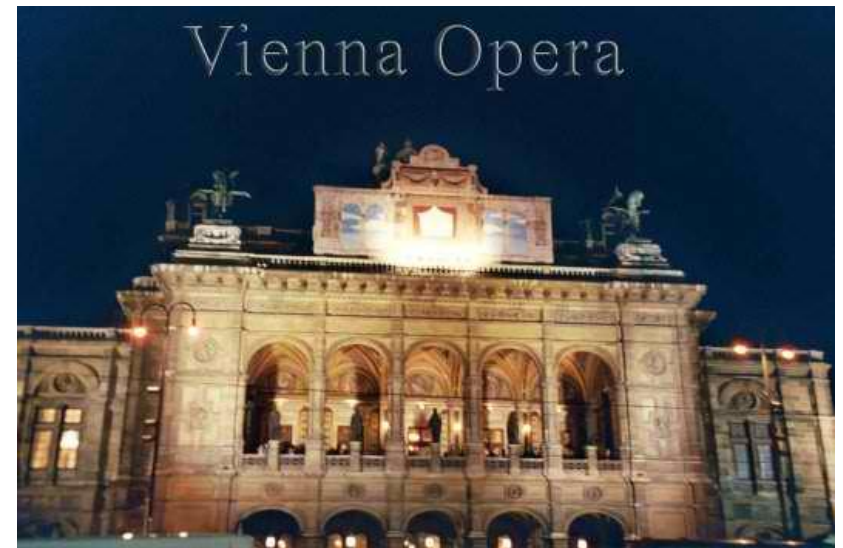


Implications for clinical practice and study design

37th ESMO Congress
Vienna, Austria
Amanda Psyrri, MD, PhD



Disclosure slide

- Advisory Board (Merck KGaA)

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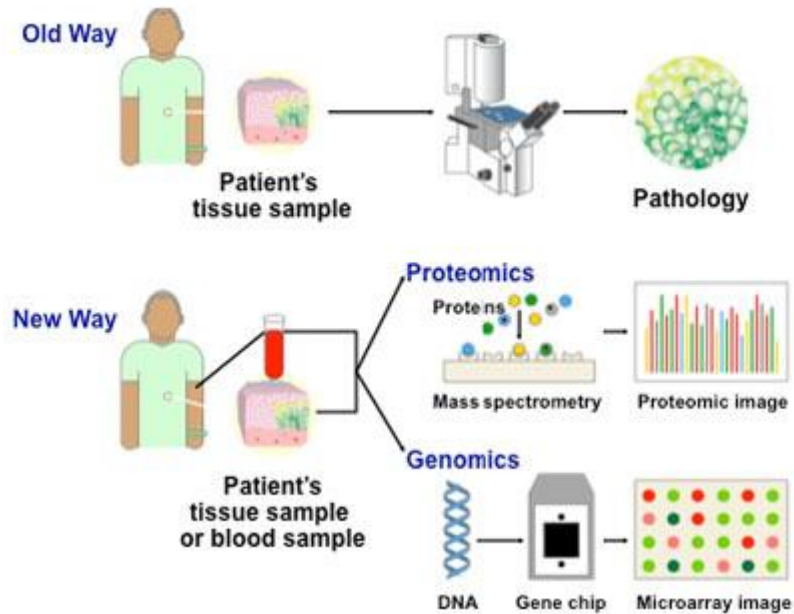
HPV(-) HPV(+)

