
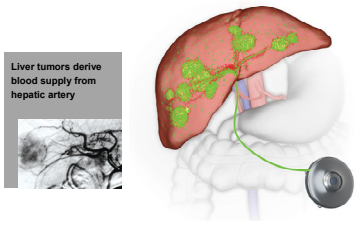


Starting a Hepatic Artery Infusion Therapy Program at WVU Medicine

Carl Schmidt, MD, FACS
 Professor of Surgery
 Chief, Division of Surgical Oncology



Principles of Hepatic Artery Infusion therapy




Liver tumors derive blood supply from hepatic artery

HAI therapy delivers ~400x higher concentration than achieved by systemic chemotherapy

First pass liver metabolism results in minimal systemic exposure of FUDR

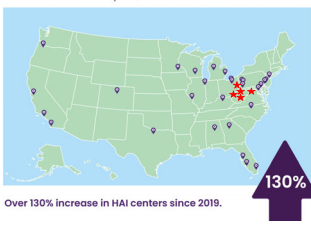
Eminger Seminars in Oncology 1983




HAI therapy use is increasing in USA

- FDA approved
- MRI safe
- Adopted by top cancer centers
- Well-established treatment protocols
- Structured training and ongoing peer-to-peer advice
- Inexhaustible power supply
- Well-established reimbursement codes
- Over 10,000 patients

Find a HAI Center near you ▶




Over 130% increase in HAI centers since 2019.

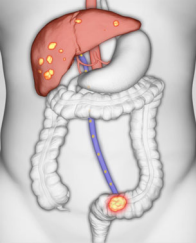


Hepatic Artery Infusion Therapy Indications

Unresectable Colorectal Liver Metastases Adjuvant Therapy after Resection




Colorectal cancer liver metastases – unmet needs



- Colorectal cancer affects 150,000 people in the US each year
- Leading cause of death in men younger than 50
- Up to 60% may develop liver metastases

- Surgical resection possible in 20% at diagnosis
- May achieve in another 15% after systemic treatment
- Recurrence after resection in 75%
- 50% recur in the liver

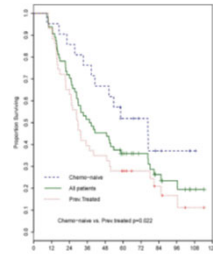
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388222/



HAI therapy for unresectable colorectal liver metastases


- Phase II trial
- N=64 unresectable
- Treated with HAI and systemic chemotherapy
- 67% prior chemo
- Median tumors = 14

- 73% response
- 86% for chemo-naïve
- 36% 5-year OS
- 52% conversion to resectable
- 63% 5-year OS if surgical resection achieved



Chemo-naïve vs. Post-treated p=0.022

Pak J Surg Oncol 2018



Adjuvant HAI therapy for resected colorectal cancer liver metastases

- Randomized clinical trial
- 156 patients
- HAI with systemic chemotherapy vs systemic chemo alone
- Fluorouracil, with or without leucovorin
- Conducted prior to introduction of newer chemotherapy
- Primary endpoint: 2-year survival

At 2 years	Systemic chemo + HAI (N=74)	Systemic chemo alone (N=82)	P value
Overall survival	86%	72%	P=0.03
Survival rate free of hepatic recurrence	90%	60%	P<0.001

Old data – no FOLFOX or FOLFIRI or bevacizumab

Kemeny *NEJM* 1999

Updated long-term survival: Adjuvant HAI therapy and systemic chemotherapy for resected colorectal liver metastases

- Retrospective, n=287
- All patients treated with HAI and systemic chemotherapy
- Two groups: before 2003 (treated with 5-FU/LV or CPT) and after 2003 (treated with FOLFOX or FOLFIRI)
- Median follow-up: 11 years.

Adjuvant HAI in Combination with Modern Chemotherapy Achieved 78% 5-year Survival and 61% 10-year Survival

Overall Survival (OS)	Entire cohort (N=278)	Treated before 2003 (N=142)	Treated after 2003 (N=136)
Median overall survival	100 months	71 months	Has not been reached
5-year OS	66%	56%	78%
10-year OS	48%	40%	61%

Kemeny *JSO* 2016

Adjuvant HAI after CRLM resection with modern chemotherapy

- Single center, N= 2,308 patients
- Complete resection of CRLM
- HAI combined with systemic vs systemic alone
- 5-FU with or without irinotecan or oxaliplatin

	Systemic chemo + HAI (N=736)	Systemic chemo alone (N=1,583)	P value
Median overall survival	67 months	44 months	<0.001
5-year survival rate	52.9%	37.9%	<0.001
10-year survival rate	38%	23.8%	<0.001

Subst analysis for recipients of modern systemic chemo (irinotecan or oxaliplatin) with or without HAI

