

12th Annual Otolaryngology Literature Update

Head & Neck Oncology III

Jason G. Newman, M.D., FACS

Professor

Director, Head & Neck Oncology

Department of Otolaryngology - Head & Neck Surgery

Medical University of South Carolina

newmajas@musc.edu

Dr. Jason G. Newman received his medical degree from Thomas Jefferson University Medical School in 1997 and completed residencies in Otolaryngology at Manhattan Eye, Ear & Throat Hospital, New York, NY, (1998-1999), New York Presbyterian Hospital of Columbia and Cornell, and Memorial Sloan Kettering Cancer Center (1999-2002).

Following residency, Dr. Newman completed his fellowship in Head and Neck Surgery/Oncology and Microvascular Surgery at the University of Pennsylvania Perelman School of Medicine in 2005. After fellowship, Dr. Newman remained on faculty at Penn until 2022. Dr. Newman is now serving as the Wendy and Keith Wellin Endowed Chair in Head and Neck Surgery, and the Chief of the Hollings Cancer Network at the Medical University of South Carolina.

Dr. Newman's areas of expertise include head and neck mucosal and cutaneous cancer surgery, robotic surgery, anterior cranial base surgery and complex thyroid surgery with special interest in minimally invasive approaches. Dr. Newman also is actively involved in research focused on head and neck cancer clinical trials, genetic signatures for head and neck cancer, and survivorship for head and neck cancer patients.

As the Chief of the Hollings Cancer Network, Dr. Newman is helping to realize the vision of a state-wide network to help care for cancer patients in South Carolina. This network intends to give patients access care closer to home when possible, while seamlessly transitioning them to tertiary care facilities when needed. This strategy will help strengthen the delivery of cancer care, improve patient outcomes, create leadership pathways, increase patient volumes, increase access to clinical trials, and minimize variations in the delivery of care.

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Berger BM, Hanna GJ, Posner MR, Genden EM, Lautersztain J, Naber SP, Del Vecchio Fitz C, Kuperwasser C. Detection of Occult Recurrence Using Circulating Tumor Tissue Modified Viral HPV DNA among Patients Treated for HPV-Driven Oropharyngeal Carcinoma. Clin Cancer Res. 2022 Oct 3;28(19):4292-4301. doi: 10.1158/1078-0432.CCR-22-0562. PMID: 35576437; PMCID: PMC9527497.

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HEAD AND NECK REVIEW

Jason G. Newman, MD
Wendy and Keith Wellin Endowed Chair in Head and Neck Surgery
Professor & Director, Division of Head & Neck Oncologic Surgery
Department of Otolaryngology-Head & Neck Surgery
Chief, Hollings Cancer Network
Medical University of South Carolina
August 26, 2023

DISCLOSURES

- Medical Board, Castle Biosciences
- Consulting, Hologic Inc
- Consulting, Merck Inc
- Consulting, OncoNano
- Consulting CelSci

INTRODUCTION

- 4 papers
- One of them will be a new “landmark” paper
- 3 of them are being presented to open a door into the current and future state of head and neck cancer surgery.

LIQUID BIOPSY

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Detection of Occult Recurrence Using Circulating Tumor Tissue Modified Viral HPV DNA among Patients Treated for HPV-Driven Oropharyngeal Carcinoma

Barry M. Berger¹, Glenn J. Hanna², Marshall R. Posner^{3,4}, Eric M. Genden^{3,5}, Julio Lautersztain⁶, Stephen P. Naber¹, Catherine Del Vecchio Fitz¹, and Charlotte Kuperwasser¹



LIQUID BIOPSY

- The National Cancer Institute states that a liquid biopsy is; “A test done on a sample of blood to look for cancer cells from a tumor that are circulating in the blood or for pieces of DNA from tumor cells that are in the blood”

LIQUID BIOPSY: WHY DID I PICK THIS STUDY?

- Already being used as a cancer screening tool
- Likely to become standard of care for many cancers
- Will change the cancer landscape
- Will impact management algorithms
 - Screening, surveillance, high risk populations

CTDNA: INTRODUCTION

- HPV-driven OP cancer exponential rise in incidence
- 15-25% of patients experience relapse
- These patient often have unusual patterns and timing of recurrence
- Many patients stop undergoing surveillance after 2 years
- Many of these patients can still undergo curative-intent treatment, which underscores the importance of early detection

CTDNA: INTRODUCTION

- Circulating tumor DNA (ctDNA) has emerged as a diagnostic tool to detect presence of cancer
- The assay detects HPV-driven cancer-specific DNA, tumor-tissue modified viral HPV DNA (**TTMV-HPV DNA**)
- This is NOT detecting presence of HPV, but is specific to the changes that occur during HPV driven cancer changes to the DNA.

