

***Update on the  
Cholangiocarcinoma in the Young  
(CITY)  
Working Group***

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# ***Cholangiocarcinoma in the Young (CITY) Working Group***

- ***Sergio Gradilone, PhD, Researcher, Mayo Clinic Rochester***
- ***Marie Halpin, CCF Volunteer***
- ***Benjamin Kipp, PhD, Cancer Genetics, Mayo Clinic Rochester***
- ***Milind Javle, MD, Medical Oncologist, MD Anderson***
- ***Jim Palma, Executive Director of TargetCancer***
- ***Tushar Patel, MB, ChB, Hepatologist, Mayo Clinic Florida***
- ***Jason Scott, PhD, CCF Board Member, Economist***
- ***Lipika Goyal, MD, MPhil, Medical Oncologist, MGH Cancer Center***

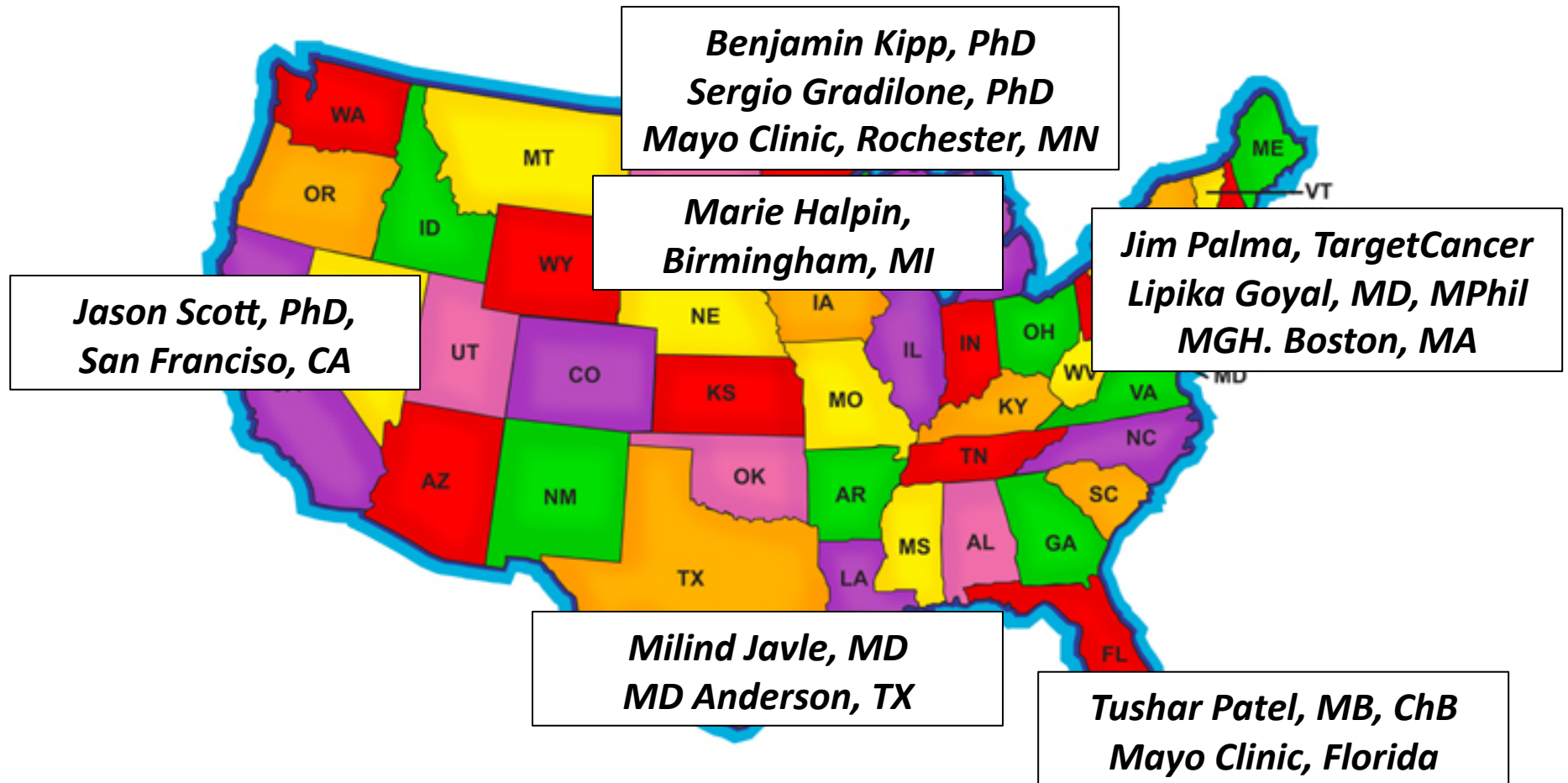
# ***CITY's Aim***

- ***Working Group #2: Profiling and Sequencing Team***
- ***Are there molecular aberrations that are driving the development of cholangiocarcinoma in young people?***
  - ***Challenges we encountered***
  - ***MGH: Single Institution Experience***
  - ***How do we maintain momentum?***

# ***6 Practical Challenges we Encountered***

- 1. Communication***
- 2. Defining the hypothesis***
- 3. Funding***
- 4. Authorship and Institutional Recognition***
- 5. Platform for data sharing***
- 6. Getting IRB approval***

# ***Challenge #1: Communication***



## ***Challenge #2: Defining the hypothesis***

- ***Defining the population:***
  - ***Intrahepatic vs extrahepatic vs both***
  - ***<30yo?, <40 yo?, <50yo?***
- ***Resources: Blood, Tissue, Chart Review***
- ***Approach: WES, WGS, RNA sequencing, proteomics? Germline vs Somatic? Internal platforms vs commercial platforms?***
- ***Prospective or Retrospective***

## ***Challenge #3: Funding***

- ***Blood/Tissue specimen retrieval, processing, and shipping***
- ***Molecular testing on blood and tissue***

# ***Our Decision: Start Small***

- ***Co-authorship is one of the most tangible and well documented ways to demonstrate scientific collaboration***
- ***Final question: What are the clinicopathologic characteristics of young patients with IHCC compared to older patients with IHCC?***



