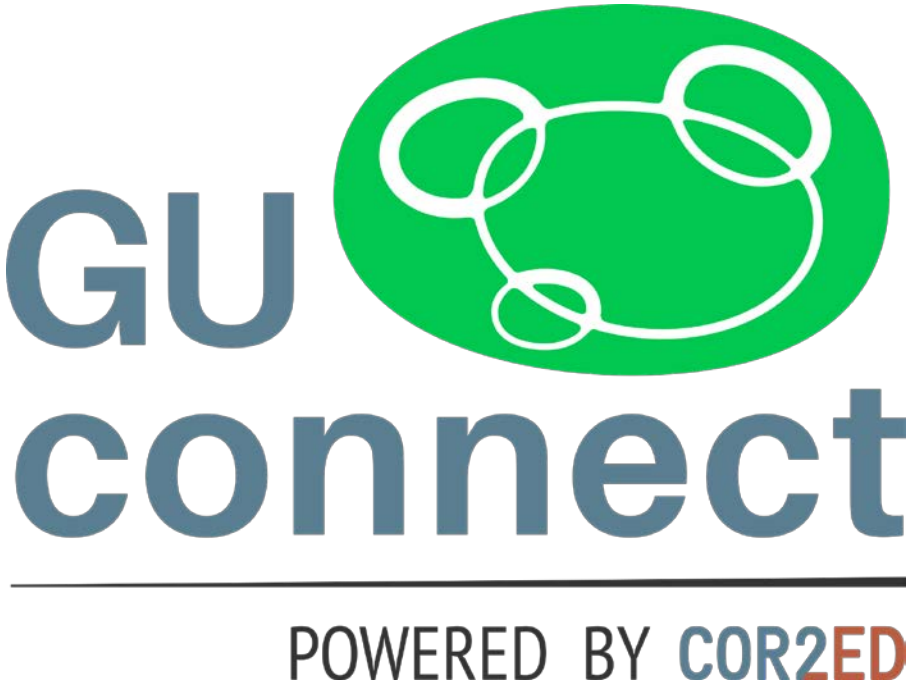

GU
connect
POWERED BY COR2ED

MEETING SUMMARY
ESMO 2018, Munich, Germany

Dr. Fabio Schutz
Beneficencia Portuguesa de Sao Paulo, Brazil

HIGHLIGHTS ON GU ONCOLOGY

DISCLAIMER

GU connect
POWERED BY COR2ED

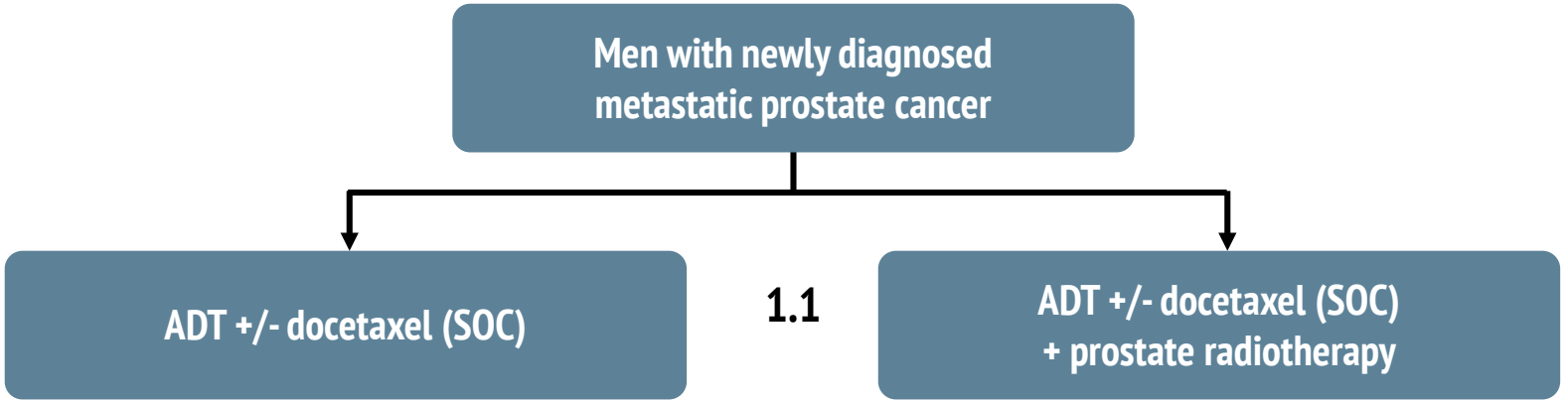
Please note: The views expressed within this presentation are the personal opinions of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GU CONNECT group

RADIOTHERAPY TO THE PRIMARY TUMOUR FOR MEN WITH NEWLY-DIAGNOSED METASTATIC PROSTATE CANCER: SURVIVAL RESULTS FROM STAMPEDE (NCT00268476)

C. Parker et al. Abst #LBA5_PR

STAMPEDE TRIAL: RT FOR LOCAL DISEASE IN M1 PATIENTS

STUDY DESIGN



36Gy/6 fractions/6 weeks **or** 55Gy/20 fractions/4 weeks
Schedule nominated before randomisation

Stratification variables

- Age (<70 vs ⩾70 years), nodal involvement (N0 vs N1 vs Nx), randomising site, WHO performance status (0 vs 1 or 2), type of ADT, aspirin or NSAID use, docetaxel use

Parker C, et al. Presented at ESMO 2018, abstract LBA5_PR
MRC CTU at UCL
ADT, androgen deprivation therapy; Gy, gray; M, metastasis; N, nodal; NSAID, nonsteroidal anti-inflammatory drug; RT, radiotherapy; SOC, standard-of-care; WHO, World Health Organization

