Kura Oncology Investor Day

November 16, 2017

KURA ONCOLOGY

DEVELOPING PRECISION MEDICINES TO TREAT CANCER

Forward Looking Statements

This presentation contains forward-looking statements. Such statements include, but are not limited to, statements regarding our research, pre-clinical and clinical development activities, plans and projected timelines for tipifarnib, KO-947 and KO-539, plans regarding regulatory filings, our expectations regarding the relative benefits of our product candidates versus competitive therapies, and our expectations regarding the therapeutic and commercial potential of our product candidates. The words "believe," "may," "will," "estimate," "promise," "plan", "continue," "anticipate," "intend," "expect," "potential" and similar expressions (including the negative thereof), are intended to identify forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: our future preclinical studies and clinical trials may not be successful; the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our product candidates; we may decide, or the FDA may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our product candidates, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; our product candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our product candidates could delay or prevent regulatory approval or commercialization; we may not be able to obtain additional financing. New risk factors and uncertainties may emerge from time to time, and it is not possible for Kura's management to predict all risk factors and uncertainties.

All forward-looking statements contained in this presentation speak only as of the date on which they were made. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Kura Oncology Investment Highlights

- Developing precision medicines for well-defined cancers with significant commercial potential
- Positive Phase 2 trial in HRAS mutant head and neck squamous cell carcinomas (HNSCC) for lead program, tipifarnib
  - 67% response rate (n=6); confirmed responses with durability > 1 year
  - Plan to initiate pivotal trial in HRAS mutant HNSCC in 2018
  - Patent exclusivity in HRAS mutant HNSCC indication in U.S. to 2036
- Additional Phase 2 trials with data in 2018 expand opportunity for tipifarnib
- Additional pipeline opportunities
  - Potent and selective ERK inhibitor (KO-947) with clinical data expected in 2018
  - Menin-MLL inhibitor (KO-539) with robust activity in preclinical models of AML
- Strong cash position: $100.8 million as of September 30, 2017*
- Leadership team with proven oncology drug development experience

* Cash, cash equivalents and short-term investments

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Kura Leadership Team

Troy Wilson, Ph.D., J.D.
Chief Executive Officer

Yi Liu, Ph.D.
Chief Scientific Officer

Pingda Ren, Ph.D.
SVP, Chemistry and Pharmaceutical Sciences

Antonio Gualberto, M.D., Ph.D.
Chief Medical Officer

Heidi Henson
Chief Financial Officer

Annette North, LLB
SVP and General Counsel

wellspring biosciences · Pfizer · intellikine · ambit · Genomics Institute of the Novartis Research Foundation · EMD SERONO · Takeda

Proven oncology drug discovery and development expertise

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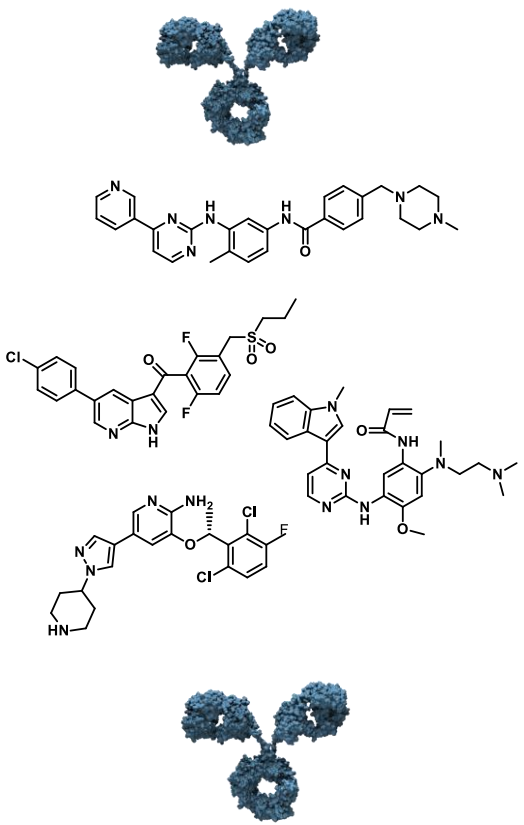
Biomarkers Have Potential to Unlock the Value of Precision Medicines



Precision Medicines

+

Protein Expression

Genetics

Histology

Biomarkers

→

Enhanced Clinical Benefit for Patients

- Zelboraf® vemurafenib (BRAF V600E)
- Herceptin® trastuzumab (HER2)
- glivec® imatinib (BCR-ABL)
- TAGRISSO™ osimertinib (EGFR T790M)
- XALKORI® CRIZOTINIB (ALK-ROS1)
- KEYTRUDA (PD-1)

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Product Candidate Pipeline

PROGRAM	PRECLINICAL	CLINICAL PROOF OF CONCEPT	PIVOTAL
Tipifarnib Farnesyl Transferase Inhibitor	HRAS Mutant Solid Tumors		*Expect to initiate pivotal trial in 2018*
	Peripheral T-cell Lymphomas		
	Myelodysplastic Syndromes		
	Chronic Myelomonocytic Leukemia		
KO-947 ERK Inhibitor	Solid Tumors		
KO-539 Menin-MLL Inhibitor	Acute Leukemias		

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Pipeline with Large Market Opportunity

PRODUCT CANDIDATE	TUMOR TYPE	TARGET POPULATION
Tipifarnib (Phase 2)	$HRAS^{mut}$ HNSCC	2,800-3,400
	$HRAS^{mut}$ Sq-NSCLC	1,000-1,700
	PTCL	1,500-2,500*
	MDS	15,000-18,000**
	CMML	750*
KO-947 (Phase 1)	HNSCC	10,000-20,000*
	$KRAS^{mut}$ NSCLC	23,000
	$BRAF^{mut}$ NSCLC	5,000
KO-539 (Preclinical)	MLL-rearranged leukemias	3,500
	$NPM1^{mut}$/$DNMT3A^{mut}$ AML	9,600

* Biomarker still under evaluation for these indications; these reflect estimates of the biomarker-positive subset for each indication

** Estimate of the prevalence of MDS patients (approx. 50,000-60,000 patients in the U.S.) who would be positive for a tipifarnib biomarker

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Anticipated Near-Term Milestones

2017

- ✓ Initiate Phase 2 trial of tipifarnib in CMML
- ✓ Initiate Phase 1 trial of KO-947
- ✓ Data from Phase 2 trial of tipifarnib in PTCL
- ✓ U.S. patent for use of tipifarnib in HRAS mutant HNSCC
- ✓ Positive Phase 2 trial of tipifarnib in HRAS mutant HNSCC
- ✓ Data for KO-539 in preclinical models of AML
- □ Preliminary results from Phase 2 trial of tipifarnib in CMML (ASH)
- □ Role of CXCL12 as potential target in hematologic malignancies (ASH)

2018

- □ Additional data from Phase 2 trial of tipifarnib in HRAS mutant HNSCC
- □ Data from Phase 2 trial of tipifarnib in MDS
- □ Additional data from Phase 2 trial of tipifarnib in PTCL
- □ Additional data from Phase 2 trial of tipifarnib in CMML
- □ Data from Phase 1 trial of KO-947
- □ Initiate pivotal trial for tipifarnib in HRAS mutant HNSCC

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Tipifarnib in HRAS Mutant Head and Neck Squamous Cell Carcinomas (HNSCC)

Head and Neck Squamous Cell Carcinomas

SIXTH MOST COMMON CANCER WORLWIDE[1]

- 63,030 new cases; 13,360 deaths in U.S. in 2017[2]
- 650,000 cases; 200,000 deaths/year WW

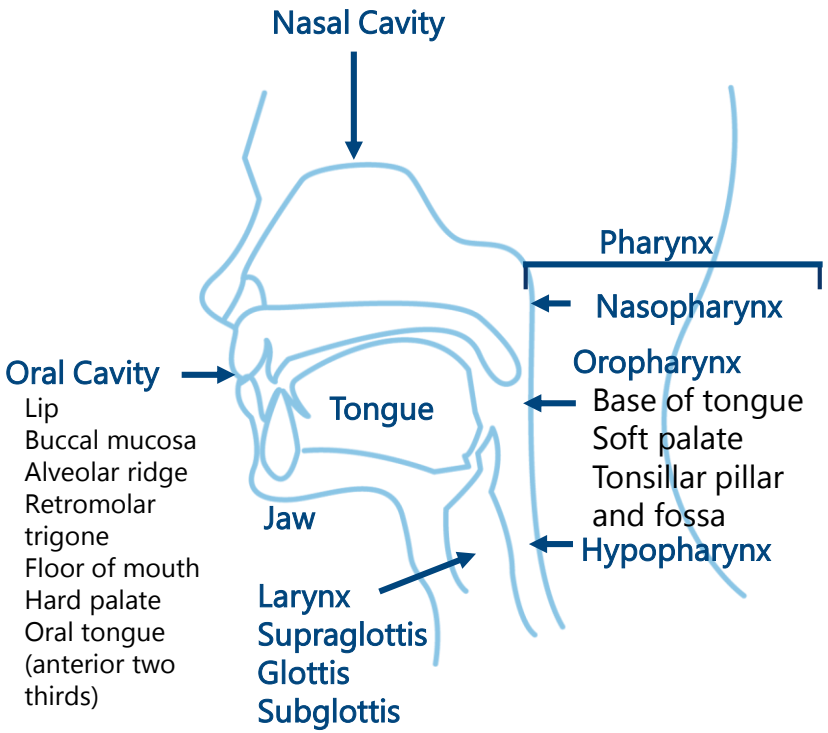
MAIN ANATOMICAL SITES[3]

- Oral cavity
- Nasopharynx/oropharynx/hypopharynx
- Larynx

SQUAMOUS HISTOLOGY OBSERVED IN 95% CASES

TWO MAIN ETIOLOGIES

- Tobacco smoking and alcohol consumption (HPV-)
- Infection with high-risk HPV (HPV+); largely limited to oropharyngeal cancers



[1] Globocaniarc.fr project. WHO
[2] Cancer.net. ASCO
[3] SEER training modules, head & neck cancer. NCI

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Recurrent / Metastatic HNSCC Treatment Paradigm[1]

LOCALIZED HNSCC

- Treated with surgery and radiation +/- chemo

RECURRENT HNSCC – FIRST LINE

- Patients with good performance status: platinum-based doublet (e.g., cisplatin/5-FU or carboplatin/paclitaxel)
  - ORR: 30% to 40%; median OS: 6-9 months regardless of specific drugs
  - Cetuximab commonly added to current treatment regimens
- Patients with poor performance status:
  - Single agent cetuximab or chemotherapy: cisplatin, carboplatin, 5-FU, taxanes, gemcitabine (for NPC)

RECURRENT HNSCC – SECOND LINE

- Taxanes; methotrexate is FDA approved but not commonly used in the U.S.
- Cetuximab single agent
- Pembrolizumab, nivolumab

[1] NCCN. Clinical practice guidelines in oncology: head and neck cancers. v.2.2013.

