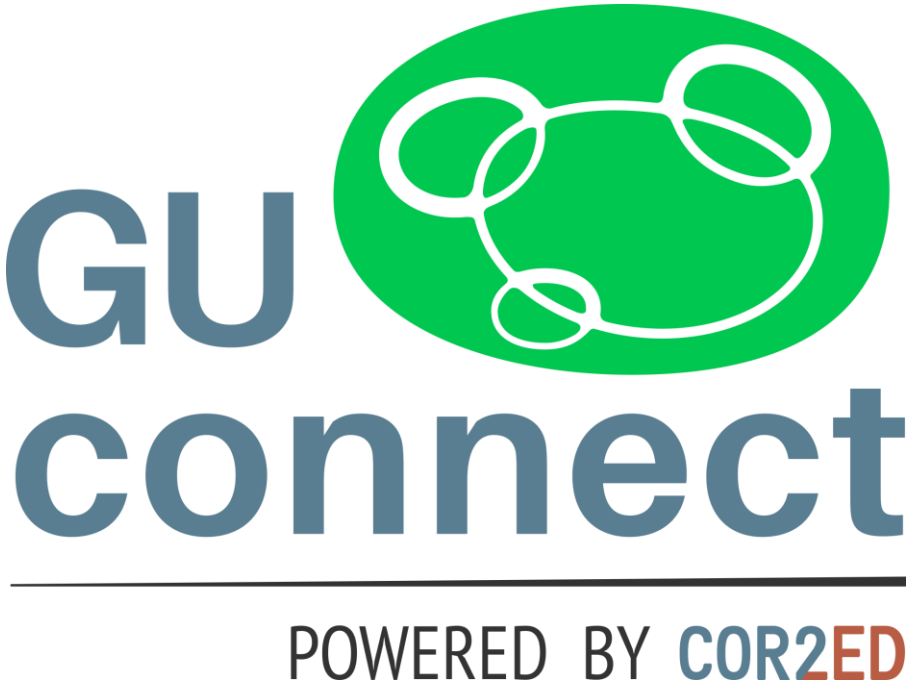
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MEETING SUMMARY

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

NEERAJ AGARWAL, MD
ASSOCIATE PROFESSOR,
HUNTSMAN CANCER INSTITUTE, UNIVERSITY OF UTAH

ADVANCEMENTS AND NEW TREATMENT PARADIGMS IN METASTATIC RCC

A PHASE II STUDY OF ATEZOLIZUMAB WITH OR WITHOUT BEVACIZUMAB VS SUNITINIB IN UNTREATED METASTATIC RENAL CELL CARCINOMA PATIENTS

DAVID McDERMOTT ET AL.

Presented at the 2017 Genitourinary Cancer Symposium
Orlando, Florida, February 2017

