

Definitive liver radiotherapy for intrahepatic cholangiocarcinoma with extrahepatic metastases

~~Cancer~~

Brian De, MD

PGY-5 Radiation Oncology Resident

MD Anderson Cancer Center

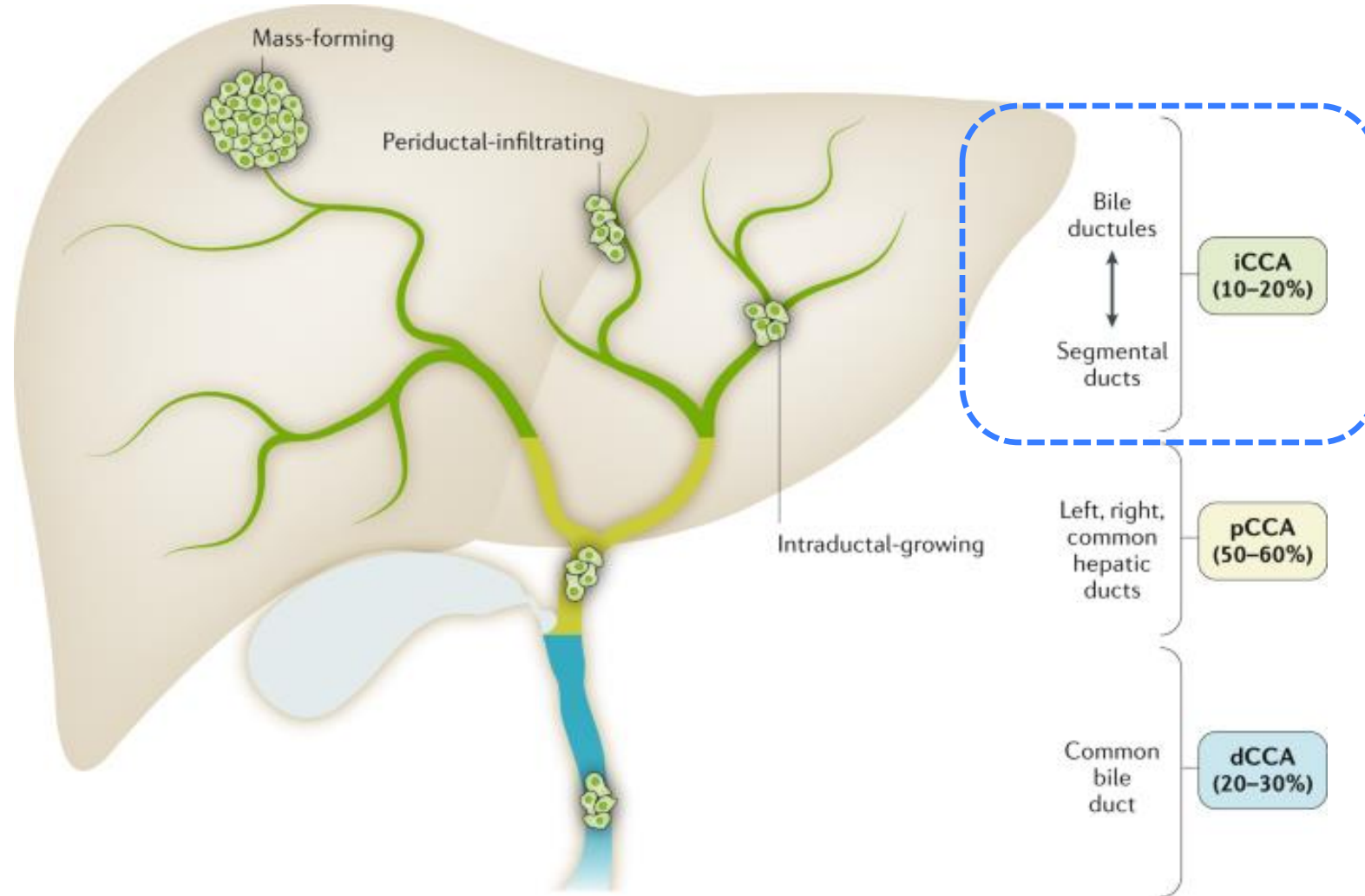
October 22nd, 2022

Disclosure of Conflicts of Interest

Brian De, MD, has no relevant financial relationships to disclose.