2nd Line Recurrent/Metastatic HNSCC Represents Significant Unmet Need

Response rates of 5-16% and limited duration of clinical benefit are observed with existing 2nd line therapies

	KEYTRUDA® (PEMBROLIZUMAB)	OPDIVO® (NIVOLUMAB)		ERBITUX® (CETUXIMAB)
Efficacy Study	Single Arm[1] N = 174	Nivolumab vs BSC[2] N = 240 vs 121		Single Arm[3] N = 103
		Nivolumab	Control[4]	
ORR	16% (CI 11 – 23)	13.3% (CI 9.3 – 18.3)	5.8% (CI 2.4 – 11.6)	13% (CI 7 – 21)
Median PFS/TTP	2.0 months	2.0 months	2.3 months	2.3 months
Median OS	8 months	7.5 months	5.1 months	6 months

Current targeted therapies have not yet capitalized on the progress in the understanding of the molecular landscape of HNSCC

[1] Keytruda Package Insert
[2] Opdivo Package Insert
[3] *J. Clin. Oncol.* 2007 Jun 1;25(16): 2171-7
[4] Investigator's choice of cetuximab, methotrexate or docetaxel

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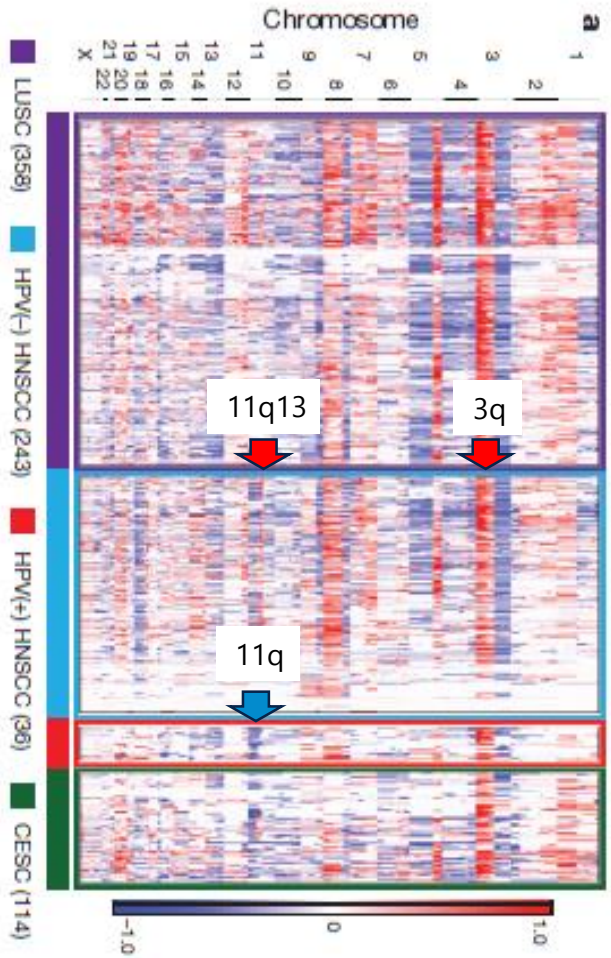
Genomic Landscape of HNSCC

- Genomic alterations are commonly seen in HNSCC regardless of HPV status[1]
- 3q amplifications containing the squamous lineage TP63 and SOX2 genes, and PIK3CA are seen in both HPV+ and HPV- tumors
- In HPV+ tumors, deletions in 14q, containing TRAF3, in 11q, including ATM1are also seen
- In HPV- tumors, 9p21.3, containing CDKN2A is commonly deleted while 11q13 containing CCND1, FADD and ANO1, and 11q22 containing BIRC2 and YAP1 are amplified
- Many of these genomic alterations are shared by other SCC tumors (e.g. lung and cervix SCC)



[1] Reviewed in Aung and Siu. Cancers of the Head & Neck (2016) 1:2

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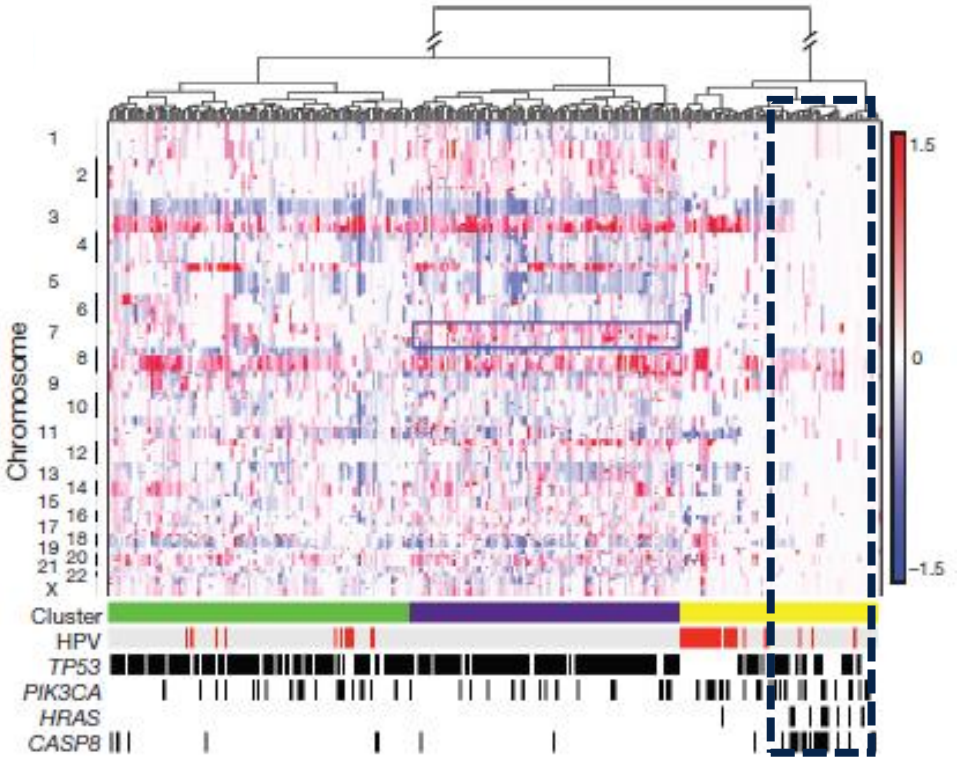
HRAS Mutations are Observed in an Unique Molecular Subset of HNSCC[1]



- HRAS mutations (~5% of tumors at diagnosis) are present in a distinctive molecular subset of HNSCC, characterized by
  - low rate of genetic alterations
  - less frequent TP53 mutation
  - frequent CASP8 inactivation
- **Hypothesis:** HRAS is the main oncogene driver of a subset of SCC tumors

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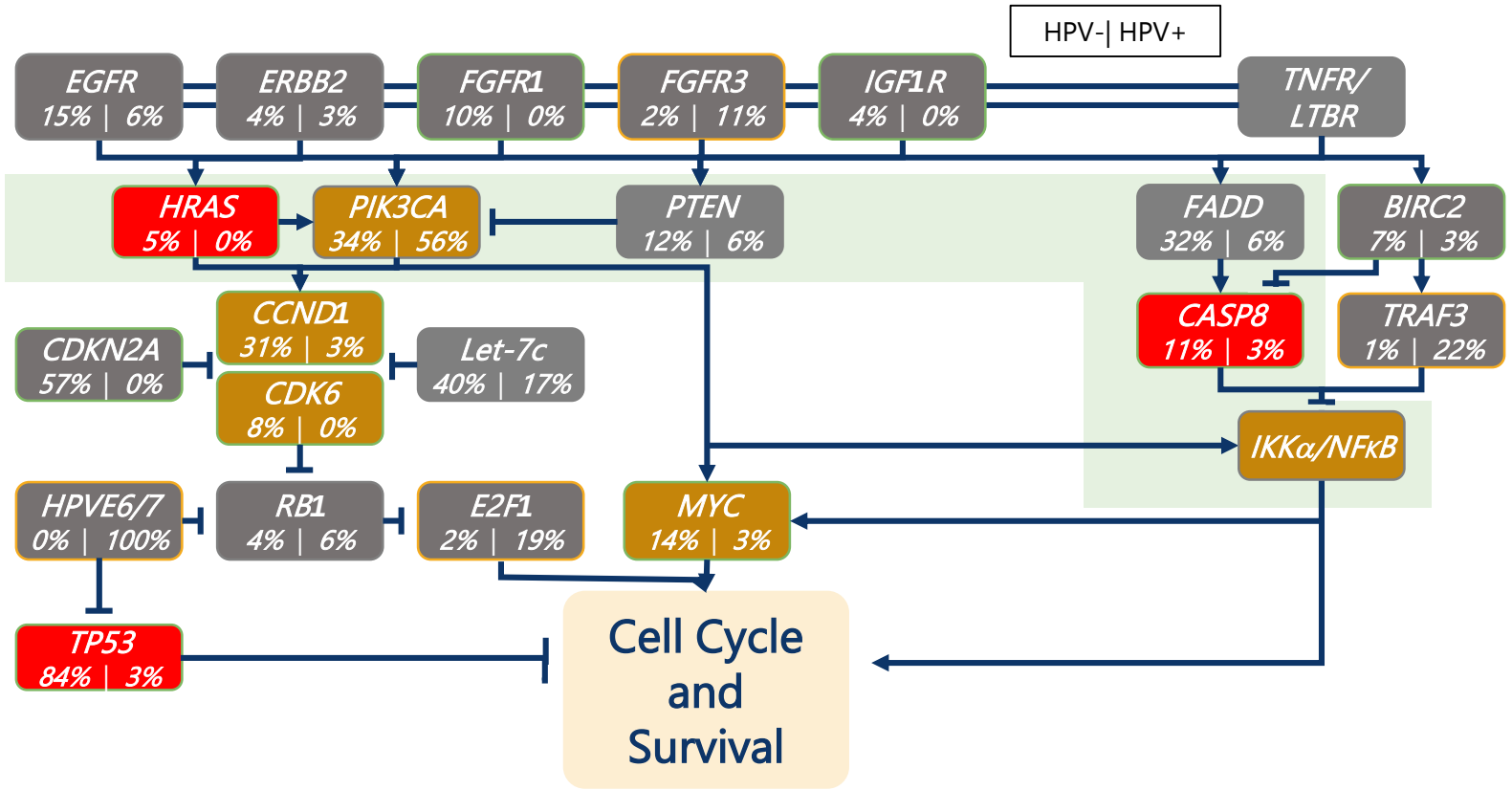
HRAS Mutations Define an Oncogenic Pathway in SCC

HRAS/CASP8 converge on IKKa/NF-kB and together with TP53 regulate cell growth and survival of SCC tumors of the head and neck, lung and skin [1,2]



[1] Cancer Genome Atlas Network 2015. *Nature* 517:576-82.
[2] Maeda 2007. *Clin Cancer Res.* 13:5041-7.