ATEZOLIZUMAB + BEVACIZUMAB

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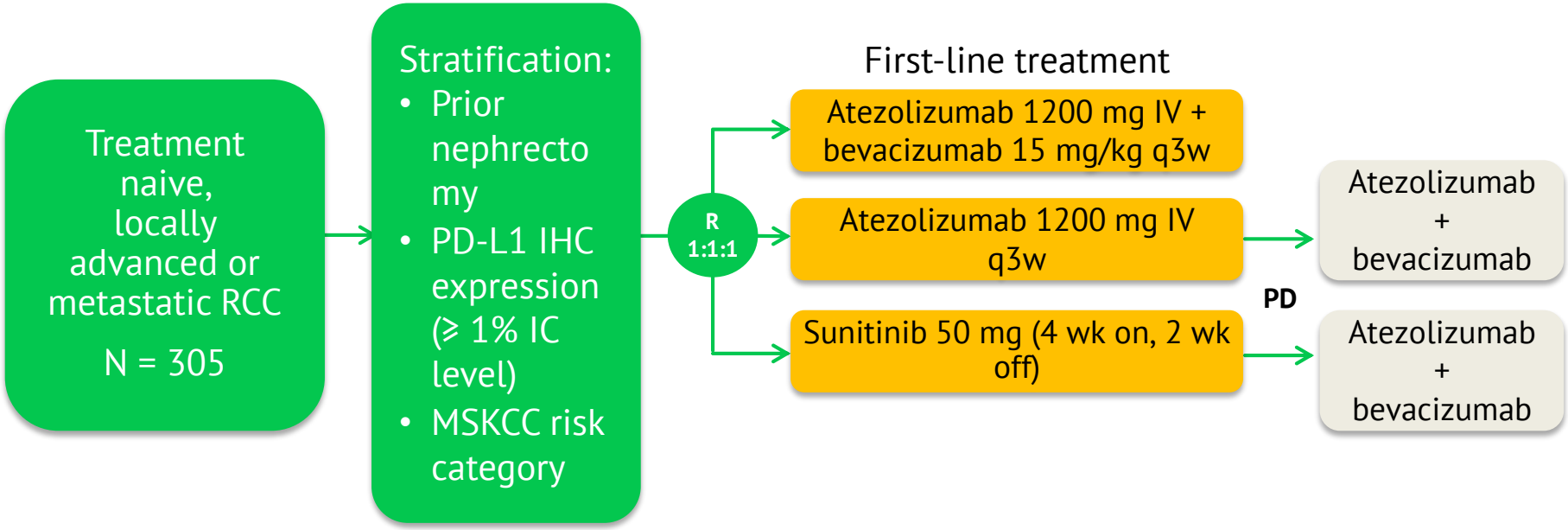
- A Phase Ib study in first-line mRCC showed anti-tumor activity and a tolerable safety profile for atezolizumab + bevacizumab[1,2]

- Sequential tumor biopsies provided preliminary evidence of improved anti-tumor immune responses following treatment with bevacizumab and atezolizumab + bevacizumab[2]

Presented at the 2017 Genitourinary Cancer Symposium.

1. Sznol, ASCO GU, 2015. 2. Wallin, Nat Commun, 2016.

IMMOTION150 (PHASE II) TRIAL DESIGN



- The coprimary endpoints: PFS (RECIST v1.1 by IRF) in ITT and PD-L1+ patients
- Designed to be hypothesis generating and inform the trial design of the Phase III study IMmotion151

Presented at the 2017 Genitourinary Cancer Symposium.
IC: tumor-infiltrating immune cells; IRF, independent review facility.

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BASELINE DEMOGRAPHICS (ITT)

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	Sunitinib n = 101	Atezolizumab + bevacizumab n = 101	Atezolizumab n = 103
Age, median (range), y	61 (25-85)	62 (32-88)	61 (27-81)
Male, n (%)	79 (78%)	74 (73%)	77 (75%)
KPS ≥ 80, n (%)	94 (93%)	99 (99%)	101 (99%)
Predominant clear cell histology, n (%)	96 (96%)	97 (96%)	95 (92%)
Sarcomatoid component, n (%)	14 (14%)	15 (15%)	16 (15%)
Prior nephrectomy, n (%)	88 (87%)	88 (87%)	89 (86%)
MSKCC risk category, n (%)			
Favorable (0)	21 (21%)	30 (30%)	26 (25%)
Intermediate (1 or 2)	70 (69%)	62 (61%)	69 (67%)
Poor (≥ 3)	10 (10%)	9 (9%)	8 (8%)
≥ 1% of IC expressing PD-L1 (PD-L1+), n (%)	60 (59%)	50 (50%)	54 (52%)

Presented at the 2017 Genitourinary Cancer Symposium.
Clinical cut-off, Oct 17, 2016. Median duration of follow-up, 20.7 mo.

