American College of Radiology
ACR Appropriateness Criteria®
Management of Liver Cancer

Variant: 1 Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.

Procedure	Appropriateness Category
Liver transplantation	Usually Appropriate
Percutaneous ablation liver	Usually Appropriate
Surgical liver resection	Usually Appropriate
Combination locoregional therapy	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Transarterial chemoembolization	May Be Appropriate
Transarterial radioembolization	May Be Appropriate
Bland transarterial embolization	May Be Appropriate
Systemic therapies	Usually Not Appropriate

Variant: 2 Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.

Procedure	Appropriateness Category
Liver transplantation	Usually Appropriate
Combination locoregional therapy	Usually Appropriate
Surgical liver resection	Usually Appropriate
Transarterial chemoembolization	Usually Appropriate
Transarterial radioembolization	Usually Appropriate
Bland transarterial embolization	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Percutaneous ablation liver	May Be Appropriate
Systemic therapies	Usually Not Appropriate

Variant: 3 Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.

Procedure	Appropriateness Category
Transarterial chemoembolization	Usually Appropriate
Transarterial radioembolization	Usually Appropriate
Bland transarterial embolization	Usually Appropriate
Systemic therapies	Usually Appropriate
Combination locoregional therapy	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Percutaneous ablation liver	Usually Not Appropriate
Surgical liver resection	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Variant: 4 Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

Procedure	Appropriateness Category
Systemic therapies	Usually Appropriate
Transarterial radioembolization	Usually Appropriate
Transarterial chemoembolization	May Be Appropriate
Bland transarterial embolization	May Be Appropriate
Combination locoregional therapy	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Percutaneous ablation liver	Usually Not Appropriate
Surgical liver resection	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Variant: 5 Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.

Procedure	Appropriateness Category
Surgical liver resection	Usually Appropriate
Percutaneous ablation liver	Usually Appropriate
Liver transplantation	May Be Appropriate
Systemic therapies	May Be Appropriate
Transarterial radioembolization	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Transarterial chemoembolization	May Be Appropriate
Bland transarterial embolization	Usually Not Appropriate

Variant: 6 Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.

Procedure	Appropriateness Category
Systemic therapies	Usually Appropriate
Transarterial radioembolization	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Bland transarterial embolization	Usually Not Appropriate
Transarterial chemoembolization	Usually Not Appropriate
Percutaneous ablation liver	Usually Not Appropriate
Surgical liver resection	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Variant: 7 Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).

Procedure	Appropriateness Category
Long-acting somatostatin analogs	Usually Appropriate
Bland transarterial embolization	Usually Appropriate
Peptide receptor radionuclide therapy	Usually Appropriate
Transarterial chemoembolization	Usually Appropriate
Transarterial radioembolization	Usually Appropriate
Systemic therapies	May Be Appropriate

External beam radiation therapy	May Be Appropriate
Percutaneous ablation liver	May Be Appropriate
Surgical liver resection	May Be Appropriate
Combination locoregional therapy	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Variant: 8 Metastatic liver disease: Solitary colorectal liver metastasis.

Procedure	Appropriateness Category
Systemic therapies	Usually Appropriate
Surgical liver resection	Usually Appropriate
Percutaneous ablation liver	Usually Appropriate
Combination locoregional therapy	May Be Appropriate
External beam radiation therapy	May Be Appropriate
Transarterial chemoembolization	May Be Appropriate
Transarterial radioembolization	May Be Appropriate
Bland transarterial embolization	Usually Not Appropriate
Hepatic arterial chemotherapy infusion	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Variant: 9 Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

Procedure	Appropriateness Category
Systemic therapies	Usually Appropriate
Hepatic arterial chemotherapy infusion	May Be Appropriate
Transarterial chemoembolization	May Be Appropriate
Transarterial radioembolization	May Be Appropriate
Bland transarterial embolization	May Be Appropriate (Disagreement)
Combination locoregional therapy	May Be Appropriate
Percutaneous ablation liver	May Be Appropriate
Surgical liver resection	May Be Appropriate
External beam radiation therapy	Usually Not Appropriate
Liver transplantation	Usually Not Appropriate

Panel Members

Erica M. Knavel Koepsel, MD[a]; Amanda R. Smolock, MD, PhD[b]; Jason W. Pinchot, MD[c]; Charles Y. Kim, MD[d]; Osmanuddin Ahmed, MD[e]; Murthy R.K. Chamarthy, MD[f]; Elizabeth M. Hecht, MD[g]; Gloria L. Hwang, MD[h]; David E. Kaplan, MD, MSc[i]; Join Y. Luh, MD[j]; Jorge A. Marrero, MD, MS[k]; Eric J. Monroe, MD[l]; George A. Poultsides, MD, MS[m]; Matthew J. Scheidt, MD[n]; Eric J. Hohenwalter, MD.[o]

Summary of Literature Review

Introduction/Background

The treatment and management of hepatic malignancies can be complex because it encompasses a variety of primary and metastatic malignancies and an assortment of local and systemic treatment options. Knowing when to use each of these treatments is critical to ensure the most appropriate care for patients. Interventional radiologists have a key role to play in the delivery of a variety of liver-directed treatments including percutaneous ablation, transarterial embolization (TAE) with bland embolic particles alone, transarterial chemoembolization (TACE) with injection of a chemotherapeutic emulsion, and transarterial radioembolization (TARE). Based on 9 clinical variants, the appropriateness of each treatment is described in this document.

Discussion of Procedures by Variant

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
A. Systemic Therapies

There is no evidence to support the use of systemic agents in very early-stage hepatocellular carcinoma (HCC).

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
B. Surgical Liver Resection

For patients with early-stage disease, treatment should be completed with curative intent in the absence of extrahepatic metastatic disease or portal vein invasion [1,2]. Patients with early-stage localized cancer with good liver function should be considered for resection [3]. Surgical resection provides a treatment pathway with comparable long-term survival to transplantation in patients without significant underlying liver disease and low-volume disease [4-6]. Patients with Child-Turcotte-Pugh (CTP) Class A cirrhosis without evidence of portal hypertension are generally appropriate candidates for resection [7]. Patients with CTP Class B and CTP Class C cirrhosis are at higher risk for decompensation and have a less favorable 5-year survival rate, making them poor resection candidates. However, they could be considered for transplantation [7,8]. The tumor location and invasion of hepatic vasculature can also limit resectability.

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
C. Liver Transplantation

For patients with 1 tumor measuring ≤5 cm or 3 tumors measuring <3 cm (ie, patients falling within the "Milan criteria"), treatment should be completed with curative intent in the absence of extrahepatic metastatic disease or portal vein invasion [2,9]. Transplant patients with limited tumor burden, as defined by the Milan criteria, have been found to have equivalent survival outcomes compared with patients who have received transplants for non-HCC indications [7]. Liver transplantation confers the best long-term survival for patients with HCC who meet the Milan criteria but can be hindered by donor organ availability [1,10-12]. For patients with more advanced liver disease, who are not surgical resection candidates, transplantation may be an excellent option to treat both their underlying liver disease and their HCC.

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
D. Percutaneous Ablation Liver

Ablative therapies include thermal (radiofrequency ablation [RFA], microwave ablation [MWA], and cryoablation) and nonthermal (percutaneous ethanol injection) modalities. Currently, thermal techniques are more commonly performed because of superior control and efficacy [13,14]. These techniques can be performed percutaneously or surgically (open or laparoscopic). Thermal ablative

techniques are an effective treatment for tumors <3 cm in diameter with good local control rates, which have been demonstrated to be similar to resection [15-21]. RFA and MWA are the most commonly used thermal techniques. MWA may have potential advantages over RFA, based on the clinical situation, because it is less susceptible to heat-sink, creates larger ablation zones in a shorter period of time, and is less susceptible to the effects of tissue impedance [9].

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
E. External Beam Radiation Therapy

Stereotactic body radiotherapy (SBRT) is generally reserved for unresectable disease [22]. However, there is some evidence to suggest the use of SBRT as a first-line therapy for HCC tumors <6 cm in diameter [22-24]. Several studies have found 1-year local control rates between 75% and 100%, with acceptable toxicity rates with lesions up to 6 to 7 cm in diameter [24-26]. There are some studies showing improved local control and mixed results for overall survival for early-stage HCC treated with SBRT compared to RFA, although they are limited by sample size and varying methodologies [27-31]. SBRT has been used to downstage or bridge patients to transplant or resection [32-35]. Unfortunately, there are limited long-term prospective data regarding SBRT for HCC [22].

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
F. Bland Transarterial Embolization

Transarterial techniques are generally unnecessary with solitary tumors <3 cm and are reserved for unresectable disease [36].

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
G. Transarterial Chemoembolization

Transarterial techniques are generally unnecessary with solitary tumors <3 cm and are reserved for unresectable disease [36]. However, TACE has been used as an adjuvant procedure before ablation using the injected lipiodol as a target for tumors with ill-defined borders or those which are difficult to see with CT or ultrasound (US) [37,38].

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
H. Transarterial Radioembolization

TARE with Yttrium-90 is a transarterial therapy that is an option for patients with multifocal HCC. Yttrium-90 emits damaging beta particles, which locally causes radiation-induced cell death, without causing vascular occlusion [39,40]. TARE has gained support for its use as an alternative to focal therapy for patients with low-volume disease with results similar to other curative intent treatment strategies, such as ablation. TARE is administered at a higher dose to targeted liver segments (usually <2), maximizing the lethal effects and minimizing damage to unaffected parenchyma [41-44].