STAMPEDE TRIAL: RT FOR LOCAL DISEASE IN M1 PATIENTS

GU connect
POWERED BY COR2ED

RESULTS: BASELINE CHARACTERISTICS

Characteristic		SOC (n=1029)	SOC+RT (n=1032)
Age (years)	Median (IQR) Range	68 (63–73) 37–86	68 (63–73) 45–87
PSA (ng/ml)	Median (IQR) Range	98 (30–316) 1–20590	97 (33–313) 1–11156
Metastatic burden	Low High Not classified	409 (42%) 567 (58%) 53	410 (43%) 553 (57%) 69
Site of metastases	Bone Liver Lung Distant lymph nodes Other	919 (89%) 23 (2%) 42 (4%) 294 (29%) 35 (3%)	917 (89%) 19 (2%) 48 (5%) 304 (29%) 33 (3%)
Docetaxel use	No Yes	845 (82%) 184 (18%)	849 (82%) 183 (18%)

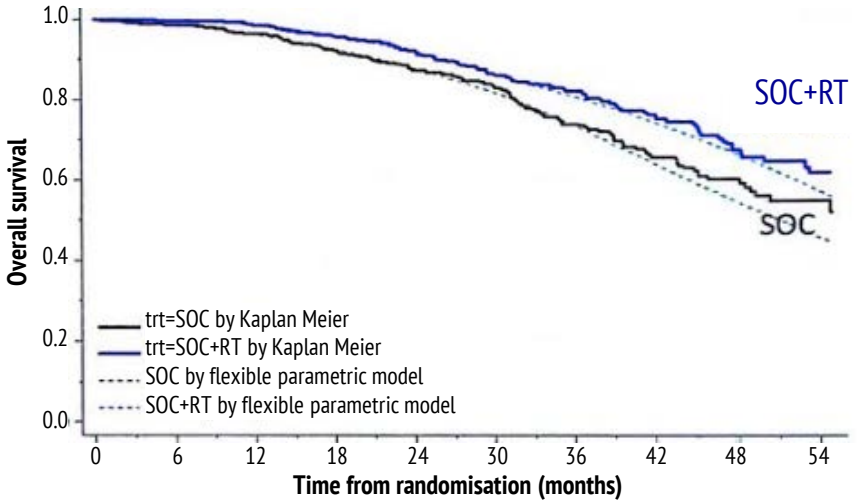
Parker C, et al. Presented at ESMO 2018, abstract LBA5_PR
MRC CTU at UCL
IQR, interquartile range; M, metastasis; PSA, prostate-specific antigen; RT, radiotherapy

STAMPEDE TRIAL: RT FOR LOCAL DISEASE IN M1 PATIENTS

GU connect
POWERED BY COR2ED

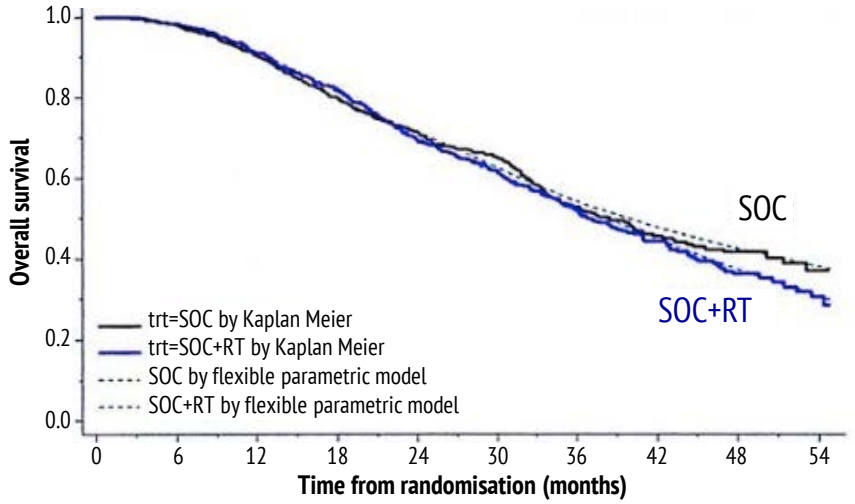
OVERALL SURVIVAL: METASTATIC BURDEN SUBGROUP ANALYSIS

Low burden



HR: 0.68 (95% CI: 0.52–0.90) p=0.007
3-year OS (%): SOC = 73%
SOC+RT = 81%

High burden



HR: 1.07 (95% CI: 0.90–1.28) p=0.420
3-year OS (%): SOC = 54%
SOC+RT = 53%

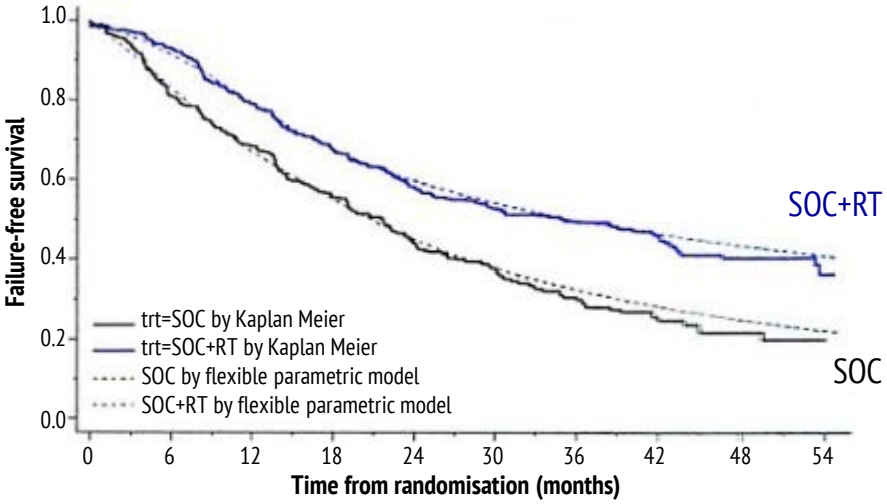
Parker C, et al. Presented at ESMO 2018, abstract LBA5_PR
MRC CTU at UCL
CI, confidence interval; HR, hazard ratio; M, metastasis; OS, overall survival; RT, radiotherapy; SOC, standard-of-care; trt, treatment