## ***Challenge #4: Authorship and Institutional Recognition***

- ***Who will get first author?***
- ***Last author?***
- ***Which institution will get the most recognition?***

# Challenge #5: Data Sharing

The screenshot displays the REDCap interface for the Biliary Tract Cancer Database. The browser address bar shows the URL [https://redcap.partners.org/redcap/redcap\\_v5.9](https://redcap.partners.org/redcap/redcap_v5.9). The user is logged in as **lg868**. The interface includes a sidebar with navigation options like **My Projects**, **Project Home**, and **Project Setup**. The main content area shows the **Pathology** section for **Study ID 1**, with fields for **Date of Diagnosis**, **Age at Diagnosis**, and **Method of Diagnosis** (Radiotherapy or Biopsy). The **TNM** section is partially visible at the bottom. The Windows taskbar at the bottom shows the time as 1:42 PM on 2/5/2015.

**REDCap™**

Logged in as **lg868** | Log out

- My Projects
- Project Home
- Project Setup

Project status: **Development**

**Data Collection** [Edit instruments](#)

- Record Status Dashboard**  
- View data collection status of all records
- Add / Edit Records**  
- Create new records or edit/view existing ones

**Study ID 1** [Select other record](#)

Data Collection Instruments:

- Demographics
- Risk Factors

## Biliary Tract Cancer Database

VIDEO: Ba

Actions: [Modify instrument](#) [Download PDF of instrument\(s\)](#)

### Pathology

[Editing existing Study ID 1](#)

<b>Study ID</b>	1
<b>Diagnosis Information</b>	
<b>Date of Diagnosis</b>	<input type="text"/> Today M-D-Y
<b>Age at Diagnosis</b>	<input type="text"/>
<b>Method of Diagnosis</b>	<input type="radio"/> Radiography <input type="radio"/> Biopsy
<b>TNM</b>	

# ***Challenge #6: Getting IRB Approval***

- ***Partners IRB***
- ***MD Anderson IRB***
- ***Mayo IRB***
- ***Data sharing agreement***

***MGH Institutional Experience  
Advanced Intrahepatic Cholangiocarcinoma  
(IHCC)***

***222 pts w/ IHCC***

***-30 pts s/p resection w/o recurrence***

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***192 advanced IHCC pts analyzed***

