NCI 9855: A Phase 2 Study of CDX-011 (Glembatumumab vedotin) for Metastatic Uveal Melanoma

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Disclosures

Amgen – advisory board
Bristol Myers-Squibb – clinical trial support
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Deciphera – clinical trial support
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Glaxo SmithKline – clinical trial support
Immunocore – data safety monitoring committee
Novartis – clinical trial support
Reata – clinical trial support, data safety monitoring board
Background – antibody drug conjugates

3 main components:

1. Antibody directed against a specific target
2. Cytotoxic agent
3. Protease-cleavable linker that covalently attaches the cytotoxin to the antibody

CDX-011: glembatumumab vedotin

1. IgG2 directed against GPNMB, a transmembrane protein involved in metastasis and invasion. 86% GPNMB expression in uveal melanoma (Williams M., Mel Res 2010)
2. Microtubule inhibitor MMAE (mono-methylauristatin E)
3. Valine-citrulline peptide linker covalently binds MMAE to anti-GPNMB

CR011: fully-human IgG2 targeting GPNMB  MMAE: dolastatin-like tubulin inhibitor
Study Schema

• Single-arm, open-label Phase 2 study

• Simon two-stage minimax design
  – 18 patients in first stage
  – 14 patients in second stage
  – Up to 34 patients total

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- Eligible uveal melanoma patients
- Baseline tissue for GPNMB IHC
- Glembatumumab 1.9 mg/kg IV every 3 weeks
- Day 21 biopsy for GPNMB IHC
- Optional biopsy for GPNMB IHC
- Treatment until progression or toxicity
STUDY ENDPOINTS

• **Primary** = Overall Response Rate using RECIST 1.1

• **Secondary** = Progression-free survival, Overall survival, GPNMB expression via IHC

• **Exploratory** = Immunophenotyping of tumors, rash as a biomarker
Enrollment to date

- UNIVERSITY OF KANSAS: 1
- NORTHWESTERN UNIVERSITY: 1
- MAYO CLINIC: 3
- WASHINGTON UNIVERSITY: 4
- UNIVERSITY OF COLORADO CANCER CENTER: 4
- OHIO STATE: 4
- MD ANDERSON CANCER CENTER: 14
Related AEs By Class View (NCI Standard Reports)
Complete response: 0
Partial response: 11% (2)
Stable disease: 68% (13)
Disease Progression: 21% (4)
Overall response rate: 11% (2)
Disease control rate: 79% (15)
Summary

• Glembatumumab vedotin 1.9 mg/kg has been well-tolerated to date in metastatic uveal melanoma
• Gr 3/4 toxicities have been mainly myelosuppression
• First stage enrollment met trigger for continuation
• Second stage enrollment near complete
• Full study results expected in 2nd Quarter 2017
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