STAMPEDE TRIAL: RT FOR LOCAL DISEASE IN M1 PATIENTS

GU connect
POWERED BY COR2ED

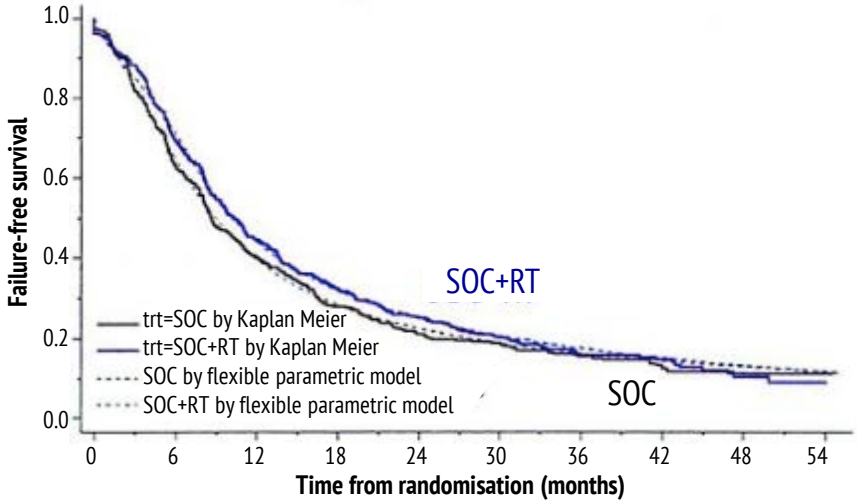
FAILURE-FREE SURVIVAL (FFS): METASTATIC BURDEN SUBGROUP ANALYSIS

Low burden



HR: 0.59 (95% CI: 0.49–0.72) $p=4.83\times10^{-3}$
3-year FFS (%): SOC = 33%
SOC+RT = 50%

High burden



HR: 0.88 (95% CI: 0.77–1.01) p=0.059
3-year FFS (%): SOC = 17%
SOC+RT = 18%

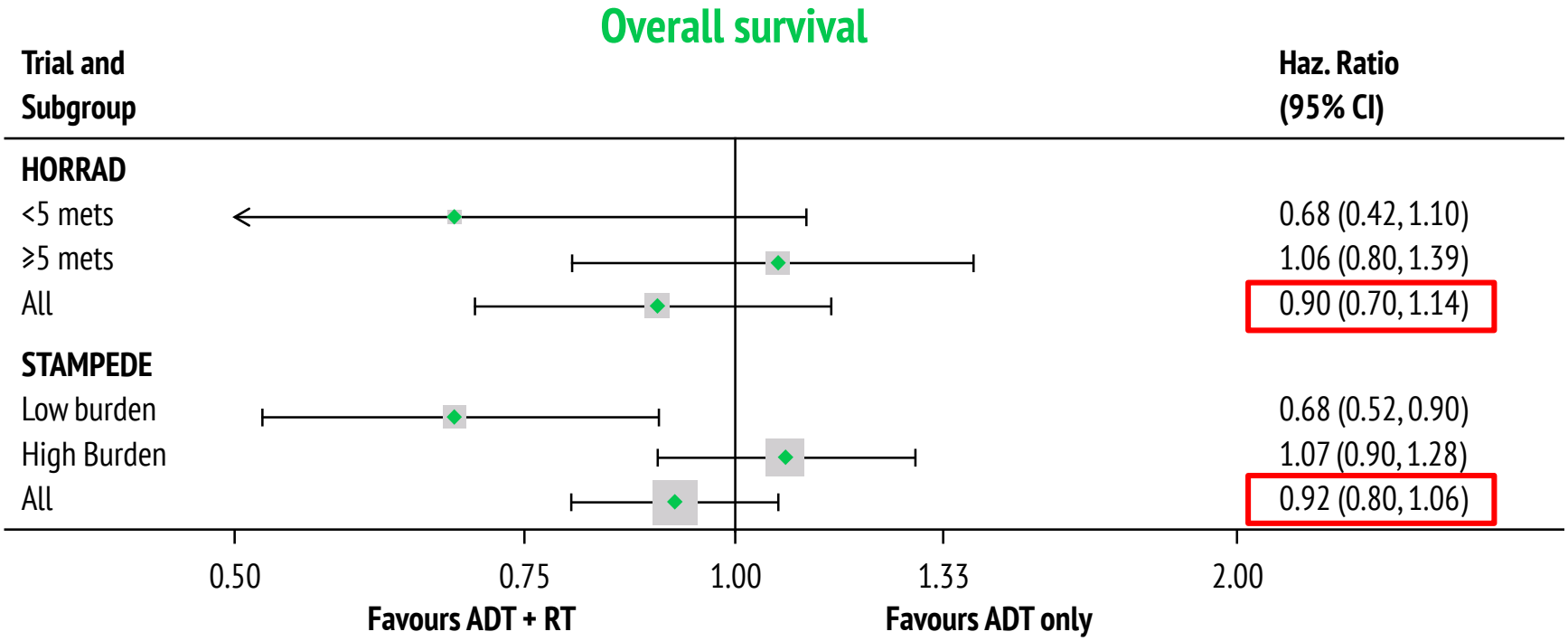
Test for interaction: p=0.0024

Parker C, et al. Presented at ESMO 2018, abstract LBA5_PR
MRC CTU at UCL
CI, confidence interval; FFS, failure-free survival; HR, hazard ratio; M, metastasis; RT, radiotherapy; SOC, standard-of-care; trt, treatment

STAMPEDE TRIAL: RT FOR LOCAL DISEASE IN M1 PATIENTS

GU connect
POWERED BY COR2ED

THE EFFECT IS CONSISTENT WITH HORRAD



Boeve et al. Eur Urol 2018
MRC CTU at UCL
ADT, androgen deprivation therapy; CI, confidence interval; Haz, hazard; M, metastasis; mets, metastases; RT, radiotherapy