RMSD protein RMSD
DNAC UNK73
H. sapiens similar to Succinate dehydrogenase [ubiquinone] flavoprotein subunit, LOC373586
NFE2L homolog 2, penta HEE
NARF, member of RAS oncogene family NARP2B
GPCR-105 protein hGPC113
home sapiens hypothetical protein DKF Z6791C121 DKF Z6791C121
ring finger protein 32, CNF3
transcriptional corepressor protein 2 SYCP2
home sapiens CNA FLJ12862 fa, clone BBAW2010548
nuclear receptor subfamily 1, group 3, member 2 NR1C2
GAAO22 protein KIAA2022
home sapiens hypothetical gene supported by AL356405, BC034005 LOC374873
germ cell specific Y-axis binding protein YBC2
home sapiens CNA FLJ12846 fa, clone T5370201172
interleukin 17 receptor 3 IL17RB
hypothetical protein FLJ14569 fa FL14569
luciferase enhancer of sp11, Drosophila HE-S1
home sapiens CNA clone IMAGE 4440313, partial cds
FLJ32363 protein FLJ32363
hypothetical protein FLJ10460 FLJ10460
cyclin-dependent kinase inhibitor ZA melanoma, p16, inhibits CDKN2A
similar to hREN CNA C72037008 gene MGC15397
nucleoporin p15 NUPP15
nucleoporin p25, NDC80 RNA
nucleoporin p35 NUP35
TAF11A RNA polymerase II, TATA box binding protein TBP associated factor, 50kDa TAF11
home sapiens, clone IMAGE 534460
home sapiens, clone IMAGE 527371
TAF11B RNA polymerase II, TATA box binding protein TBP associated factor, 50kDa TAF11
home sapiens LOC374817 LOC374817
hypothetical protein NC042424 MGC2542
hypothetical protein FLJ31992 FA FLJ31992
potassium voltage-gated channel, delayed-rectifier, subfamily S, member 1 KCNS1
home sapiens LOC375195 LOC375195
neurofilament, heavy polypeptide 200kDa NFH
inhibitor of growth family, member 1 like ING1L
argininosuccinate lyase ASB1
ZNF 2796-2646 protein DKF Z27965646
hypothetical protein LOC226128 LOC226128
GIA4541 protein KIA04541
TfII alpha receptor associated protein TRA15 TRA16
CRIS-like gene, PPRX
hypothetical protein LOC283129 LOC283129
hypothetical protein FLJ10460 FLJ10460
SCORIN related, matrix-associated case-dependent regulator of chromatin, subfamily A, SMARCA3
transcription factor Dsp-EZF differentiation partner 2 TFDP2
topoisomerase I DNA binding protein TOPBP1
chromosome 9 open reading frame 40 C9orf40
v-type ATP domain transfer factor TFA, absent 5' splice, tRNA EFY85
hypothetical protein FLJ33794 FLJ33794
hypocretin, hypocretins 18 HTAN
MCMI microchromosome maintenance deficient 2, miton S, consensive MCMI2
myc C-terminal A, myeloid acute leukemia C-terminal A dithiolase EPHACH
BAF53 BAF53A
home sapiens, clone IMAGE 530675
home sapiens mRNA cDNA DKF Z65A01016 from clone DKF Z65A01016
replication fork co-factor 14, 27kDa CFK14
polymerase RNA II Div. directed polyphosphatase IN POLDH
mitochondrial ribosomal protein L47 MRPL47
MCMI2 microchromosome maintenance deficient 2, miton S, consensive MCMI2
organismal cell death 10 PCOLCE10
zinc alpha 1 metalloprotein domain DP1A
hypothetical protein NC042465 MGC24660
dihydrofolate reductase DHFR
ribonucleic acid-specific protein 1 USP1
nucleoside triphosphate dependent glyoxylate 6 homology type, alpha 1 3-glucosyltransferase AGI6
CCZ-1 cell surface cysteine 7.1, consensive CCZ7
hypothetical protein FLJ12888 FLJ12888
hypothetical protein FLJ12573 FLJ12573
tissue zipper protein FKSG124 FKSG124
MCMI microchromosome maintenance deficient 6 MISS homolog, S, pome 5, consensive MCMI5
enhancer of zeste homolog 2 Drosophila EZH1
brain-like FMSL2
home sapiens CNA FLJ41872 fa, clone BSNAC2003897
home sapiens CNA FLJ12839 fa, clone KBM00100589
home sapiens CNA FLJ28559 fa, clone SLV00568
myosin MYIN
cyclin-dependent kinase inhibitor 2C p18, inhibits CDK4 CDKN2C
Spax1 CNA, AT17-dependent G12
muscle LIM1
ME1 myofibril associated viral replication site 1 homology mouse ME1S1
hypothetical protein LOC360771 LOC360771
taglin X mental retardation TMFMT1
helium ion channel K-C auto-inhibition 2 HSK2
null, home sapiens 1 colon cancer; noroglycosyl type 2 E, col MLH1
hypothetical protein LOC134541 LOC134541
chaperone, EGF LAG seven-pass transmembrane receptor 3 flamingo homology, Drosophila CELSR3
hypothetical protein H090107 LOC1011618
kin IV BRIC like Drosophila vBRIC1
noscapene acetylase protein 2 NAPI2