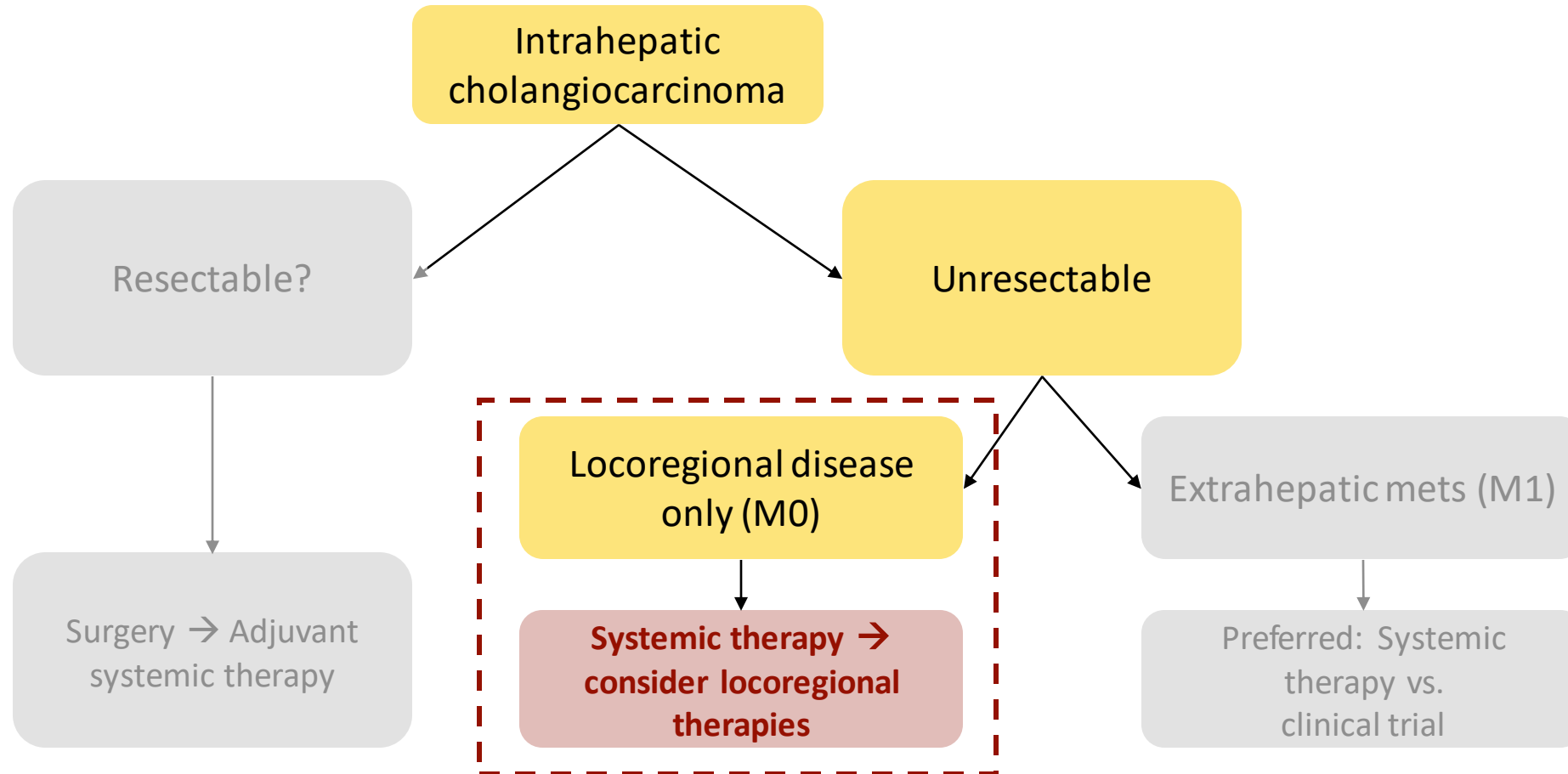


Intrahepatic cholangiocarcinoma is associated with a median survival of ~12 months