	Modern systemic chemo + HAI (N=643)	Modern systemic chemo alone (N=759)	P value
Median overall survival	67 months	47 months	<0.001

The benefit of approximately 2 year longer survival remained in the era of modern chemotherapy

Addition of HAI to systemic chemotherapy resulted in approx. 2 years increase in median survival

Koerkamp *JCO* 2017

Hepatic Artery Infusion Therapy Indications

Unresectable Intrahepatic Cholangiocarcinoma

Intrahepatic cholangiocarcinoma- unmet needs

- Affects 5,000 people in the US each year
- Median survival 13-17 months
- Zero 3-year survivors with systemic chemotherapy alone in ABC trial

1. Mousaoui NH, El-Sherpieny M. Epidemiology of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *Cancer Control*. 2017 Jul; 24(4):427-434. doi: 10.1177/1073274817702924. 2. Valle J, Wain H, Palmer DH, et al. ABC-2 Trial Investigators. Cisplatin plus gemtacin versus gemtacin alone for biliary tract cancer. *N Engl J Med*. 2010 Apr 8;363(14):1221-1. doi: 10.1056/NEJMoa0907191. PMID: 20373064.

HAI therapy for unresectable intrahepatic cholangiocarcinoma

- Systematic review and meta-analysis of 9 publications
- 154 unique patients included in pool analysis
- Unresectable ICC patients treated with HAI

Overall Survival Rate	154 patients pooled data*
1-year OS	86.4%
2-year OS	55.5%
3-year OS	38.5%
5-year OS	9.7%

- Weighted median Overall Survival of patients with unresectable ICC treated with HAI - **29.0 months**
- 39.5% survive to 3 years**
- Median survival 16.7 months with gemcitabine/cisplatin alone in patients without metastatic disease per ABC trial

Holster *Ann Surg Oncol* 2022
Valle *NEJM* 2010

Can HAI help my patient?



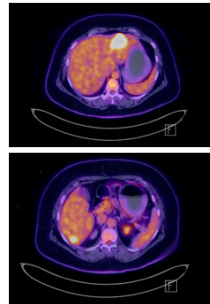
Case #1: Colorectal cancer

- 46 y/o woman – metastatic rectal cancer to liver dx 2017
- FOLFOX-panitumumab x 6 cycles
- Jan 2018 - Laparoscopic anterior resection and ablation 3 liver masses
- FOLFOX-panitumumab x 6 cycles

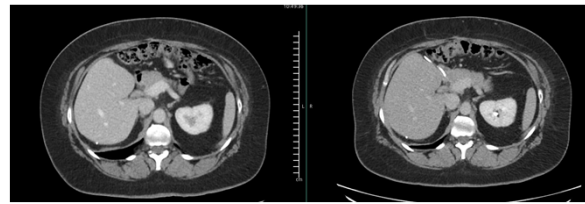


Case #1: Colorectal cancer Recurrence in liver only

- March 2019 - removal of left liver mass, right liver mass and microwave ablation of posterior right liver mass, cholecystectomy, **HAI**
- Adjuvant FUDR x 4 cycles
- August 2019 - pump removed
- Surveillance alternating CT CAP and MRI
- Remains NED as of Sept 2023



Case #1: Colorectal cancer Surveillance CT scans



May 2023

Jan 2022



Case #2: Unresectable intrahepatic cholangiocarcinoma

- 61 y/o man with fatigue and abnormal labs
- CT scan - multiple liver masses
- Percutaneous biopsy c/w cholangiocarcinoma
- EGD and colonoscopy clear
- Local tumor board declares not resectable
- Gem/cis for 8 cycles and well tolerated
- Imaging after cycle 8 shows progression – still liver only disease
- Referral to surgical oncology



Case #2: Unresectable intrahepatic cholangiocarcinoma

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULTS	THERAPY ASSOCIATION	BIOMARKER LEVEL*
ERBB2 (HER2/Neu)	IHC	DNA Tumor	Not Analyzed	LACK OF EFFECT	Lowest
	IHC	Protein	Negative (0)	panitumumab, trastuzumab	

* Biomarker reporting classification Level 1 – Computer diagnosed (CDx) and 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines. Level 3 – Minimal clinical significance. Biopsy result requires further testing to confirm the most clinically significant therapy.

Important Note

An AI CDx result was not reported for this case because the algorithm was not able to match the sample to any of the tested tumor types with a sufficient level of confidence.