# ***MGH IHCC Database by Age***

<b>Age Group</b>	<b>n (%)</b>
Overall Population	192 (100%)
< 40 years old	12 (6%)
≥ 40 years old	180 (94%)
< 50 years old	38 (20%)
≥ 50 years old	154 (80%)
< 60 years old	89 (46%)
≥ 60 years old	103 (54%)

# **MGH: Overall IHCC Population (n=192)**

<b>Variable</b>	<b>n (%)</b>
<b>Median Age at Advanced Diagnosis (years)</b>	<b>60.8 (23.1 - 86.5)</b>
<b>Gender</b>	
<b>Male</b>	<b>95 (49.5%)</b>
<b>Female</b>	<b>97 (50.5%)</b>
<b>Presentation</b>	
<b>Primary Metastatic</b>	<b>144 (75%)</b>
<b>Recurrent Metastatic</b>	<b>48 (25%)</b>
<b>Baseline Median CA 19-9 (U/mL)</b>	<b>78.0 (1.0 - 94432)</b>
<b>Baseline Median CEA (ng/mL)</b>	<b>2.9 (0.2 - 887.5)</b>
<b>Total Tumor Volume (cm<sup>3</sup>)</b>	<b>132.9 (0.8 - 1488)</b>
<b>CA 19-9 / Tumor Volume Ratio</b>	<b>0.6 (0.0 - 1010)</b>

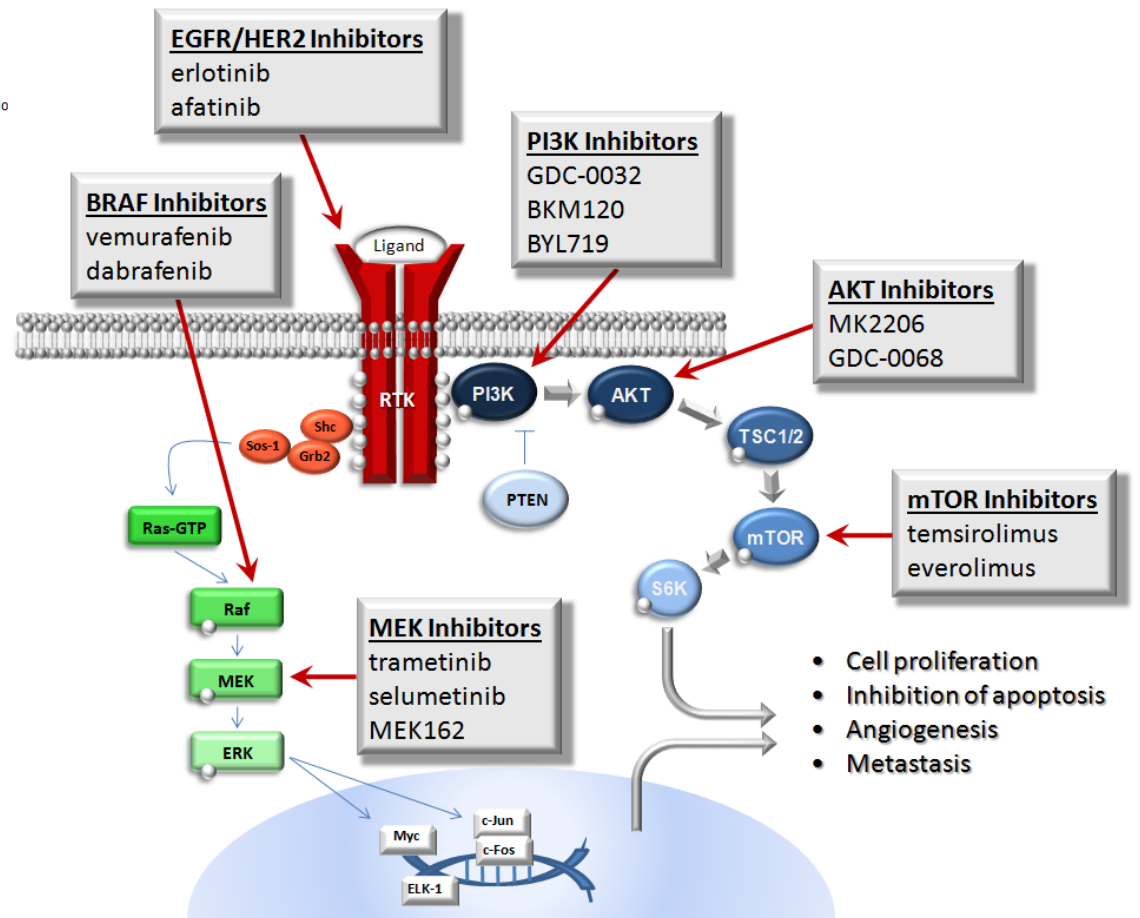
# MGH: Overall IHCC Population (n=192)