CTDNA: INTRODUCTION

- Earlier studies published the results of sensitivity, specificity, and retrospective outcomes for this test.
- Test has been available clinically since February 2020
 - Bhisham Chera worked with colleagues at UNC to develop this test*
- Important stepping stone
- This is the first prospectively designed retrospective consecutive clinical case series (N=1,076) evaluating circulating TTMV-HPV DNA for surveillance of patients with HPV driven OPSCC after definitive treatment in 108 US sites.

CTDNA: METHODS

- IRB approval
- Waiver of consent due to nature of the study
- Eligible patients included any patient treated for primary HPV-driven OPSCC without known distant metastasis
 - At least 3 months s/p definitive treatment (any modality)
 - Confirmation of HPV status by P16 IHC, or direct HPV detection with ISH, or PCR
 - Pre-treatment testing was not performed as a part of this study

CTDNA: METHODS

- Patient demographics collected
- Stage, treatment, dates of treatment, interval of follow-up, current disease status, HPV strain
- TTMV-HPV DNA assay (NavDx, Naveris, Inc) is provided by a single national reference laboratory, CLIA certified.
- Quantification of the result has been described in previous papers
- Depending upon the high-risk strain of HPV, score greater than 7 or 12 were considered positive
- Score between 5-7 or 5-12 are considered indeterminate
- Score below 5 are considered negative

CTDNA: METHODS

- Lab results compiled along with clinical findings
- All positive tests were compared to clinical and radiologic findings at the time to establish evidence of recurrence
- Physical exam, Endoscopy, CT, MRI, PET-CT, biopsy

CTDNA: RESULTS

- 108 sites
- Each site median of 3 cases
- 27 sites contributed 10 or more
- 5 sites contributed 59% of cases

Table 1. Summary of patient characteristics.

	N = 1,076 (%)
Mean age, years (range)	63 (27-97)
Sex	
Female	133 (12)
Male	943 (88)
p16 status	
Positive	1,069 (99)
Negative ^a	1 (1)
Unknown ^a	6 (1)
# NavDx TTMV-HPV DNA test results	
1	837 (78)
2	190 (18)
3	43 (4)
4	6 (1)
Time posttreatment ^b	
3-6 months	249 (23)
6-12 months	238 (22)
>12 months	589 (55)

^ap16 status was negative unknown at baseline as noted on the test requisition but reported as positive for HPV status on the test requisition or was positive for TTMV-HPV DNA.

^bFor patients with more than one TTMV-HPV DNA test, this was the interval posttreatment reported for the first test result obtained in surveillance.

CTDNA: RESULTS

- Of the 1,076 patients, 80 (7.4%) had at least one positive test result
- 21 of the 80 (26%) had a known clinical recurrence at the time of the test
- The remaining 59 of 80 (74%) were either IND or NED.
- Notably, nearly half of those 59 patients were tested more than 12 months after definitive treatment
- Of the 59 patients with IND or NED at the time of positive ctDNA, 55 (93%) were later proven to have recurrent disease.
 - This suggests the presence of subclinical recurrence at the time of positive ctDNA testing

CTDNA: RESULTS

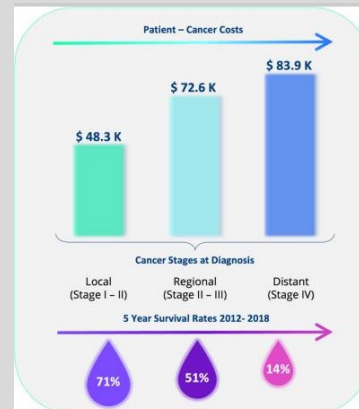
- Amongst patients with clinical disease at the time of testing, the PPV was 100% (N=21/21)
- PPV for patients with IND or NED was 93% (N=55/59)
- Longer follow-up may ultimately identify these remaining 4 patients to have recurrence. 2 of them have clinically suspicious lesions
- Overall NPV, defined as a negative test correlating with a patient with no clinical evidence of disease was 95% (1,198/1,256)