EFFECTS OF ABIRATERONE ACETATE PLUS PREDNISONE/PREDNISOLONE IN HIGH AND LOW RISK METASTATIC HORMONE SENSITIVE PROSTATE CANCER

A. Hoyle et al. Abst #LBA4

STAMPEDE TRIAL: BENEFIT OF ABIRATERONE FOR LOW/HIGH RISK/VOLUME

GU connect
POWERED BY COR2ED

BACKGROUND

	Pt No.	Median F/U (mo)	HR
LATITUDE M1 "high risk"	1199	30.4	**0.62** (0.51–0.76)
STAMPEDE AAP M0+M1	1917	40	**0.63** (0.52–0.76)
STAMPEDE AAP (M1)	1002	40	**0.61** (0.49–0.75)
STAMPEDE AAP (M0)	915	40	**0.75** (0.48–1.18)

What do we mean by "Risk" or "Volume?"

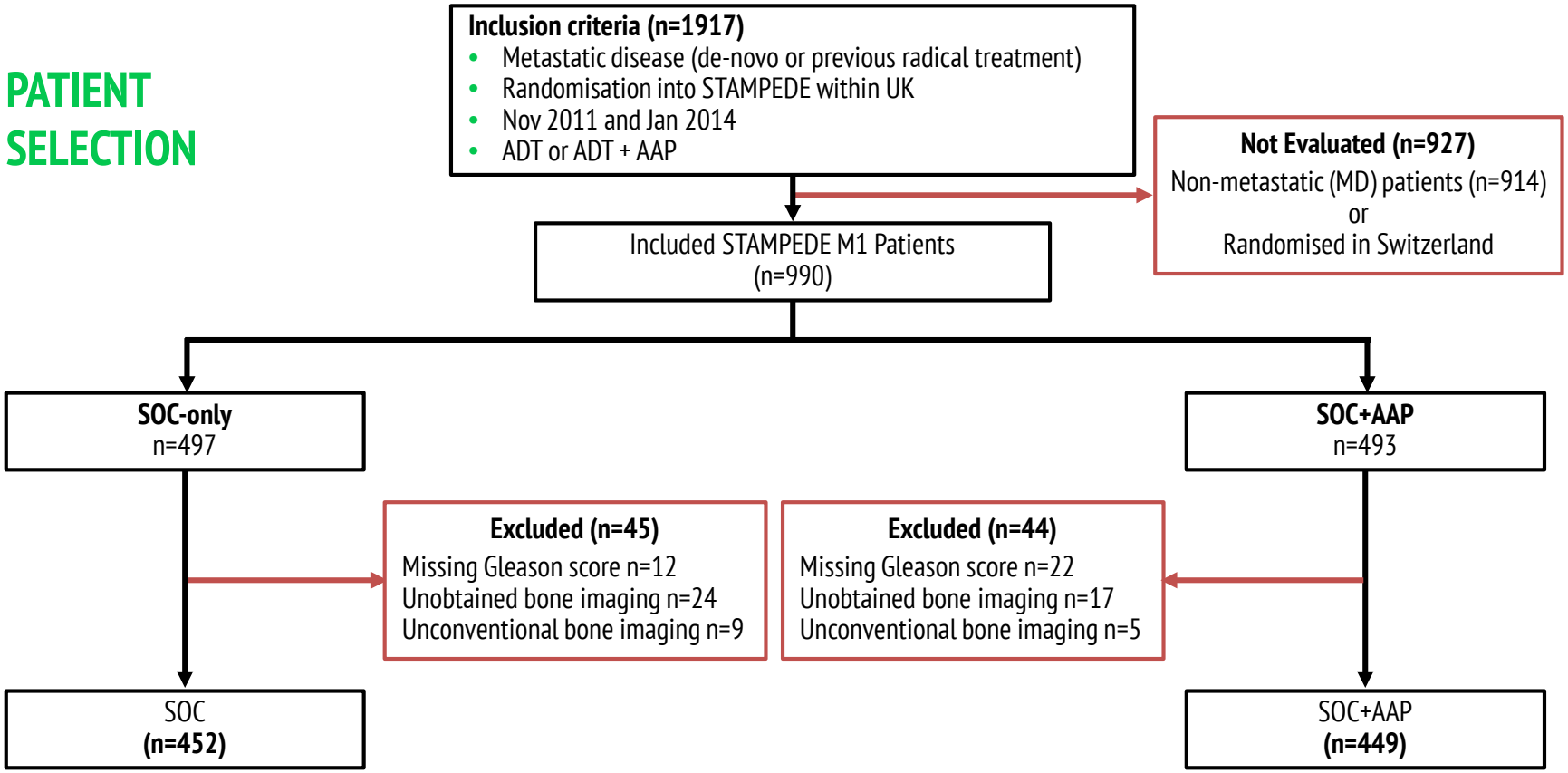
Definition		
CHAARTED (volume)	High	Visceral metastases AND/OR ≥4 Bone metastases (≥1 outside vertebral column or pelvis)
LATITUDE (risk)	High	≥2 high risk features • ≥3 Bone metastases • Visceral metastases • ≥Gleason 8

Hoyle A, et al. Presented at ESMO 2018, abstract LBA4
AAP, abiraterone acetate plus prednisone/prednisolone; F/U, follow-up; HR, hazard ratio; M, metastasis