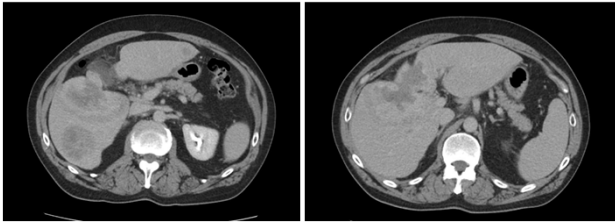
Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result	Biomarker	Method	Analyte	Result
MSI	Seq	DNA Tumor	Stable	FGFR2	Seq	DNA Tumor	Mutation Not Detected
Microsatellite Status	IHC	Protein	Stable	WNT1	Seq	WNA Tumor	Mutation Not Detected
MSI-High	Seq	WNA Tumor	Mutation Not Detected	FGFR3	Seq	WNA Tumor	Mutation Not Detected
Tumor Microsatellite Instability	Seq	DNA Tumor	Low, 4-14.8%	EGFR	Seq	DNA Tumor	Mutation Not Detected
MSI-H	Seq	DNA Tumor	Mutation Not Detected	EGFR2	Seq	DNA Tumor	Mutation Not Detected
BRCA1	Seq	DNA Tumor	Mutation Not Detected	BRCA2	Seq	WNA Tumor	Mutation Not Detected
BRCA2	Seq	DNA Tumor	Mutation Not Detected	BRCA1	Seq	DNA Tumor	Mutation Not Detected
ERBB2 (HER2/Neu)	IHC	Protein	Negative (0)	PD-L1 (SP142)	IHC	Protein	Negative (0%)
ERBB2 (HER2/Neu)	IHC	Protein	Negative (0)	MSI-H	Seq	DNA Tumor	Mutation Not Detected
ERBB2 (HER2/Neu)	IHC	Protein	Negative (0)				

OTHER FINDINGS (see below for additional results)



Case #2: Unresectable intrahepatic cholangiocarcinoma



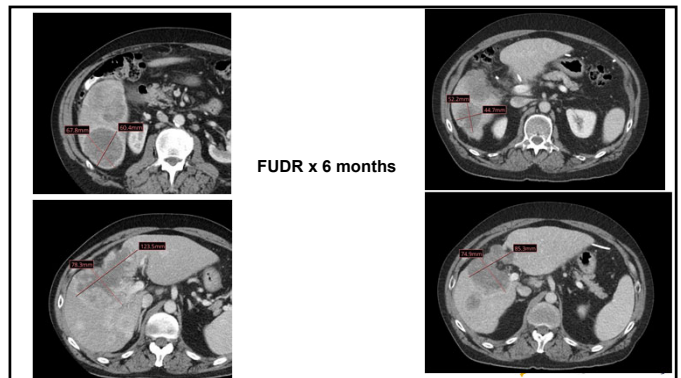
Case #2: Unresectable intrahepatic cholangiocarcinoma

Surgical resection not feasible...

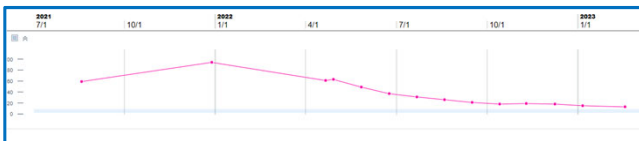


**Case #2: Unresectable intrahepatic cholangiocarcinoma
HAI therapy**

- Robotic cholecystectomy and placement pump
- Indocyanine green perfusion angiography
- FUDR x 3 cycles
- Imaging consistent with response



**Case #2: Unresectable intrahepatic cholangiocarcinoma
Tumor marker (AFP)**



**Case #2: Unresectable intrahepatic cholangiocarcinoma
HAI therapy for over 1 year**

- Imaging after 6 and 9 cycles – ongoing tumor **response**
- Imaging after 12 cycles – stable and no metastatic disease
- Completed 14 cycles FUDR then developed abdominal pain possibly related to FUDR infusions (rare side effect)
- Treated with Y-90 SIRT x 3
- Still alive 2 years after diagnosis of unresectable ICC

Why start an HAI program at your hospital?

HAI therapy is a commitment for patients

HAI therapy requires close collaboration of multidisciplinary teams and shared decision making between medical and surgical oncologists

- HAI therapy initiated 2-4 weeks postop
- HAI pump refilled every two weeks alternating floxuridine and heparinized saline
- Bi-weekly refills administered by infusion center
- FUOR dosing adjustments made at each refill based on liver labs
- Pump may be kept implanted indefinitely in case of recurrence – glycerin refills done every 2-3 months



How can we partner to bring HAI to more patients?

- Oncology nurses familiar with accessing ports can learn the procedure and teach colleagues how to refill pumps
- Oncology pharmacist trained on dosing protocols
- Intera Oncology supports on-site training
- WVU Morgantown team will also support - carl.schmidt@hsc.wvu.edu

Questions?

Carl Schmidt, MD, FACS
 Professor of Surgery
 Chief, Division of Surgical Oncology
 Contact – mobile 614-545-8913
 Email – carl.schmidt@hsc.wvu.edu