CC-1, a bispecific PSMAxCD3 antibody

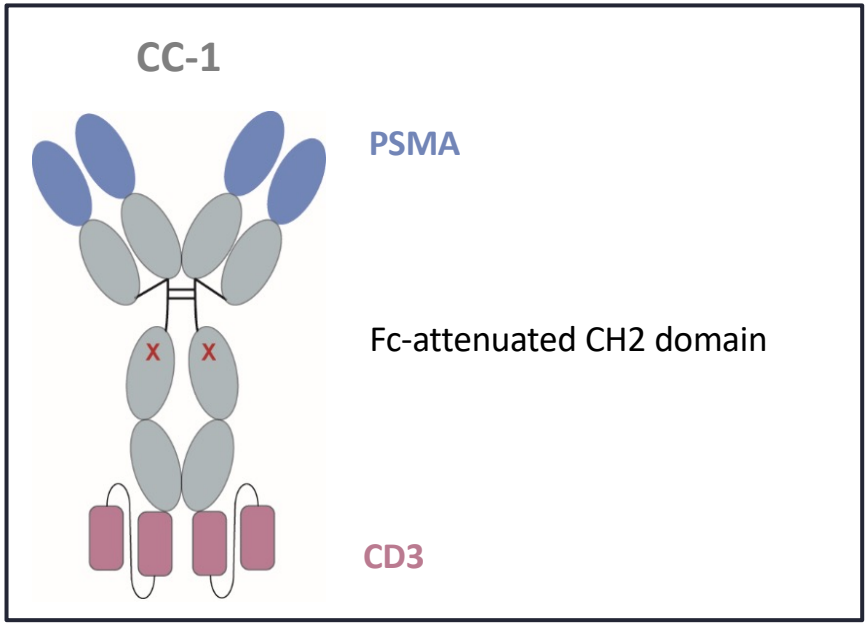
Current status of the clinical trials

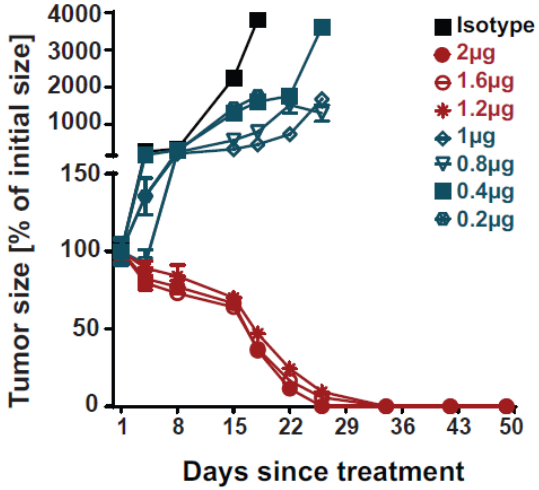
Dr. Jonas Heitmann

5th ForTra Workshop for Translational Research

Universitätsklinikum Tübingen

CC-1 (PSMAxCD3)





Zekri et al, 2021

Preclinical:

- Optimized bispecific format and targeting of both, tumor cells and neovasculature in a variety of tumor entities
- Binding to PSMA in prostate cancer and squamous cell cancer (SCC) of the lung
- Favorable safety and efficacy data in vitro and in mice

CC-1 – Ongoing clinical trials

PSMAxCD3_CRPC:

CC-1 in **CRPC** (castration resistant prostate cancer)

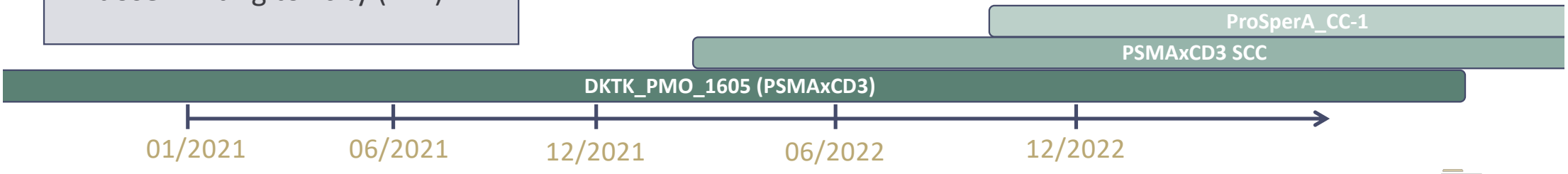
- Recruitment completed in Q1/2023
- Preliminary results on safety and efficacy
- Target dose reached without dose limiting toxicity (DLT)

