

First-in-human study of CDR404, a novel bivalent and bispecific, antibody-derived, T cell engager in MAGE-A4-positive advanced solid cancers



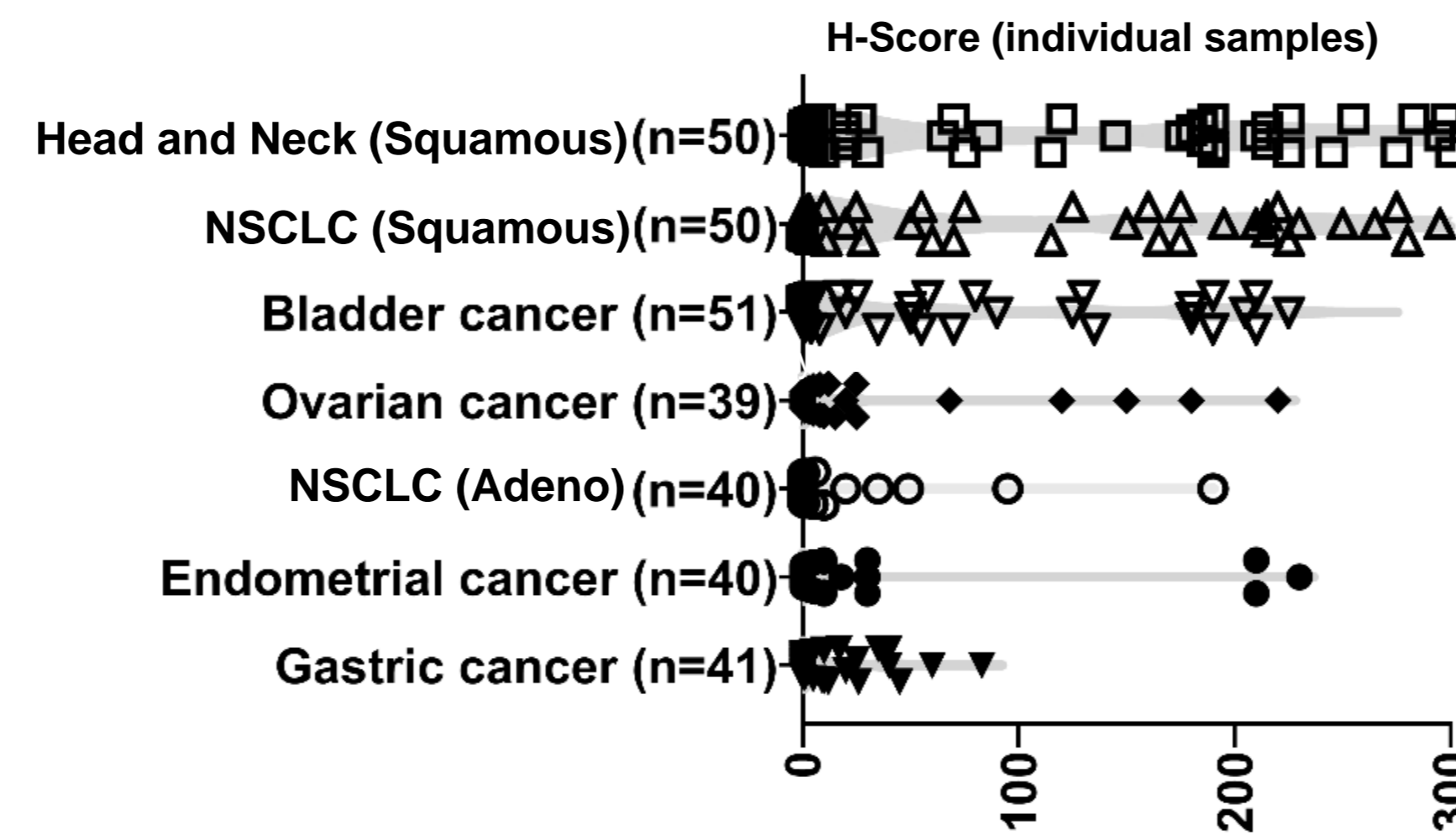
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1 Background

- The use of T cell engaging bispecifics redirecting T cells towards human leukocyte antigen (HLA)-presented peptides is emerging as a promising treatment modality for patients with solid tumors
- Melanoma-associated antigen A4 (MAGE-A4) is an intracellular cancer testis antigen highly expressed in multiple solid cancers
- CDR404 is a stable, highly potent bispecific and bivalent, antibody fragment-based T cell engager (TCE) which has a Fab-(scFv)₂ format targeting a MAGE-A4₂₃₀₋₂₃₉ peptide
- Here we present the Phase 1 study design for the TCE candidate CDR404 in HLA-A*02:01 patients with advanced/recurrent MAGE-A4 positive solid tumors (NCT06402201)