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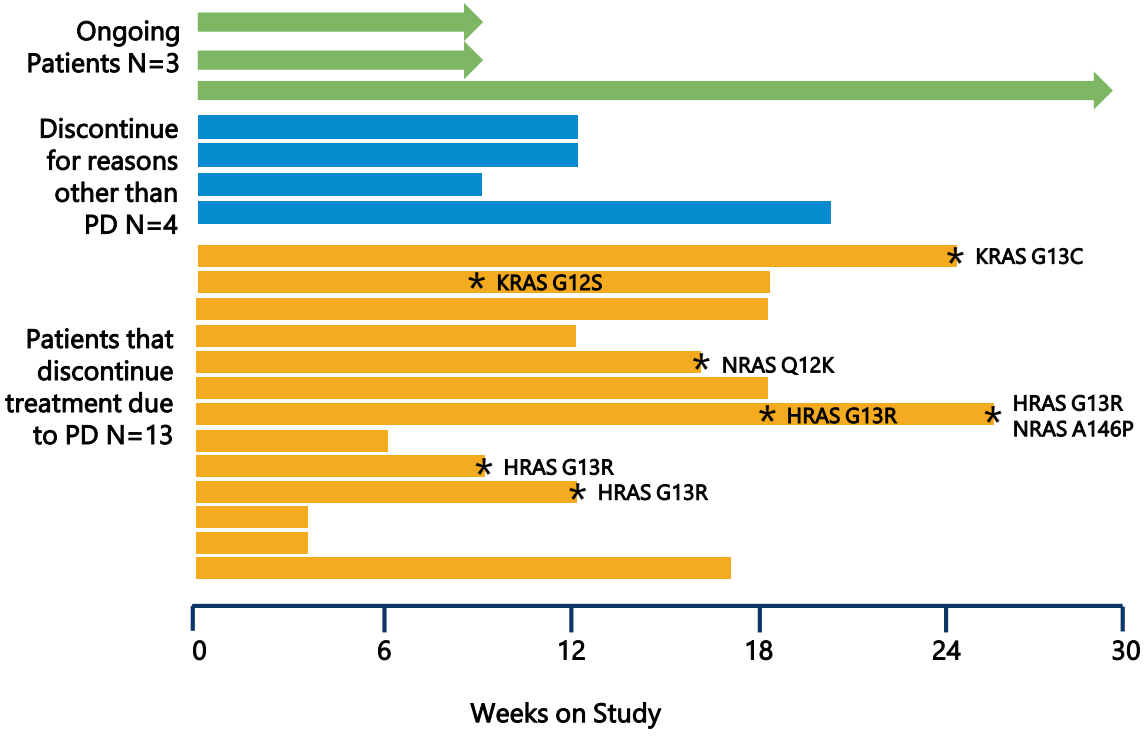
Acquired HRAS Mutations Develop During 1st Line Therapy[1]

- Braig *et al.* studied onset of resistance in 20 patients treated with cetuximab / platinum / 5-fluorouracil followed by cetuximab maintenance using liquid biopsies. Subjects were selected for RAS WT status at study entry



RESULTS

- RAS mutations detected in 6 of 13 patients that developed PD
- PD observed within 6 months of 1st line therapy
- 3 patients (3/20, 15%) developed HRAS mutations

CONCLUSIONS

- Results suggest a ~20% rate of HRAS mutation in 2nd line
  - 5% at diagnosis
  - 15% de novo treatment resistance related mutations

[1] Braig *et al.*, *Oncotarget* 7:42988-42995, 2016

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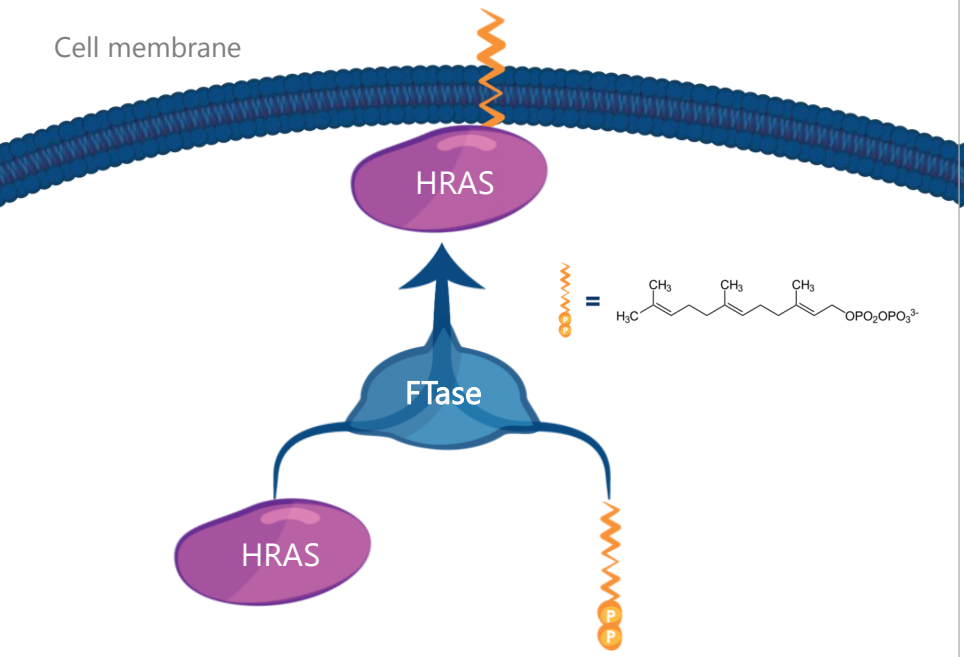
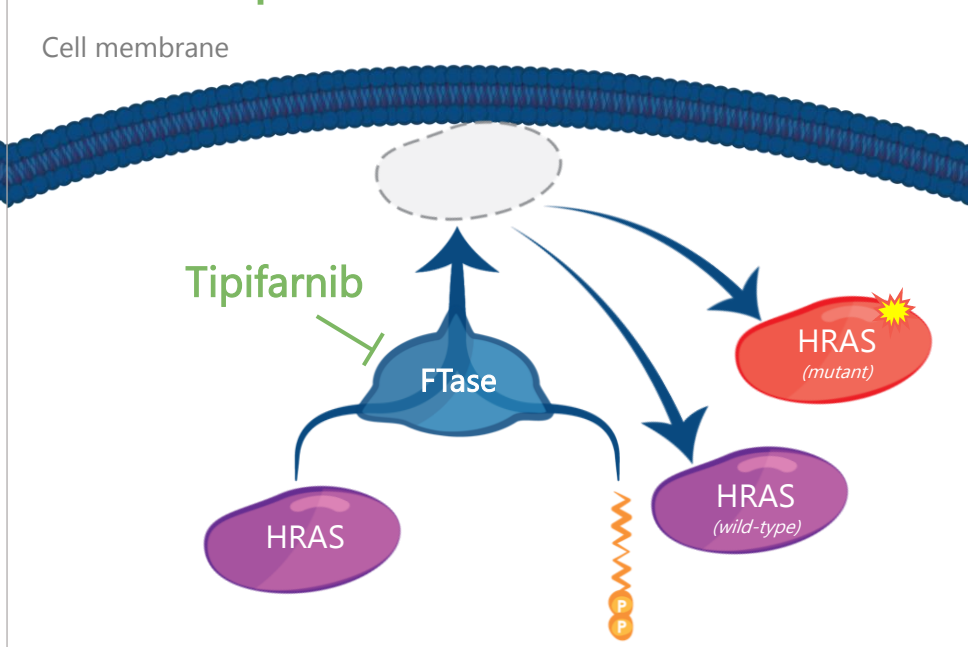
Farnesylation is Required for HRAS Activity

Normal FTase



- **Farnesyl transferase (FTase) attaches farnesyl group to proteins**, facilitating localization to the inner cell membrane
- Membrane localization is **required for HRAS signal transduction activity**

Tipifarnib Inhibits FTase



- Blocking farnesylation **prevents WT and mutant HRAS membrane localization**
- NRAS and KRAS are susceptible to redundant forms of prenylation, but **HRAS can only be farnesylated**

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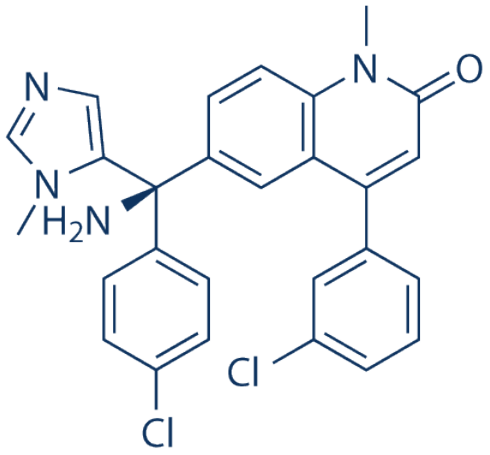
Tipifarnib: Selective FTase Inhibitor with Substantial Prior Clinical Experience

- Extremely potent and selective inhibitor of FTase[1] in-licensed from Janssen
- Well characterized > 5,000 patients treated in prior studies in >70 studies
- Anecdotal activity of durable responses but developed before advent of personalized medicine approaches, including genetic selection
- Manageable safety profile as single agent therapy (< 25% treatment discontinuation)
- Tipifarnib adverse events (reported from 472 solid tumors patients):
  - Myelosuppression (neutropenia 25%, anemia 31%, thrombocytopenia 19%)
  - Non-heme > 25%: fatigue (41%) and GI unspecific (nausea 47%, anorexia 33%, diarrhea 32%, vomiting 32%)



Tipifarnib

[1] End et al. 2001 Cancer Res 61:131-37

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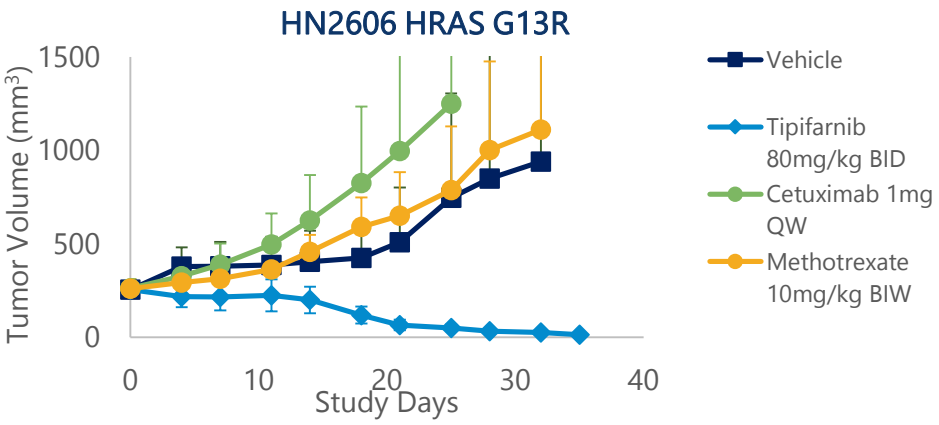
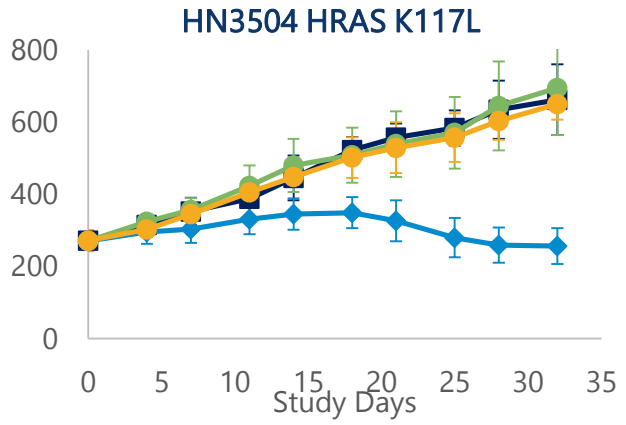
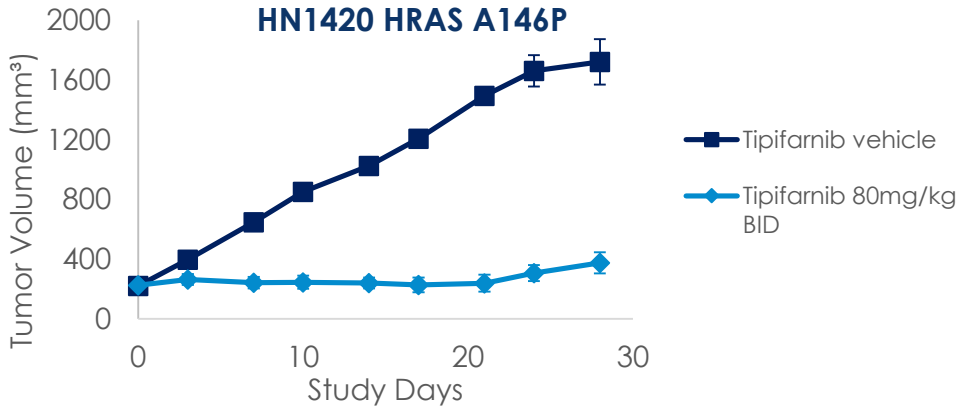
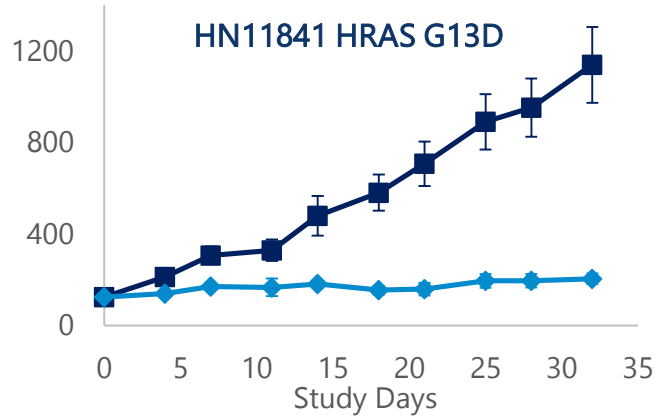
HRAS Mutant HNSCC PDX Models Are Sensitive to Tipifarnib and Resistant to Standards-of-Care