For localized disease, ICC is treated with systemic therapy +/- local therapies

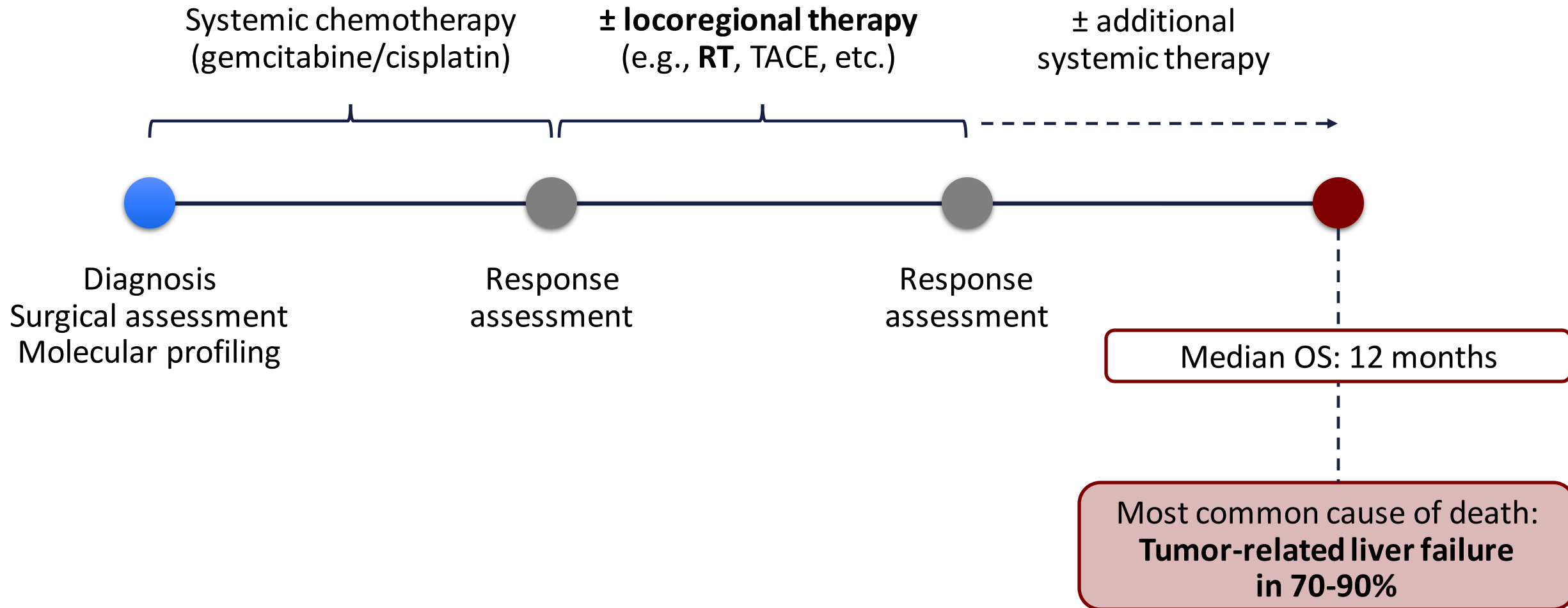


Source: NCCN Clinical Practice Guidelines in Oncology; Hepatobiliary Cancers; Version 2.2022 (July 15, 2022)

Kubo et al. Liver Cancer Study Group of Japan Clinical Practice Guidelines for Intrahepatic Cholangiocarcinoma. Liver Cancer 2022;11:290-314.



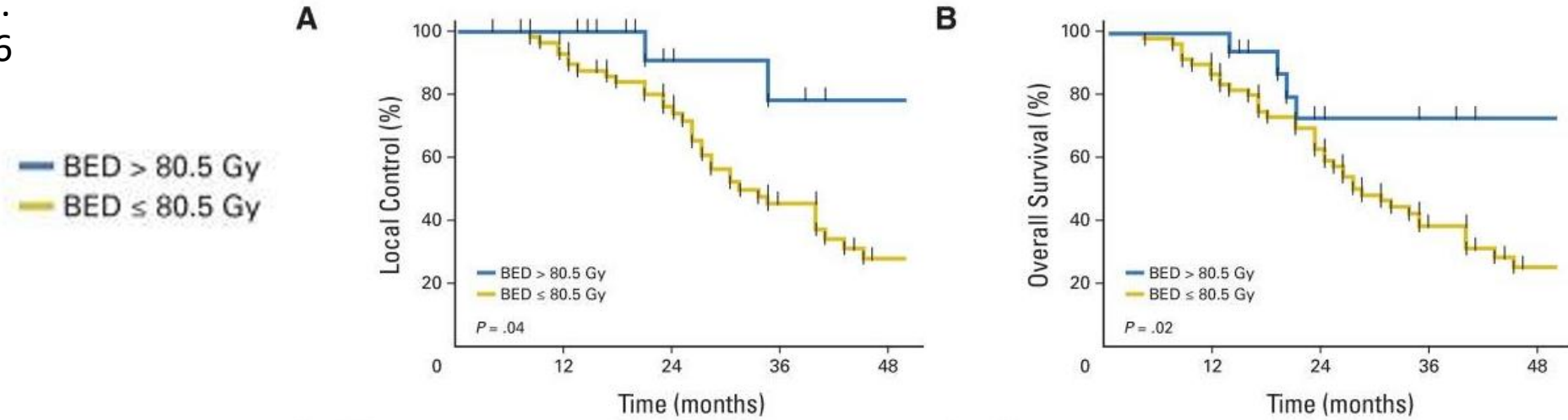
For localized disease, RT is used to reduce the risk of tumor-related liver failure (TRLF)