Presented by: Dr. Thomas Powles

PROGRESSION FREE SURVIVAL OUTCOMES

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All Patients	PFS (Months)	Stratified HR (as % CI)	$_{a}$ Value
Atezo + Bev (n=101) vs. Sunitinib (n=101)	11.7 vs 8.4	1.00 (0.69 - 1.45)	0.982
Atezo (n=103) vs. Sunitinib (n=101)	6.1 vs 8.4	1.19 (0.82 – 1.7)	0.358
Patients with ⩾ 1% IC expressing PD – L1			
Atezo + Bev (n=50) vs. Sunitinib (n=60)	14.7 vs 7.8	0.64 (0.38-1.08)	0.095
Atezo (n=54) vs. Sunitinib (n=60)	5.5 vs 7.8	1.03 (0.63 – 1.67)	0.917

- Similar baseline demographics, MSKCC risk category, with >90% clear cell predominant mRCC

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[a] *P*values are for descriptive purposes only and not adjusted for multiple comparisons.

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CONCLUSIONS

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- Atezolizumab + bevacizumab resulted in encouraging efficacy vs sunitinib in the PD-L1+ subgroup of first-line mRCC patients
- The efficacy of atezolizumab + bevacizumab vs sunitinib is being evaluated in the ongoing Phase III trial (IMmotion151; NCT02420821)
- Safety in the atezolizumab arm and the atezolizumab + bevacizumab arm was consistent with previous data of each drug alone

EVOLUTION OF CIRCULATING TUMOR DNA (CTDNA) PROFILE FROM FIRST-LINE (1L) TO SECOND-LINE (2L) THERAPY IN METASTATIC RENAL CELL CARCINOMA (MRCC)

SUMANTA K. PAL, MD ET AL.

Presented at the 2017 Genitourinary Cancer Symposium
Orlando, Florida, February 2017

INTRODUCTION

- Multiple targeted therapies approved for mRCC[1]
- Efforts such as TCGA have revealed insights into tumor biology[2]
  - Data may reflect earlier disease states
  - No predictive biomarkers clinically implemented

- Circulating biomarkers represent a practical means of serially assessing tumor biology[3]
  - Advanced cancers shed DNA in blood
  - Circulating tumor DNA (ctDNA) can account for tumor heterogeneity

- Objective was to determine the mutational landscape of advanced RCC using ctDN, and to assess changes across patients receiving 1st-line and subsequent treatment

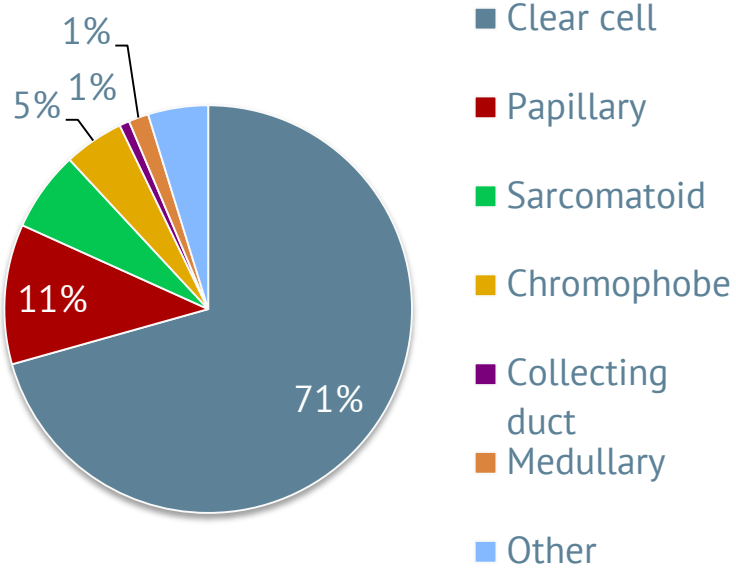
Presented at the 2017 Genitourinary Cancer Symposium.