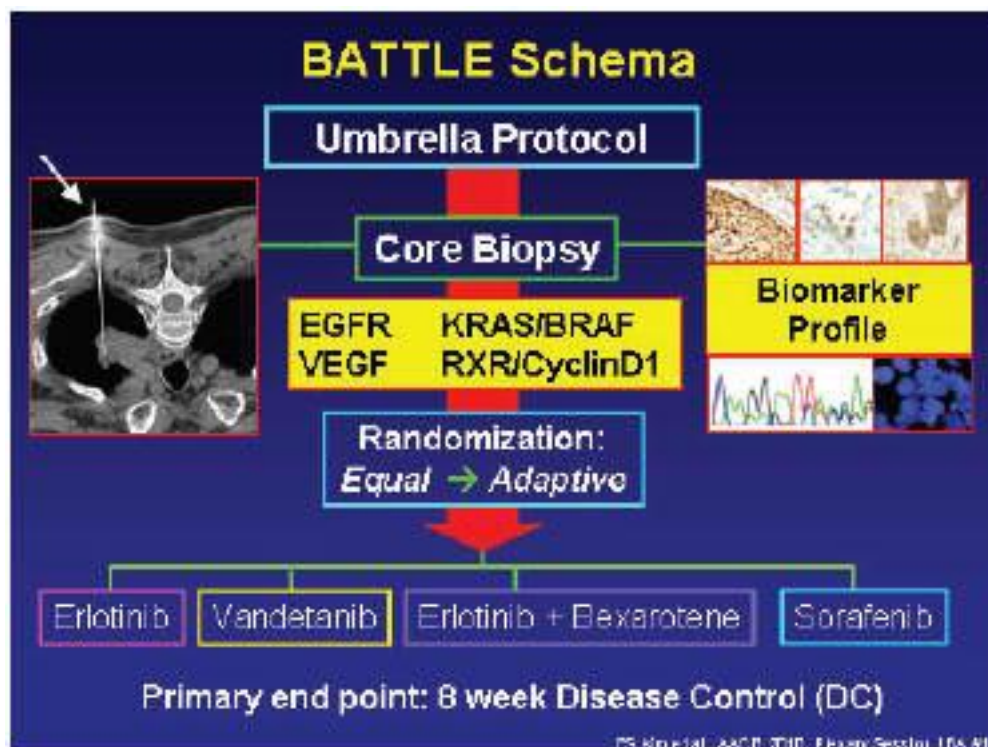


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Personalized Medicine



Biomarker-integrated Approaches of Targeted Therapy for Lung cancer Elimination

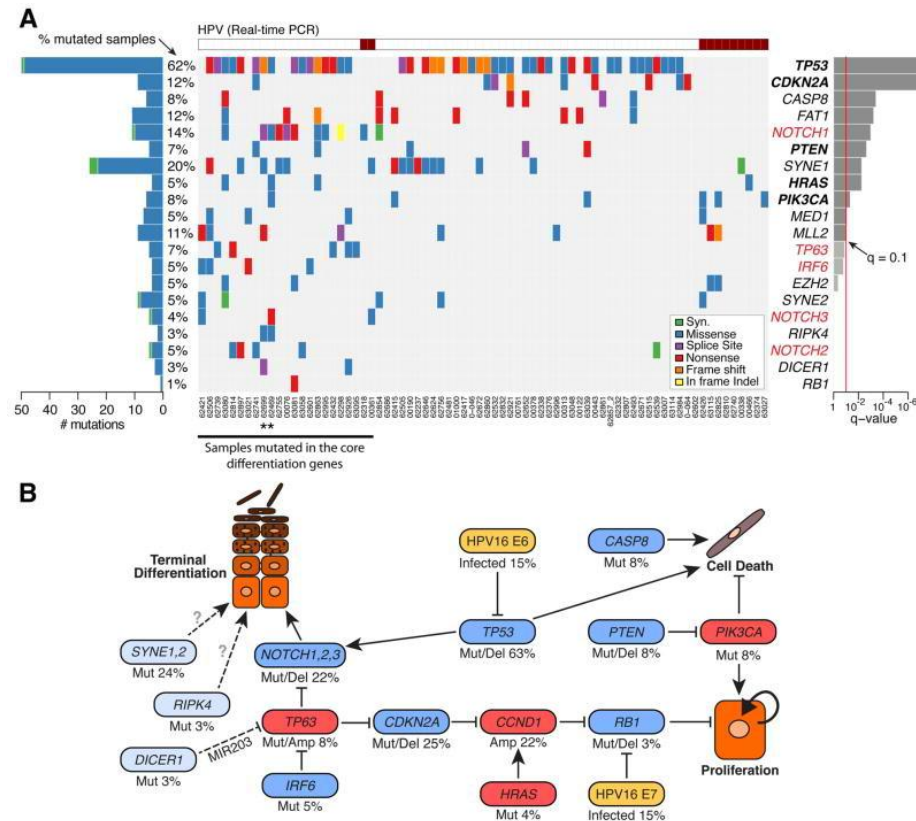


Molecular characterization of head and neck cancer: how close to personalized targeted therapy?

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