CTDNA: DISCUSSION

- Overall PPV of 95%
- Overall NPV of 95%
- The ability of a novel test to serve as a sensitive, specific tool with high PPV and NPV for HPV cancers is intriguing
- This test may be an important tool in surveillance of HPV driven OPSCC
- Patients with a positive test warrant close and further follow-up
- Relatively easy and (becoming) widely available test
- May identify patients earlier in recurrence, increase rate of salvage

CTDNA: TRANSLATIONAL IMPLICATIONS

- How do we incorporate into routine clinical care?
- Is it relevant to order a baseline test?
- How often should this be done?
- Do negative tests at certain intervals predict the rate or recurrence?
- Should this be incorporated into any screening protocols?



CTDNA: MY THOUGHTS

- I am currently using this for all HPV related patients
- Pre and post treatment
- Spotty use after first post-treatment test
- Helpful in a few scenarios:
 - Equivocal exam
 - Equivocal scans
- Clinical trial opportunities
 - TORS trial
 - CRT trial

ROBOTIC SURGERY

original reports

Phase II Randomized Trial of Transoral Surgery and Low-Dose Intensity Modulated Radiation Therapy in Resectable p16+ Locally Advanced Oropharynx Cancer: An ECOG-ACRIN Cancer Research Group Trial (E3311)

Robert L. Ferris, MD, PhD¹; Yael Flamand, MS²; Gregory S. Weinstein, MD³; Shuli Li, PhD²; Harry Quon, MD⁴; Ramee Mehra, MD⁵; Joaquin J. Garcia, MD⁶; Christine H. Chung, MD⁷; Maura L. Gillison, MD, PhD⁸; Umamaheswar Duvvuri, MD, PhD⁹; Bert W. O'Malley Jr, MD³; Enver Ozer, MD³; Giovana R. Thomas, MD¹⁰; Wayne M. Koch, MD⁴; Neil D. Gross, MD⁴; R. Bryan Bell, MD¹¹; Nabil F. Saba, MD¹²; Miriam Lango, MD¹³; Eduardo Méndez, MD^{14,1}; and Barbara Burtress, MD¹⁵

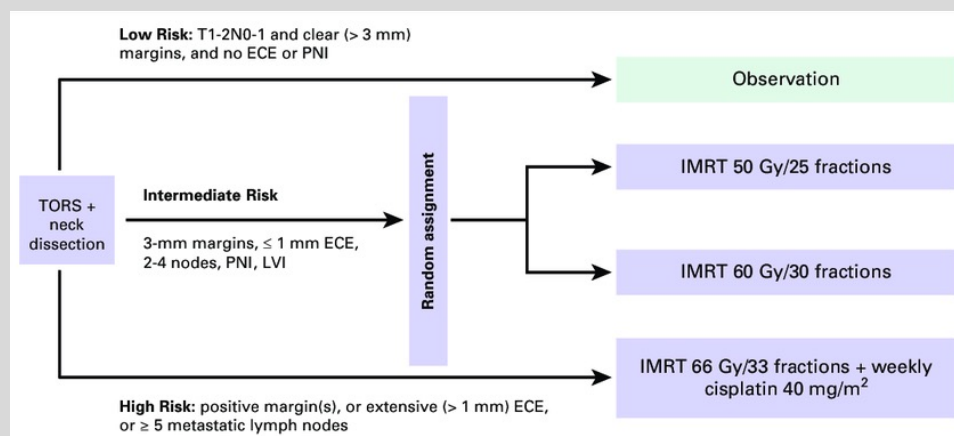
ROBOTIC SURGERY- WHY DID I PICK THIS PAPER?

- TORS is now a standard of care
- Lots of unanswered questions still
- This paper helps answer SOME of the questions
- The field and technology continue to evolve

3311: INTRO

- Definitive CRT is curative for HPV associated oropharynx cancer, but is associated with significant toxicity
- We have suspected for over a decade that treatment de-intensification in a subset of patients is reasonable
- There are many strategies looking at deintensifying treatment for these patients
- This paper studies the strategy of transoral surgery (TOS) and reduced post-operative RT in intermediate risk patients
- Outcomes include 2 year progression-free survival
- QOL and Swallowing outcomes collected