Activity observed in both hot spot (12, 13, 61) and non hot spot (exon 4) HRAS mutants consistent with MOA





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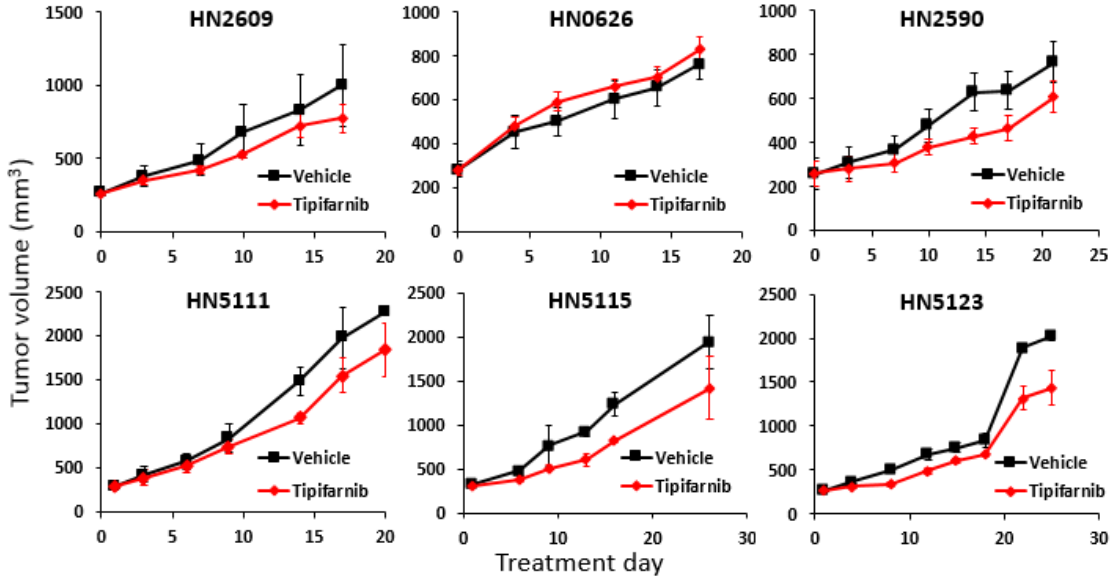
Tipifarnib Inactive in HNSCC Tumors with Wild-Type HRAS



- Preclinical data in HNSCC PDX models with wild-type HRAS status demonstrates tipifarnib has minimal to no activity
- Specificity of HRAS mutation as an FTI target in HNSCC is further supported by clinical data – Lonafarnib demonstrated 0/15 responses in relapsed/refractory HNSCC patients with unknown HRAS status (ruled out effectiveness of FTI in unselected HNSCC with 97% probability)[1]

[1] *Am J Clin Oncol.* 2009; 32:274-9

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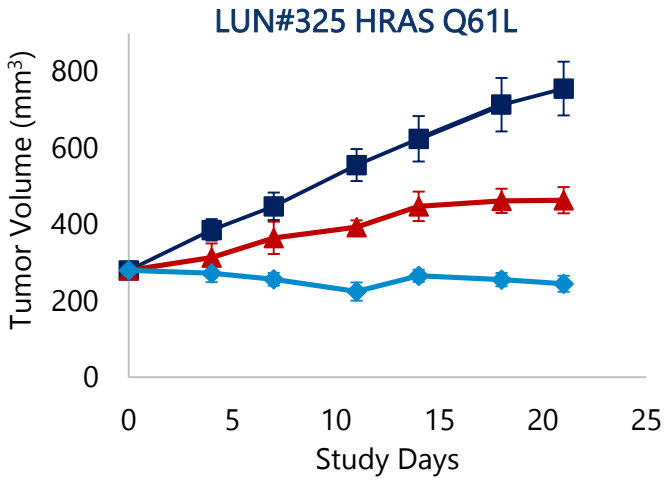
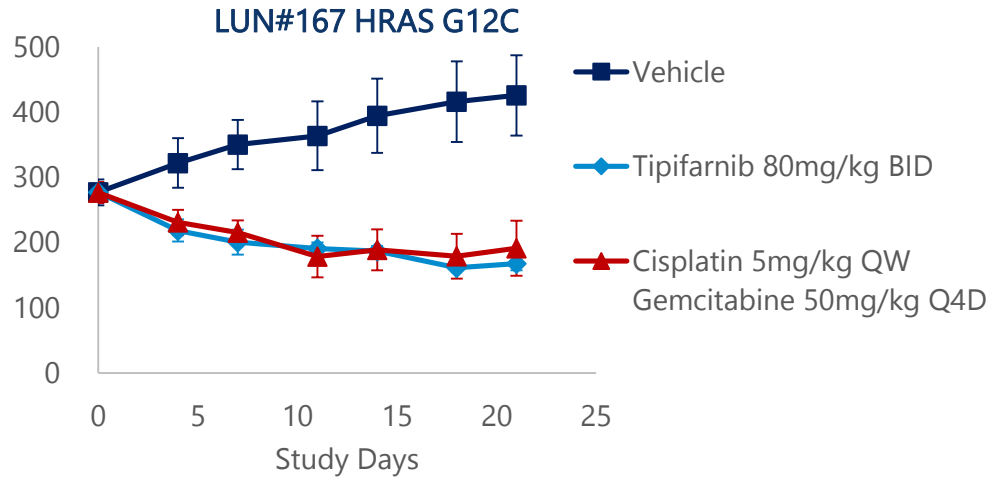
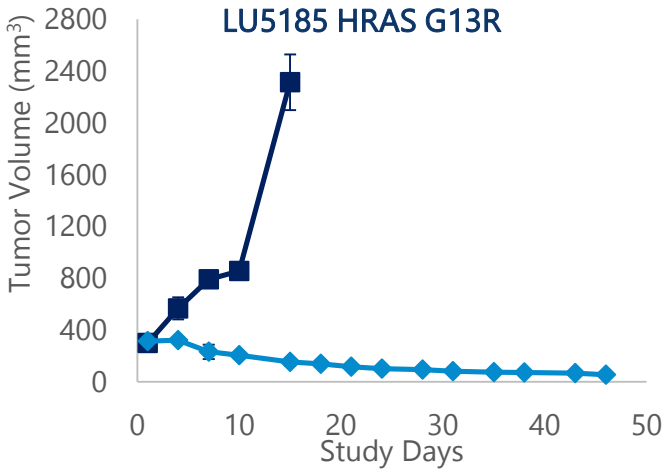
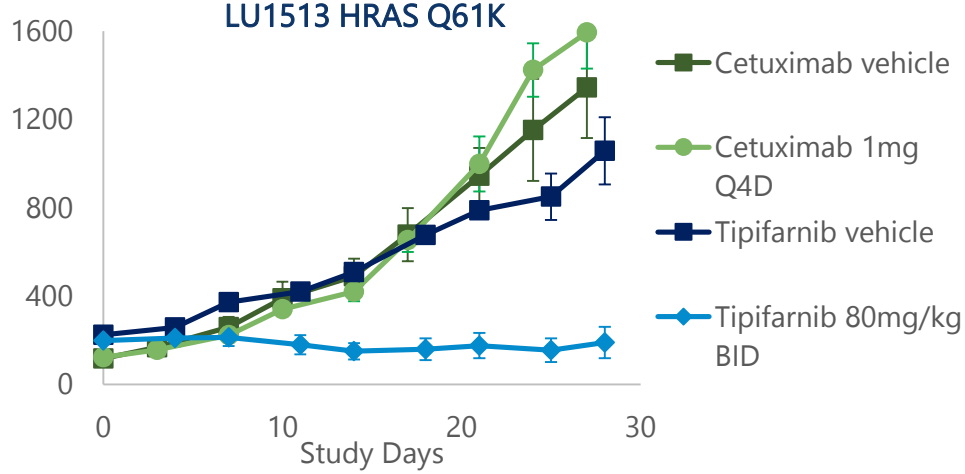
Tipifarnib Demonstrates Robust Activity in Other HRAS Mutant SCC, Lung SCC PDX Models









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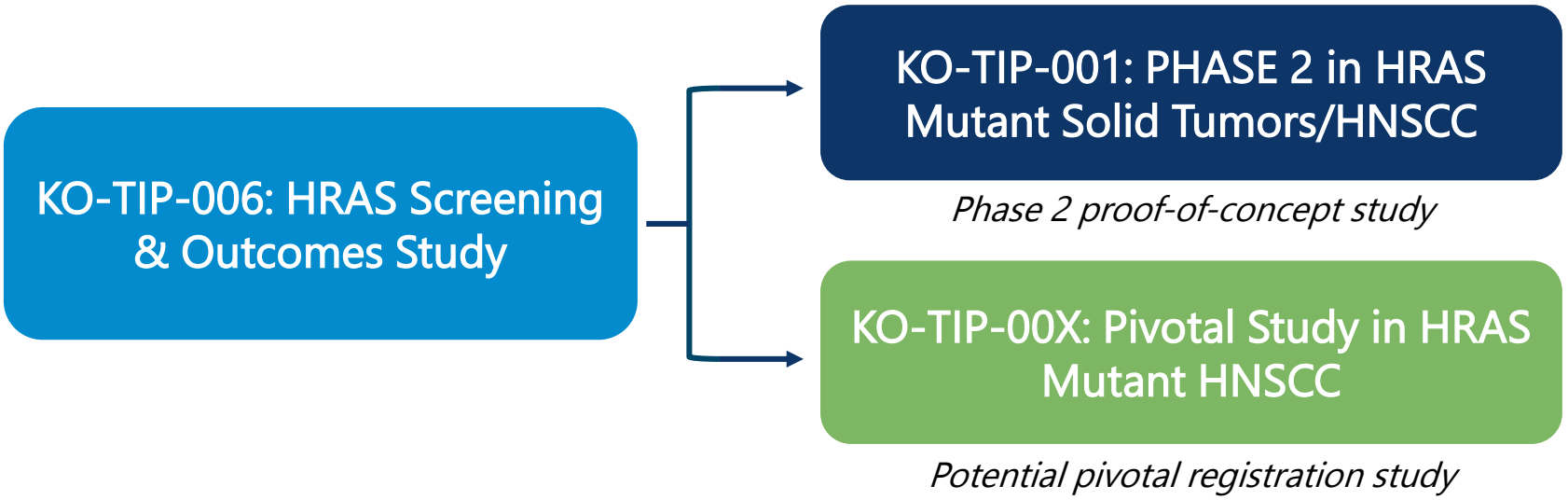
Tipifarnib Development Program in HRAS Mutant HNSCC