TARE has been used to downstage or bridge patients to transplant or resection [3,32,35,36,45-47]. Initial studies seemed to favor TARE for downstaging, but a recent study demonstrated similar posttreatment outcomes [32,45,48]. In general, TARE and other transarterial techniques are unnecessary with solitary tumors <3 cm and are reserved for unresectable disease, but additional applications have been developed.

Variant 1: Hepatocellular cancer: Solitary tumor less than 3 cm, cirrhotic.
I. Combination Locoregional Therapy

Combination locoregional therapies (ablation plus TACE or TAE) can be used to improve

tumoricidal effects and increase the size of the ablation by reducing the heat-sink effect but are usually indicated for intermediate size lesions >3 to 4 cm, or those lesions with poorly defined margins [9,49-55]. Combination therapy can also be advantageous for poorly visible tumors on US or CT, and preablation TACE can aid in localizing and targeting the tumor for ablation [38].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
A. Systemic Therapies

There is no evidence to support the use of systemic agents in early-stage HCC.

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
B. Surgical Liver Resection

For patients with 1 tumor measuring ≤5 cm, treatment should be completed with curative intent in the absence of extrahepatic metastatic disease or vascular invasion [1,2]. The patient's underlying liver disease, the location of the tumor, and the presence of vascular invasion may exclude them from these surgical approaches [56]. Patients with CTP Class A cirrhosis without evidence of portal hypertension are generally appropriate candidates for resection [7]. Patients with CTP Class B and CTP Class C cirrhosis are at higher risk for decompensation and less favorable 5-year survival, making them poor resection candidates, but they could be considered for transplantation [7,8].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
C. Liver Transplantation

Solitary tumors between 3 and 5 cm still meet the Milan criteria for liver transplantation, and long-term survival in patients with solitary tumors has been shown to be 70% after 5 years [1,57]. Liver transplantation confers the best long-term survival for patients with HCC who meet the Milan criteria but can be hindered by donor organ availability [1,10-12]. For patients with more advanced liver disease who are not surgical resection candidates, transplantation may be an excellent option for treating both their underlying liver disease and their HCC.

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
D. Percutaneous Ablation Liver

Ablation therapies can still be used in this scenario but are commonly combined with TACE or TAE to improve tumoricidal effects and increase the size of the ablation for intermediate size lesions >3 cm in diameter [49-55]. MWA, which is less susceptible to heat-sink and tissue impedance, has shown effectiveness as a monotherapy for tumors >3 cm in diameter [58,59].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
E. External Beam Radiation Therapy

Unfortunately, there is limited long-term prospective data regarding SBRT for HCC, and it is usually reserved for unresectable disease [22]. However, there is some evidence to suggest including SBRT as a first-line therapy for HCC <6 cm in diameter [22-24]. Several studies have found 1-year local control rates between 75% and 100% with acceptable toxicity rates with lesions up to 6 to 7 cm in diameter [24-26]. There are some studies showing improved local control and mixed results for overall survival for early-stage HCC treated with SBRT compared with RFA, although they are limited by sample size and varying methodologies [27-31]. SBRT has been used to downstage or bridge patients to transplant or resection [32-35].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
F. Bland Transarterial Embolization

There is variable evidence in the literature regarding the superiority of TACE, drug-eluting beads (DEB)-TACE, or bland TAE, with limited evidence that TAE is similar in effectiveness to TACE or DEB-TACE [60-63]. However, DEB-TACE may have less systemic toxicity compared with TACE [64-67].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
G. Transarterial Chemoembolization

For patients with acceptable liver function and unresectable disease, TACE has shown a survival advantage compared with supportive care in several small randomized controlled studies [68,69]. However, there have been additional conflicting studies that have failed to demonstrate a survival advantage compared with conservative management [70-72]. These studies are also small in size and use variable TACE techniques and chemotherapeutics. There is variable evidence in the literature regarding the superiority of TACE, DEB-TACE, or TAE, with limited evidence that TAE is similar in effectiveness to TACE/DEB-TACE [60-63]. However, DEB-TACE may have less systemic toxicity [64-66,73]. TACE has also been used to control tumor progression for those awaiting transplant or as adjuvant treatment before resection [74-80].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
H. Transarterial Radioembolization

TARE has gained support for its use as an alternative to focal therapy for patients with low-volume disease, with results similar to other curative intent treatment strategies, such as ablation. TARE is administered at a higher dose to targeted liver segments (usually <2), maximizing the lethal effects and minimizing damage to unaffected parenchyma [41-44].

TARE has been used to downstage or bridge patients to transplant or resection [3,32,45-47,81]. Initial studies comparing TACE versus TARE for downstaging seemed to favor TARE, but a recent larger study demonstrated similar posttreatment outcomes [32,45,48]. TARE as a bridging therapy may be especially important if the time on a wait list is >6 months [82].

Variant 2: Hepatocellular cancer: Solitary tumor 3 to 5 cm, cirrhotic.
I. Combination Locoregional Therapy

Combination locoregional therapies (ablation plus TACE or TAE) can be used to improve tumoricidal effects and increase the size of the ablation by reducing the heat-sink effect but are usually indicated for intermediate size lesions >3 to 4 cm or those lesions with poorly defined margins [9,49-55]. Several studies have shown improved overall survival with combination therapy of MWA and TACE for the treatment of HCC (>5 cm in diameter) compared with patients who underwent TACE alone or MWA alone [83,84].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
A. Systemic Therapies

Systemic therapies can be an option for patients with more advanced multifocal disease. Treatment with sorafenib, a tyrosine kinase inhibitor (TKI), has shown a statistically significant increase in median overall survival compared with placebo (2-3 months over placebo) [85,86]. However, recently, atezolizumab and bevacizumab given to patients with Child-Pugh A and Eastern Cooperative Oncology Group (ECOG) 0 or 1 in combination resulted in better overall and progression-free survival than sorafenib alone (overall survival at 12 months, 67.2% in combination

group compared with 54.6% in sorafenib alone group) [87].

Regorafenib is an additional TKI, which has been approved for patients previously treated with sorafenib. It has shown improved overall survival compared with placebo (10.6 versus 7.8 months) [88]. Lenvatinib is a vascular endothelial growth factor inhibitor, approved for first-line treatment of unresectable HCC. The REFLECT trial demonstrated noninferiority to sorafenib with improved overall survival (13.6 months versus 12.3 months). Nivolumab and pembrolizumab, PD-1 immune checkpoint inhibitors, and cabozantinib, an inhibitor of multiple tyrosine kinases, are additional developing treatments for HCC with promising findings on overall survival and disease progression [89-91].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
B. Surgical Liver Resection

Curative therapy with surgical resection is not a first-line therapy for multifocal HCC. Adjuvant ablation, SBRT, TAE, TACE, or Yttrium-90 could potentially be used to downstage to resection [3,32,33,35,36,45-47,54,75,81,92-97].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
C. Liver Transplantation

Liver transplantation for multifocal HCC outside of the Milan criteria is not a first-line treatment strategy. Adjuvant ablation, SBRT, TAE, TACE, or Yttrium-90 could potentially be used to downstage to transplant [3,32,33,35,36,45-47,54,75,81,92-97].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
D. Percutaneous Ablation Liver

In the setting of multifocal HCC, ablation may serve an adjunctive role to other locoregional and systemic treatments. In this setting, it would not be considered for curative intent or as initial therapy.

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
E. External Beam Radiation Therapy

SBRT can be used for inoperable HCC. Several studies have found 1-year local control rates between 75% and 100%, with acceptable toxicity rates with lesions up to 6 to 7 cm in diameter [22,24-26]. SBRT has been used to downstage or bridge patients to transplant or resection [32-35]. Unfortunately, there are limited long-term prospective data regarding SBRT for HCC [22]. Feasibility of SBRT will depend on number of lesions and lesion location, but unfortunately, there is a lack of literature to define a strict cutoff for treatment candidates [98]. SBRT may also play a role in palliation of symptomatic lesions and can also be used as salvage therapy post-TAE or TACE [99].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.
F. Bland Transarterial Embolization

There is variable evidence in the literature regarding the superiority of TACE, DEB-TACE, or TAE, with limited evidence that TAE is similar in effectiveness to TACE or DEB-TACE [60-63]. However,

DEB-TACE may have less systemic toxicity compared with TACE [64-67]. Severe underlying liver dysfunction and tumor burden limits the use of these techniques. TACE or TAE could also be used for selective embolization of multiple lesions if technically feasible [100,101].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.

G. Transarterial Chemoembolization

For patients with acceptable liver function and unresectable disease, TACE has shown a survival advantage compared with supportive care in several small randomized controlled studies [68,69]. However, there have been additional conflicting studies that have failed to demonstrate a survival advantage compared with conservative management [70-72]. These studies are also small in size and use variable TACE techniques and chemotherapeutics. There is variable evidence in the literature regarding the superiority of TACE, DEB-TACE, or TAE, with limited evidence that TAE is similar in effectiveness to TACE or DEB-TACE [60-63]. However, DEB-TACE may have less systemic toxicity [64-67]. Severe underlying liver dysfunction and tumor burden limits the use of these techniques. TACE could also be used for selective embolization of multiple lesions if technically feasible [100,101].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.