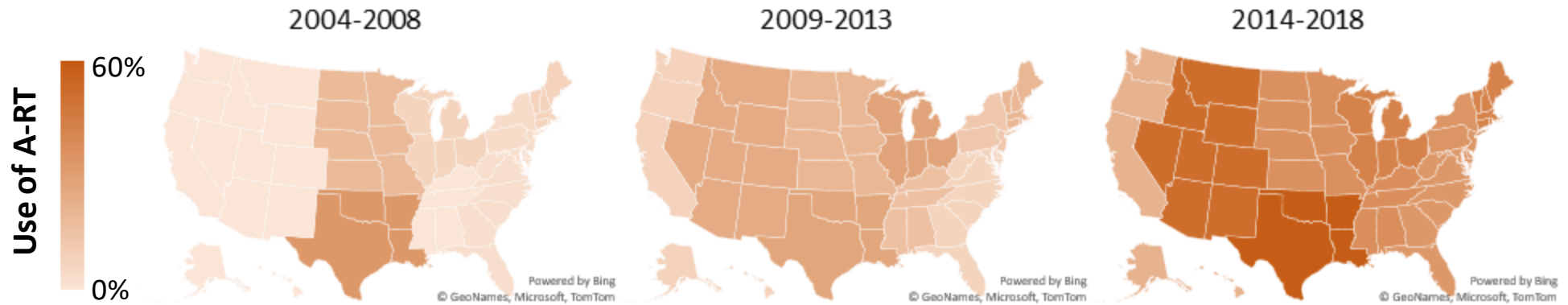
For localized disease, ablative radiotherapy (A-RT) with $BED_{10} \geq 80.5$ Gy is associated with more durable LC and longer OS