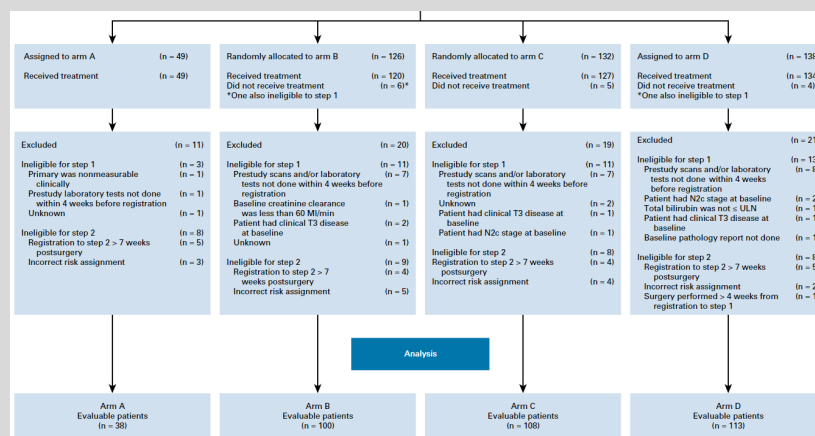
3311: STUDY DESIGN: RANDOMIZED PHASE II



3311: STUDY DESIGN

- 68 surgeons at 59 sites
- Comment made that amendment to protocol was made to strongly recommend ligation of cervical vessels
 - 1/256 fatal bleed after this recommendation
- 495 patients enrolled
 - 443 underwent TORS, 41 underwent TLM, 11 underwent headlight surgery
- 11% assigned to Arm A, about 30% each randomized to B and C, and **30% to Arm D**

3311: STUDY DESIGN: RANDOMIZED PHASE II



3311: RESULTS

- Median Age 58, 89% male, tonsil primary 66%, 30% with >10pack year smoking
- Arm D eligibility: >1mm ENE (77%), >4 nodes (27%), positive margins (11%)
- At time of analysis, 21 recurrences, 10 LR and 11 DM
- Smoking history did not impact survival

3311: RESULTS

TABLE 2. 2-Year PFS, Overall PFS Events, and Sites of Recurrence

Arm	Patients (No.)	2-Year PFS (%)	90% CI	Deaths (without recurrence)	Recurrences	LRF	DM
A	38	96.9	91.9 to 100	0	1	0	1
B	100	94.9	91.3 to 98.6	1	4	2	2
C	108	96.0	92.8 to 99.3	0	4	0	4
D	113	90.7	86.2 to 95.4	3	7	4	3

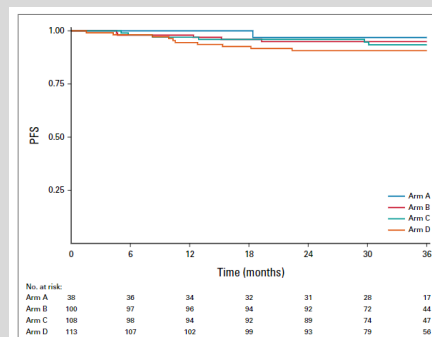


FIG 2. Kaplan-Meier estimates of PFS by arm for 359 evaluable patients. PFS, progression-free survival.

3311: RESULTS

- The 2-year overall survival (OS) Kaplan-Meier estimate was 100% for arm A, 99.0% (90% CI, 9.3 to 100) for arm B, 98.1% (90% CI, 95.9 to 100) for arm C, and 96.3% (90% CI, 93.3 to 99.3) for arm D.

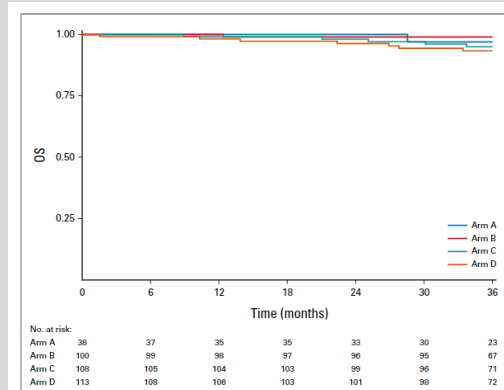


FIG 3. Kaplan-Meier estimates of OS by arm for 359 evaluable patients. OS, overall survival.