H. Transarterial Radioembolization

This treatment can be used to treat an entire hepatic lobe if there is extensive multifocal disease but can also be administered to a segment at high dose to minimize normal parenchyma injury and maximize radiation deposition within the lesion [41-44,47]. Studies comparing TARE and TACE have shown similar survival rates and complication rates with potentially less postprocedural pain and toxicity with TARE [102-108]. TARE traditionally requires a planning angiogram, calculation of hepatopulmonary shunting, and dose calculation before treatment, which has required 2 separate visits to complete, but some high-volume centers have demonstrated the feasibility of same-day and single-session treatments [109,110] TARE has been used to downstage or bridge patients to transplant or resection [3,32,35,36,45-47].

Variant 3: Hepatocellular cancer: Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic.

I. Combination Locoregional Therapy

Combination locoregional therapies could be used with palliative intent or to downstage patients in this setting. Several studies have shown improved overall survival with combination therapy of MWA and TACE for the treatment of HCC (>5 cm in diameter) compared with patients who underwent TACE alone or MWA alone [83,84].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

A. Systemic Therapies

Systemic therapies can be an option for patients with advanced-stage disease. Treatment with sorafenib, a TKI, showed a statistically significant increase in medial overall survival compared with placebo (2-3 months over placebo) [85,86]. However, recently, atezolizumab and bevacizumab given to patients with Child-Pugh A and ECOG 0 or 1 in combination resulted in better overall and

progression-free survival than sorafenib alone (overall survival at 12 months, 67.2% in combination group compared with 54.6% in sorafenib alone group) [87]. Regorafenib is an additional TKI, which has been approved for patients previously treated with sorafenib. It has shown improved overall survival compared with placebo (10.6 versus 7.8 months) [88]. Lenvatinib is a vascular endothelial growth factor inhibitor approved for first-line treatment of unresectable HCC. The REFLECT trial demonstrated noninferiority to sorafenib with improved overall survival (13.6 months versus 12.3 months). Nivolumab and pembrolizumab, PD-1 immune checkpoint inhibitors, and cabozantinib, an inhibitor of multiple tyrosine kinases, are additional developing treatments for HCC with promising findings on overall survival and disease progression [89-91].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

B. Surgical Liver Resection

Patients with solitary or multifocal disease with vascular invasion would not be candidates for resection. However, a retrospective study showing improved overall survival with hepatic resection compared with TACE for patients with intermediate- and advanced-stage disease has suggested expanding the surgical criteria, as long as the patient's preoperative liver function and postoperative liver remnant are appropriate for surgery [111].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

C. Liver Transplantation

Patients with solitary or multifocal disease with vascular invasion would not be candidates for transplantation. Patients with macrovascular invasion are at increased risk for HCC recurrence and decreased survival [112,113].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

D. Percutaneous Ablation Liver

Patients with solitary or multifocal disease with vascular invasion would not be candidates for ablation.

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

E. External Beam Radiation Therapy

SBRT can be used as palliative therapy for inoperable HCC. Several studies have found 1-year local control rates between 75% and 100%, with acceptable toxicity rates with lesions up to 6 to 7 cm in diameter [24-26]. Feasibility of SBRT will depend on the number of lesions and lesion location; unfortunately, there is a lack of literature to define a strict cutoff for treatment candidates [98]. SBRT may also play a role in palliation of symptomatic lesions and can also be used as salvage therapy post-TAE or TACE [99].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

F. Bland Transarterial Embolization

Generally, TAE or TACE is not ideal in cases of macroscopic portal vein invasion given that occlusive embolization of the hepatic artery could increase the risk of liver failure [114]. However, there have been some recent studies showing a survival benefit of TACE over conservative therapy when portal vein thrombus is present; however, this benefit, although still statistically significant, was less

pronounced in patients with advanced vascular invasion [115,116].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

G. Transarterial Chemoembolization

Generally, TAE or TACE is not ideal in cases of macroscopic portal vein invasion given that occlusive embolization of the hepatic artery could increase the risk of liver failure [114]. However, there have been some recent studies showing a survival benefit of TACE over conservative therapy when portal vein thrombus is present; however, this benefit, although still statistically significant, was less pronounced in patients with advanced vascular invasion [115,116].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

H. Transarterial Radioembolization

TARE has been used for patients with advanced disease, even safely with portal vein thrombosis, to prolong survival. Underlying liver function, performance status, and/or hepatopulmonary shunting can limit the use of this technique [81]. Patients with multifocal disease usually require staged lobar treatment, which can increase the risk for radiation-induced liver disease. Studies comparing TARE and TACE have shown similar survival rates and complication rates with potentially less postprocedural pain and toxicity with TARE [46,102-106,108]. TARE traditionally requires a planning angiogram, calculation of hepatopulmonary shunting, and dose calculation before treatment, which has required 2 separate visits to complete, but some high-volume centers have demonstrated feasibility of same-day and single-session treatments [109,110].

Variant 4: Hepatocellular cancer: Solitary or multifocal disease with vascular invasion, cirrhotic.

I. Combination Locoregional Therapy

Limited evidence is available regarding combination therapy for patients with vascular invasion. One study using a combination of SBRT and TACE showed an improved survival benefit over systemic therapy alone for macroscopic vascular invasion [117].

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.

A. Systemic Therapies

The efficacy of chemotherapy regimens for the treatment of intrahepatic cholangiocarcinoma is usually poor. With that in mind, systemic chemotherapy is generally reserved for unresectable intrahepatic cholangiocarcinoma. A combined analysis of the ABC-02 and BT22 trials in recent years [118,119] has led to widespread adoption of gemcitabine plus cisplatin as the standard palliative regimen for locally advanced or metastatic intrahepatic cholangiocarcinoma.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.

B. Surgical Liver Resection

Currently, surgical resection is the only curative treatment option and the only treatment that can provide a chance at long-term survival [120]. Unfortunately, at the time of diagnosis, many patients have locally advanced or metastatic disease, with only 15% to 30% of patients presenting with resectable disease [121]. The goals of surgical resection are to obtain a microscopically negative margin while maintaining an adequate future liver remnant. Still, 5-year survival remains poor.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
C. Liver Transplantation

Liver transplantation is only considered in select patients because recurrence rates, and survival data have been poor for this population [121]. A review of the Cincinnati Transplant Tumor Registry demonstrated a 5-year survival rate of 28%. This study also reported a 51% recurrence rate after transplantation with a median time to recurrence of 9.7 months [122].

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
D. Percutaneous Ablation Liver

Heat-based thermal ablation modalities have also shown a treatment advantage for tumors <5 cm in diameter [123]. Ablation can be used for small (<3 cm in diameter) and intermediate (3-5 cm in diameter) intrahepatic cholangiocarcinomas, which are inoperable, with a median overall survival ranging from 33 to 38.5 months [123-125]. A meta-analysis of RFA performed for intrahepatic cholangiocarcinoma found a survival benefit for this treatment in patients who are not surgical candidates [126].

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
E. External Beam Radiation Therapy

There is currently no evidence for the use of radiotherapy alone for intrahepatic cholangiocarcinoma. Radiotherapy has been used in conjunction with systemic chemotherapy.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
F. Bland Transarterial Embolization

The use of TAE is supported for more advanced intrahepatic cholangiocarcinoma.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
G. Transarterial Chemoembolization

The use of TACE is supported for more advanced intrahepatic cholangiocarcinoma.

Variant 5: Intrahepatic cholangiocarcinoma: Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases.
H. Transarterial Radioembolization

An early study of radioembolization at a single center demonstrated improved survival in patients with peripheral cholangiocarcinoma [127].

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
A. Systemic Therapies

Limited systemic chemotherapy options are available currently. Systemic chemotherapy with gemcitabine and cisplatin remains the standard of care for patients with advanced disease. Gemcitabine plus cisplatin compared with gemcitabine alone was associated with improved survival for patients with advanced biliary tract cancer in a randomized controlled phase III trial. In this trial, patients treated with gemcitabine plus cisplatin lived on average 3.6 months longer and did not have an increase in adverse events [119].

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
B. Surgical Liver Resection

Surgical resection is not a treatment option in this scenario.

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
C. Liver Transplantation

Liver transplantation is not a treatment option for advanced cholangiocarcinoma.

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
D. Percutaneous Ablation Liver

Ablation therapy has a limited role in the treatment of advanced and central ductal cholangiocarcinoma.

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
E. External Beam Radiation Therapy

Radiotherapy alone has not been used for this scenario and has only been used in conjunction with systemic chemotherapy. Postoperative adjuvant chemoradiation may reduce local recurrence and improve overall survival, particularly in high-risk patients. Definitive chemoradiation along with biliary stenting in the nonoperative setting may confer a small survival benefit [128].

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
F. Bland Transarterial Embolization

Bland embolization has been studied less than chemoembolization but could be considered in patients with inoperable disease [129].

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
G. Transarterial Chemoembolization

TACE has been demonstrated to prolong survival in patients with unresectable disease (9.1-30

months median survival after procedure) [130]. There is no consensus in the literature in regard to the superiority of DEB-TACE or TACE.