1. Choueiri et al. NEJM 2017; 2. TCGA Investigators Nature 2013; 3. Zill O et al ASCO 2016

Presented by: Sumanta K. Pal, MD

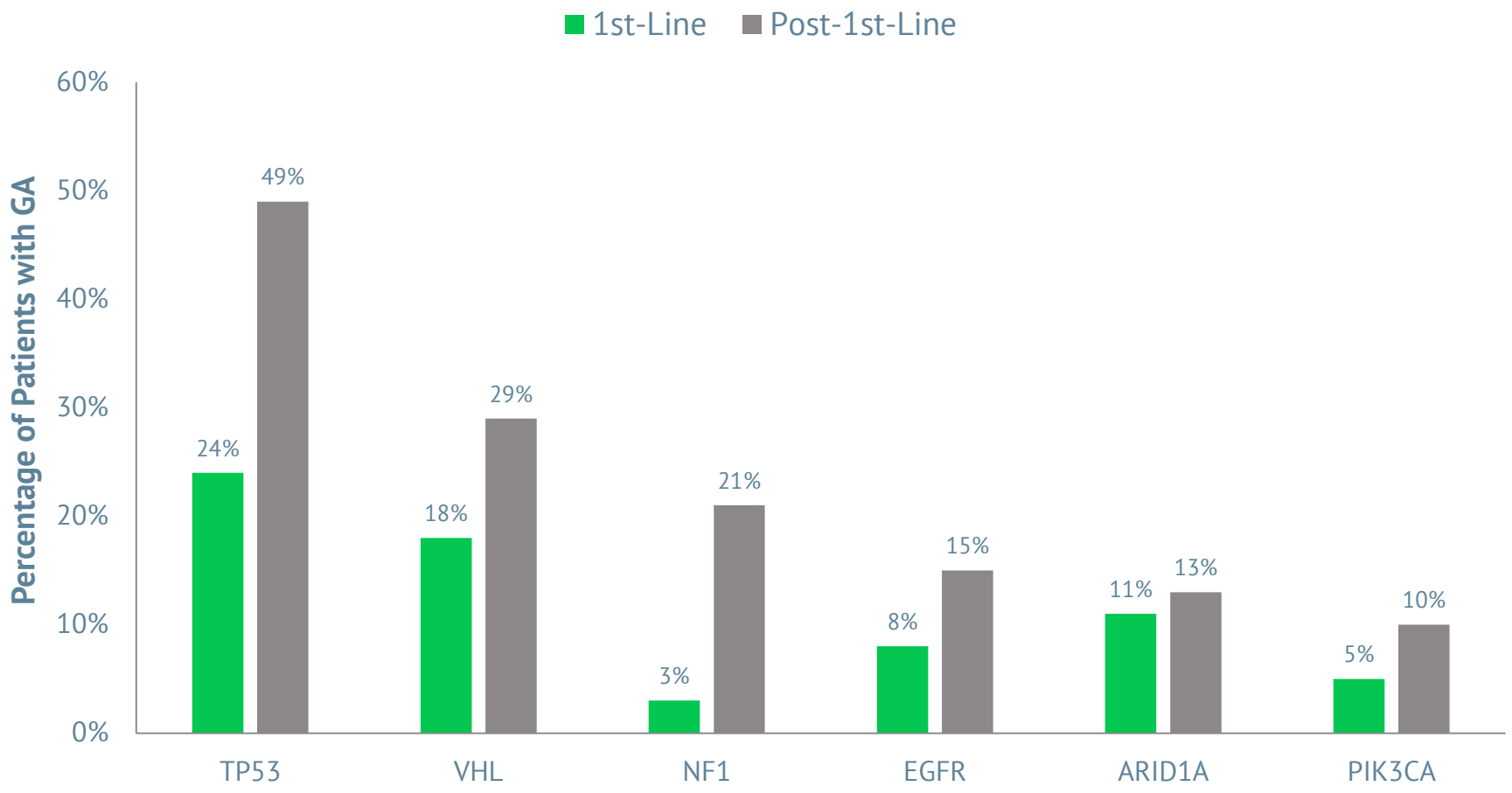
RESULTS

- ctDNA collected from 224 patients
- Average age 61 (range, 23-87)
- M:F 149:75
- Histologic subtype specified in 128 cases
  - 71% clear cell
  - 11% papillary
- ctDNA detected in 79% of patients with an average of 3.3 genomic alterations (GAs) detected per patient.
- Of 633 GAs identified, preponderance of single nucleotide variants (SNVs) and small insertions/deletions (indels) (89% of all mutations)



RESULTS

Selected GAs by Line of Therapy



Presented at the 2017 Genitourinary Cancer Symposium.