<b>Variable</b>	<b>n (%)</b>
<b>Histology</b>	
<b>Well</b>	<b>12 (9.2%)</b>
<b>Well to Moderately</b>	<b>1 (0.8%)</b>
<b>Moderately</b>	<b>52 (40.0%)</b>
<b>Moderately to Poor</b>	<b>19 (14.6%)</b>
<b>Poor</b>	<b>46 (35.4%)</b>
<b>Sites of Metastasis on Last Radiological Scans</b>	
<b>Liver</b>	<b>146 (76.8%)</b>
<b>Lymph Node</b>	<b>97 (51.1%)</b>
<b>Peritoneal</b>	<b>70 (36.8%)</b>
<b>Lung</b>	<b>69 (36.1%)</b>
<b>Bone</b>	<b>23 (12.2%)</b>
<b>Other</b>	<b>16 (8.4%)</b>

# Clinical **SNAPSHOT** Genotyping Assay

## 25 cancer genes – 160 mutations

Gene	Amino Acid - cDNA Residue	Gene	Amino Acid - cDNA Residue
<b>AKT1</b>	E17 - 49G	<b>IDH1</b>	R132 - 394C/395G
<b>ALK</b>	L1196 - 4493C	<b>IDH2</b>	R140 - 418C/419G R172 - 514A/515G
<b>APC</b>	R1114 - 3340C Q1338 - 4012C R1450 - 4348C T1556fs*3 - 4666_4667insA	<b>KIT</b>	D816 - 2447A Exon 11 deletions/insertio
<b>BRAF</b>	G466 - 1397G G469 - 1406G L597 - 1789C/1790T V600 - 1798G/1799T	<b>KRAS</b>	G12 - 34G/35G G13 - 37G/38G G61 - 181C/182A/183A A146 - 436G/437C
<b>CTNNB1</b>	D32 - 94G/95A S33 - 98C G34 - 101G S37 - 109T/110C T41 - 121A/122C S45 - 133T/134C	<b>MAP2K1</b>	Q56 - 167A K57 - 171G D67 - 199G
<b>EGFR</b>	G719 - 2155G/2156G E746_A750del - 2235_2249del15 E746_A750del - 2236_2250del15 T790 - 2369C L858 - 2573T L861 - 2582T Exon 19 deletions Exon 20 insertions	<b>NOTCH1</b>	L1575 - 4724T L1601 - 4802T
<b>ERBB2</b>	Exon 20 insertions	<b>NRAS</b>	G12 - 34G/35G G13 - 37G/38G Q61 - 181C/182A/183A
<b>FGFR3</b>	S249 - 746C G370 - 1108G Y373 - 1118A	<b>PIK3CA</b>	R88 - 263G E542 - 1624G E545 - 1633G/1634A Q546 - 1636C/1637A H1047 - 3139C/3140A G1049 - 3145G
<b>GNA11</b>	Q209 - 626A	<b>PTEN</b>	R130 - 388C R173 - 517C R233 - 697C K267fs*9 - 800delA
<b>GNAQ</b>	Q209 - 626A	<b>RET</b>	M918 - 2753T
<b>GNAS</b>	R201 - 601C/602G	<b>TP53</b>	R175 - 524G G245 - 733G R248 - 742C/743G R273 - 817C/818G R306* - 916C
<b>HRAS</b>	G12 - 34G/35G G13 - 37G/38G Q61 - 181C/182A/183G		





# ***MGH: Overall IHCC Population with Molecular Genotyping (n=103)***

<b>Mutation</b>	<b>n (%)</b>
Wildtype	48 (46.6%)
IDH1	26 (25.2%)
IDH2	4 (3.9%)
KRAS	9 (8.7%)
BRAF	3 (2.9%)
PIK3CA	5 (4.9%)
TP53	4 (3.9%)
Other Mutation	6 (5.8%)