Variant 6: Ductal cholangiocarcinoma: Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy.
H. Transarterial Radioembolization

TARE may be beneficial for unresectable intrahepatic cholangiocarcinoma after failed first-line chemotherapy, with a disease control rate reported at 81.8% [131]. TARE has shown a survival benefit in multiple studies in patients with unresectable intrahepatic cholangiocarcinoma [132].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).

Neuroendocrine cancers include carcinoid tumors, with the primary tumor located most commonly in the gastrointestinal tract and lungs, as well as pancreatic islet cell malignancies. These tumors can secrete a variety of hormones (glucagon, vasoactive intestinal peptide, insulin, and gastrin) causing related symptoms. Patients usually become symptomatic once the disease has metastasized to the liver, thus presenting with more advanced disease. Treatment of neuroendocrine cancers has focused on symptom management and controlling disease progression.

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
A. Long-Acting Somatostatin Analogs

A majority of neuroendocrine tumors express somatostatin receptors. Somatostatin analogs, like octreotide, have been a steadfast part of the treatment regimen for symptomatic neuroendocrine cancers to control symptoms but may have limited effect on overall survival [133,134]. Over time, decreased effectiveness of somatostatin analogs limits symptomatic control.

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
B. Systemic Therapies

Chemotherapeutic agents (eg, streptozocin, 5-fluorouracil, doxorubicin, capecitabine) or molecularly targeted agents (eg, everolimus sunitinub) are not commonly used as initial treatment but can be used for patients with rapidly progressive disease, rapidly progressive symptoms, or failure of initial therapy [135-139]. Alpha interferon has also been used as a systemic treatment, but its adverse effects have limited its use [135].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
C. Surgical Liver Resection

Surgical resection, when feasible, can reduce symptoms by cytoreduction. It has also been shown to improve survival [140-143]. If complete resection is not possible, removal of 90% of the disease is thought to be necessary to achieve symptom control. However, this can be difficult to accomplish if the disease is diffuse [144].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
D. Liver Transplantation

Liver transplant has been performed and can confer a survival benefit for patients with advanced,

diffuse disease, but it is unfortunately fraught with high recurrence rates of 31% to 56% [145].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
E. Percutaneous Ablation Liver

Thermal ablation, like surgical resection, can help with cytoreduction and is less invasive than surgery [135]. Ablation can be an important treatment option for patients who are not surgical candidates, in combination with surgery performed intraoperatively, or in the treatment of recurrences for those patients who have already undergone surgery [135].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
F. External Beam Radiation Therapy

SBRT (an advanced technique of hypofractionated external beam radiation therapy that delivers ablative doses of radiation) can be performed based on liver tolerance [146]. If the liver is diffusely involved or constraints cannot be met, external beam radiation therapy via 3-D conformational radiation or intensity modulated radiation therapy can be performed [147]. Whole-liver radiation is an effective palliative intervention [148].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
G. Bland Transarterial Embolization

Transarterial therapies are an important treatment strategy for multifocal liver dominant metastatic neuroendocrine tumors. TAE, TACE, DEB-TACE, and TARE have all shown efficacy for overall survival, tumor growth reduction, and symptom control, without clear superiority of one transarterial therapy over the others [132,133,149-156].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
H. Transarterial Chemoembolization

Transarterial therapies are an important treatment strategy for multifocal liver dominant metastatic neuroendocrine tumors. TAE, TACE, DEB-TACE, and TARE have all shown efficacy for overall survival, tumor growth reduction, and symptom control, without clear superiority of one transarterial therapy over the others [132,133,149-156]. However, embolization with DEB-TACE has been associated with an increased risk of biloma formation [152,157].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
I. Transarterial Radioembolization

Transarterial therapies are an important treatment strategy for multifocal liver dominant metastatic neuroendocrine tumors. TAE, TACE, DEB-TACE, and TARE have all shown efficacy for overall survival, tumor growth reduction, and symptom control, without clear superiority of one transarterial therapy over the others [132,133,149-156]. Patients treated with TARE can have fewer side effects following treatment, but one study found that overall survival may be worse than with TAE or TACE [158]. TARE may also be associated with long-term liver toxicity with lobar and bilobar treatment [159].

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
J. Combination Locoregional Therapy

No high-quality evidence exists for the use of combination locoregional therapy for the treatment of metastatic neuroendocrine tumors.

Variant 7: Metastatic liver disease: Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas).
K. Peptide Receptor Radionuclide Therapy

Yttrium-90 (beta-emitter)–and lutetium-177 (beta and gamma-emitter)–labeled somatostatin analogs selectively bind to somatostatin receptors, which are internalized and cause radiation-induced cell death known as PRRT [160]. PRRT has shown to have an effect on disease control with decreased tumor size, increased progression-free survival, and improvement in overall survival compared with octreotide long-acting repeatable [160-162]. PRRT treatment can be expensive and may or may not be covered by insurance.

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
A. Systemic Therapies

Systemic therapies are first-line therapies for metastatic colorectal cancer. Therapy options are increasing in number and are becoming more selective based on known biomarkers [163]. Fluorouracil forms the basis of multiple combination therapies, including with irinotecan (FOLFIRI), oxaliplatin (FOLFOX), or capecitabine (CAPOX or XELOX), resulting in similar outcomes [164]. Recently, triple therapy with fluorouracil, oxaliplatin, and irinotecan (FOLFOXIRI) has shown superiority over FOLFIRI [165-167]. Additionally, the above regimens have also been combined with biologic agents, with some studies demonstrating survival benefits [164,168].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
B. Surgical Liver Resection

Surgical resection remains the best chance for potential cure and has the best overall survival for patients with metastatic colorectal cancer. However, very few patients (<20%) with colorectal liver cancer have metastases that are resectable at the time of diagnosis [169,170]. Resectability is generally considered with limited metastatic disease: up to 5 tumors with adequate intervening nontumor liver parenchyma. Portal vein embolization is an adjunctive procedure before surgery used to hypertrophy the future liver remnant to ensure adequate liver function following resection [171].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
C. Liver Transplantation

The use of liver transplantation is limited before the high risk of disease recurrence [172].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
D. Percutaneous Ablation Liver

Thermal ablation (RFA and MWA) is an ideal treatment option for carefully selected patients with results similar to resection [173-175]. Ablation of a limited number of smaller tumors (<3 cm) with an ablation margin >5 mm confers the best chance for local tumor control [176]. With less morbidity compared to resection, ablation can be a good option for poor surgical candidates [175].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
E. External Beam Radiation Therapy

SBRT is a treatment proposed as an additional local therapy option in place of percutaneous

thermal ablation. A single retrospective study suggested an advantage of SBRT over MWA for local disease control particularly for metastases >3 cm in diameter, but this study was performed on a lesion-by-lesion basis without accounting for additional clinical factors in a retrospective review of a small number of cases [177].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
F. Hepatic Arterial Chemotherapy Infusion

Hepatic arterial chemotherapy infusion is not conventionally used for solitary disease.

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
G. Bland Transarterial Embolization

TAE may serve an adjunctive role to surgery for resectable colorectal liver metastasis.

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
H. Transarterial Chemoembolization

Chemoembolization may serve a role in improving surgical outcomes for resectable colorectal hepatic metastasis [178].

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
I. Transarterial Radioembolization

TARE should be reserved for the treatment of multifocal disease that has failed other therapies.

Variant 8: Metastatic liver disease: Solitary colorectal liver metastasis.
J. Combination Locoregional Therapy

Larger lesions (3-5 cm in diameter) can be treated with a combination of TACE/TAE and ablation with excellent local tumor control and survival benefit [179].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).
A. Systemic Therapies

Systemic therapy is vital first-line therapy for multifocal metastatic colorectal cancer. Fluorouracil can be combined with irinotecan (FOLFIRI), oxaliplatin (FOLFOX), or capecitabine (CAPOX or XELOX), resulting in similar outcomes [164]. Recently, FOLFOXIRI has shown superiority over FOLFIRI [165-167]. Additionally, these regimens have also been combined with biologic agents, with some studies demonstrating survival benefits [164,168]. Systemic therapies have also been used for downstaging to resection [169], and one study showed bevacizumab plus FOLFOXIRI may outperform bevacizumab plus modified FOLFOX in terms of resectability rate in initially unresectable disease. Other chemotherapy regimens such as FOLFOX or FOLFOXIRI plus cetuximab have also been shown to convert some unresectable metastatic disease to resectability [180].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).
B. Surgical Liver Resection

Feasibility of surgical resection is based on volume of disease and conventionally limited to <5 hepatic metastases with adequate remnant nontumor liver. FOLFOX and FOLFOXIRI plus cetuximab may promote resectability of initially unresectable disease [180].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

C. Liver Transplantation

Liver transplantation has a limited role for multifocal colorectal liver metastases because of a risk of recurrence in this volume of disease.