- Non-treatment study to define the medical need in HRAS mutant patients
- Supports screening of HRAS in HNSCC patients for potential enrollment into a tipifarnib trial
- Could provide a measure of tipifarnib's effectiveness in the HRAS mutant HNSCC population post-approval



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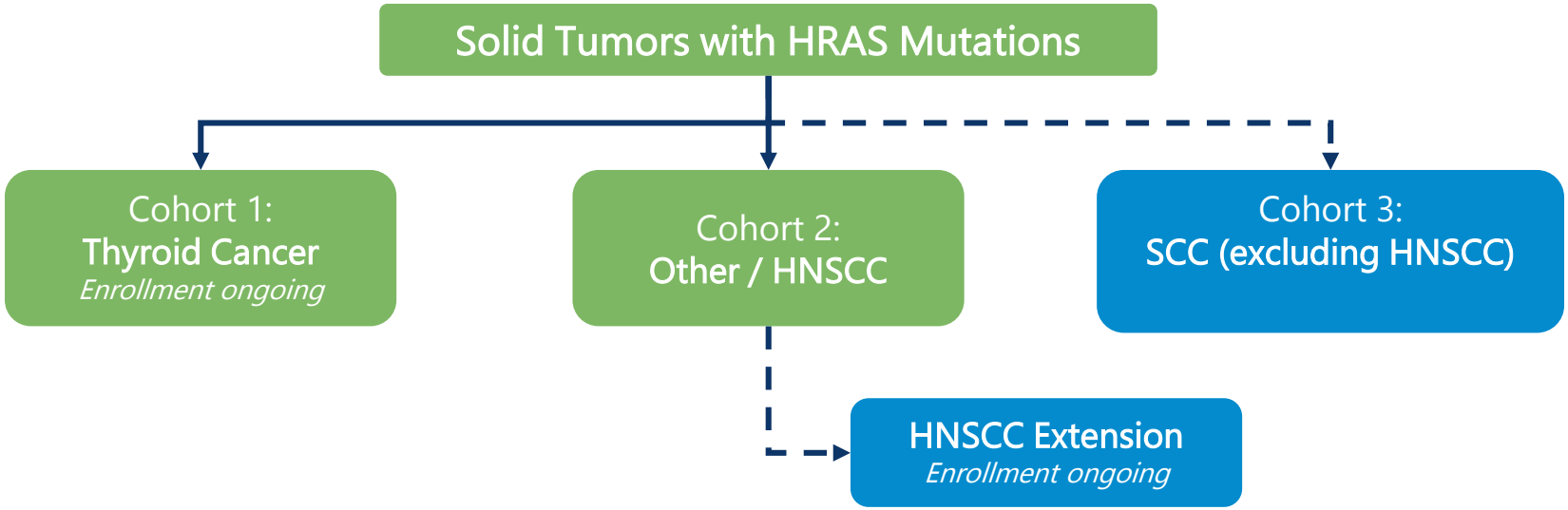
KO-TIP-001: Phase 2 Proof-of-Concept Trial in HRAS Mutant Solid Tumors



- Key Eligibility:
  - R/M disease in PD
  - No curative therapy available
  - HRAS mutation
  - Measurable disease (RECIST v1.1)
  - ECOG PS 0 - 1

- Primary Objective: ORR[1]
- Design: Simon 2-stage (11+7 pts)
- Hypothesis: 10% (H0) vs 30% (H1) ORR, a=0.05, 80% power (4 responses needed)
- No hypothesis testing in the up to 30 HNSCC extension

[1] Objective response includes ≥ 30% tumor shrinkage as defined in RECIST 1.1 guideline (See A. Eisenhauer *et al., Eur. J. Cancer* 45 (2009): 228-247)

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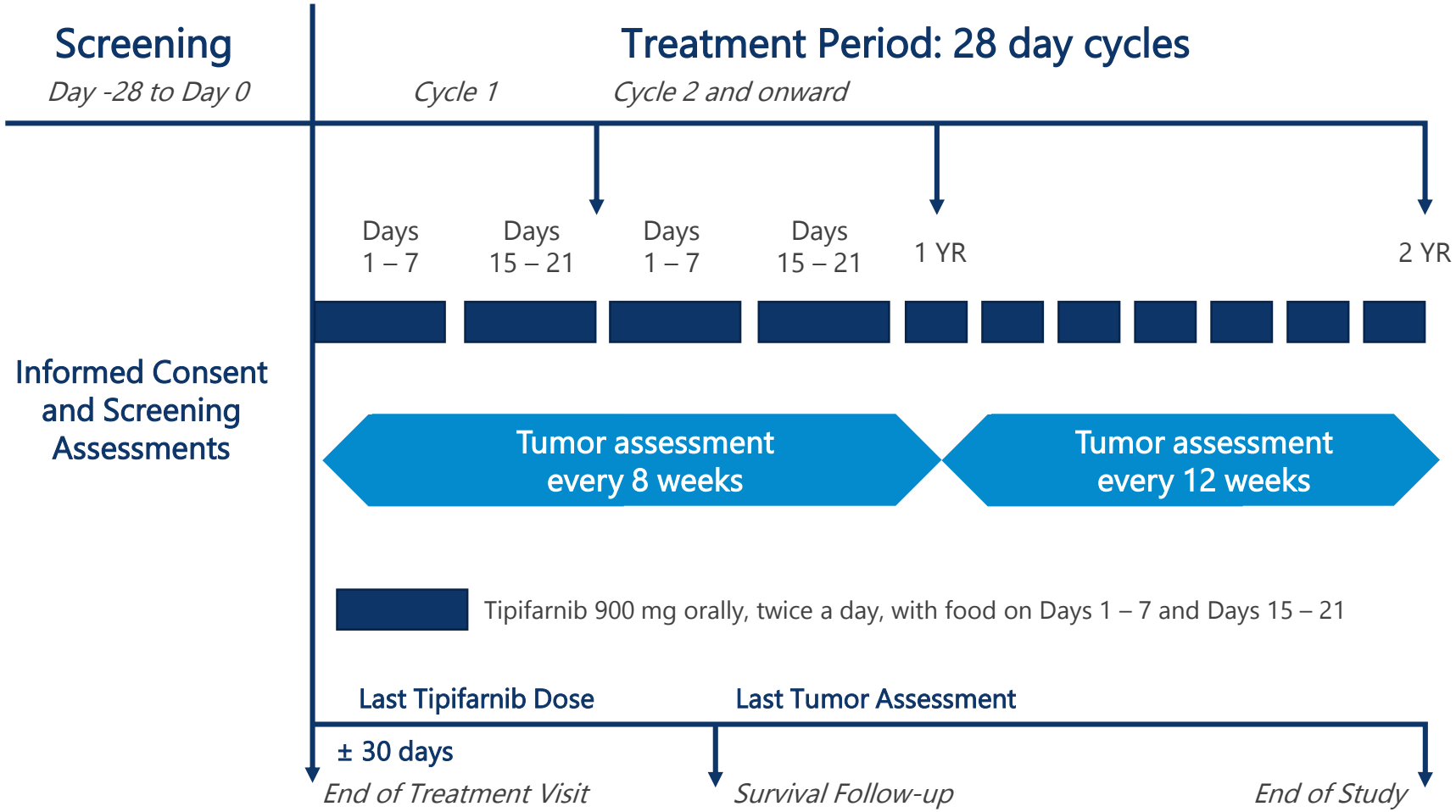
KO-TIP-001 Study Design



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Alternate Week Dosing for Tipifarnib Previously Evaluated

PHASE 1 ALTERNATE WEEK DOSING REGIMEN IN SOLID TUMORS (N=22)[1]

- DLTs: fatigue, myelosuppression was moderate and manageable
- **MTD: 600 mg BID alternate week schedule**

PHASE 1 ALTERNATE WEEK DOSING REGIMEN IN MDS (N=63)[2]

- DLTs: ataxia (n = 1), fatigue (n = 1), nausea (n = 1) and neutropenic fever (n = 2) at doses > 1200 mg/d
- **MTD: 600 mg BID alternate week schedule**

PHASE 1 ALTERNATE WEEK DOSING REGIMEN IN R/R AML (N=44)[3]

- Evaluated doses up to 1600 mg bid. Sixteen patients were treated at the 1000 - 1200 mg dose levels, with 3 of them experiencing CRs. No responses at lower dose levels.
- DLTs: Gr 5 hepatorenal failure (n=1), Gr 2 - 3 creatinine elevation (n=5), Gr 4 hypotension (n=1), Gr 3 LFTs (n=1)
- **MTD: 1200 mg BID alternating week schedule**

[1] *Anticancer Drugs.* 2005;16:317-21.
[2] *Clin Cancer Res.* 2008;14:509-14.
[3] *Leukemia.* 201;25:1543-7.

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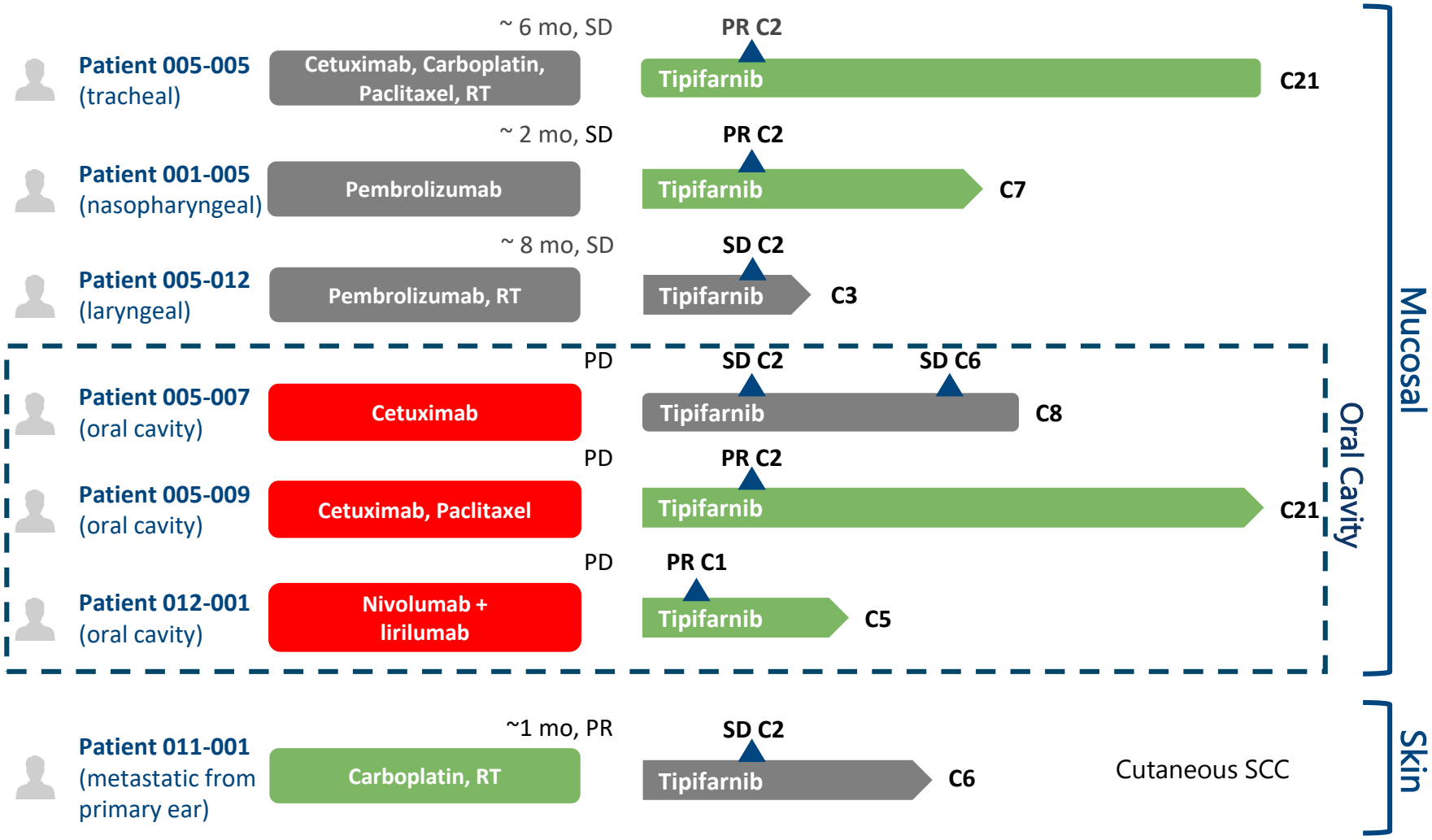
Summary of HRAS Mutant HNSCC and Skin SCC Patients



Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

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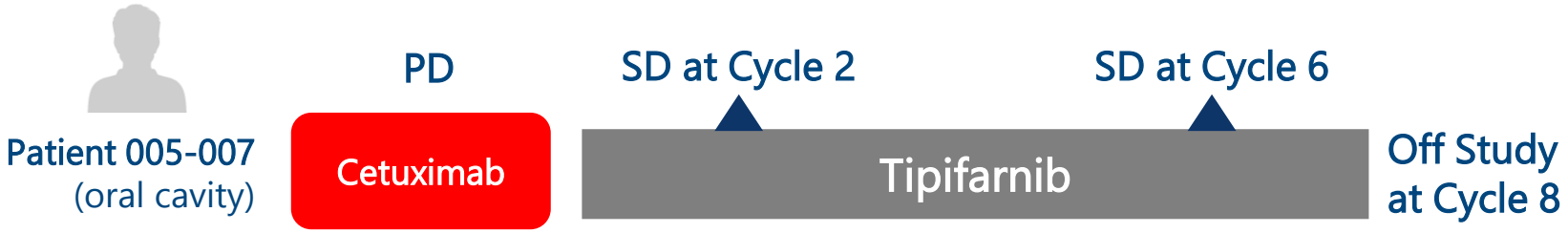
Stable Disease on Tipifarnib Monotherapy after Cetuximab Failure



- Only subject to experience SD as best response
- Unusual case: 20 year old male with dyskeratosis congenita, medullary cystic kidney disease and small bowel lymphoma. HPV UNK, no tobacco/alcohol - Suggest potential germinal issue
- SCC of the maxilla with HRAS Q61K and 16 additional mutations including MAPK1 E322K (ERK)
- Prior treatment with maxillectomy and adjuvant RT, and cetuximab
- Discontinues treatment at C8 due to investigator decision (tumor imaging appearance of extension – non-measurable)

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

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Durable Response on Tipifarnib After Cetuximab / Chemo / Radiation Treatment

Patient 005-005
(tracheal)

~ 6 mo, SD

Cetuximab, Carboplatin, Paclitaxel, RT

~ 8 mo

PR at Cycle 2

Tipifarnib

Off Therapy Cycle 21

- Elderly white male with HNSCC metastatic to tracheal tumor and prior history of nasal HNSCC
- Received 2 cycles of paclitaxel, carboplatin and cetuximab with a mixed response
- Further treatment with paclitaxel and cetuximab followed by RT
- Non hotspot HRAS Q22K, CDKN2Adel (WT for TP53, CASP8, PIK3CA)
  - HRASQ22K Observed in Costello syndrome (tumor predisposition syndrome due to germline HRAS mutations)
  - Equivalent KRASQ22K known to be tumor-related
- Partial response at C2, on tipifarnib for > 1.5 years

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

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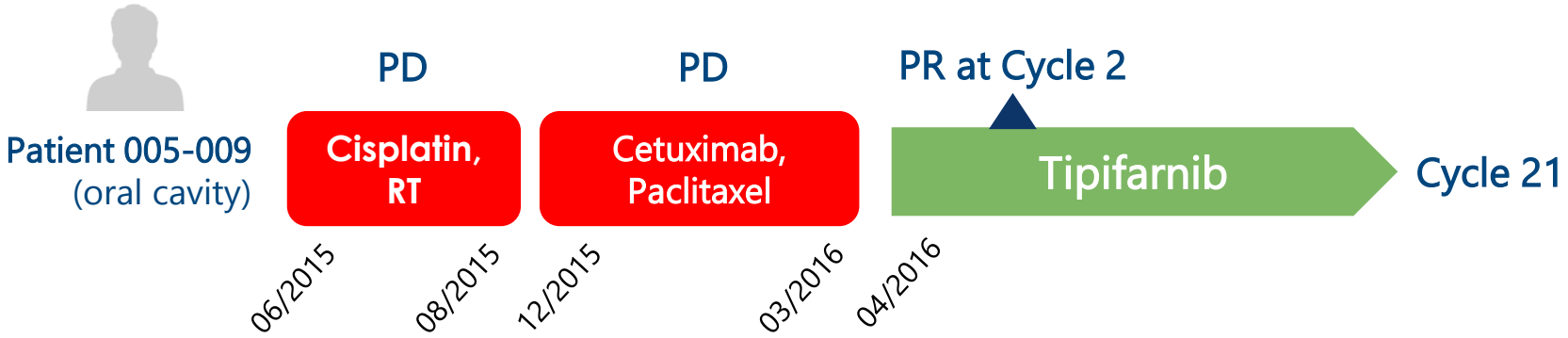
Rapid and Durable Response on Tipifarnib in 3rd Line Refractory Disease



- 58 year old male presenting with oral cavity SCC
- HPV/p16 (-) with no history of tobacco or alcohol abuse
- HRAS Q61K and a TP53 splice variant, wild type for CASP8 and PIK3CA
- Multiple surgeries, adjuvant and palliative RT
- Highly progressive disease refractory to platinum/RT and cetuximab/paclitaxel

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

Tipifarnib Response in Nasopharyngeal Carcinoma Post-Immunotherapy Failure[1]

Patient 001-005
(nasopharynx)

~ 6 mo, SD

Cisplatin

~2 mo SD

Pembrolizumab

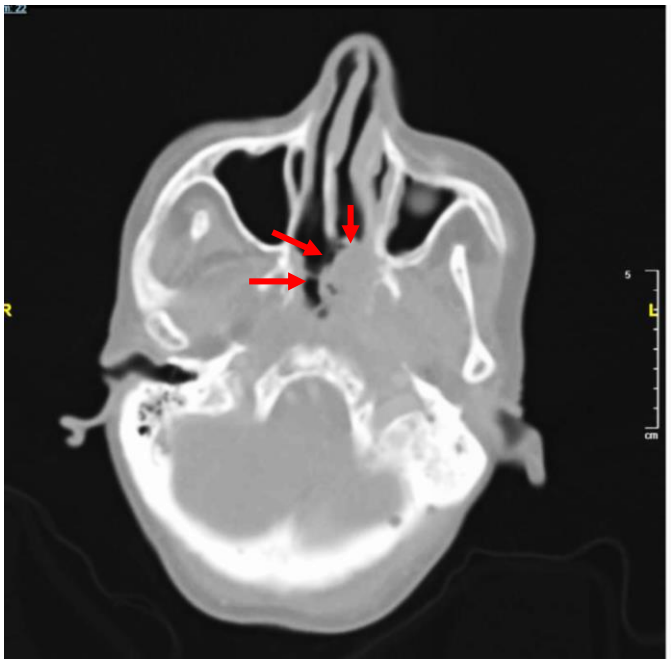
PD

PR at Cycle 2

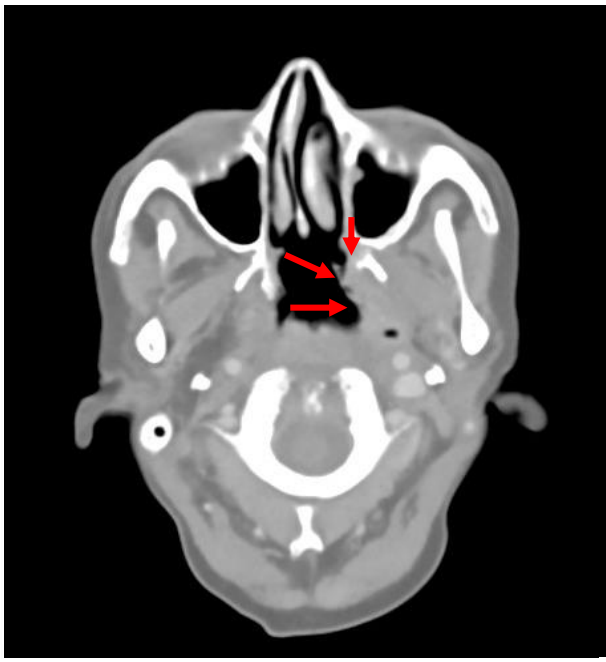
Tipifarnib

Cycle 7

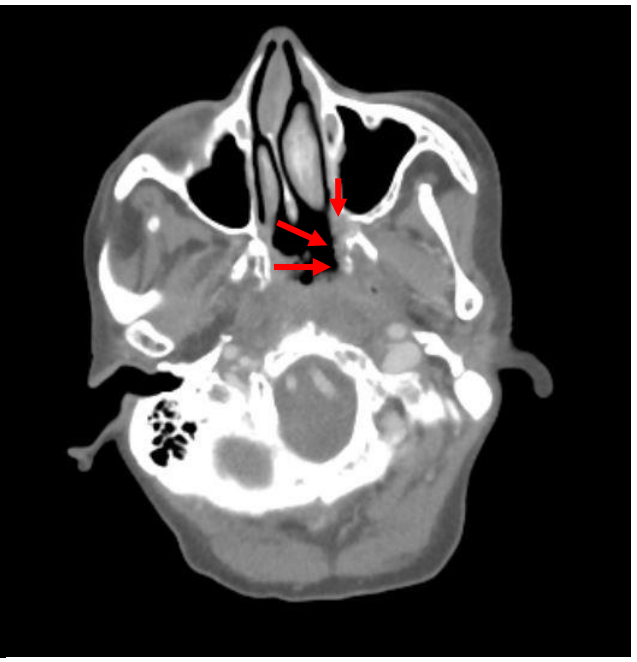
- 59 year old female with nasopharynx SCC carrying HRAS G12D



Baseline



Cycle 2, 40% reduction



Cycle 6, 49% reduction

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)
Images provided by Dr. Nicole Chau, DFCI, Boston