SCC PSMAxCD3:

CC-1 in **SCC of the lung**

ProSperA_CC-1:

CC-1 in **BCR (biochemical relapse) of PC (prostate cancer)**



PSMAxCD3_CRPC - Trial design

Part I

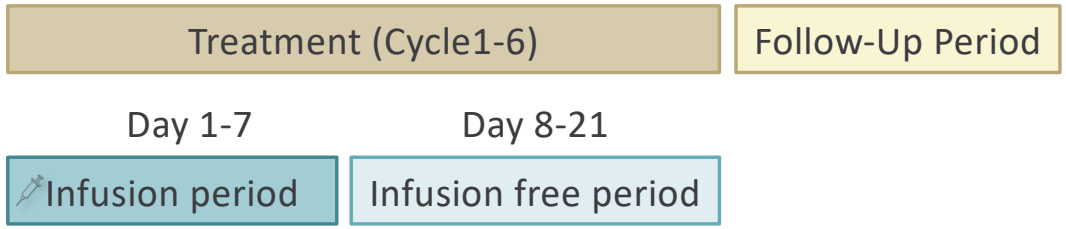
Dose escalation
- Intraindividual dose escalation
- Aim: Determine maximum tolerated dose (MTD) of CC-1

Part II

Dose expansion
- Application of MTD
- Aim: Define recommended phase 2 dose (RP2D)

- First-in-human trial
- Multi-center

- Indication: CRPC after third line
- Prophylactic tocilizumab
- CC-1 as 24hr continuous infusion



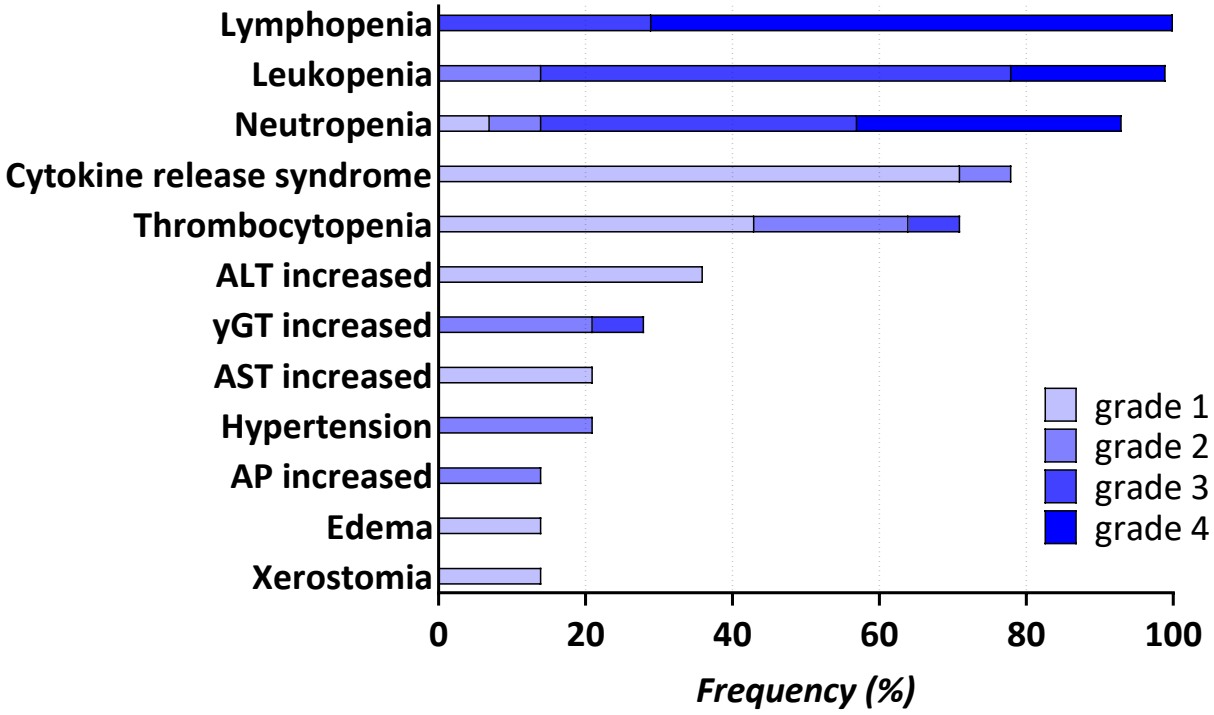
PSMAxCD3_CRPC – Included subjects

Characteristics	Patients (n = 22)
age, median (range), years	70.5 (43 - 82)
PSA, median (range), µg/ml	123.5 (0.5 – 1,053)
ECOG, n (%)	
0	14 (64)
1	8 (36)
Metastasis, n (%)	
Bone	21 (95)
Lymphnodes	17 (77)
Hepatic	6 (27)
Others	5 (23)