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

D. Percutaneous Ablation Liver

A phase II clinical trial (CLOCC study) demonstrated a survival benefit for early aggressive local treatment of unresectable colorectal liver metastases using RFA with or without surgical resection in conjunction with systemic therapy compared to systemic therapy alone. In this study, the median overall survival was higher for the combined treatment arm at 45.6 months compared with 40.5 months for the systemic treatment group, and the median progression-free survival was significantly longer at 16.8 months in the combined group compared with 9.9 months for systemic treatment alone [181].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

E. External Beam Radiation Therapy

The conventional role for radiotherapy in unresectable colorectal liver metastases has been limited to palliation for tumor burden and related pain. Early data on the use of SBRT for disease control in this setting suggest a possible role, but data are continuing to emerge [182].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

F. Hepatic Arterial Chemotherapy Infusion

Hepatic arterial chemotherapy infusion has been used for treatment of unresectable disease [183-185]. Hepatic arterial chemotherapy infusion along with systemic therapy can convert some disease into resectable disease, possibly improving survival [186]. Direct arterial administration can result in an increased drug concentration within the liver but can be limited by procedural complexity and liver toxicity [183]. This therapy has conventionally involved surgical implantation, but a clinical trial in Japan demonstrated the ability to safely perform image-guided hepatic arterial infusion [187].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

G. Bland Transarterial Embolization

TAE can be used for unresectable colorectal liver metastases. This can be combined with other techniques such as ablation.

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

H. Transarterial Chemoembolization

TACE, in addition to TAE, is a treatment option for unresectable disease providing a survival benefit without data demonstrating superiority of one over the other [68,69]. DEBIRI chemoembolization may show a survival benefit on par with systemic chemotherapy for unresectable colorectal liver metastases [188]. Chemoembolization can provide local disease control and may be of the most benefit earlier in therapy after 0 to 2 lines of systemic chemotherapy as opposed to salvage

therapy following several failed lines of systemic chemotherapy [189].

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

I. Transarterial Radioembolization

TARE provides no additional survival benefit when added to systemic chemotherapy as first-line therapy [190,191]. However, subgroup analysis from 2 randomized controlled trials did identify a survival benefit of TARE plus systemic chemotherapy for colorectal liver metastases from right-sided colon primary tumors compared with left-sided primaries (22 versus 17.1 months) [192]. TARE has, however, been shown to be associated with a survival benefit for patients with colorectal liver metastases that have failed multiple prior systemic chemotherapy options [193,194]. Therefore, this therapy should be reserved as salvage therapy in the treatment of chemo-refractory colorectal liver metastases.

Variant 9: Metastatic liver disease: Multifocal bilobar colorectal carcinoma (liver dominant or isolated).

J. Combination Locoregional Therapy

The strategy of combining transarterial therapies with ablation to enhance therapeutic effect can also be used in multifocal colorectal liver metastases. One prospective study demonstrated good control of tumor treated with combination chemoembolization and RFA [179].

Summary of Recommendations

- **Variant 1**: Liver transplantation or percutaneous ablation liver or surgical liver resection is usually appropriate for hepatocellular cancer in which the solitary tumor is <3 cm in a patient with cirrhosis. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2**: Liver transplantation or combination locoregional therapy or surgical liver resection or TACE or TARE is usually appropriate for hepatocellular cancer in which the solitary tumor is 3 to 5 cm in a patient with cirrhosis. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 3**: TACE or TARE or bland TAE or systemic therapies are usually appropriate for hepatocellular cancer that is multifocal and bilobar with at least 1 tumor >5 cm in a patient with cirrhosis. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 4**: Systemic therapies or TARE is usually appropriate for hepatocellular cancer that is solitary or multifocal disease with vascular invasion in a cirrhotic patient. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 5**: Surgical liver resection or percutaneous liver ablation is usually appropriate for peripheral intrahepatic lobar cholangiocarcinoma that is <3 cm with no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 6**: Systemic therapies are usually appropriate for hilar ductal cholangiocarcinoma that is >3 cm with poorly defined margins, vascular invasion, and periportal

lymphadenopathy.

- **Variant 7**: Long-acting somatostatin analogs or bland TAE or peptide receptor radionuclide therapy or TACE or TARE is usually appropriate for multifocal metastatic neuroendocrine tumor to the liver, including carcinoid tumors as well as islet cell tumors of the pancreas. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 8**: Systemic therapies or surgical liver resection or percutaneous ablation liver is usually appropriate for solitary colorectal liver metastasis. These procedures are comparable alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 9**: Systemic therapies are usually appropriate for multifocal bilobar colorectal carcinoma where the liver is dominant or isolated. Bland TAE may be appropriate for this clinical scenario, but the experts could not agree on the exact appropriateness category.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

References

1. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996;334(11):693-699.
2. Llovet JM, Bru C, Bruix J. Prognosis of hepatocellular carcinoma: the BCLC staging classification. Semin Liver Dis 1999;19:329-38.
3. Toso C, Mentha G, Kneteman NM, Majno P. The place of downstaging for hepatocellular carcinoma. J Hepatol 2010;52:930-6.
4. Teh SH, Christein J, Donohue J, et al. Hepatic resection of hepatocellular carcinoma in patients with cirrhosis: Model of End-Stage Liver Disease (MELD) score predicts perioperative mortality. J Gastrointest Surg 2005;9:1207-15; discussion 15.
5. Yamashita Y, Taketomi A, Itoh S, et al. Longterm favorable results of limited hepatic resections for patients with hepatocellular carcinoma: 20 years of experience. J Am Coll Surg. 2007;205(1):19-26.
6. Sapisochin G, Bruix J. Liver transplantation for hepatocellular carcinoma: outcomes and novel surgical approaches. Nat Rev Gastroenterol Hepatol 2017;14:203-17.
7. Akoad ME, Pomfret EA. Surgical resection and liver transplantation for hepatocellular carcinoma. [Review]. Clin Liver Dis. 19(2):381-99, 2015 May.
8. Taura K, Ikai I, Hatano E, et al. Influence of coexisting cirrhosis on outcomes after partial hepatic resection for hepatocellular carcinoma fulfilling the Milan criteria: an analysis of 293 patients. Surgery 2007;142:685-94.
9. Meloni MF, Chiang J, Laeseke PF, et al. Microwave ablation in primary and secondary liver tumours: technical and clinical approaches. Int J Hyperthermia 2017;33:15-24.
10. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol. 2012;56(4):908-943.
11. Jiang L, Liao A, Wen T, Yan L, Li B, Yang J. Living donor liver transplantation or resection for Child-Pugh A hepatocellular carcinoma patients with multiple nodules meeting the Milan criteria. Transpl Int. 27(6):562-9, 2014 Jun.
12. Squires MH 3rd, Hanish SI, Fisher SB, et al. Transplant versus resection for the management of hepatocellular carcinoma meeting Milan Criteria in the MELD exception era at a single institution in a UNOS region with short wait times. J Surg Oncol. 109(6):533-41, 2014 May.
13. Majumdar A, Roccarina D, Thorburn D, Davidson BR, Tsochatzis E, Gurusamy KS. Management of people with early- or very early-stage hepatocellular carcinoma: an attempted network meta-analysis. Cochrane Database Syst Rev 2017;3:CD011650.
14. Orlando A, Leandro G, Olivo M, Andriulli A, Cottone M. Radiofrequency thermal ablation vs. percutaneous ethanol injection for small hepatocellular carcinoma in cirrhosis: meta-analysis of randomized controlled trials. Am J Gastroenterol. 2009;104(2):514-524.
15. Chen MS, Li JQ, Zheng Y, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg. 2006;243(3):321-328.
16. Feng K, Yan J, Li X, et al. A randomized controlled trial of radiofrequency ablation and surgical resection in the treatment of small hepatocellular carcinoma. J Hepatol. 2012;57(4):794-802.

17. Fujimori M, Takaki H, Nakatsuka A, et al. Survival with up to 10-year follow-up after combination therapy of chemoembolization and radiofrequency ablation for the treatment of hepatocellular carcinoma: single-center experience. J Vasc Interv Radiol. 2013;24(5):655-666.

18. Huang J, Yan L, Cheng Z, et al. A randomized trial comparing radiofrequency ablation and surgical resection for HCC conforming to the Milan criteria. Ann Surg. 2010;252(6):903-912.

19. Livraghi T, Meloni F, Di Stasi M, et al. Sustained complete response and complications rates after radiofrequency ablation of very early hepatocellular carcinoma in cirrhosis: Is resection still the treatment of choice? Hepatology. 2008;47(1):82-89.

20. Peng ZW, Lin XJ, Zhang YJ, et al. Radiofrequency ablation versus hepatic resection for the treatment of hepatocellular carcinomas 2 cm or smaller: a retrospective comparative study. Radiology. 2012;262(3):1022-1033.

21. Tohme S, Geller DA, Cardinal JS, et al. Radiofrequency ablation compared to resection in early-stage hepatocellular carcinoma. HPB. 15(3):210-7, 2013 Mar.

22. Schaub SK, Hartvigson PE, Lock MI, et al. Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma: Current Trends and Controversies. Technol Cancer Res Treat 2018;17:1533033818790217.

23. Andolino DL, Johnson CS, Maluccio M, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. Int J Radiat Oncol Biol Phys. 2011;81(4):e447-453.

24. Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. J Clin Oncol. 2013;31(13):1631-1639.

25. Mendez Romero A, Wunderink W, Hussain SM, et al. Stereotactic body radiation therapy for primary and metastatic liver tumors: A single institution phase i-ii study. Acta Oncol 2006;45:831-7.