3311: RESULTS

- PRO: Functional assessment of cancer therapy (FACT-HN)
- MD Anderson Dysphagia Index (MDADI)
- Consistent decline in QOL and swallowing during treatment.
- Recovery to baseline in arm A-C
- Slightly lower scores in Arm D

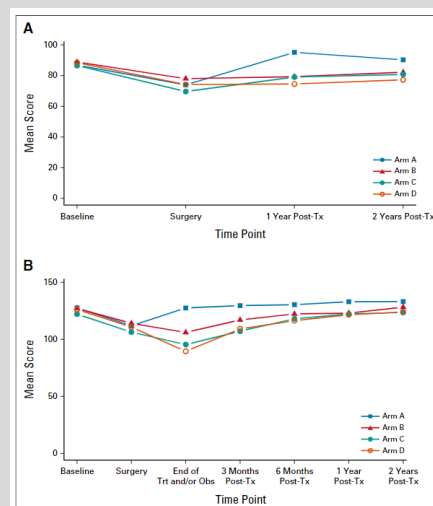


FIG 4. (A) Swallowing and (B) QOL. QOL, quality of life; Trt and/or Obs, treatment and/or observation; Tx, treatment.

3311: DISCUSSION

- 95% 2 year progression free survival amongst intermediate risk patients who undergo TOS and lower-dose RT at 50GY; amongst the best results in the literature
- TOS and 50GY PORT is oncologically appropriate in intermediate risk patients
- Clear decrease in PRO during treatment, with recovery to baseline.
- Unclear if the reduced RT dose and avoidance of chemotherapy will lead to better long term PRO

3311: TRANSLATION

- TORS with deintensified post-operative therapy, is an excellent option for management of HPV related OPSCC
- Patients should be given this option as a standard of care.
- Patients should meet with a head and neck surgeon
- How do I look at this?
 - Rare home run- surgery without additional therapy
 - Many patients- deciding on the morbidity of surgery and reduced dose RT vs the morbidity of chemotherapy and radiation
 - With some exceptions, we should try to avoid tri-modality therapy

NEXT GENERATION SEQUENCING

Current Trends in Precision Medicine and Next-Generation Sequencing in Head and Neck Cancer

Roberto N. Solis, MD, Dustin A. Silverman, MD, Andrew C. Birkeland, MD*

Department of Otolaryngology-Head and Neck Surgery, University of California, Davis, 2521 Stockton Blvd., Suite 7200, Sacramento, CA, 95817, USA.

NGS- WHY DID I PICK THIS PAPER?

- Next Generation Sequencing (NGS) has gained significant popularity amongst medical oncologists
- Multiple commercial entities and academic centers have designed tests to help guide individual patient decisions on managing their cancers
- This technology is in its infancy, and is beginning to be applied to head and neck cancer
- This paper is an overview of the current state of the art

NGS- WHAT IS IT?

- Next Generation Sequencing (NGS) is a host of technologies that explores the molecular alterations of tumors
- Precision medicine is the science of applying patient-specific genetic alterations to medical decision-making or intervention

NGS- INTRODUCTION

- In the last few decades, 5 year overall survival (OS) for head and neck SCCa has not meaningfully changed
- On a yearly basis, about 14,000 patients will die of mucosal head and neck cancer in the US
- With the rise of new types of HNC, including HPV mediated cancers, and aggressive oral cavity cancers in younger patients without known risk factors, we know that the current staging system is a poor predictor of outcomes
- We need additional tools to help us analyze the factors that contribute to successful outcomes

NGS: INTRO

- NGS explores the molecular aspects of Head and neck Cancer with 2 goals
 - Identify prognostic markers
 - Identify actionable genomic alterations
- Currently, cetuximab (anti-EGFR antibody) is the only FDA approved targeted therapy for HNSCC
- The significant number of genetic mutations and variables in tumor make a single “magic bullet” challenging

NGS: CURRENT UNDERSTANDING

- In 2006 the Cancer Genome Atlas (TCGA) advanced our understanding of cancer genetics.
- In 2015, a comprehensive analysis of 279 head and neck SCCa patients who were part of TCGA was published
- Described some of the early mutational targets: TP53 mutations, activation mutation of PIK3CA, amplification of E2F1
- Therapies can be designed to target these mutations
- Despite that, we still have no approved targeted therapy (except Cetuximab)

NGS: CURRENT UNDERSTANDING

- Recent large trial, NCI-MATCH, has helped change the NGS landscape
- Using NGS to screen a large (5,954 patients) cohort with various types of refractory cancers. (None head and neck)
- 38% of tumors had an actionable mutation, 12% had multiple actionable mutations
- However, 71% of tumors have therapy-resistance mutations
- Highlights the need for combination therapies, to overcome resistance
- Successor study NCI-ComboMATCH