3 MAGE-A4 is expressed in a variety of solid tumors



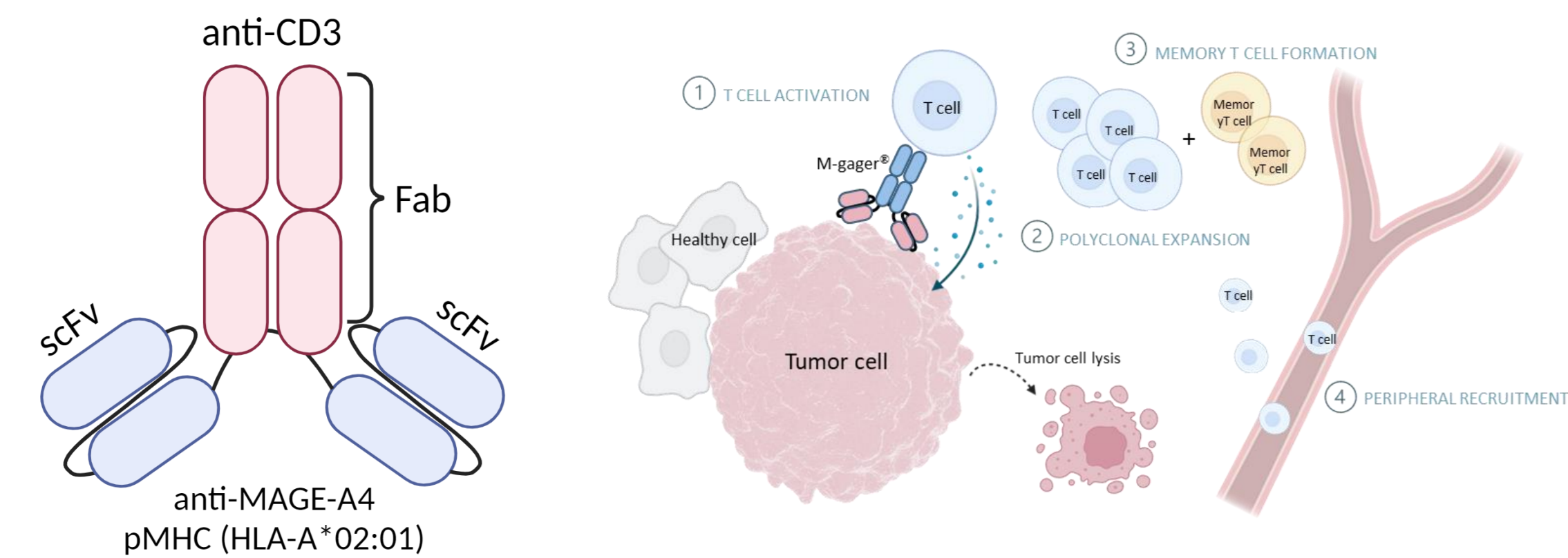
Immunohistochemistry (IHC) staining of 311 solid tumor samples from 7 histologies showing distribution of MAGE-A4 protein expression

4 CDR404 addresses a large cancer population with unmet need

	MAGE-A4 prevalence ¹ based on IHC patient samples	Addressable population ² (IHC and HLA eligibility) (US + EU)
Head & Neck (Squamous)	62%	42'903
NSCLC (Squamous)	52%	31'893
Bladder	47%	40'912
Gynecological	29%	32'131
NSCLC (Adeno)	15%	12'267
Gastric	27%	13'992
SS**	70%	< 1'000
MRCLS	20%	< 1'000

1. Data generated by CDR-Life using IHC with a 1% (2+/3+ intensity) cut-off and public data. 2: International Agency for Cancer Research, WHO. Incidence p.a. of HLA-A*02+ & MAGE-A4+ cases in US, CA & EU 2020 numbers. MRCLS: Myxoid/round cell liposarcoma; NSCLC: Non-small cell lung cancer; SS: Synovial sarcoma. *Ovarian, Cervical and Endometrial cancer

2 Drug characteristics and mechanism of action



- Bivalent format to increase potency through an avidity effect
- Large therapeutic window through high target specificity and a tailored low affinity CD3 binding
- CDR404 is engineered to have a low CRS profile in patients
- Highly stable and producible in scalable industry standard process
- Strong and durable anti-tumor activity *in-vivo*

5 Phase 1 clinical trial evaluating safety, tolerability and antitumor activity of CDR404

Key inclusion criteria:

- Age ≥ 18 years
- Advanced or metastatic disease, which has exhausted all standard-of-care regimens
- ECOG score ≤ 1
- Participant is germline HLA-A*02:01+
- Tumor MAGE-A4+ by IHC at a central laboratory
- Measurable disease per RECIST 1.1

Screening

PART A Dose exploration

Agnostic tumor recruitment but focus on lung, head and neck, esophageal, bladder and sarcoma tumors

Identification of the pharmacologically effective dose range

Initially weekly iv infusion

QSP-modelling derived starting dose

Dose escalation based on BOIN12 model assisted 3+3 design

Primary endpoint

Safety/tolerability
Dose-limiting toxicities, TEAEs and TRAEs

Secondary endpoints:

Anti-tumor efficacy
ORR, DCR, DOR, PFS per RECISTv1.1, OS

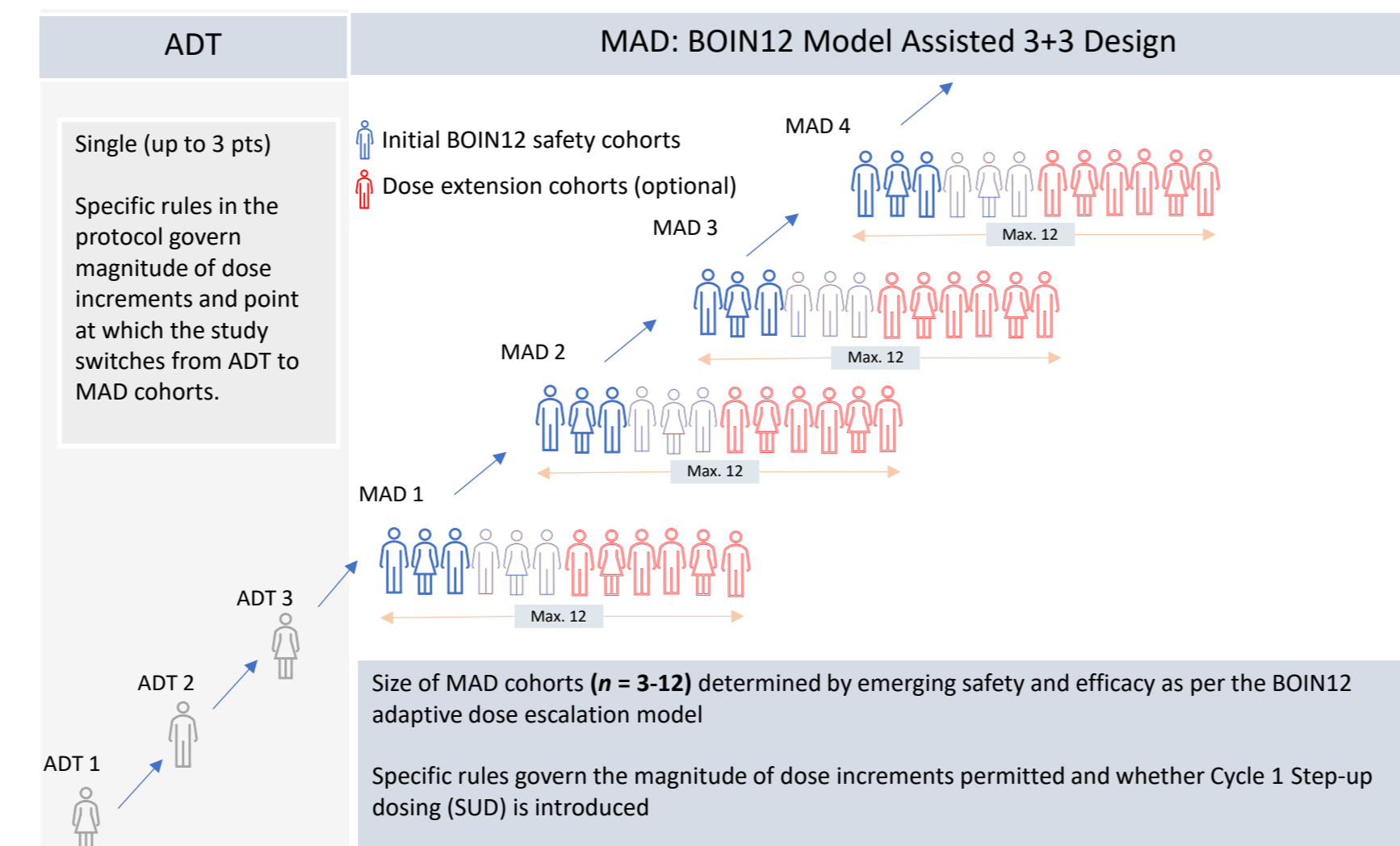
Exploratory endpoints:

Circulating tumor DNA (ctDNA) molecular response
evaluation of PK and PD parameters

PART B Dose Expansion

Identification of the optimal biological dose(s) of iv/sc CDR404 associated with reproducible anti-tumor responses in selected tumor types

ADT: Accelerated dose titration; BOIN12: Bayesian Optimal Interval Phase I/II, DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; IHC: Immunohistochemistry; HLA, human leukocyte antigens; IV, intravenous; MAD: Multiple ascending doses; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; QSP Quantitative system pharmacology; RECIST, Response Evaluation Criteria in Solid Tumors; TEAE, treatment-emergent adverse events; TRAE, treatment-related adverse events;



6 Study Locations



Enrolment started in Summer 2024 with a target of 17 sites open for patient recruitment. Up to 40 patients planned for enrollment in part A.

For more information, contact CDR-Life at cdr404-001_study@cdr-life.com or visit:

- Clinicaltrials.gov: <https://clinicaltrials.gov/study/NCT06402201>
- EudraCT: 2023-508808-38-00

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