STAMPEDE TRIAL: BENEFIT OF ABIRATERONE FOR LOW/HIGH RISK/VOLUME

GU connect
POWERED BY COR2ED

PATIENT SELECTION



Hoyle A, et al. Presented at ESMO 2018, abstract LBA4

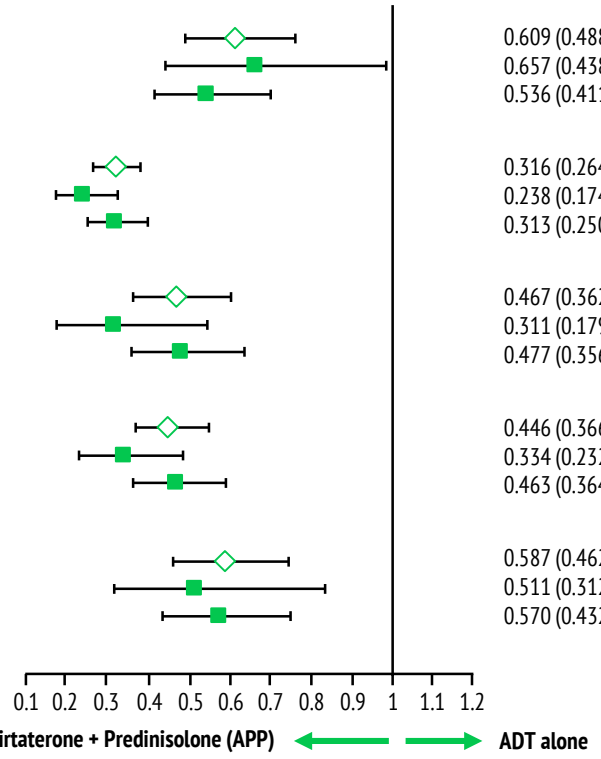
AAP, abiraterone acetate plus prednisone/prednisolone; ADT, androgen deprivation therapy; M, metastasis, SOC, standard-of-care

STAMPEDE TRIAL: BENEFIT OF ABIRATERONE FOR LOW/HIGH RISK (LATITUDE)

GU connect
POWERED BY COR2ED

RESULTS: LATITUDE RISK STRATIFICATION

		ADT alone	AAP	Adjusted HR* (95% CI)	p-value	Interaction by metastatic volume p-value
		No. of events/No. of patients				
Overall survival						
	All patients	195/452	135/449	0.609 (0.488–0.789)	<0.001	
	Low risk	59/220	41/208	0.657 (0.438–0.983)	0.041	0.385
	High risk	136/232	94/241	0.536 (0.411–0.699)	<0.001	
Failure free survival						
	All patients	354/452	191/449	0.316 (0.264–0.378)	<0.001	
	Low risk	152/220	56/208	0.238 (0.174–0.325)	<0.001	0.294
	High risk	202/232	135/241	0.313 (0.250–0.392)	<0.001	
Skeletal related events						
	All patients	164/452	93/449	0.467 (0.362–0.602)	<0.001	
	Low risk	49/220	17/208	0.311 (0.179–0.543)	<0.001	0.207
	High risk	115/232	76/241	0.477 (0.356–0.639)	<0.001	
Progression free survival						
	All patients	267/452	158/449	0.446 (0.366–0.544)	<0.001	
	Low risk	101/220	41/208	0.334 (0.232–0.482)	<0.001	0.159
	High risk	166/232	117/241	0.463 (0.364–0.588)	<0.001	
Prostate cancer specific death*						
	All patients	172/452	114/449	0.587 (0.462–0.746)	<0.001	
	Low risk	49/220	27/208	0.511 (0.312–0.836)	0.008	0.728
	High risk	123/232	87/242	0.570 (0.432–0.754)	<0.001	



Hoyle A, et al. Presented at ESMO 2018, abstract LBA4

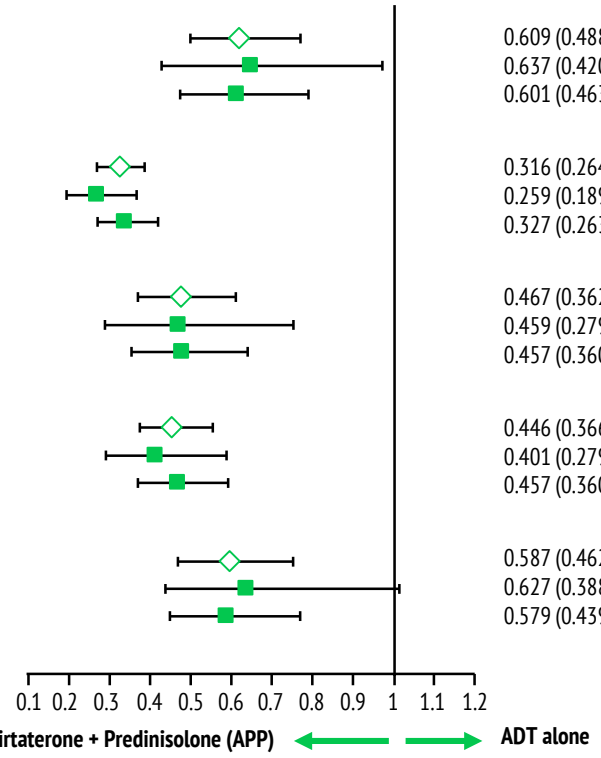
AAP, abiraterone acetate plus prednisone/prednisolone; ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio

STAMPEDE TRIAL: BENEFIT OF ABIRATERONE FOR LOW/HIGH VOLUME (CHAARTED)

GU connect
POWERED BY COR2ED

CHAARTED VOLUME CRITERIA

		ADT alone	AAP	Adjusted HR* (95% CI)	p-value	Interaction by metastatic volume p-value
		No. of events/No. of patients				
Overall survival						
	All patients	195/452	135/449	0.609 (0.488–0.789)	<0.001	
	Low volume	53/196	39/206	0.637 (0.420–0.966)	0.034	0.771
	High volume	142/256	96/243	0.601 (0.463–0.779)	<0.001	
Failure free survival						
	All patients	354/452	191/449	0.316 (0.264–0.378)	<0.001	
	Low volume	133/196	57/206	0.259 (0.189–0.356)	<0.001	0.472
	High volume	221/256	134/243	0.327 (0.263–0.408)	<0.001	
Skeletal related events						
	All patients	164/452	93/449	0.467 (0.362–0.602)	<0.001	
	Low volume	46/196	25/206	0.459 (0.279–0.577)	0.002	0.981
	High volume	118/256	68/243	0.457 (0.360–0.579)	<0.001	
Progression free survival						
	All patients	267/452	158/449	0.446 (0.366–0.544)	<0.001	
	Low volume	86/196	45/206	0.401 (0.279–0.577)	<0.001	0.670
	High volume	181/256	113/243	0.457 (0.360–0.579)	<0.001	
Prostate cancer specific death*						
	All patients	172/452	114/449	0.587 (0.462–0.746)	<0.001	
	Low volume	43/196	31/206	0.627 (0.388–1.013)	0.057	0.740
	High volume	129/256	83/243	0.579 (0.439–0.764)	<0.001	



