Glycoprotein NMB (gpNMB) -

- Internalized transmembrane glycoprotein overexpressed in multiple tumor types including ~80% of melanomas
- High tumor gpNMB expression associated with shorter metastasis-free and overall survival
- Upregulated in BRAFV600 mutant melanoma following BRAF/MEK inhibition

The gpNMB-targeting antibody, CR011, is linked to the potent cellular toxin monomethylauristatin E (MMAE) using Seattle Genetics proprietary technology. Delivers MMAE to gpNMB-expressing tumor cells.

Three completed clinical studies in melanoma and breast cancer - Rash, neuropenia, and neuropathy most common treatment-related toxicities

- Promising overall response rate (ORR) - ORR = 15% in Ph 1/2 melanoma study
- Rash associated with greater clinical benefit in breast cancer and melanoma
- Overexpression of gpNMB associated with improved outcome in breast cancer

- Prevention of recurrence in high risk patients
- gpNMB overexpression with >10% gpNMB+ over time in primary vs. metastatic tumors

FUTURE DIRECTIONS & RATIONALE FOR COMBINATION WITH IMMUNOTHERAPY

- Preclinical data suggest antimetastatic activity of ADC-MMAE may be enhanced when combined with variullumab, an anti-CD27 monoclonal antibody or CPI
- Microtubule-depolymerizing cytotoxic agents such as MMAE also convert tumor-resident tolerogenic dendritic cells into active antigen-presenting cells
- Building upon the positive monotherapy results, an additional cohort evaluating GV in combination with variullumab is enrolling (NCT02032339). Subsequent cohorts will evaluate combination with CPI
- Pre-entry skin biopsies will be obtained to investigate potential predictors of response to GV, given the association of rash and outcome

CDX011-05 STUDY DESIGN

Patient Population
- Unresectable Stage III or IV melanoma
- Refractory to checkpoint inhibitor (CPI)
- > anti-CTLA-4, PD-1, or PD-L1
- BRAF/MEK inhibition in BRAFV600 mutant melanoma
- ≤ 1 prior cytotoxic regimen

Study Design
- Single arm, open-label, Phase 2 trial
- GV 1.9 mg/kg IV infusion, 90 minutes
- Every three weeks dosing schedule
- Tumor assessments every 6 weeks for 6 months, then every 9 weeks

Patient Characteristics, Exposure, and Tolerability

- Male (n=62) 34 (55)
- Age, years (median [min, max]) 67.0 (19, 86.0)
- ECOG PS 0-1 (n=62) 52 (84)
- Stage (n=62)
  - I 1 (2)
  - II 41 (66)
  - III 10 (16)
- Duration of Advanced Disease, months (median, min, max) 1.9 (1, 3.188)
- BRAF Mutation (n=59) 12 (19)
- RAS Mutation (n=56) 2 (3.4)
- 2+ Disease Sites (n=51) 27 (44)
- Prior Revisions (n=57)
  - 1+ 30 (52)
- Prior Therapies (n=55)
  - Checkpoint Inhibitor 62 (100)
  - Anti-CTLA-4 50 (91)
  - PD-1/PD-L1 inhibitor 58 (94)
  - BRAF/MEK inhibitor 8 (15)
  - Chemotherapy 13 (23)
  - Cytokines 21 (39)

Toxicities (n=57)

<table>
<thead>
<tr>
<th>toxicity</th>
<th>toxicity grade ≥3</th>
<th>toxicity overall</th>
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<tbody>
<tr>
<td>Alopecia</td>
<td>NA</td>
<td>47%</td>
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<tr>
<td>Neutropenia</td>
<td>5%</td>
<td>47%</td>
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<tr>
<td>Rash</td>
<td>10%</td>
<td>47%</td>
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<tr>
<td>Fatigue</td>
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<td>40%</td>
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<tr>
<td>Neutropenia</td>
<td>19%</td>
<td>34%</td>
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<tr>
<td>Nausea</td>
<td>0%</td>
<td>32%</td>
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<tr>
<td>Decreased appetite</td>
<td>0%</td>
<td>27%</td>
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<tr>
<td>Pruritus</td>
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<tr>
<td>Diarrhea</td>
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<tr>
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<tr>
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</tr>
<tr>
<td>Leukopenia</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Maximum Tumor Shrinkage

- Duration of Response (n=57)
  - Complete Response (CR) 6 (10, 11 months)
  - Partial Response (PR) 10 (10, 11 months)

Endpoints / Statistical Design

- Primary endpoint: ORR
- Secondary endpoints:
  - Progression-Free Survival (%)
  - Overall Survival (%)
  - Safety
  - gpNMB expression vs. outcome

Endpoints for positive study
- Threshold for positive study: 6 weeks from baseline
- Includes pts without progression for 3 weeks

GPNMB Expression

- Pre-entry tumor tissues analyzed by immunohistochemistry at a centralized laboratory
- Tumors were gpNMB+ for all 58 pts with available tissue, and 79% had tumors with 100% epithelial cells gpNMB+
- No clear correlation of gpNMB expression and outcome in this population

ACTIVITY

Examples of Responses in gpNMB-Expressing Patients

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