- 22 patients were treated, among them 14 patients at the MTD
- Heavily pretreated patient population
- Definition of target dose with 14th patient:

Days	1	2	3	4	5	6	7
Dose (µg)	78	215	826	826	826	826	826

PSMAxCD3_CRPC - Summary of related adverse events in patients treated at MTD

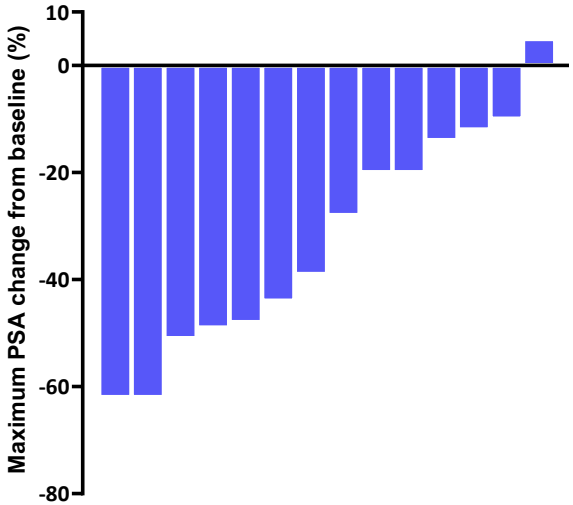


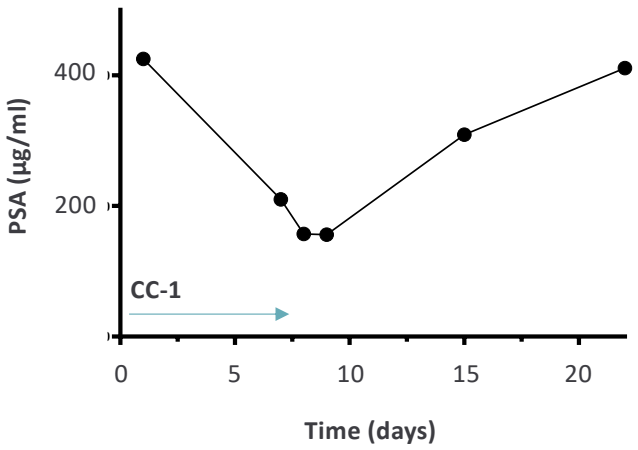
- 80% cytokine release syndrome ≦ Grade 2
- 22% hypertension
- Laboratory alterations → tocilizumab

→ Favorable safety profile

Only AEs occurring ≥2-times are displayed in this graph. Note at MTD only data of n=14 patients are available

PSMAxCD3_CRPC: Preliminary efficacy





- 7 patients received multiple treatment cycles
- 13/14 patients with PSA reduction
  - Transient effect in metastasized patients

→ Efficacy at earlier disease stages (lower tumor burden)

CC-1 – Ongoing clinical trials

PSMAxCD3_CRPC:

CC-1 in **CRPC**

- Recruitment completed in Q1/2023
- Preliminary results on safety and efficacy
- Target dose reached without DLT

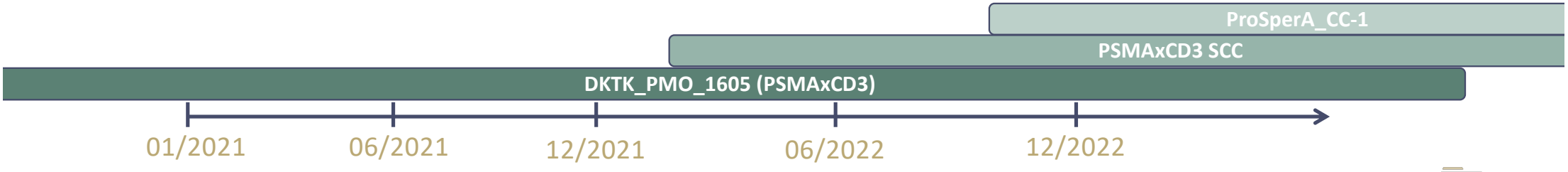
SCC PSMAxCD3:

CC-1 in **SCC of the lung**

- No DLT

ProSperA_CC-1:

CC-1 in **BCR of PC**



SCC PSMAxCD3 – Trial design

Part Ia

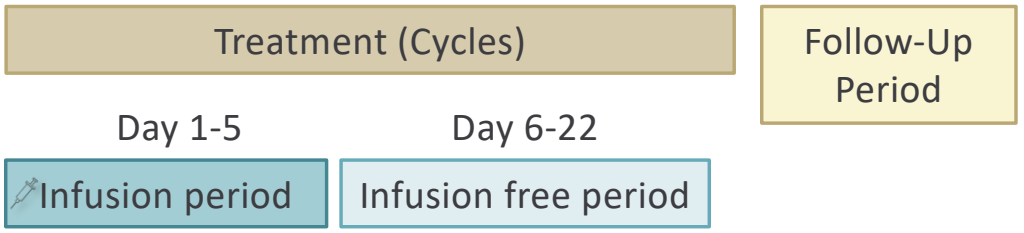
Dose escalation
- Intraindividual dose escalation
- Aim: Determine MTDa of CC-1

Part Ib

Dose escalation
- rule based 3+3 design
- Aim: Determine MTDb of CC-1 in combination with ICB

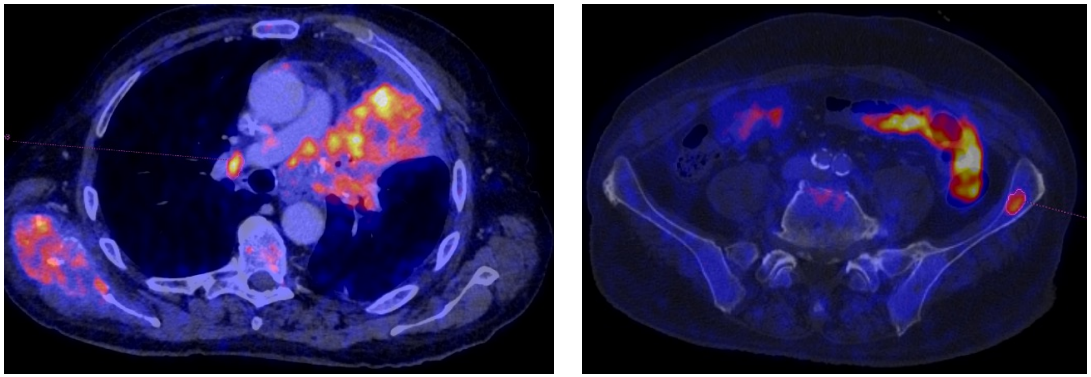
Part II

Dose expansion
- Application of MTDb
- Aim: Define RP2D



- Indication: SCC of the lung after second line
- CC-1 is administered as **3hr infusion**
- Prophylactic application of tocilizumab
- Second Part Ib to combine CC-1 with immune checkpoint blockade (ICB)

SCC PSMAxCD3 - Preliminary results



PSMA-PET scan
A patient with metastatic lung SCC was imaged by contrast enhanced [18F]-PSMA-1007 PET/CT. Left, osseous and lymphonodal metastases as well as primary cancer site (left upper lobe); Right, Single PSMA-expressing bone metastases, which notably were not noticed on CT scan.

- 1 patient treated
  - PSMA imaging valid for imaging of PSMA expression
  - No DLT, no CRS observed
  - Discontinued due to tumor progression

CC-1 – Ongoing clinical trials

PSMAxCD3_CRPC:

CC-1 in **CRPC**

- Recruitment completed in Q1/2023
- Preliminary results on safety and efficacy
- Target dose reached without DLT

SCC PSMAxCD3:

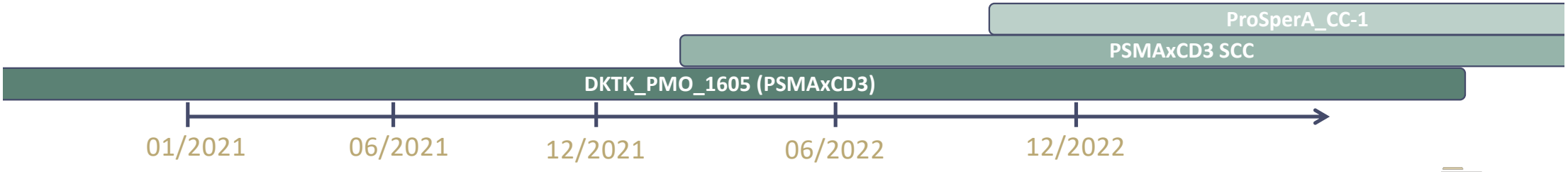
CC-1 in **SCC of the lung**

- No DLT

ProSperA_CC-1:

CC-1 in **BCR of PC**

- Recruiting
- 7 Patients treated
  - So far, no DLT



ProSperA_CC-1 - Trial design

Part I

Dose escalation
- Application of CC-1 as 3hr infusion
- Rule based 3+3 design
- Aim: Determine MTD of CC-1

Part II

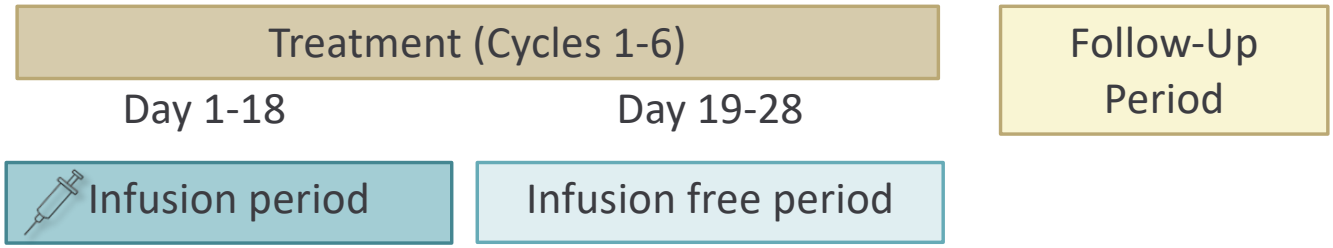
Dose expansion
- Application of MTD
- Aim: Define RP2D

- Phase I trial
- Single-center

- Indication: low risk PC with biochemical recurrence

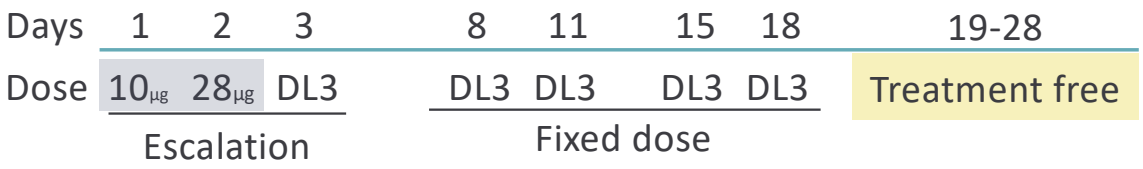
→ Favorable tumor:immune cell ratio

- CC-1 is administered twice weekly as **3hr infusion**



ProSperA_CC-1 – Dose and dose escalation

Dose escalation of CC-1 (Cycle 1) – Cohort 1



Dose levels of cohorts

Cohort	#1	#2	#3	#4	#5	#6	#7
DL_{max} (µg)	78	110	150	210	300	400	600

Conclusion

- **FIH trial in CRPC completed**
  - Favorable safety profile of CC-1, MTD reached without DLT
  - Early efficacy in heavily pretreated patient population
- **Phase I trial in SCC of the lung**
  - No DLT observed
- **Phase I trial in PC with BCR ongoing**
  - Good safety/tolerability
  - Dose escalation ongoing

KKE Translationale Immunologie
Helmut Salih
Gundram Jung
Juliane Walz
Martin Pflügler

ZKS Tübingen

NCT Heidelberg
Richard Schlenk

Urologie Essen
Boris Hadaschik

Charité
Sebastian Ochsenreither

Helmholtz-Validierungsfonds

HELMHOLTZ GEMEINSCHAFT

KKE Translationale Immunologie
Medizinische Klinik
Universitätsklinikum Tübingen

EBERHARD KARLS UNIVERSITÄT TÜBINGEN
MEDIZINISCHE FAKULTÄT

dkfz.
Deutsches Konsortium für Translationale Krebsforschung
Partnerstandort Tübingen

Else Kröner Fresenius Stiftung

ForTra gGmbH für Forschungstransfer

DKTK German Cancer Consortium