Hoyle A, et al. Presented at ESMO 2018, abstract LBA4

AAP, abiraterone acetate plus prednisone/prednisolone; ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio

JAVELIN RENAL 101: A RANDOMIZED, PHASE 3 STUDY OF AVELUMAB + AXITINIB VS SUNITINIB AS FIRST-LINE TREATMENT OF ADVANCED RENAL CELL CARCINOMA

R. Motzer et al. Abst #LBA6_PR

JAVELIN RENAL 101

GU connect
POWERED BY COR2ED

Key eligibility criteria:
- Treatment-naïve aRCC with a clear cell component
- ⩾1 measurable lesion as defined by RECIST v1.1
- Tumor tissue available for PD-L1 staining
- ECOG PS 0 or 1

Stratification:
- ECOG PS (0 vs 1)
- Geographic region (USA vs Canada/Western Europe vs ROW)

R 1:1

Avelumab 10 mg/kg IV Q2W + Axitinib 5 mg PO BID (6-week cycle)

Sunitinib 50 mg PO QD (4 weeks on, 2 weeks off)

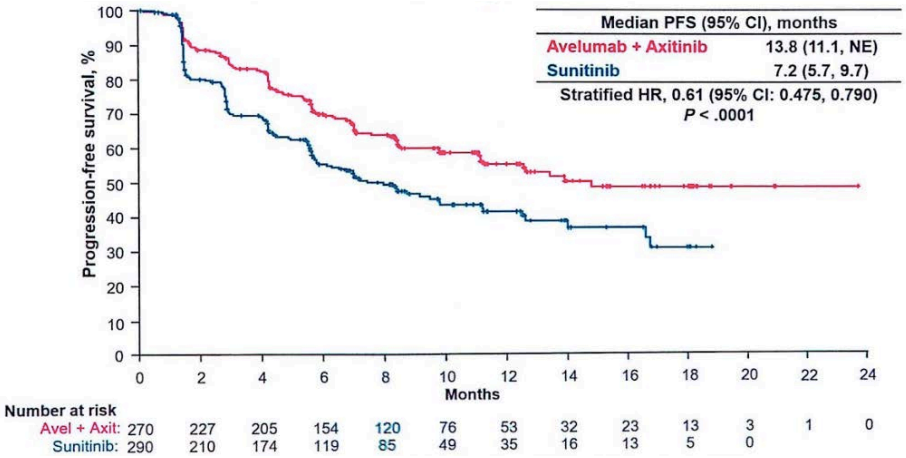
Characteristic	PD-L1+ group (N=560)		Overall population (N=886)	
	Avelumab + Axitinib (N=270)	Sunitinib (N=290)	Avelumab + Axitinib (N=442)	Sunitinib (N=444)
Median age, years	62	61	62	61
Male, %	75	77	72	78
Prior nephrectomy, %	86	87	80	80
ECOG performance status, %				
0/1	62/38	67/33	63/37	63/37
IMDC prognostic risk, %*				
Favourable	19	20	21	22
Intermediate/poor	64/16	66/13	61/16	62/16
MSKCC Prognostic risk, %†				
Favourable	19	21	22	23
Intermediate/poor	67/12	69/8	64/12	66/10
Geographic region, %				
United States	28	28	29	30
Canada/Western Europe	30	28	29	29
Rest of the World	43	44	42	42

* Not reported in <1% of patients; † Not reported in <3% of patients

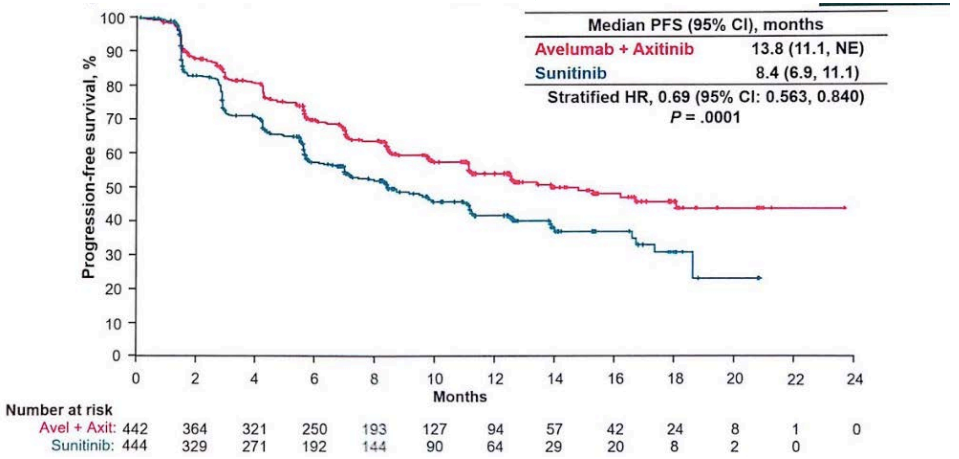
aRCC, advanced renal cell carcinoma; BID, twice a day; ECOG PS, Eastern Cooperative Oncology Group performance status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; IV, intravenous; MSKCC, Memorial Sloan Kettering Cancer Center; PD-L1, programmed death-ligand 1; PO, orally; Q2W, once every 2 weeks; QD, once a day; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; ROW, rest of the world