NGS: CURRENT UNDERSTANDING

- Despite very few standard of care options, in a recent national survey, 75% of oncologists are using NGS to guide patient care
- Tumor is sent to lab for sequencing to determine if there are targets
- There are currently dozens of FDA approved NGS platforms
 - Single gene mutations, eg. BRAF, EGFR
 - Several hundred gene panels
- Cost of sequencing a cancer genome has gone from \$1 million in 2007 to \$600 today.
 - This sequencing can now be applied to a patient's individual tumor
 - Often covered by insurance

NGS: CHALLENGES

- In theory, should be able to identify an actionable target, treat the patient with the appropriate drug, and see tumor response.
- BUT...
- Not always clear that the mutations are clinically significant (passenger mutations)
- Our understanding of WHICH mutations are significant is still limited
- Intratumor heterogeneity
- Drug resistance (tumor burden, immune mediators, heterogeneity etc)
- Still have limited actionable mutations (38% according to NCI-MATCH)

NGS: CURRENT UTILITY

- Should be considered on patients who have failed SOC therapies
 - Gene panels, and not single gene tests
- Should be used in experimental settings to help create new pathways of care.
 - Identifying signatures that might help us manage differently
 - Create better prognostic models
 - Identify new targets for therapy
- No doubt that this is only the beginning

NGS: MY THOUGHTS

- Consider for patients for whom limited options exist (recs from TB)
- When a patient is not responding the way we expect
- When cure is not likely
- Can use previous biopsy, or consider a new biopsy
- When it is unclear if a lesion is a primary site or metastasis from a previous cancer

Final Report

Patient

Name: Patient, Test
Date of Birth: XX/Mon/19XX
Sex: Female
Case Number: TN19-XXXXXX
Diagnosis: Carcinoma, metastatic, NGS

Specimen Information

Primary Tumor Site: Breast, NOS
Specimen Site: Pleura, NOS
Specimen ID: ABC-12345-XYZ
Specimen Collected: XX-Mon-2019
Completion of Testing: XX-Mon-2019

Ordered By

Ordering Physician, MD
Cancer Center
123 Main Street
Springfield, NY 12345, USA
11234 456 7890

High Impact Results

BIOMARKER	METHOD	RESULT	THERAPY ASSOCIATION	BIOMARKER LEVEL*
BRCA1	NGS	Mutated, Pathogenic Exon 21 [p.R145G]	BENEFIT olaparib, talazoparib	Level 1
			BENEFIT abiraterone, enzalutamide	Level 1
ER	IHC	Positive [2+, 90%]	BENEFIT tamoxifen, toremifene, endocrine therapy	Level 2
			BENEFIT endocrine therapy	Level 1
PR	IHC	Positive [2+, 3%]	BENEFIT abiraterone, enzalutamide, endocrine therapy	Level 2
			BENEFIT abiraterone, enzalutamide, endocrine therapy	Level 2
ERBB2 (HER2)	ISH	Not Amplified	adjuvant trastuzumab emtansine (T-DM1), lapatinib, neratinib, pertuzumab, trastuzumab	Level 1
	IHC	Negative [1+, 10%]		

* Biomarker reporting classification: Level 1 - highest level of clinical evidence and/or biomarker association included on the drug label; Level 2 - strong evidence of clinical significance and is included by standard clinical guidelines; Level 3 - general clinical significance (i.e., evidence exists in patient's tumor type, but evidence exists in another tumor type).

Additional Results

BIOMARKER	METHOD	RESULT
MSI	NGS	Stable
Tumor Mutational Burden	NGS	High
AKT1	NGS	Mutation Not Detected
AR	IHC	Positive [2+, 90%]
BRCA2	NGS	Mutation Not Detected
ERBB2 (HER2)	NGS	Mutation Not Detected
ERBB3	NGS	Mutation Not Detected
PD-L1	SP142 IHC	Negative [0]

The selection of any, all, or none of the matched therapies includes solely with the discretion of the treating physician. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, using into consideration all available information concerning the patient's condition. The NGS sequencing information for any therapeutic, and its accordance with the applicable standard of care, whether or not a particular patient will benefit from a selected therapy is based on many factors and can vary significantly. All trademarks are registered trademarks are the property of their respective owners.