26. Cardenes HR, Price TR, Perkins SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. Clin Transl Oncol 2010;12:218-25.

27. Eriguchi T, Takeda A, Tateishi Y, et al. Comparison of stereotactic body radiotherapy and radiofrequency ablation for hepatocellular carcinoma: Systematic review and meta-analysis of propensity score studies. Hepatol Res 2021;51:813-22.

28. Pan YX, Fu YZ, Hu DD, et al. Stereotactic Body Radiotherapy vs. Radiofrequency Ablation in the Treatment of Hepatocellular Carcinoma: A Meta-Analysis. Front Oncol 2020;10:1639.

29. Parikh ND, Marshall VD, Green M, et al. Effectiveness and cost of radiofrequency ablation and stereotactic body radiotherapy for treatment of early-stage hepatocellular carcinoma: An analysis of SEER-medicare. J Med Imaging Radiat Oncol 2018;62:673-81.

30. Rajyaguru DJ, Borgert AJ, Smith AL, et al. Radiofrequency Ablation Versus Stereotactic Body Radiotherapy for Localized Hepatocellular Carcinoma in Nonsurgically Managed Patients: Analysis of the National Cancer Database. J Clin Oncol 2018;36:600-08.

31. Seo YS, Kim MS, Yoo HJ, et al. Radiofrequency ablation versus stereotactic body radiotherapy for small hepatocellular carcinoma: a Markov model-based analysis. Cancer Med 2016;5:3094-101.

32. Lewandowski RJ, Kulik LM, Riaz A, et al. A comparative analysis of transarterial

downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. Am J Transplant. 2009;9(8):1920-1928.

33. Katz AW, Chawla S, Qu Z, Kashyap R, Milano MT, Hezel AF. Stereotactic hypofractionated radiation therapy as a bridge to transplantation for hepatocellular carcinoma: clinical outcome and pathologic correlation. International journal of radiation oncology, biology, physics 2012;83:895-900.

34. O'Connor JK, Trotter J, Davis GL, Dempster J, Klintmalm GB, Goldstein RM. Long-term outcomes of stereotactic body radiation therapy in the treatment of hepatocellular cancer as a bridge to transplantation. Liver Transpl. 2012;18(8):949-954.

35. Mohamed M, Katz AW, Tejani MA, et al. Comparison of outcomes between SBRT, yttrium-90 radioembolization, transarterial chemoembolization, and radiofrequency ablation as bridge to transplant for hepatocellular carcinoma. Adv Radiat Oncol 2016;1:35-42.

36. Bryce K, Tsochatzis EA. Downstaging for hepatocellular cancer: harm or benefit? Transl Gastroenterol Hepatol 2017;2:106.

37. Zheng XH, Guan YS, Zhou XP, et al. Detection of hypervascular hepatocellular carcinoma: Comparison of multi-detector CT with digital subtraction angiography and Lipiodol CT. World J Gastroenterol 2005;11:200-3.

38. Gandhi S, Iannitti DA, Mayo-Smith WW, Dupuy DE. Technical report: Lipiodol-guided computed tomography for radiofrequency ablation of hepatocellular carcinoma. Clin Radiol 2006;61:888-91.

39. Salem R, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for hepatocellular carcinoma using Yttrium-90 microspheres: a comprehensive report of long-term outcomes. Gastroenterology. 2010;138(1):52-64.

40. Mazzaferro V, Sposito C, Bhoori S, et al. Yttrium-90 radioembolization for intermediate-advanced hepatocellular carcinoma: a phase 2 study. Hepatology 2013;57:1826-37.

41. Titano J, Voutsinas N, Kim E. The Role of Radioembolization in Bridging and Downstaging Hepatocellular Carcinoma to Curative Therapy. Semin Nucl Med 2019;49:189-96.

42. Lewandowski RJ, Gabr A, Abouchaleh N, et al. Radiation Segmentectomy: Potential Curative Therapy for Early Hepatocellular Carcinoma. Radiology 2018;287:1050-58.

43. Vouche M, Habib A, Ward TJ, et al. Unresectable solitary hepatocellular carcinoma not amenable to radiofrequency ablation: multicenter radiology-pathology correlation and survival of radiation segmentectomy. Hepatology 2014;60:192-201.

44. Riaz A, Gates VL, Atassi B, et al. Radiation segmentectomy: a novel approach to increase safety and efficacy of radioembolization. International journal of radiation oncology, biology, physics 2011;79:163-71.

45. Gabr A, Abouchaleh N, Ali R, et al. Comparative study of post-transplant outcomes in hepatocellular carcinoma patients treated with chemoembolization or radioembolization. Eur J Radiol. 93:100-106, 2017 Aug.

46. Kulik LM, Atassi B, van Holsbeeck L, et al. Yttrium-90 microspheres (TheraSphere) treatment of unresectable hepatocellular carcinoma: downstaging to resection, RFA and bridge to transplantation. J Surg Oncol. 2006;94(7):572-586.

47. Salem R, Gabr A, Riaz A, et al. Institutional decision to adopt Y90 as primary treatment for

hepatocellular carcinoma informed by a 1,000-patient 15-year experience. Hepatology 2018;68:1429-40.

48. Parikh ND, Waljee AK, Singal AG. Downstaging hepatocellular carcinoma: A systematic review and pooled analysis. Liver Transpl 2015;21:1142-52.

49. Bharadwaz A, Bak-Fredslund KP, Villadsen GE, et al. Combination of radiofrequency ablation with transarterial chemoembolization for treatment of hepatocellular carcinoma: experience from a Danish tertiary liver center. Acta Radiol. 57(7):844-51, 2016 Jul.

50. Iezzi R, Pompili M, La Torre MF, et al. Radiofrequency ablation plus drug-eluting beads transcatheter arterial chemoembolization for the treatment of single large hepatocellular carcinoma. Dig Liver Dis. 47(3):242-8, 2015 Mar.

51. Lu Z, Wen F, Guo Q, Liang H, Mao X, Sun H. Radiofrequency ablation plus chemoembolization versus radiofrequency ablation alone for hepatocellular carcinoma: a meta-analysis of randomized-controlled trials. Eur J Gastroenterol Hepatol. 2013;25(2):187-194.

52. Peng ZW, Zhang YJ, Liang HH, Lin XJ, Guo RP, Chen MS. Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial. Radiology 2012;262:689-700.

53. Sheta E, El-Kalla F, El-Gharib M, et al. Comparison of single-session transarterial chemoembolization combined with microwave ablation or radiofrequency ablation in the treatment of hepatocellular carcinoma: a randomized-controlled study. European journal of gastroenterology & hepatology 2016;28:1198-203.

54. Yao FY, Kerlan RK, Jr., Hirose R, et al. Excellent outcome following down-staging of hepatocellular carcinoma prior to liver transplantation: an intention-to-treat analysis. Hepatology 2008;48:819-27.

55. Yin X, Zhang L, Wang YH, et al. Transcatheter arterial chemoembolization combined with radiofrequency ablation delays tumor progression and prolongs overall survival in patients with intermediate (BCLC B) hepatocellular carcinoma. BMC Cancer 2014;14:849.

56. Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. 67(1):358-380, 2018 01.

57. Mazzaferro V, Bhoori S, Sposito C, et al. Milan criteria in liver transplantation for hepatocellular carcinoma: an evidence-based analysis of 15 years of experience. Liver Transpl 2011;17 Suppl 2:S44-57.

58. Zhang NN, Lu W, Cheng XJ, Liu JY, Zhou YH, Li F. High-powered microwave ablation of larger hepatocellular carcinoma: evaluation of recurrence rate and factors related to recurrence. Clin Radiol 2015;70:1237-43.

59. Medhat E, Abdel Aziz A, Nabeel M, et al. Value of microwave ablation in treatment of large lesions of hepatocellular carcinoma. J Dig Dis 2015;16:456-63.

60. Brown KT, Do RK, Gonen M, et al. Randomized Trial of Hepatic Artery Embolization for Hepatocellular Carcinoma Using Doxorubicin-Eluting Microspheres Compared With Embolization With Microspheres Alone. J Clin Oncol 2016;34:2046-53.

61. Kluger MD, Halazun KJ, Barroso RT, et al. Bland embolization versus chemoembolization of

hepatocellular carcinoma before transplantation. Liver Transpl. 2014;20(5):536-543.

62. Maluccio MA, Covey AM, Porat LB, et al. Transcatheter arterial embolization with only particles for the treatment of unresectable hepatocellular carcinoma. J Vasc Interv Radiol. 2008;19(6):862-869.

63. Marelli L, Stigliano R, Triantos C, et al. Transarterial therapy for hepatocellular carcinoma: which technique is more effective? A systematic review of cohort and randomized studies. Cardiovasc Intervent Radiol. 2007;30(1):6-25.

64. Dhanasekaran R, Kooby DA, Staley CA, Kauh JS, Khanna V, Kim HS. Comparison of conventional transarterial chemoembolization (TACE) and chemoembolization with doxorubicin drug eluting beads (DEB) for unresectable hepatocelluar carcinoma (HCC). J Surg Oncol. 2010;101(6):476-480.

65. Huang K, Zhou Q, Wang R, Cheng D, Ma Y. Doxorubicin-eluting Bead versus Conventional Transarterial Chemoembolization for the Treatment of HCC: a Meta-Analysis. J Gastroenterol Hepatol. 2013.