JAVELIN RENAL 101: PFS PER IRC

PFS per IRC in the PD-L1+ group (Primary endpoint)



PFS per IRC in the overall population (Key secondary endpoint)



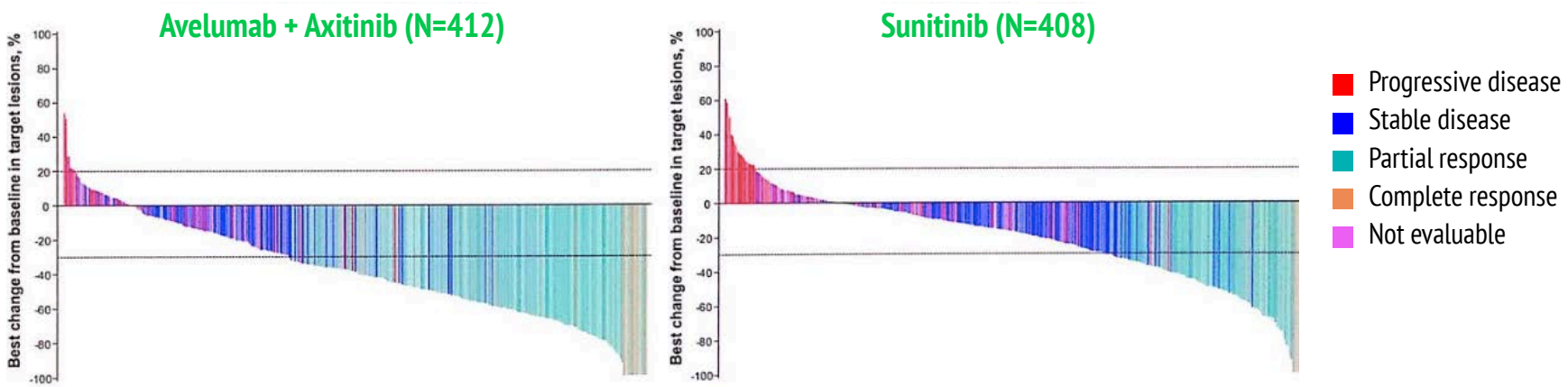
Motzer R, et al. Presented at ESMO 2018, abstract LBA6_PR

CI, confidence interval; HR, hazard ratio; IRC, independent review committee; NE, not estimable; PD-L1, programmed death-ligand 1; PFS, progression-free survival

JAVELIN RENAL 101: OVERALL RESPONSE RATE

GU connect
POWERED BY COR2ED

Per IRC	PD-L1+ group (N=560)		Overall population (N=886)	
	Avelumab + Axitinib (N=270)	Sunitinib (N=290)	Avelumab + Axitinib (N=442)	Sunitinib (N=444)
Objective response rate (95% CI), %	**55 (49.0, 61.2)**	**26 (20.6, 30.9)**	**51 (46.6, 56.1)**	**26 (21.7, 30.0)**
Best overall response, %*				
Complete response	4	2	3	2
Partial response	51	23	48	24
Stable disease	27	43	30	46
Progressive disease	11	22	12	19
Not evaluable†	4	7	6	8
Patients with ongoing response, %‡	73	65	70	71
Per investigator assessment				
Objective response rate (95% CI), %	**62 (55.8, 67.7)**	**30 (24.5, 35.3)**	**56 (51.1, 60.6)**	**30 (25.9, 34.7)**
Best overall response, %				
Complete response	4	3	3	2
Partial response	58	27	53	28



Motzer R, et al. Presented at ESMO 2018, abstract LBA6_PR

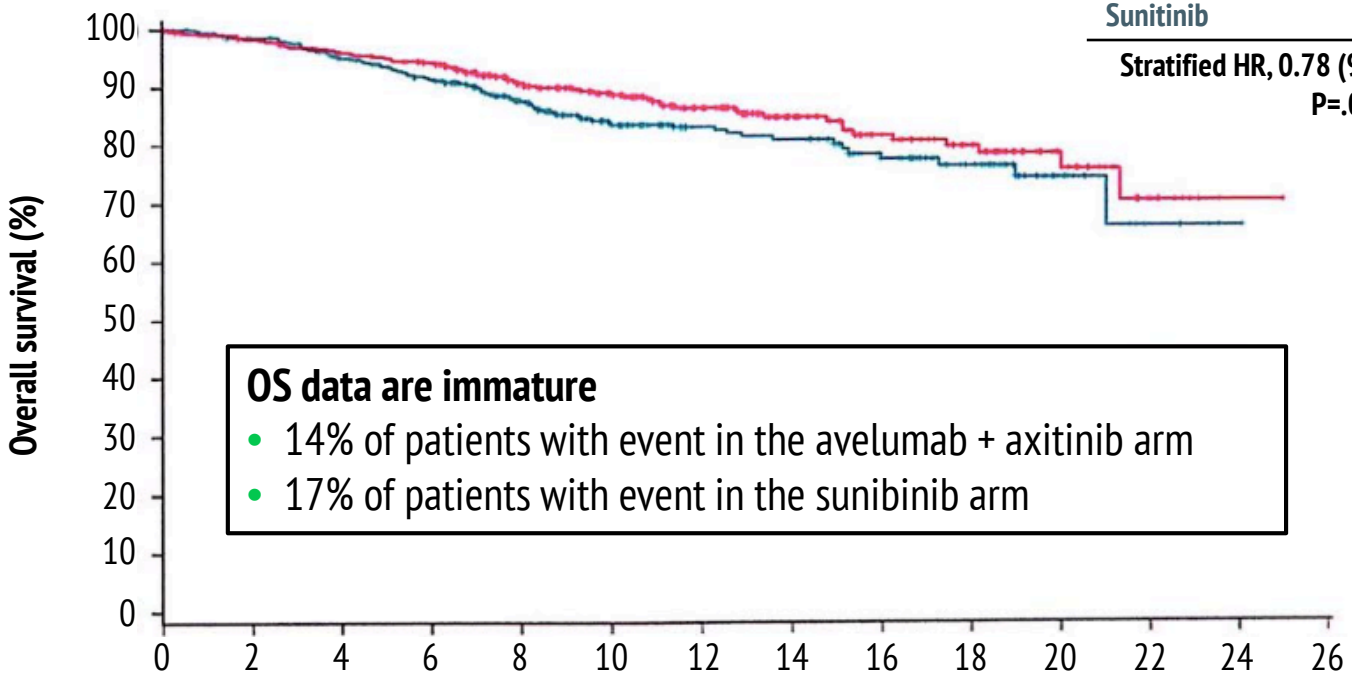
* Patients without target lesions at baseline per IRC who achieved non-complete response/non-progressive disease: 3% (avelumab + axitinib) and 2% (sunitinib) in the PD-L1+ group, 2% (avelumab + axitinib) and 2% (sunitinib) in the overall population; † Including patients with no post-baseline assessments; ‡ In patients with confirmed complete or partial response. CI, confidence interval; IRC, independent review committee; PD-L1, programmed death-ligand 1