Presented by: Sumanta K. Pal, MD

CONCLUSIONS

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- ctDNA detected in the majority of patients (79%) with mRCC
- Most frequent GAs in the overall cohort included *TP53,VHL, EGFR, NF1* and *ARID1A*
- Compared to patients receiving 1st-line therapy, patients receiving post-1st-line agents had increased GAs in *TP53, NF1, EGFR*, and *PIK3CA*
- These alterations underscore potential mechanisms of resistance and may guide treatment selection upon disease progression after first line therapy

A SINGLE-ARM BIOMARKER-BASED PHASE II TRIAL OF SAVOLITINIB IN PATIENTS WITH ADVANCED PAPILLARY RENAL CELL CANCER

TONI K. CHOUEIRI ET AL.

Presented at the 2017 Genitourinary Cancer Symposium
Orlando, Florida, February 2017

BACKGROUND AND INTRODUCTION

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- Of the non-clear cell renal carcinomas, papillary RCC (PRCC) is the most common with no drug approved for specifically for PRCC
- MET and its ligand, hepatocyte growth factor, are known to play an important role in the molecular events underlying oncogenesis in PRCC[1,2]
- Savolitinib (AZD6094, HMPL-504, volitinib) is a potent, selective MET inhibitor which has shown activity in patients with MET-driven PRCC in a phase I study[3]
- A phase II study of savolitinib for patients with PRCC, in whom anti-tumor activity was correlated with MET pathway alterations is reported (Clinicaltrials.gov identifier: NCT02127710)

Presented at the 2017 Genitourinary Cancer Symposium.
Presented by: Toni Choueiri, MD

1. Albiges L, et al. *Clin Cancer Res* 2014;20:3411–21.
2. Linehan WM, et al. *N Engl J Med* 2016;374:135–45.
3. Gan HK, et al. *J Clin Oncol* 2015;33:abstr 487.

PATIENTS AND METHODS

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- **Single-arm, multicenter, global, phase II study** designed to evaluate the safety and efficacy of savolitinib (600 mg orally daily) in patients with PRCC, irrespective of prior treatment
- **Primary objective**: to assess the objective response rate (ORR) to savolitinib in all patients with PRCC and by MET status
- **Secondary objectives**: change in target lesion tumor size from baseline, progression-free survival (PFS) and duration of response (DoR)
- **Key inclusion criteria**: histologically confirmed locally advanced or metastatic PRCC, predicted life expectancy ⩾12 weeks, age ⩾18 years and adequatehematologic, hepatic and renal function
- **Exclusion criteria**: prior or current MET inhibitor treatment

RESULTS

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Tumor responses in the overall treatment population and by MET status

RECIST response, n (%)	MET-driven (n=44)	MET-independent (n=46)	MET Unknown (n=19)	Total (N=109)
PR†	8 (18)*	0 (0)	0 (0)	8 (7)
SD	22 (50)	11 (24)	5 (26)	38 (35)
PD	11 (25)	28 (61)	9 (47)	48 (44)
NE	3 (7)	7 (15)	5 (26)	15 (14)

*p=0.002 vs MET-independent subgroup (Fisher exact test). Responses assessed according to RECIST version 1.1.
†Unconfirmed responses excluded. PD, progressive disease; NE, not evaluable.

SUMMARY AND CONCLUSIONS

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- 8 of 44 (18%) patients with MET- driven PRCC achieved a PR
- PFS was significantly longer in patients with MET-driven PRCC compared with MET-independent disease (6.2 versus 1.4 months, respectively ($p<0.0001$)
- Treatment with savolitinib was generally well tolerated, with the majority of AEs being grade 1 or 2
- These data support the hypothesis that savolitinib has anti-tumor activity in patients with MET-driven PRCC

Presented at the 2017 Genitourinary Cancer Symposium.
Presented by: Toni Choueiri, MD