66. Lammer J, Malagari K, Vogl T, et al. Prospective randomized study of doxorubicin-eluting-bead embolization in the treatment of hepatocellular carcinoma: results of the PRECISION V study. Cardiovasc Intervent Radiol. 2010;33(1):41-52.

67. Martin R, Geller D, Espat J, et al. Safety and efficacy of trans arterial chemoembolization with drug-eluting beads in hepatocellular cancer: a systematic review. Hepatogastroenterology. 2012;59(113):255-260.

68. Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet. 2002;359(9319):1734-1739.

69. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology. 2002;35(5):1164-1171.

70. Doffoel M, Bonnetain F, Bouche O, et al. Multicentre randomised phase III trial comparing Tamoxifen alone or with Transarterial Lipiodol Chemoembolisation for unresectable hepatocellular carcinoma in cirrhotic patients (Federation Francophone de Cancerologie Digestive 9402). Eur J Cancer 2008;44:528-38.

71. Pelletier G, Ducreux M, Gay F, et al. Treatment of unresectable hepatocellular carcinoma with lipiodol chemoembolization: a multicenter randomized trial. Groupe CHC. J Hepatol 1998;29:129-34.

72. Groupe d'Etude et de Traitement du Carcinome H. A comparison of lipiodol chemoembolization and conservative treatment for unresectable hepatocellular carcinoma. N Engl J Med 1995;332:1256-61.

73. Martin RC, Joshi J, Robbins K, et al. Hepatic intra-arterial injection of drug-eluting bead, irinotecan (DEBIRI) in unresectable colorectal liver metastases refractory to systemic chemotherapy: results of multi-institutional study. Ann Surg Oncol. 2011;18(1):192-198.

74. Cescon M, Cucchetti A, Ravaioli M, Pinna AD. Hepatocellular carcinoma locoregional therapies for patients in the waiting list. Impact on transplantability and recurrence rate. J Hepatol. 2013;58(3):609-618.

75. Chapman WC, Majella Doyle MB, Stuart JE, et al. Outcomes of neoadjuvant transarterial chemoembolization to downstage hepatocellular carcinoma before liver transplantation. Ann Surg. 2008;248(4):617-625.

76. Chua TC, Liauw W, Saxena A, et al. Systematic review of neoadjuvant transarterial chemoembolization for resectable hepatocellular carcinoma. Liver Int. 2010;30(2):166-174.

77. De Giorgio M, Vezzoli S, Cohen E, et al. Prediction of progression-free survival in patients presenting with hepatocellular carcinoma within the Milan criteria. Liver Transpl. 2010;16(4):503-512.

78. Heckman JT, Devera MB, Marsh JW, et al. Bridging locoregional therapy for hepatocellular carcinoma prior to liver transplantation. Ann Surg Oncol. 2008;15(11):3169-3177.

79. Lesurtel M, Mullhaupt B, Pestalozzi BC, Pfammatter T, Clavien PA. Transarterial chemoembolization as a bridge to liver transplantation for hepatocellular carcinoma: an evidence-based analysis. Am J Transplant. 2006;6(11):2644-2650.

80. Maddala YK, Stadheim L, Andrews JC, et al. Drop-out rates of patients with hepatocellular cancer listed for liver transplantation: outcome with chemoembolization. Liver Transpl. 2004;10(3):449-455.

81. Habib A, Desai K, Hickey R, Thornburg B, Lewandowski R, Salem R. Locoregional therapy of hepatocellular carcinoma. [Review]. Clin Liver Dis. 19(2):401-20, 2015 May.

82. Victor DW, 3rd, Monsour HP, Jr., Boktour M, et al. Outcomes of Liver Transplantation for Hepatocellular Carcinoma Beyond the University of California San Francisco Criteria: A Single-center Experience. Transplantation 2020;104:113-21.

83. Xu LF, Sun HL, Chen YT, et al. Large primary hepatocellular carcinoma: transarterial chemoembolization monotherapy versus combined transarterial chemoembolization-percutaneous microwave coagulation therapy. J Gastroenterol Hepatol 2013;28:456-63.

84. Liu C, Liang P, Liu F, et al. MWA combined with TACE as a combined therapy for unresectable large-sized hepotocellular carcinoma. Int J Hyperthermia 2011;27:654-62.

85. Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med. 2008;359(4):378-390.

86. Cheng AL, Kang YK, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. The Lancet. Oncology 2009;10:25-34.

87. Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-905.

88. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2017;389:56-66.

89. Kelley RK, Ryoo BY, Merle P, et al. Second-line cabozantinib after sorafenib treatment for advanced hepatocellular carcinoma: a subgroup analysis of the phase 3 CELESTIAL trial. ESMO Open 2020;5.

90. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. The Lancet. Oncology 2018;19:940-52.

91. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. Lancet 2017;389:2492-502.

92. Bova V, Miraglia R, Maruzzelli L, Vizzini GB, Luca A. Predictive factors of downstaging of hepatocellular carcinoma beyond the Milan criteria treated with intra-arterial therapies. Cardiovasc Intervent Radiol 2013;36:433-9.

93. DuBay DA, Sandroussi C, Kachura JR, et al. Radiofrequency ablation of hepatocellular carcinoma as a bridge to liver transplantation. HPB (Oxford). 2011;13(1):24-32.

94. Graziadei IW, Sandmueller H, Waldenberger P, et al. Chemoembolization followed by liver transplantation for hepatocellular carcinoma impedes tumor progression while on the waiting list and leads to excellent outcome. Liver Transpl 2003;9:557-63.

95. Lau WY, Lai EC. The current role of radiofrequency ablation in the management of hepatocellular carcinoma: a systematic review. Ann Surg. 2009;249(1):20-25.

96. Ravaioli M, Grazi GL, Piscaglia F, et al. Liver transplantation for hepatocellular carcinoma: results of down-staging in patients initially outside the Milan selection criteria. Am J Transplant 2008;8:2547-57.

97. Sun PL, Chen CL, Hsu SL, et al. The significance of transarterial embolization for advanced hepatocellular carcinoma in liver transplantation. Transplant Proc 2004;36:2295-6.

98. Baumann BC, Wei J, Plastaras JP, et al. Stereotactic Body Radiation Therapy (SBRT) for Hepatocellular Carcinoma: High Rates of Local Control With Low Toxicity. Am J Clin Oncol 2018;41:1118-24.

99. Jang WI, Bae SH, Kim MS, et al. A phase 2 multicenter study of stereotactic body radiotherapy for hepatocellular carcinoma: Safety and efficacy. Cancer 2020;126:363-72.

100. Miyayama S, Yamashiro M, Ikuno M, Okumura K, Yoshida M. Ultraselective transcatheter arterial chemoembolization for small hepatocellular carcinoma guided by automated tumor-feeders detection software: technical success and short-term tumor response. Abdom Imaging 2014;39:645-56.

101. Miyayama S, Matsui O, Yamashiro M, et al. Ultraselective transcatheter arterial chemoembolization with a 2-f tip microcatheter for small hepatocellular carcinomas: relationship between local tumor recurrence and visualization of the portal vein with iodized oil. J Vasc Interv Radiol 2007;18:365-76.

102. Carr BI, Kondragunta V, Buch SC, Branch RA. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a two-cohort study. Cancer. 2010;116(5):1305-1314.

103. Kooby DA, Egnatashvili V, Srinivasan S, et al. Comparison of yttrium-90 radioembolization and transcatheter arterial chemoembolization for the treatment of unresectable hepatocellular carcinoma. J Vasc Interv Radiol. 2010;21(2):224-230.

104. Lance C, McLennan G, Obuchowski N, et al. Comparative analysis of the safety and efficacy of transcatheter arterial chemoembolization and yttrium-90 radioembolization in patients with unresectable hepatocellular carcinoma. J Vasc Interv Radiol. 2011;22(12):1697-1705.

105. Lobo L, Yakoub D, Picado O, et al. Unresectable Hepatocellular Carcinoma:

Radioembolization Versus Chemoembolization: A Systematic Review and Meta-analysis. [Review]. Cardiovasc Intervent Radiol. 39(11):1580-1588, 2016 Nov.

106. Moreno-Luna LE, Yang JD, Sanchez W, et al. Efficacy and safety of transarterial radioembolization versus chemoembolization in patients with hepatocellular carcinoma. Cardiovasc Intervent Radiol. 2013;36(3):714-723.

107. Salem R, Lewandowski RJ, Kulik L, et al. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterology. 2011;140(2):497-507 e492.

108. Sangro B, Carpanese L, Cianni R, et al. Survival after yttrium-90 resin microsphere radioembolization of hepatocellular carcinoma across Barcelona clinic liver cancer stages: a European evaluation. Hepatology 2011;54:868-78.

109. Gabr A, Kallini JR, Gates VL, et al. Same-day 90Y radioembolization: implementing a new treatment paradigm. Eur J Nucl Med Mol Imaging. 43(13):2353-2359, 2016 Dec.

110. Gates VL, Marshall KG, Salzig K, Williams M, Lewandowski RJ, Salem R. Outpatient single-session yttrium-90 glass microsphere radioembolization. J Vasc Interv Radiol 2014;25:266-70.