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Regression of Widely Metastatic/High Tumor Burden Laryngeal SCC

Patient 05-012
(Laryngeal)

~2 mo, PD

Cetuximab + Paclitaxel + Carboplatin

~8 mo, SD

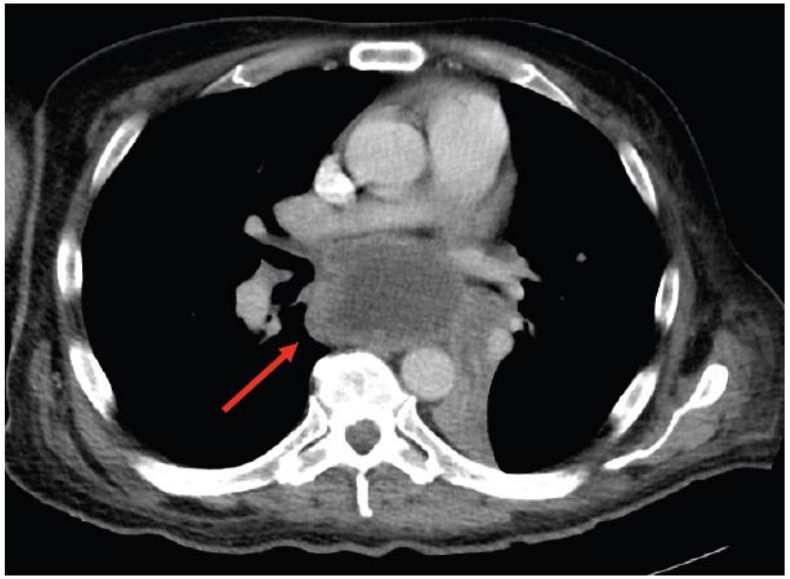
Pembrolizumab + palliative RT

SD at Cycle 2

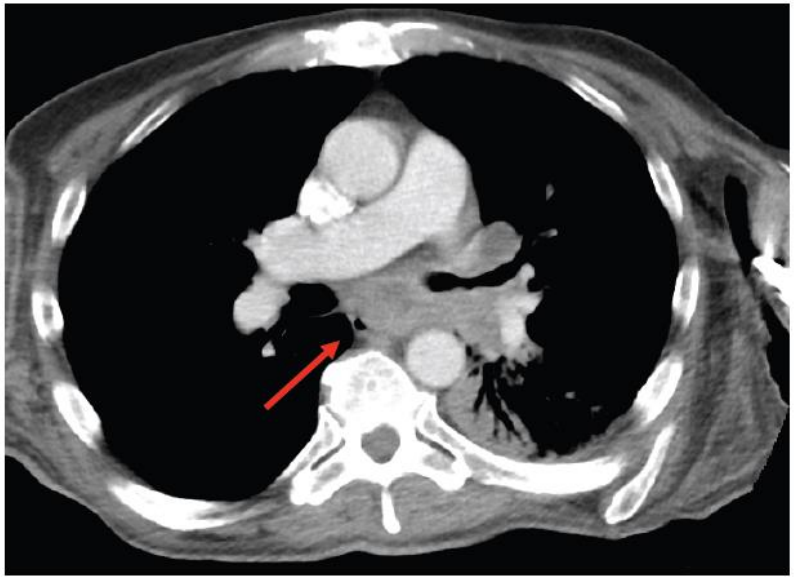
Tipifarnib

Cycle 3

- 55 year old male with metastatic laryngeal SCC (mediastinal LNs, muscle, adrenal gland, lung, bone)
- 80 pack-years, no current alcohol use



Baseline



Cycle 2, 22% reduction

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)
Images provided by Dr. Alan Ho, MSKCC, New York

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Tumor Response and Resolution of Disfiguring Skin Lesions post Immunotherapy Failure

Patient 012-001
(oral cavity)

SD, 5 mo

Cisplatin, Docetaxel, Cetuximab

PD

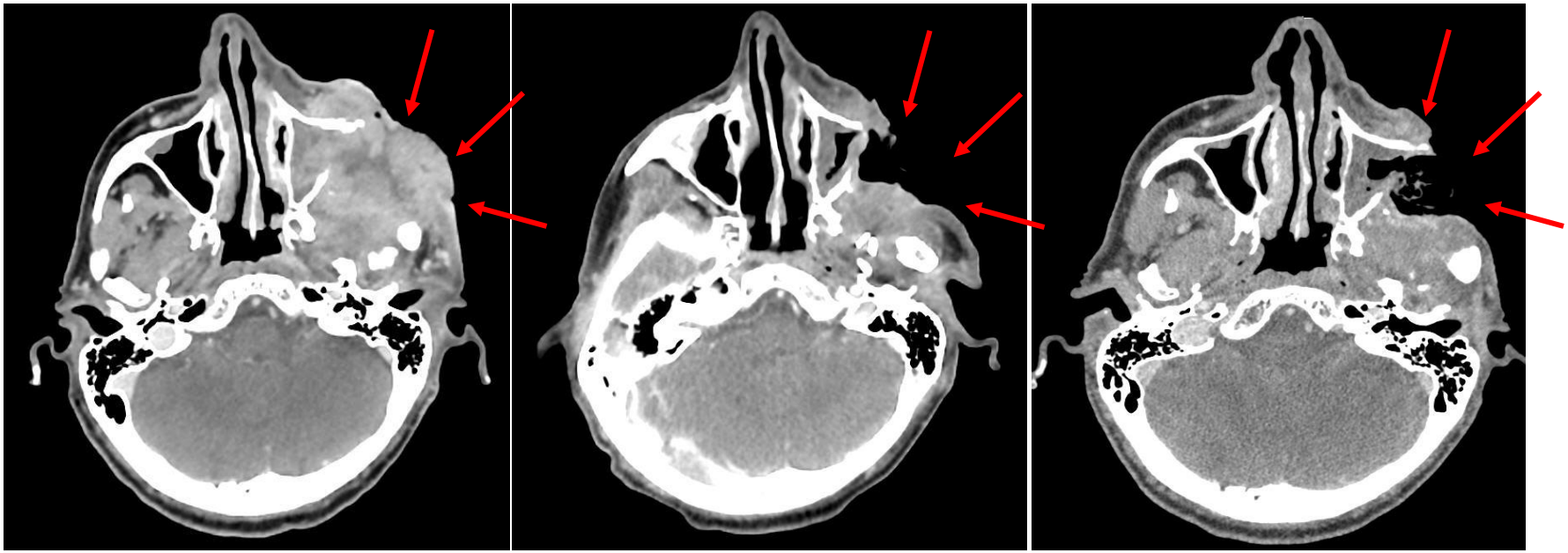
Nivolumab + lirilumab

PR at Cycle 1

Tipifarnib

Cycle 5

- 69 year old male with recurrent oral cavity SCC. No history of tobacco or alcohol abuse
- HPV – tumor carrying HRAS G12S, TP53 R248Q
- Initial PR (40% tumor reduction) observed on Cycle 1 Day 15 (7 days tipifarnib + 7 days



Baseline | **Cycle 1, 40% reduction** | **Cycle 3, 56% reduction**

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)
Images provided by Dr. Caroline Even and Dr. Charles Ferte, IGR, Paris

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Resolution of Disfiguring Skin Lesions with Tipifarnib post Immunotherapy Failure (cont'd)

Patient 012-001
(oral cavity)

SD, 5 mo

Cisplatin, Docetaxel, Cetuximab

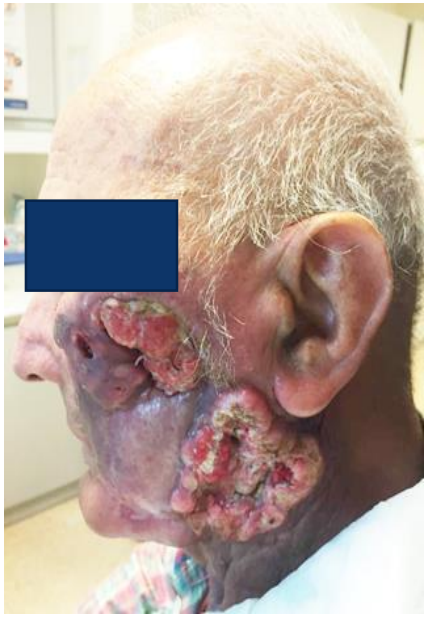
PD

Nivolumab + lirilumab

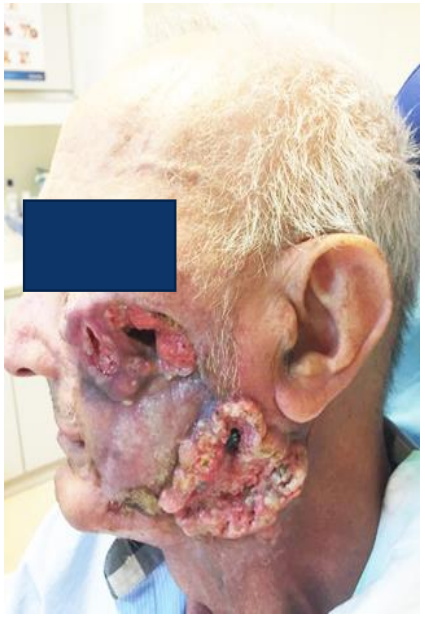
PR at Cycle 1

Tipifarnib

Cycle 5

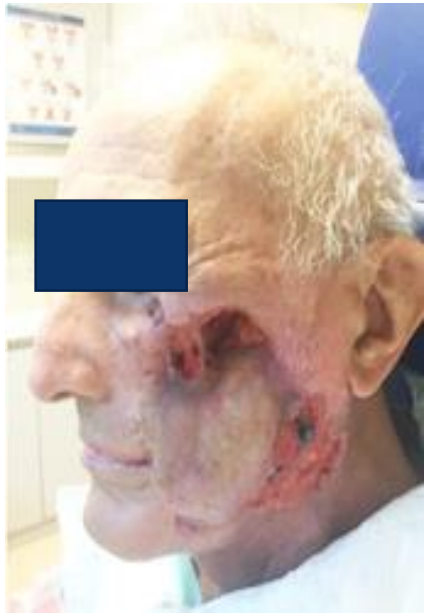


C1D1



C1D7

C1D20



C2D1

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)
Images provided by Dr. Caroline Even and Dr. Charles Ferte, IGR, Paris