Tao et al.
JCO 2016



> 80.5 Gy
 BED_{10}
associated
with ↓ TRLF

De et al.
Cancer 2022

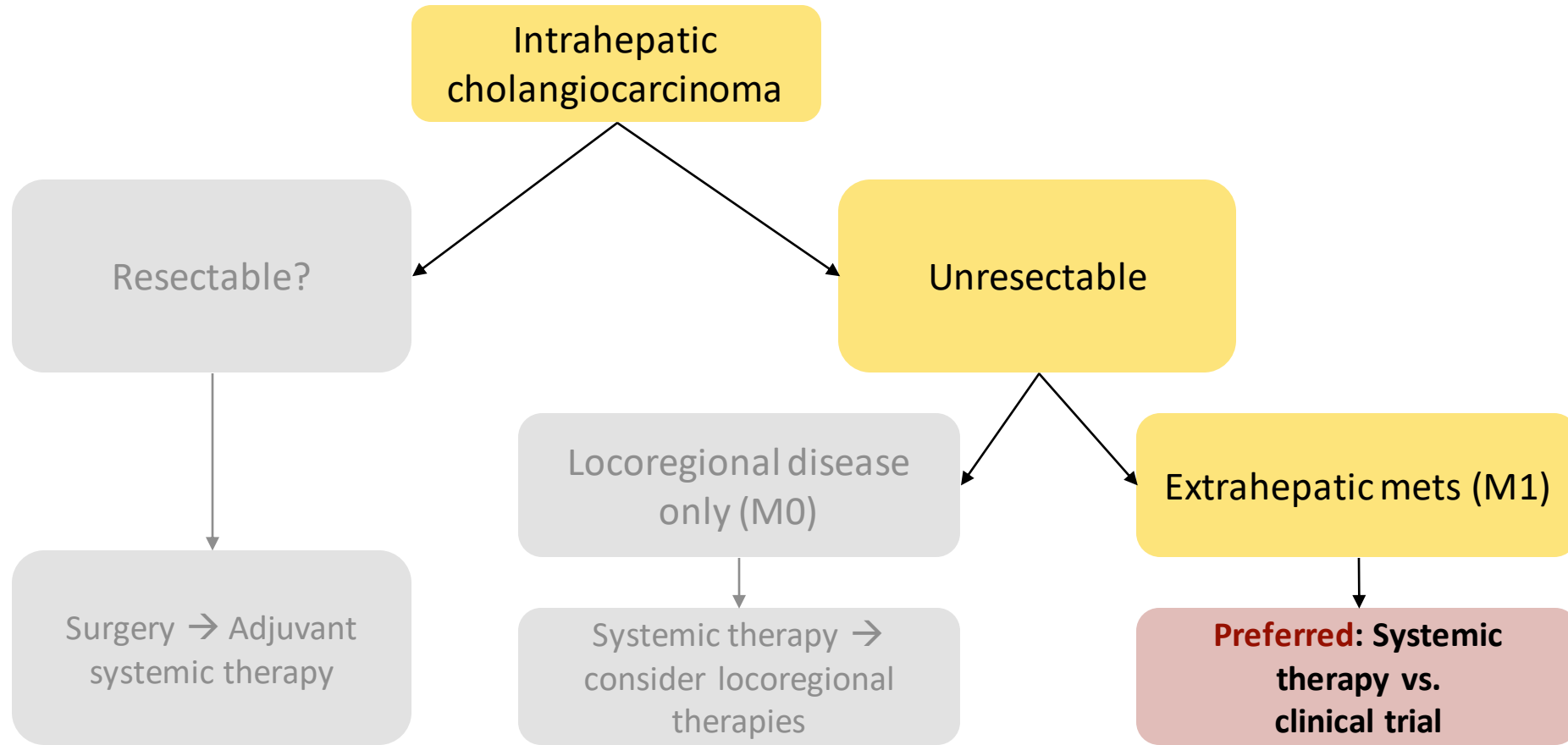


Sources: Tao et al. Ablative radiotherapy doses lead to a substantial prolongation of survival in patients with inoperable intrahepatic cholangiocarcinoma: a retrospective dose response analysis. Journal of Clinical Oncology. 2016 Jan 20;34(3):219.

De et al. Ablative liver radiotherapy for unresected intrahepatic cholangiocarcinoma: Patterns of care and survival in the United States. Cancer. 2022.



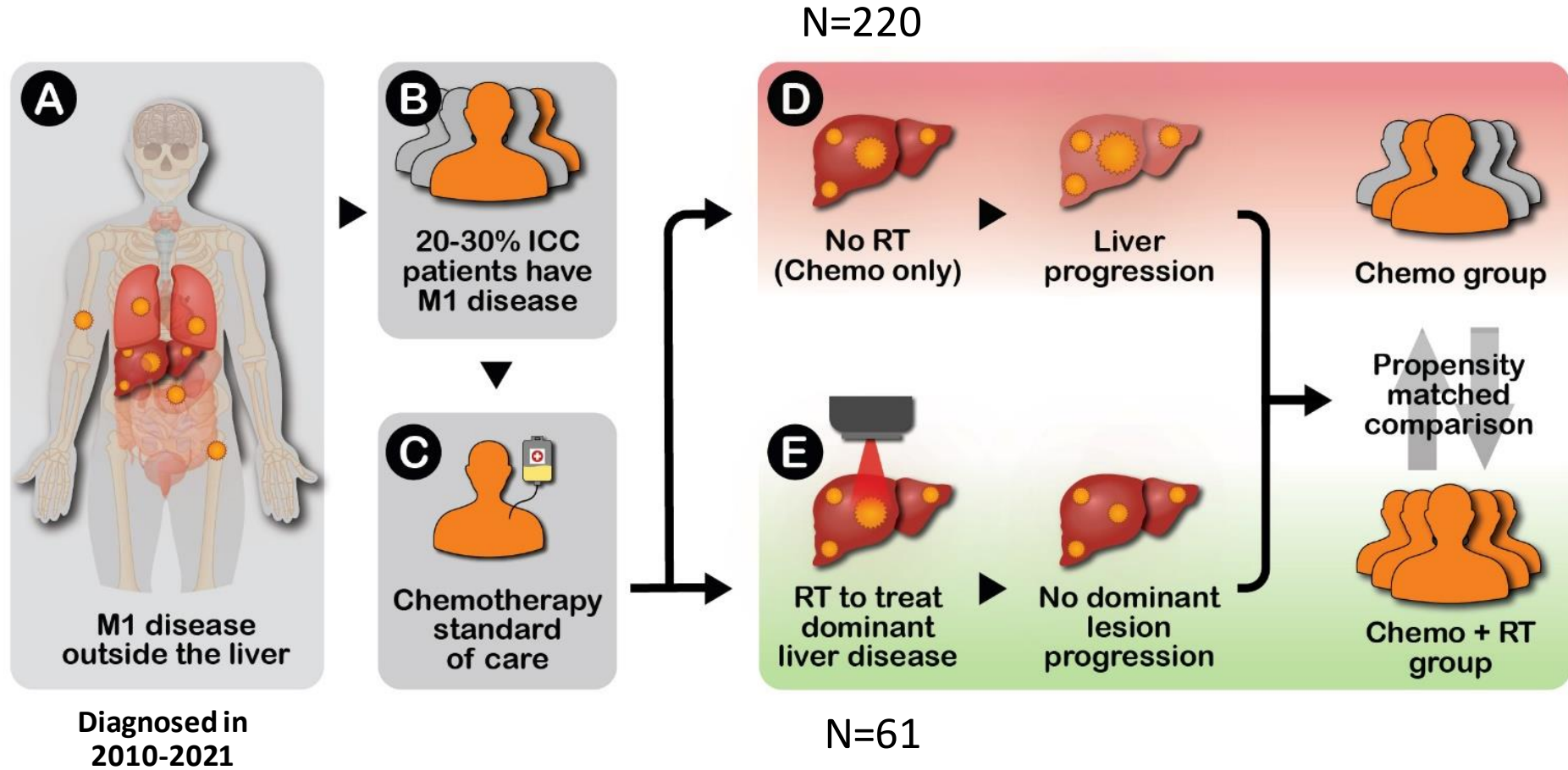
The standard of care for ICC with extrahepatic metastases is systemic therapy alone