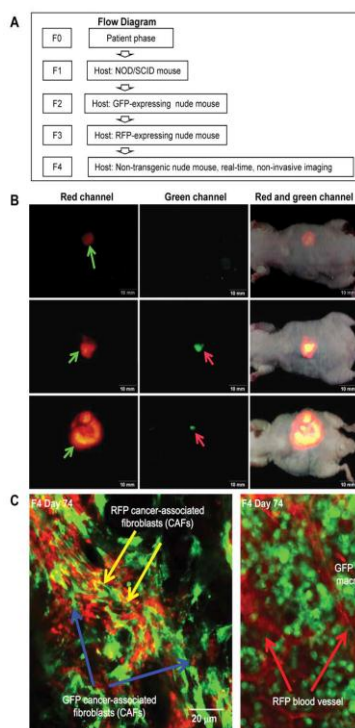
The mutational landscape of HNSCC



[Stransky et al: Science. 2011 August 26; 333\(6046\): 1157–1160.](#)

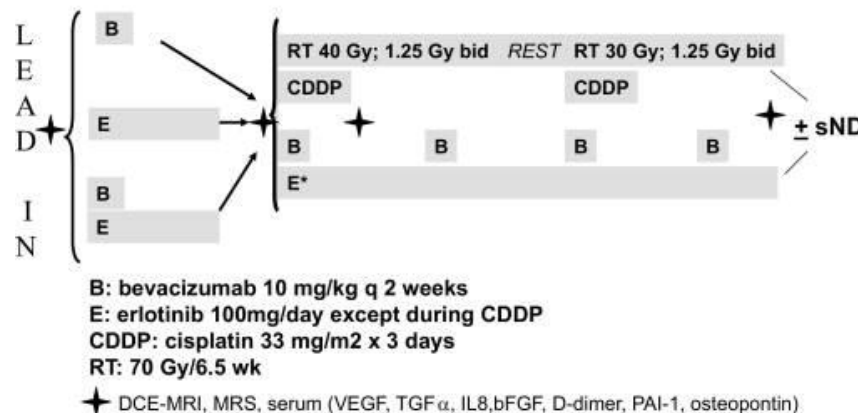
Clinical Trial Design and Target Validation

Heterotopic Tumorgrafts



“Window of opportunity” studies

Bevacizumab and Erlotinib in Newly Diagnosed SCCHN Duke Trial 7077 Schema



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