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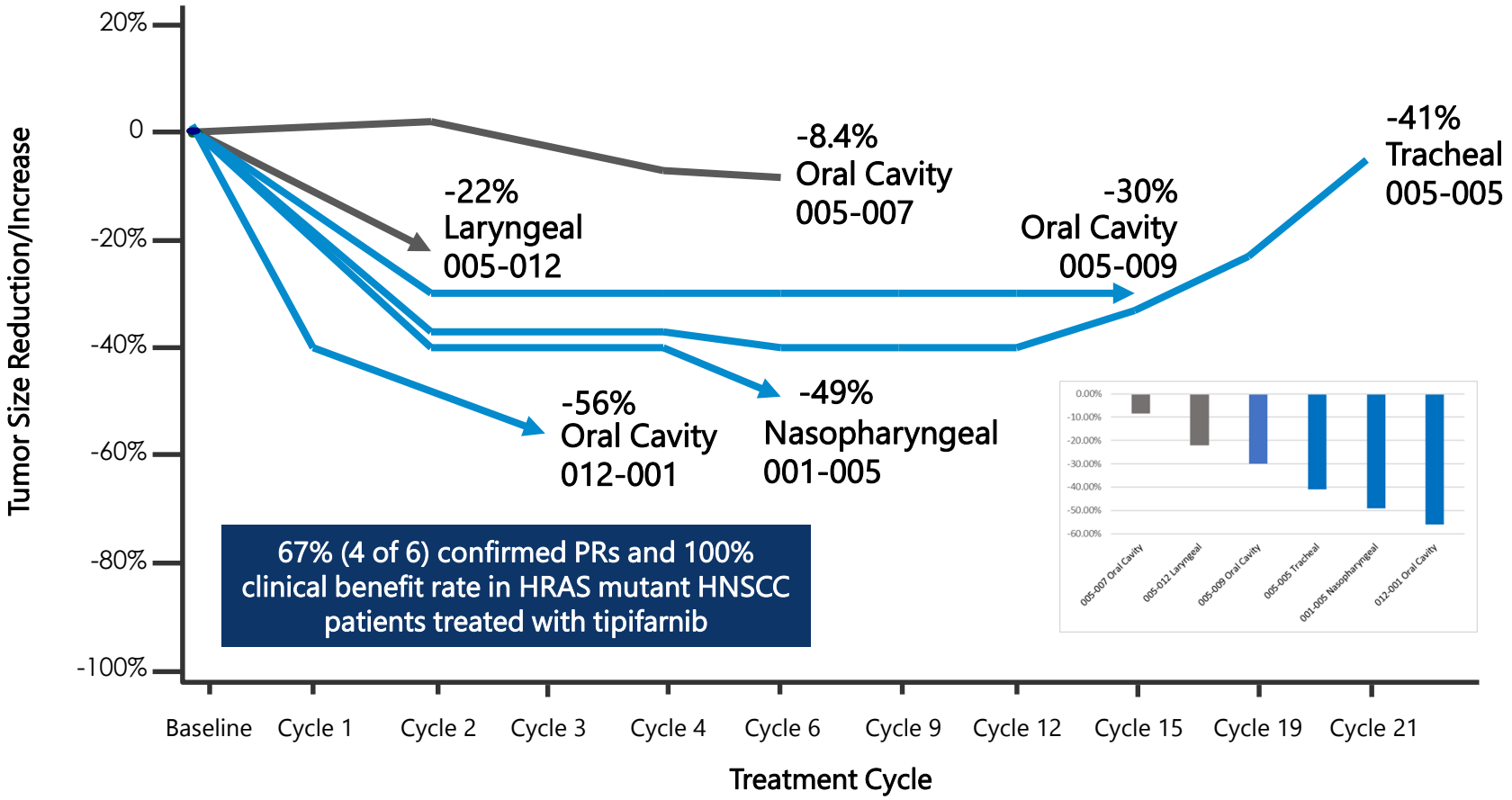
Significant Tumor Size Reduction and Durable Responses Observed with Tipifarnib



Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

Stable Disease and Symptomatic Improvement on Tipifarnib Monotherapy in Cutaneous SCC

Patient 011-001
(metastatic from primary ear)

1 mo, PR

Carboplatin, RT

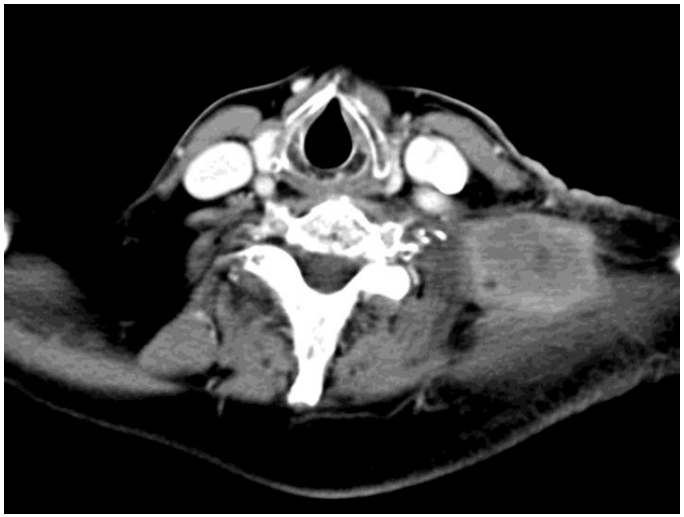
~ 3 mo

SD at Cycle 2

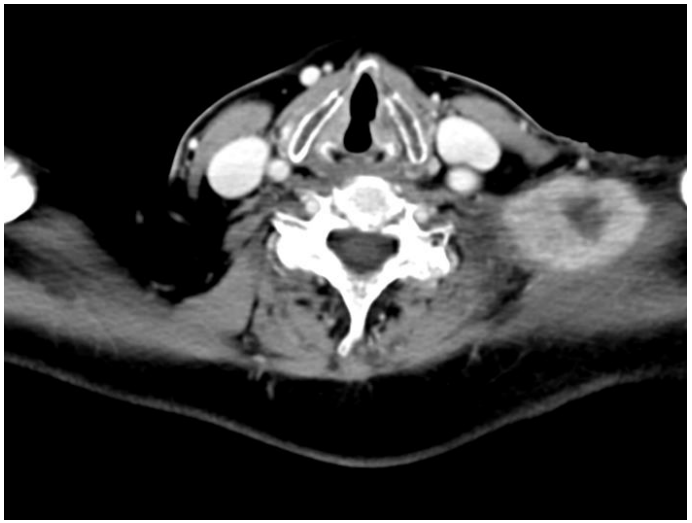
Tipifarnib

Cycle 6

- 81 yo male diagnosed with SCC arising from right ear; History of aggressive disease with short-lived benefit of prior therapies
- HRAS G12D, TP53 R110P and R248W



Baseline



Cycle 2

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)
Images provided by Dr. Irene Braña, VHIO, Barcelona

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SD and Symptomatic Improvement on Tipifarnib Monotherapy in Cutaneous SCC (cont'd)

Patient 011-001
(metastatic from primary ear)

1 mo, PR

Carboplatin, RT

~ 3 mo

SD at Cycle 2

Tipifarnib

Cycle 6

- Symptomatic benefit: Dramatic reduction in required pain medication

DATE	PAIN MEDICATION
5/May/2017	Fentanyl patch 100 mcg/h Transmucosal fentanyl 200 mcg for breakthrough pain
16/May/2017	Methadone 5 mg Q 8 hours Transmucosal fentanyl 200 mcg for breakthrough pain
24/May/2017	C1D1 Tipifarnib – grade 2 pain
28/May/2017	Pain grade 1. No breakthrough medication needed
5/Jul/2017	Fentanyl patch 50 mcg/h

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

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Safety Summary: ≥ Grade 3 related AEs (≥ 5% of subjects)

	TOTAL (N=27)	> GR 3, TOTAL (N=27)	HNSCC (N=6)
Blood and lymphatic system disorders	14 (51.9)	4 (14.8) Gr 4	1 (14.3) Gr 3
Neutropenia	8 (29.6)	3 (11.1) Gr 4	0
Anemia	6 (22.2)	0	1 (14.3) Gr 3
Thrombocytopenia	4 (14.8)	0	0
Lymphopenia	3 (11.1)	0	0
Leukopenia	2 (7.4)	1 (3.7) Gr 4	0
Gastrointestinal disorders	4 (14.8)	0	1 (14.3) Gr 3
Diarrhea	2 (7.4)	0	1 (14.3) Gr 3
Nausea	2 (7.4)	0	0
Vomiting	2 (7.4)	0	0
Investigations	3 (11.1)	0	0
Blood creatinine increased	3 (11.1)	0	0
Renal and urinary disorders	2 (7.4)	0	0
Acute kidney injury	2 (7.4)	0	0

Reporting period from study start (May 6, 2015)
Note: Percentages are based on number of subjects in ASaT Population. Version 19.0 of MedDRA was used to code AE.

Preliminary data presented at AACR-NCI-EORTC (as of October 4, 2017)

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Observed Myelosuppression May Be Related to CXCL12/CXCR4 Pathway Inhibition

- ≥ Grade 3 TEAEs in the KO-TIP-001 study included myelosuppression, GI disturbances and increased creatinine/AKI. Grade 2 neurotoxicity was also observed in some patients
- GI toxicity is common with agents of the EGFR > RAS > MEK > ERK pathway but bone marrow, renal and neurotoxicity are not common[1]
- Kura has recently identified the CXCL12/CXCR4 pathway as a potential target of tipifarnib[2]
  - CXCL12 is a chemokine involved in bone marrow homing and maturation[3], that also plays key functions in the kidney[4] and nerve systems[5]
  - Downregulated CXCL12 expression in bone marrow mesenchymal stem cells has been shown to be associated with aplastic anemia[6]
- Subjects in tipifarnib studies are being tested for circulating CXCL12 levels, CXCL12 gene expression and genetic variation

[1] Dy 2013. CA Cancer J Clin 63:249-79
2 EHA 2017, abstract P571
3 Sugiyama 2006. I*mmunity.* ;25:977-88
4 Takabatake 2009. *J Am Soc Nephrol.* 20:1714-23
5 Chen 2014. *PLoS One* 9:e92227
6 Chao 2015 *Ann Hematol* 94: 13

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Phase 2 HRAS Mutant HNSCC – Key Takeaways

- HRAS is a targetable oncogene with tipifarnib
- Clinical proof-of-concept achieved in recurrent/metastatic HRAS mutant HNSCC
- Compelling efficacy in a subset of HNSCC unresponsive to standard therapies
  - Confirmed PRs in 4 of 6 patients (67%, 22-95% 95% CI)
  - Rapid and durable responses (2 responses with DoR >1 year)
  - Activity in disease resistant to chemo, cetuximab and immune therapy
  - Resolution of disfiguring lesions
  - Decrease in pain and use of pain medication (cutaneous SCC)
- Adverse events consistent with known safety profile of tipifarnib
  - Most common severe toxicities included myelosuppression (neutropenia 31%, anemia 19%, thrombocytopenia 15%), GI disturbances (15%) and increased creatinine (11%) (N=27, overall study)
  - 3/27 (11%) patients (0/6 HNSCC) discontinued for reasons other than disease progression

Looking Ahead: Key Themes for Development of Tipifarnib in HRAS Mutant HNSCC

- Continue to add clinical sites and increase enrollment in Phase 2 trial
- Engage regulatory authorities
- Engage patient advocacy groups
- Complete development and validation of companion diagnostic
- Refine the potential market opportunity

Goal: Initiate registration-enabling study in HRAS mutant HNSCC in 2018

Anticipated Milestones

PROGRAM	MILESTONES	ESTIMATED
Tipifarnib Farnesyl Transferase Inhibitor	Positive Phase 2 clinical trial in HRAS mutant HNSCC	✓
	Preliminary data from Phase 2 clinical trial in CMML	Dec 2017
	Role of CXCL12 as potential target in hematologic malignancies	Dec 2017
	Updated results from Phase 2 clinical trial in HRAS mutant HNSCC	Feb 2018
	Data from Phase 2 clinical trial in MDS	2018
	Data from Phase 2 clinical trial in PTCL	2018
	Data from Phase 2 clinical trial in CMML	2018
	Initiate registration-enabling clinical trial in HRAS mutant HNSCC	2018
KO-947 ERK Inhibitor	Initiate Phase 1 clinical trial	✓
	Data from Phase 1 clinical trial	2018
KO-539 Menin-MLL Inhibitor	Report anti-tumor activity in preclinical models of AML	✓

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DEVELOPING PRECISION MEDICINES TO TREAT CANCER