Liver Cancer Study Group of Japan:
“... radiotherapy may be considered
for unresectable ICC with tumor
diameter ≤5 cm **in the absence of
metastasis**”

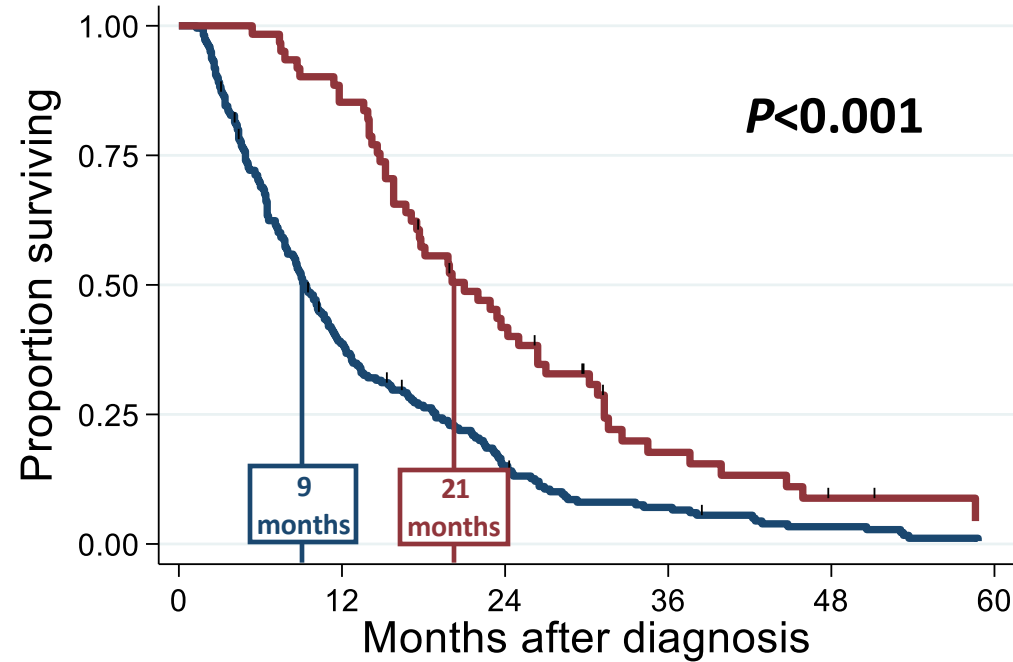


Can local therapy to the liver benefit patients with metastatic ICC?



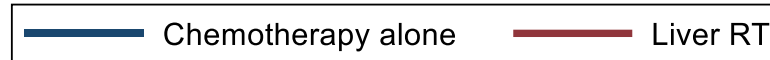


Chemo followed by RT to dominant liver lesion is associated with substantially longer survival