*I want to put these data in a pie graph*

# MGH IHCC: < 50yo vs ≥50yo

Variable	Overall Population (n=192)	< 50 years (n=38)	≥50 Years (n=154)	p-value
Median Age (years)	60.8 (23.1 - 86.5)	45.3 (23.1 - 49.9)	64.1 (50.1 - 86.5)	.
Male Gender	49.5% (95)	47.4% (18)	50.0% (77)	0.771
Presentation				
Primary Metastatic	144 (75%)	22 (57.9%)	122 (79.2%)	0.007
Recurrent Metastatic	48 (25%)	16 (42.1%)	32 (20.8%)	
Baseline Median CA 19-9 (U/mL)	78.0 (1.0 - 94432)	81.0 (1.0 - 48768)	74.0 (1.0 - 94432)	0.740
Baseline Median CEA (ng/mL)	2.9 (0.2 - 887.5)	1.9 (0.2 - 134.5)	3.3 (0.3 - 887.5)	0.085

# ***MGH IHCC: < 50yo vs ≥50yo***

<b>Variable</b>	<b>Overall Population (n=192)</b>	<b>&lt; 50 years (n=38)</b>	<b>≥50 Years (n=154)</b>	<b>p-value</b>
<b>Histology</b>				
Well	12 (9.2%)	0 (0%)	12 (11.9%)	0.249
Well to Moderately	1 (0.8%)	0 (0%)	1 (1.0%)	
Moderately	52 (40.0%)	15 (51.7%)	37 (36.6%)	
Moderately to Poor	19 (14.6%)	5 (17.2%)	14 (13.9%)	
Poor	46 (35.4%)	9 (31.0%)	37 (36.6%)	
<b>Sites of Metastasis</b>				
Liver	146 (76.8%)	31 (83.8%)	115 (75.2%)	0.547
Lymph Node	97 (51.1%)	20 (54.1%)	77 (50.3%)	
Peritoneal	70 (36.8%)	18 (48.6%)	52 (34.0%)	
Lung	69 (36.1%)	12 (32.4%)	57 (37.0%)	
Bone	23 (12.2%)	4 (10.8%)	19 (12.5%)	
Other	16 (8.4%)	3 (8.1%)	13 (8.5%)	

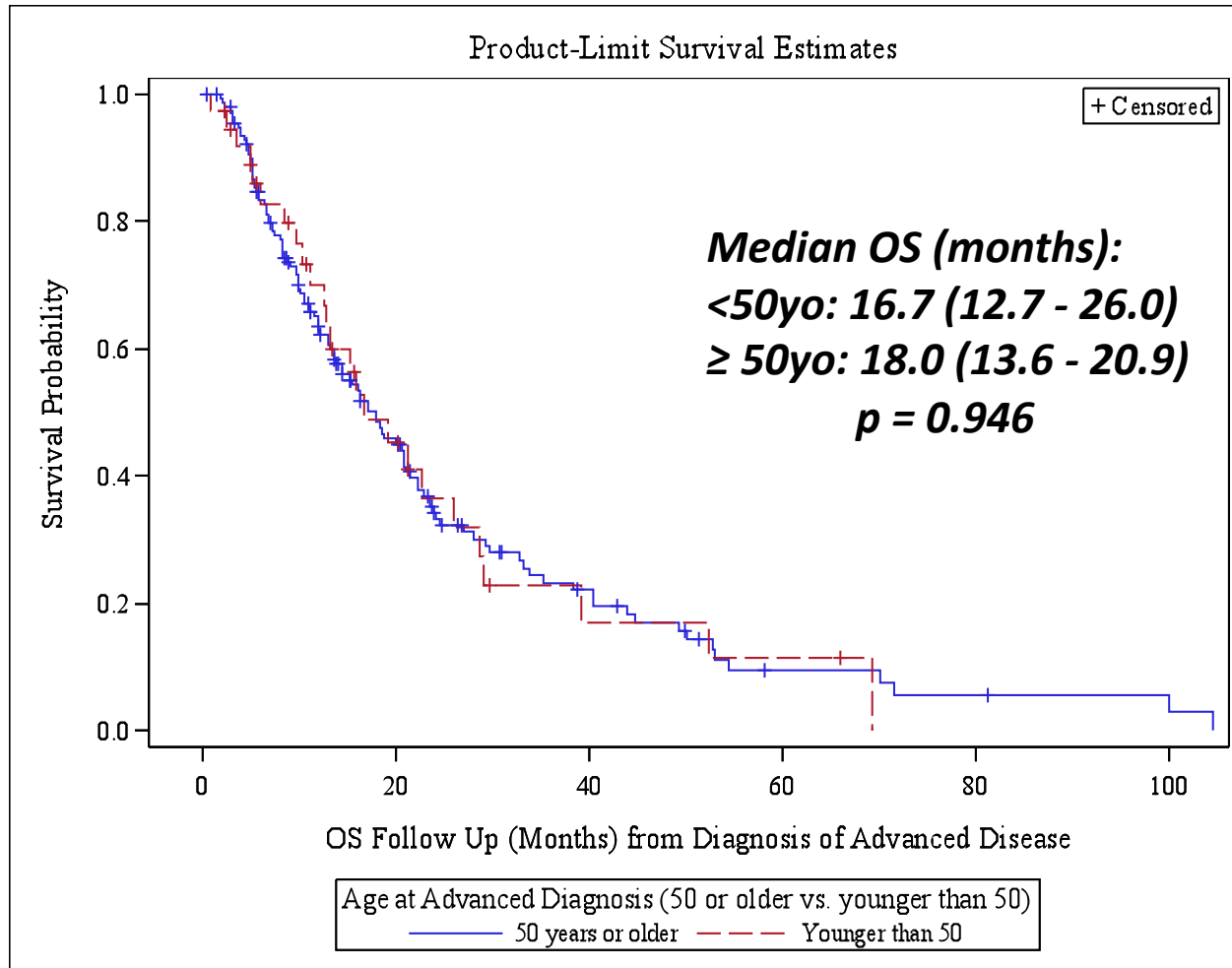
# ***MGH IHCC: < 50yo vs ≥50yo Molecular Genotyping (n=103)***

