Introduction
Current therapeutic options have inherent challenges for patients with r/r MM
• Bispecifics: treatment burden from frequent dosing over several months
• Autologous CART cell therapy: need for apheresis or bridging therapy, constrained manufacturing capacity, long manufacturing timelines, manufacturing failures, and variable quality

There is a significant unmet need for an off-the-shelf CART cell therapy as a readily available treatment option for patients with r/r MM

Allogeneic CART cell therapies may offer a significant benefit to patients who are:
• Refractory to or relapsed on prior systemic anti-cancer therapies
• Ineligible for autologous CART cell therapies
• At risk for manufacturing failure
• Facing issues with access to autologous CART therapy
• At risk of disease progression while on bridging therapy or awaiting long manufacturing timelines for autologous CART therapies

CB-011: anti-BCMA allogeneic CART cell therapy with immune cloaking to blunt rejection

KEY ATTRIBUTES

<table>
<thead>
<tr>
<th>CB-011</th>
<th>Conventional allogeneic CART cell therapy</th>
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<tbody>
<tr>
<td>CASTa-2×RMDA editing for enhanced genetic integrity</td>
<td>Reduced off-target editing and enhanced insertion rates</td>
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<td>Reduced TRAC knockout (KD)</td>
<td>TRAC gene knockout reduces GVHD risk</td>
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<tr>
<td>Humanized anti-BCMA CAR T cells specifically engineered to the TRAC gene</td>
<td>Enriches cytokine production, targets tumor antigen</td>
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<td>Blunt NK-mediated rejection</td>
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<td>Reduced TRAC and BCMA expression</td>
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CB-011 uses a patient-specific, potent, humanized anti-BCMA T cell therapy

CB-011: Healthy donor leukapheresis-derived T cells

Tumor antigen: BCMA

Indication: r/r multiple myeloma (MM)

Status: ongoing Phase 1 trial enrolling in dose escalation

CBMoufflage Phase 1 trial design

Part A: 3+3 dose escalation to determine safety, MTD, RP2D

Part B: dose expansion to determine tumor response

r/r MM

Lymphodepletion

<table>
<thead>
<tr>
<th>CB-011</th>
<th>GRF-0</th>
<th>3 DAYS</th>
<th>5 DAYS</th>
<th>3 MONTHS</th>
<th>6 MONTHS</th>
<th>9 MONTHS</th>
<th>12 MONTHS</th>
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<tr>
<td>Safety and tolerability</td>
<td>Response assessment</td>
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Cyclophosphamide (300 mg/m²) or Fludarabine (30 mg/m²) in patients with prior BCMA-directed therapy.

Dose level 1: 50 × 10^6 CART cells (enrolling patients)

NCT05722418 on clinicaltrials.gov

CBMoufflage key inclusions

• Documented diagnosis of multiple myeloma based on IMWG 2016 criteria
• Measurable disease at screening:
  • Serum M-protein > 1.0 g/dL or urine M-protein > 200 mg/24 h
  • Light chain MM without measurable disease in the serum or urine: serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio
• Received ≥ 3 MM prior lines of therapy (must include a PI, an IMID, and/or an anti-CD38 monoclonal antibody)
• Documented evidence of PD on or within 12 months of last line of therapy. Patients with documented evidence of PD within the previous 6 months and who are refractory or non-responsive to their most recent line of therapy are eligible
• ECOG grade 0 or 1
• Prior BCMAMO-directed therapy allowed (except CART) and if ≤ 3 months from last dose of BMCA-targeted therapy

IMIDs: immunomodulatory drugs; PI: proteasome inhibitor; ECOG: Eastern Cooperative Oncology Group; IMWG: International Myeloma Working Group

CBMoufflage trial participating sites

- New York: Memorial Sloan Kettering Cancer Center, New York, NY
- OHIO: Oncology Hematology Care (OHCH)
- TENNESSEE: Sarah Cannon Cancer Institute

Additional sites planned

CBMoufflage key inclusion criteria

• Allogeneic CART-T cell therapy is an investigational treatment that may address the unmet needs of r/r MM patients
• CB-011 is an allogeneic anti-BCMA CART cell therapy engineered using Cas12a chRMDA technology.
• CB-011 is the first allogeneic CART-T cell therapy in the clinic, to our knowledge, that is engineered to improve antitumor activity through an immune cloaking strategy with a B2M knockout and insertion of a B2M-HLA-E fusion protein to blunt immune-mediated rejection, and it is derived from healthy donor T cells

CB-011CaMoufflage trial summary

This is a first-in-human trial investigating the safety and efficacy of CB-011 as a single infusion in patients with r/r MM at clinical sites across the United States

Patient enrollment is ongoing in the dose escalation phase of the CBMoufflage trial

CBMoufflage key exclusion criteria

• Prior treatment with CART-T cell therapy directed at any target
• Monoclonal antibody for treatment of MM within 21 days
• BITE/ADC within 90 days; IMID within 7 days; PI or chemo within 14 days; XRT within 14 days
• AllSCCT within 6 months prior to LDC
• AllSCCT > 6 months prior without GVHD and immunosuppressive therapy can enroll
• Auto SCT < 12 weeks prior to LDC
• Known active or prior history of CNS involvement
• Seropositive for HIV, active HBV/HCV infection
• Plasma-cell leukemia, WM, POEMS, clinically significant AL
• Malignancy within 2 years (unless treated with curative intent and NED > 2 years; adequately treated non-malignant skin cancers)
• Clinically significant organ dysfunction

BITE: bispecific T cell engager; ADC: antibody drug conjugate; GVHD: graft-vs-host disease; CNS: central nervous system; LDC: lymphodepleting chemotherapy; POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder; WM: Waldenstrom macroglobulinemia; AL: amyloidosis; HIV: human immunodeficiency virus; HBV: hepatitis B virus; HCV: hepatitis C virus; NED: no evidence of disease

ACCEPTED Manuscript

A first-in-human Phase 1, multicenter, open-label study of CB-011, a next-generation CRISPR-genome edited allogeneic anti-BCMA immune-cloaked CART cell therapy, in patients with relapsed/refractory multiple myeloma (CaMMouflage trial)

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