Number at risk

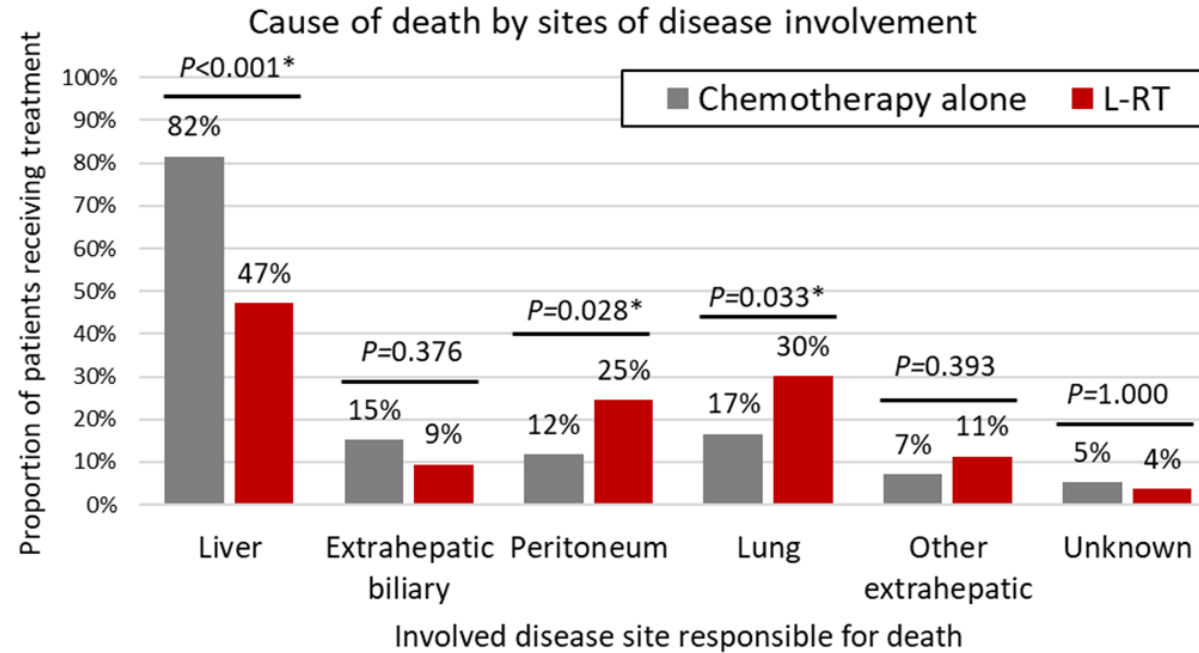
	0	12	24	36	48	60
Chemotherapy alone	220	82	31	14	6	1
Liver RT	61	52	24	8	3	1



Associated with longer survival	Associated with shorter survival
Chemotherapy duration (HR 0.85)	Age (HR 1.01)
Liver RT (HR 0.45)	ECOG 2-3 (HR 2.01)



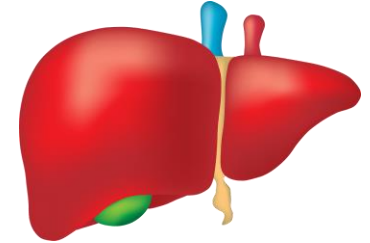
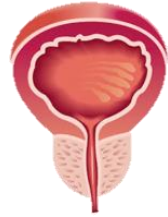
Liver RT is associated with shifts in causes of death



Attribute	Chemo alone	Chemo + RT
Median OS	Median 9 months	Median 21 months (↑)
Causes of death	Liver failure: 82% Lung: 17% Peritoneum: 12%	Liver failure: 47% (↓) Lung: 30% (↑) Peritoneum: 25% (↑)
Latency to liver failure	9 months	18 months



Comparison with selected other disease sites with benefit shown for primary site-only RT



	Prostate	Nasopharynx	Intrahepatic cholangiocarcinoma
Study	STAMPEDE (Arm H)	You et al. (China)	<i>Present study</i>
Subgroup deriving benefit	Low metastatic disease burden	Responsive to upfront chemotherapy	At risk for TRLF
OS benefit with primary site RT	81% at 3 years (vs. 73%)	76% at 2 years (vs. 55%)	Median 21 months (vs. 9 months)
Proposed <u>primary</u> mechanism	Immune modulation and eradication of resistant subclones	Eradication of resistant subclones	Mitigation of TRLF