JAVELIN RENAL 101: OVERALL SURVIVAL

OS IN THE OVERALL POPULATION

Median OS (95% CI), months	
Avelumab + Axitinib	Not reached
Sunitinib	Not reached

Stratified HR, 0.78 (95% CI: 0.554, 1.084)
P=.0679



OS data are immature

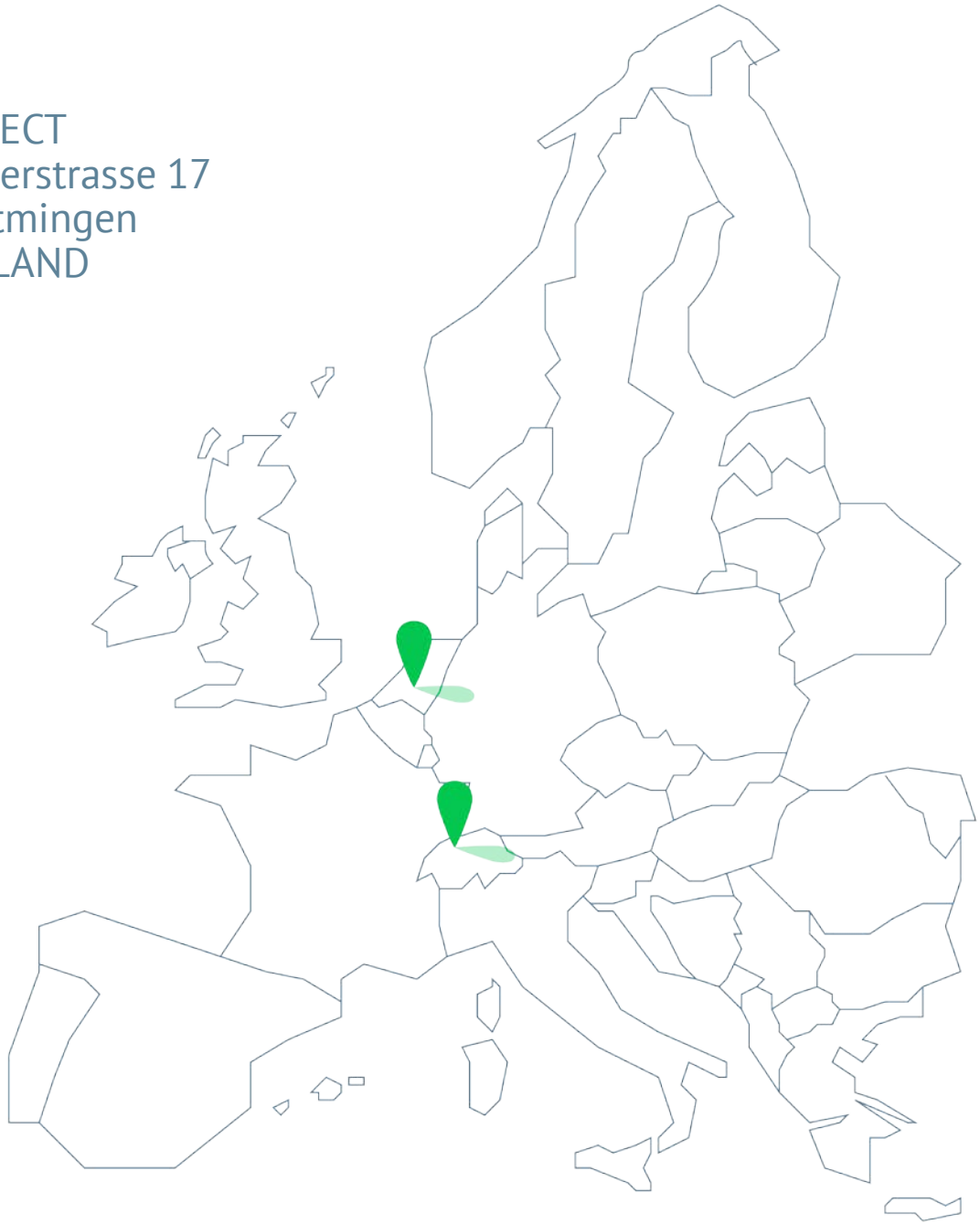
- 14% of patients with event in the avelumab + axitinib arm
- 17% of patients with event in the sunibinib arm

Number at risk													
Avel + Axit:	442	426	412	396	319	252	187	121	93	70	27	8	1	0
Sunitinib:	444	426	401	373	295	224	175	113	84	59	17	5	1	0

Motzer R, et al. Presented at ESMO 2018, abstract LBA6_PR
CI, confidence interval; HR, hazard ratio; OS, overall survival

GU connect
POWERED BY COR2ED

GU CONNECT
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