<b>Mutation</b>	<b>Overall Population (n=103)</b>	<b>&lt; 50 years (n=21)</b>	<b>≥50 Years (n=82)</b>	<b>p-value</b>
Wildtype	48 (46.6%)	11 (52.4%)	37 (45.1%)	0.552
IDH1	26 (25.2%)	5 (23.8%)	21 (25.6%)	0.865
IDH2	4 (3.9%)	1 (4.8%)	3 (3.7%)	0.815
KRAS	9 (8.7%)	1 (4.8%)	8 (9.8%)	0.470
BRAF	3 (2.9%)	1 (4.8%)	2 (2.4%)	0.572
PIK3CA	5 (4.9%)	1 (4.8%)	4 (4.9%)	0.982
TP53	4 (3.9%)	0 (0%)	4 (4.9%)	0.302
Other Mutation	6 (5.8%)	1 (4.8%)	5 (6.1%)	0.816

***I want to put these data in pie graphs***

# MGH IHCC: < 50yo vs ≥50yo

## Overall Survival



# MGH IHCC Database: < 50yo vs ≥50yo

Variable	Overall Population (n=192)	< 50 years (n=38)	≥50 Years (n=154)	p-value
Median Age (years)	60.8 (23.1 - 86.5)	45.3 (23.1 - 49.9)	64.1 (50.1 - 86.5)	.
Male Gender	49.5% (95)	47.4% (18)	50.0% (77)	0.771
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Baseline Median CEA (ng/mL)	2.9 (0.2 - 887.5)	1.9 (0.2 - 134.5)	3.3 (0.3 - 887.5)	0.085

# ***Where do we go from here?***

- ***We have a question but may need to refine it***
- ***We have a data sharing platform***
- ***We are awaiting IRB approval***

# ***How do we maintain the momentum?***

- ***Thank you to Stacey and Donna and the team at the Cholangiocarcinoma Foundation***
- ***Monthly teleconference***
- ***Point person for the project and for each site***
- ***Deadline: Abstract for GI ASCO 2016***
- ***This is Step 1 in a larger collaborative effort***



# ***Acknowledgements***

- ***Cholangiocarcinoma Foundation***
- ***CITY Working Group***
- ***Andrew Zhu, MD, PhD***
- ***Erin McDonnell, MPH, Statistician***
- ***Aparna Govindan, Research Assistant***