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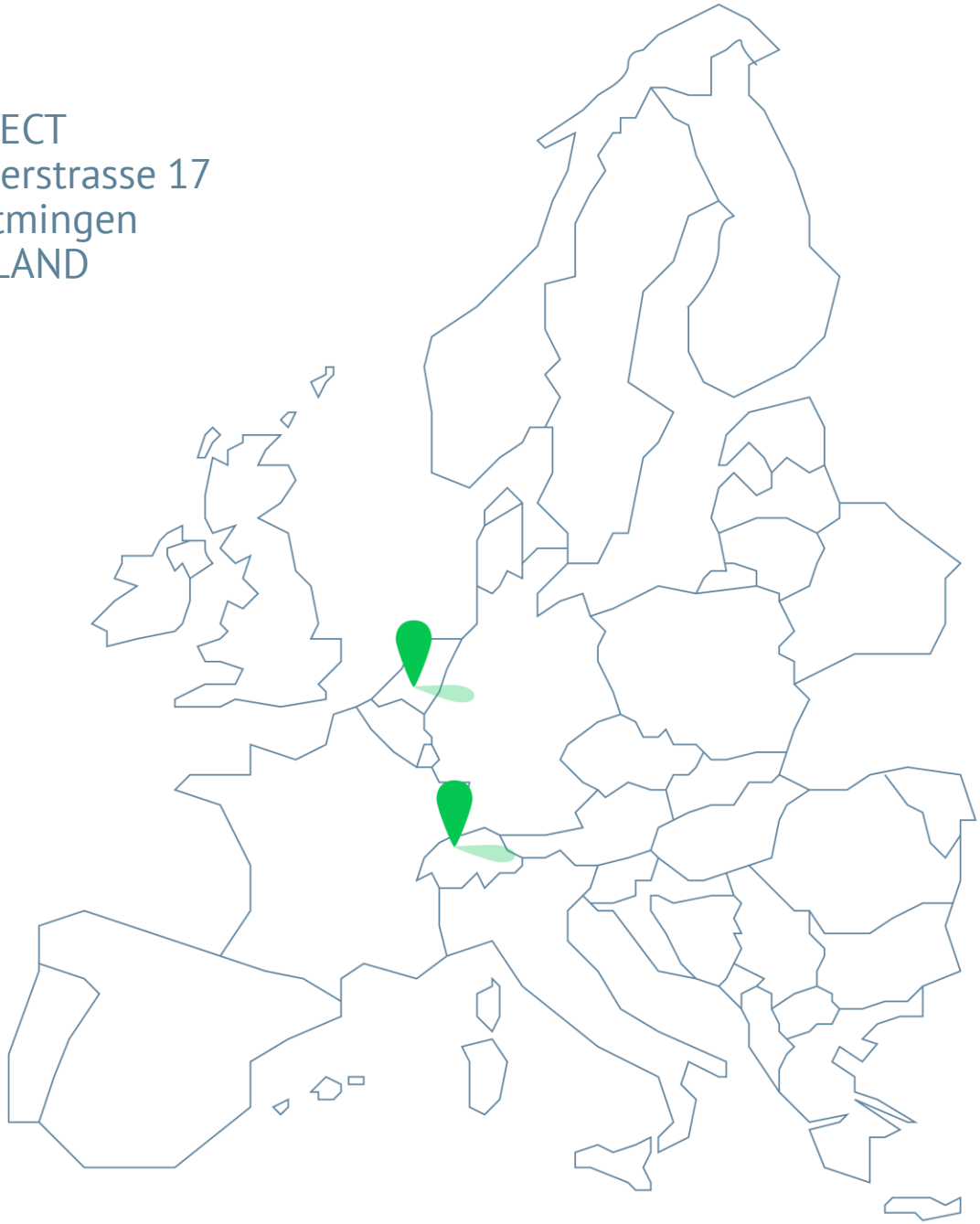
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND



Dr. Antoine Lacombe
Pharm D, MBA
Phone: +41 79 529 42 79
antoine.lacombe@cor2ed.com

Dr. Froukje Sosef
MD
Phone: +31 6 2324 3636
froukje.sosef@cor2ed.com