Key conclusions and unmet needs in M1 ICC



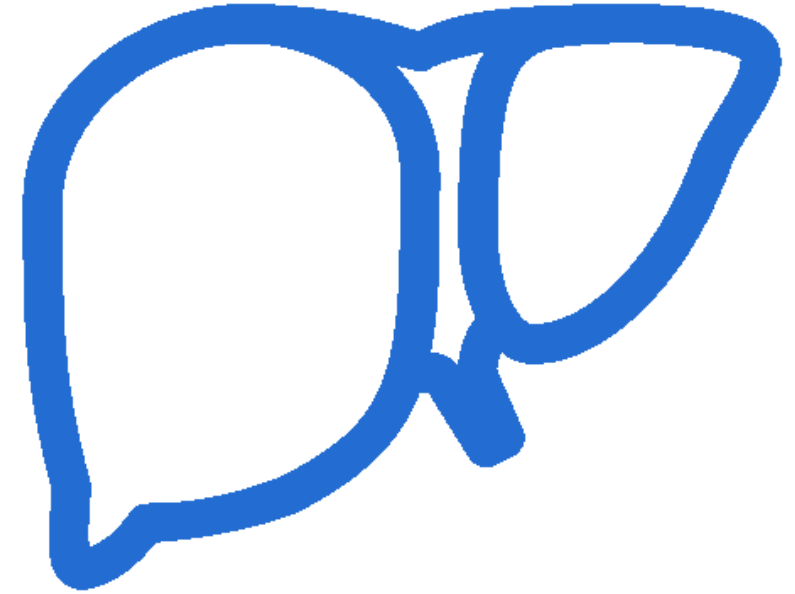
Conclusions:

- Primary site RT for M1 ICC may mitigate risk of death due to liver failure and ↑ OS



Unmet needs:

- There currently is no way to identify those patients at risk for death due to liver failure
- No prospective evidence yet exists for primary site RT



**RT to the dominant
liver lesion warrants
prospective validation**

Acknowledgments

Research mentors

Eugene J. Koay, MD PhD

Ethan Ludmir, MD

Benjamin D. Smith, MD

Grace Smith, MD

Chad Tang, MD

Emma B. Holliday, MD

Jing Li, MD PhD

Arnold Paulino, MD

Karen Hoffman, MD MPH

Vivek Verma, MD

Amol Ghia, MD

Joe Y. Chang, MD PhD

Saumil Gandhi, MD PhD

Ahsan Farooqi, MD PhD

Nikhil Thaker, MD MHA

MDACC residency program

Albert C. Koong, MD PhD

Prajnan Das, MD

Chelsea Pinnix, MD PhD

Emma B. Holliday, MD

Andrew Bishop, MD

Denise De La Cruz, Ed.D

Annette Eakes Ponnice, BA

Janice Mathew, BA

Hepatobiliary collaborators

Milind Javle, MD

Sunyoung Lee, MD

Mohamed Zaid, MD

Bruce Minsky, MD

Cullen M. Taniguchi, MD PhD

Hop Tran Cao, MD

Jean-Nicolas Vauthey, MD

Janwal P.S. Raghav MBBS MD

Ching-Wei D. Tzeng MD

Ahmed Kaseb, MD

Priya Bhosale, MD

Janio Szklaruk, MD

Kristy Brock, PhD

Lawrence Kwong, PhD

Fernando C. Carapeto DVM

Mohamed Zaid, MD

Bioinformatics mentors

C. David Fuller, MD PhD

Amy C. Moreno, MD

Co-residents & alumni

Matt S. Ning, MD MPH

Eric Brooks, MD MHA

Sean Maroongroge, MD MBA

Kelsey Corrigan, MD MPH

Gohar Manzar, MD PhD

Michael Rooney, MD

Rituraj Upadhyay, MD

External collaborators

Jennifer Y. Wo, MD (Harvard)

Chris Crane, MD (MSKCC)

Ted Hong, MD (Harvard)

Clemens Grassberger, PhD (Harvard)

Ibrahim Chamseddine, PhD (Harvard)

Imraan Jan, DO (Rutgers)

Anita Mahajan, MD (Mayo)

Bruce Haffty, MD (Rutgers)

Prashant Dogra, PhD (Methodist)

Dan Barocas, MD (Vanderbilt)

Students

Marcus Florez, BS (Baylor)

Grace Dodoo, BS (Baylor)

Arie Van Wieren, BS (JHU)

Joey Abi Jaoude, MD (Stanford)

Christopher Shi (Rice)

Tiffany Kumala (UT Austin)

Grace Waterman (Rice)

Daniela Tovar (Univ. of Houston)

Esther Lee (Rice)

Statistical Support

Graciela Nogueras-Gonzalez, PhD

Shuangshuang Fu, PhD

Suyu Liu, PhD

Funding support



Radiological Society
of North America

Definitive liver radiotherapy for intrahepatic cholangiocarcinoma with extrahepatic metastases

~~Cancer~~

Brian De, MD

PGY-5 Radiation Oncology Resident

MD Anderson Cancer Center

October 22nd, 2022