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CLIA ID: 050104940 - CAP 7195577 - ISO 15189:2013 - Caris Life Sciences, MD, LLC, Medical Director - ©2019 Caris Life Sciences. All rights reserved.

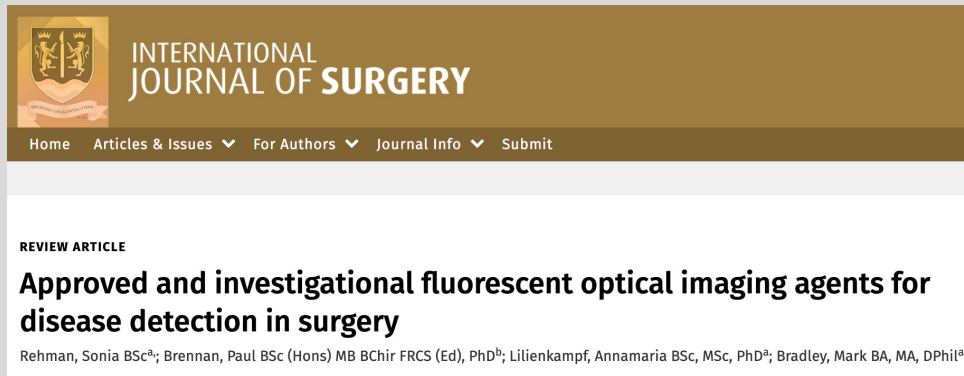
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Final Report

Other Findings

BRCA1, BRCA2, ERBB2, ERBB3, ERBB4, ERBB5, ERBB6, ERBB7, ERBB8, ERBB9, ERBB10, ERBB11, ERBB12, ERBB13, ERBB14, ERBB15, ERBB16, ERBB17, ERBB18, ERBB19, ERBB20, ERBB21, ERBB22, ERBB23, ERBB24, ERBB25, ERBB26, ERBB27, ERBB28, ERBB29, ERBB30, ERBB31, ERBB32, ERBB33, ERBB34, ERBB35, ERBB36, ERBB37, ERBB38, ERBB39, ERBB40, ERBB41, ERBB42, ERBB43, ERBB44, ERBB45, ERBB46, ERBB47, ERBB48, ERBB49, ERBB50, ERBB51, ERBB52, ERBB53, ERBB54, ERBB55, ERBB56, ERBB57, ERBB58, ERBB59, ERBB60, ERBB61, ERBB62, ERBB63, ERBB64, ERBB65, ERBB66, ERBB67, ERBB68, ERBB69, ERBB70, ERBB71, ERBB72, ERBB73, ERBB74, ERBB75, ERBB76, ERBB77, ERBB78, ERBB79, ERBB80, ERBB81, ERBB82, ERBB83, ERBB84, ERBB85, ERBB86, ERBB87, ERBB88, ERBB89, ERBB90, ERBB91, ERBB92, ERBB93, ERBB94, ERBB95, ERBB96, ERBB97, ERBB98, ERBB99, ERBB100, ERBB101, ERBB102, ERBB103, ERBB104, ERBB105, ERBB106, ERBB107, ERBB108, ERBB109, ERBB110, ERBB111, ERBB112, ERBB113, ERBB114, ERBB115, ERBB116, ERBB117, ERBB118, ERBB119, ERBB120, ERBB121, ERBB122, 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PRECISION SURGERY/ FLUORESCENT MOLECULE SURGERY-



PRECISION SURGERY/ FLUORESCENT MOLECULE SURGERY- WHY DID I PICK THIS PAPER?

- Because surgeons are jealous of precision medicine
- Enhanced-visualization surgery and molecular imaging are fields that are expanding rapidly
- Tailoring the surgery and surgical decision-making based upon enhanced information from patient and tumor specific factors
- This is an early but expanding area of interest as we can target molecules for diagnostics and therapeutics

PRECISION SURGERY- INTRO

- Medical imaging has revolutionized the practice of medicine
- MRI, PET, even CT and X-Ray have changed how we practice
- No significant technology to aid in imaging intra-op
- Molecular imaging can fill this gap
- Imaging based upon biomarkers that are disease dependent
- Disease can be monitored at the cellular/molecular level

