Implications for clinical practice and study design

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Disclosure slide

• Advisory Board (Merck KGaA)
HNSCC: One disease, different subsets

Personalized Medicine

Old Way

Patient's tissue sample

Pathology

New Way

Patient's tissue sample or blood sample

Proteomics

Proteins

Mass spectrometry

Proteomic image

Genomics

DNA

Gene chip

Microarray image

“I can’t explain it—it’s just a funny feeling that I’m being Googled.”
Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination
Molecular characterization of head and neck cancer: how close to personalized targeted therapy?
Targeted Therapies in HNSCC

- While targeted therapies have the potential to be personalized, their current use in HNSCC is not personalized.
- Cetuximab remains the sole US FDA-approved molecular targeted therapy available for HNSCC but EGFR as a molecular target has yet to be individualized for HNSCC.
- Only a small subset of HNSCC patients derives clinical benefit from cetuximab.
- Toxicity and cost of treatment with cetuximab are substantial and should be considered.
The mutational landscape of HNSCC

Clinical Trial Design and Target Validation

Heterotopic Tumografts

“Window of opportunity” studies

Bevacizumab and Erlotinib in Newly Diagnosed SCCCHN

Duke Trial 7077 Schema

B: bevacizumab 10 mg/kg q 2 weeks
E: erlotinib 100mg/day except during CDDP
CDDP: cisplatin 33 mg/m2 x 3 days
RT: 70 Gy/5.5 wk
DCE-MRI, MRS, serum (VEGF, TGF-α, IL8,bFGF, D-dimer, PAI-1, osteopontin)
Clinical Trial Design for predictive biomarker validation

- Efficient development of targeted therapies that may only benefit a fraction of patients requires clinical trial designs that use biomarkers to identify sensitive subpopulations
- Well-designed retrospective analyses of well-conducted prospective randomized trials can bring forward effective treatments to marker-defined subgroups of patients in a timely manner
- Randomized phase II biomarker trial design, which, after completion, recommends the type of phase III trial to be used for the definitive testing of the therapy and the biomarker are crucial in the development of targeted therapies
CONCLUSIONS

• Molecular targeted therapy in HNSCC continues to make strides, and holds much promise
• While targeted therapies have the potential to be personalized, their current use in HNSCC is not personalized
• Future research needs to identify factors that correlate with response and the underlying genotype-phenotype relationship that dictates this response
• Comprehensive exploration of genetic and epigenetic landscapes in HNSCC is opening new frontiers to further enlighten and mechanistically inform newer as well as existing molecular targets, and to set a course for eventually translating these discoveries into therapies for patients
Thank you