Personalized medicine in head and neck cancer

CONCLUSION AND CLINICAL PERSPECTIVES

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Disclosures

• **SF**: Honoraria from Merck, Novartis.
Trials of 2e line for advanced HNSCC in ALL COMERS...

1st line including EGFR inhibitors

Other Targeted Therapies (PI3K-I, CXCR4-I)

Optimisation EGFR-I (Broad spectrum inhibitors)
The PI3K/mTOR pathway is frequently activated in HNSCC

(No RAS mutation)

PI3k gene amplification (18-22%) or mutation


Receptor activation EGFR >90%

PTEN Loss of function: gene mutation (10-15%), deletion or promoter methylation

Everolimus

Prognostic value of the chemokine receptor CXCR4 and epithelial-to-mesenchymal transition in patients with squamous cell carcinoma of the mobile tongue

CXCR4 Expression (IHC)

Albert S, Oral Oncol 2012
Deciphering ACC biology using molecular genetics
Active immunotherapy for head and neck cancers: Induction of T cell response

Tumor immunotherapy:
Antibodies to endogenous suppressor pathways (anti-PD1, anti-CTLR4) block Tregs & unleash autoimmune anti-tumor effector immunity.
From all comers... to PERSONALIZED therapeutic approach

EGFR overexpressing tumors (SCC)

Determination of drugable targets (PI3K/mTOR, PD1...)

Identification of resistance pathways
Patients with refractory cancer (all tumor types) → Informed consent signed → Tumor biopsy → NGS+ Cytoscan HD +IHC → Bioinformatics

Non eligible patient → Molecular biology board → Specific therapy available

Eligible patient → Informed consent signed

Targeted therapy based on molecular profiling

Conventional therapy at physicians’ discretion

SHIVA – Randomized proof-of-concept phase II trial comparing molecularly targeted therapy based on tumor molecular profiling versus conventional therapy in patients with refractory cancer (PI: Christophe Le Tourneau)

Ex Vivo evaluation of drugs in HNSCC

Biopsy under local anesthesia

Fresh tumor-tissue cultured for 48h
To test targeted therapies

Biomarkers analysis by immunofluorescence

Control
Drug A
Drug B

Inteligence Medicine  Protein and nucleic acid expressions
26–30 September 2014, Madrid, Spain

Chemo-biogram  Effects of drugs on tissue biomarkers  esmo.org
Conclusions

✓ New biological techniques allow better characterization of HN cancers

✓ Several targets (PI3K/mTOR, PD1) are currently emerging as promising to improve therapeutic options

✓ Modern design of clinical trials are warranted to include tumor biological profile

✓ A real breakthrough will result from testing new drugs in selected HN cancer patient subpopulations