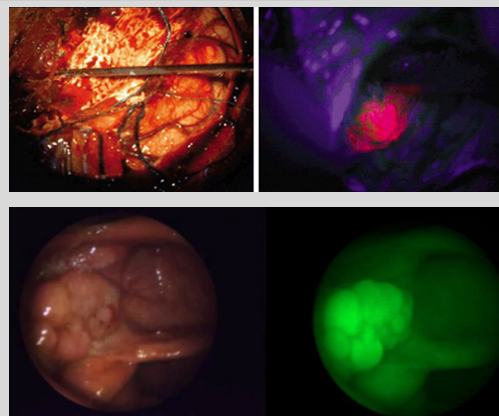


PRECISION SURGERY: INTRO

- Optical imaging is a group of technologies that allows one to interrogate structures, cells and tissues using visible light.
- Allows visualization of disease at the molecular level.
- Uses fluorescence for diagnosis, to follow disease progression, and to aid in the performance of surgery
- Surgical roles:
 - Margin delineation- reduce positive margins AND reduce removal of unnecessary tissue in high risk areas
 - Identifying multifocal disease
 - Identifying drainage patterns

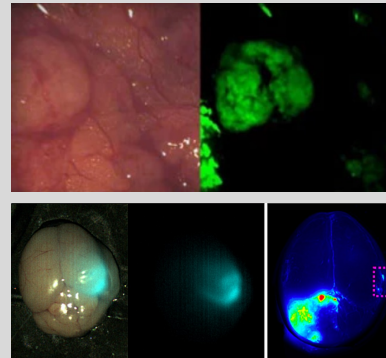
PRECISION SURGERY: CURRENT AGENTS

- 5-Aminolevulinic Acid (5-ALA)
 - Used in glioma surgery by neurosurgeons
 - Targets the hemoglobin biosynthesis pathway
 - 5-ALA levels rise in gliomas, especially high-grade ones
 - Drug was approved by FDA in 2017 for visualization and removal of high-grade gliomas
 - No other clear cancer targets
- EMI-137
 - Targets c-MET receptor, part of the tyrosine kinase family
 - Overexpression of c-MET found in tumor growth
 - EMI-137 is a fluorophore labelled peptide that binds c-MET.
 - C-MET is overexpressed in colon cancer
 - May be overexpressed in glioblastoma, Barrett's esophagus, colitis
 - Phase IIb trials in colon cancer are ongoing



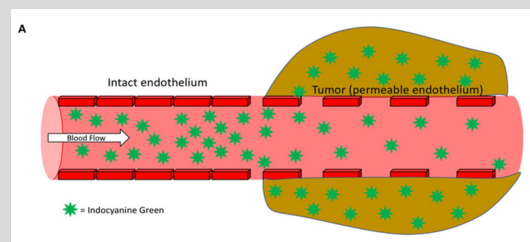
PRECISION SURGERY: CURRENT AGENTS

- OTL38
 - A near infrared (NIR) imaging probe based on folic acid coupled with an indole cyanine-like green dye (SO456)
 - Targets folate receptor alpha (FR α) overexpression
 - Approved in 2021 for imaging and resection of FR α positive ovarian and lung cancers
- BLZ-100- Part of the Tumour Paint series by Blaze Bioscience
 - Chlorotoxin (CTX), isolated from scorpion venom binds to chloride ion channels
 - Chloride ion channels are overexpressed in glioblastomas, lung and skin cancers
- LUM015
 - Targets the microenvironment around tumors
 - In Phase III trials to detect residual breast cancer



PRECISION SURGERY: CURRENT AGENTS

- Indocyanine Green
 - A tricarbocyanine dye
 - Flouresces in the NIR window
 - Has been used for decades to provide blood vessel contrast
 - When given in higher doses, seems to concentrate in tumor tissue
 - Leaky vessel theory in tumors in the “second window”



Front Surg, 2019 Mar 12;6:11. Indocyanine-Green for Fluorescence-Guided Surgery of Brain Tumors: Evidence, Techniques, and Practical Experience. Steve S Cho 1 2, Ryan Salinas 2, John Y K Lee

PRECISION SURGERY: CURRENT USE



PRECISION SURGERY: THE FUTURE

- Fluorescent optical imaging is a powerful technology, just beginning to show its full potential
- Already being used in some cancers, but will be used more broadly as more agents come to market
 - Nerve targeting peptide
 - Fungal imaging
 - Disease diagnosis

PRECISION SURGERY: MY THOUGHTS

- A powerful aid in surgical medicine
- Especially helpful in minimally invasive surgery, where haptic feedback is limited
- Very much in its infancy

THANK YOU!