111. Zhong JH, Ke Y, Gong WF, et al. Hepatic resection associated with good survival for selected patients with intermediate and advanced-stage hepatocellular carcinoma. Ann Surg 2014;260:329-40.

112. Andreou A, Bahra M, Schmelzle M, et al. Predictive factors for extrahepatic recurrence of hepatocellular carcinoma following liver transplantation. Clin Transplant. 30(7):819-27, 2016 Jul.

113. Finkenstedt A, Vikoler A, Portenkirchner M, et al. Excellent post-transplant survival in patients with intermediate stage hepatocellular carcinoma responding to neoadjuvant therapy. Liver Int 2016;36:688-95.

114. Xue TC, Xie XY, Zhang L, Yin X, Zhang BH, Ren ZG. Transarterial chemoembolization for hepatocellular carcinoma with portal vein tumor thrombus: a meta-analysis. BMC Gastroenterol 2013;13:60.

115. Niu ZJ, Ma YL, Kang P, et al. Transarterial chemoembolization compared with conservative treatment for advanced hepatocellular carcinoma with portal vein tumor thrombus: using a new classification. Med Oncol

116. Luo J, Guo RP, Lai EC, et al. Transarterial chemoembolization for unresectable hepatocellular carcinoma with portal vein tumor thrombosis: a prospective comparative study. Ann Surg Oncol 2011;18:413-20.

117. Yoon SM, Ryoo BY, Lee SJ, et al. Efficacy and Safety of Transarterial Chemoembolization Plus External Beam Radiotherapy vs Sorafenib in Hepatocellular Carcinoma With Macroscopic Vascular Invasion: A Randomized Clinical Trial. JAMA Oncol 2018;4:661-69.

118. Valle JW, Furuse J, Jitlal M, et al. Cisplatin and gemcitabine for advanced biliary tract cancer: a meta-analysis of two randomised trials. Ann Oncol 2014;25:391-8.

119. Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med. 2010;362(14):1273-1281.

120. Guro H, Kim JW, Choi Y, Cho JY, Yoon YS, Han HS. Multidisciplinary management of

intrahepatic cholangiocarcinoma: Current approaches. [Review]. Surg Oncol. 26(2):146-152, 2017 Jun.

121. Squires MH, Cloyd JM, Dillhoff M, Schmidt C, Pawlik TM. Challenges of surgical management of intrahepatic cholangiocarcinoma. [Review]. Expert rev. gastroenterol. hepatol.. 12(7):671-681, 2018 Jul.

122. Meyer CG, Penn I, James L. Liver transplantation for cholangiocarcinoma: results in 207 patients. Transplantation. 2000;69(8):1633-1637.

123. Kim JH, Won HJ, Shin YM, Kim KA, Kim PN. Radiofrequency ablation for the treatment of primary intrahepatic cholangiocarcinoma. AJR Am J Roentgenol. 2011;196(2):W205-209.

124. Mosconi C, Cappelli A, Ascanio S, et al. Yttrium-90 microsphere radioembolization in unresectable intrahepatic cholangiocarcinoma. Fut Oncol. 13(15):1301-1310, 2017 Jun.

125. Xu HX, Wang Y, Lu MD, Liu LN. Percutaneous ultrasound-guided thermal ablation for intrahepatic cholangiocarcinoma. Br J Radiol. 2012;85(1016):1078-1084.

126. Han K, Ko HK, Kim KW, Won HJ, Shin YM, Kim PN. Radiofrequency ablation in the treatment of unresectable intrahepatic cholangiocarcinoma: systematic review and meta-analysis. J Vasc Interv Radiol 2015;26:943-8.

127. Saxena A, Bester L, Chua TC, Chu FC, Morris DL. Yttrium-90 radiotherapy for unresectable intrahepatic cholangiocarcinoma: a preliminary assessment of this novel treatment option. Ann Surg Oncol. 2010;17(2):484-491.

128. Mansour JC, Aloia TA, Crane CH, Heimbach JK, Nagino M, Vauthey JN. Hilar cholangiocarcinoma: expert consensus statement. HPB. 17(8):691-9, 2015 Aug.HPB. 17(8):691-9, 2015 Aug.

129. Hyder O, Marsh JW, Salem R, et al. Intra-arterial therapy for advanced intrahepatic cholangiocarcinoma: a multi-institutional analysis. Ann Surg Oncol 2013;20:3779-86.

130. Ray CE, Jr., Edwards A, Smith MT, et al. Metaanalysis of survival, complications, and imaging response following chemotherapy-based transarterial therapy in patients with unresectable intrahepatic cholangiocarcinoma. J Vasc Interv Radiol 2013;24:1218-26.

131. Jia Z, Paz-Fumagalli R, Frey G, Sella DM, McKinney JM, Wang W. Resin-based Yttrium-90 microspheres for unresectable and failed first-line chemotherapy intrahepatic cholangiocarcinoma: preliminary results. Journal of Cancer Research & Clinical Oncology. 143(3):481-489, 2017 Mar.J Cancer Res Clin Oncol. 143(3):481-489, 2017 Mar.

132. Padia SA. Y90 Clinical Data Update: Cholangiocarcinoma, Neuroendocrine Tumor, Melanoma, and Breast Cancer Metastatic Disease. [Review]. Techniques in Vascular & Interventional Radiology. 22(2):81-86, 2019 Jun.

133. Jia Z, Paz-Fumagalli R, Frey G, Sella DM, McKinney JM, Wang W. Single-institution experience of radioembolization with yttrium-90 microspheres for unresectable metastatic neuroendocrine liver tumors. J Gastroenterol Hepatol. 32(9):1617-1623, 2017 Sep.

134. Rinke A, Wittenberg M, Schade-Brittinger C, et al. Placebo-Controlled, Double-Blind, Prospective, Randomized Study on the Effect of Octreotide LAR in the Control of Tumor Growth in Patients with Metastatic Neuroendocrine Midgut Tumors (PROMID): Results of Long-Term Survival. Neuroendocrinology 2017;104:26-32.

135. Atwell TD, Charboneau JW, Que FG, et al. Treatment of neuroendocrine cancer metastatic

to the liver: the role of ablative techniques. Cardiovasc Intervent Radiol. 2005;28(4):409-421.

136. Fazio N, Kulke M, Rosbrook B, Fernandez K, Raymond E. Updated Efficacy and Safety Outcomes for Patients with Well-Differentiated Pancreatic Neuroendocrine Tumors Treated with Sunitinib. Target Oncol 2021;16:27-35.

137. Yao JC, Fazio N, Singh S, et al. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study. Lancet 2016;387:968-77.

138. Pavel ME, Hainsworth JD, Baudin E, et al. Everolimus plus octreotide long-acting repeatable for the treatment of advanced neuroendocrine tumours associated with carcinoid syndrome (RADIANT-2): a randomised, placebo-controlled, phase 3 study. Lancet 2011;378:2005-12.

139. Yao JC, Lombard-Bohas C, Baudin E, et al. Daily oral everolimus activity in patients with metastatic pancreatic neuroendocrine tumors after failure of cytotoxic chemotherapy: a phase II trial. J Clin Oncol 2010;28:69-76.

140. Que FG, Nagorney DM, Batts KP, Linz LJ, Kvols LK. Hepatic resection for metastatic neuroendocrine carcinomas. Am J Surg 1995;169:36-42; discussion 42-3.

141. Sarmiento JM, Heywood G, Rubin J, Ilstrup DM, Nagorney DM, Que FG. Surgical treatment of neuroendocrine metastases to the liver: a plea for resection to increase survival. J Am Coll Surg. 2003;197(1):29-37.

142. Saxena A, Chua TC, Perera M, Chu F, Morris DL. Surgical resection of hepatic metastases from neuroendocrine neoplasms: a systematic review. Surgical oncology 2012;21:e131-41.

143. Boudreaux JP, Wang YZ, Diebold AE, et al. A single institution's experience with surgical cytoreduction of stage IV, well-differentiated, small bowel neuroendocrine tumors. J Am Coll Surg 2014;218:837-44.

144. McEntee GP, Nagorney DM, Kvols LK, Moertel CG, Grant CS. Cytoreductive hepatic surgery for neuroendocrine tumors. Surgery 1990;108:1091-6.

145. Moris D, Tsilimigras DI, Ntanasis-Stathopoulos I, et al. Liver transplantation in patients with liver metastases from neuroendocrine tumors: A systematic review. Surgery 2017;162:525-36.

146. Wahl DR, Stenmark MH, Tao Y, et al. Outcomes After Stereotactic Body Radiotherapy or Radiofrequency Ablation for Hepatocellular Carcinoma. J Clin Oncol 2016;34:452-9.

147. Hoffe SE, Finkelstein SE, Russell MS, Shridhar R. Nonsurgical options for hepatocellular carcinoma: evolving role of external beam radiotherapy. Cancer control : journal of the Moffitt Cancer Center 2010;17:100-10.

148. Edyta WR, Jakub L, Jerzy W. Whole Liver Palliative Radiotherapy for Patients with Massive Liver Metastases. Asian Pac J Cancer Prev 2015;16:6381-4.

149. Gupta S, Johnson MM, Murthy R, et al. Hepatic arterial embolization and chemoembolization for the treatment of patients with metastatic neuroendocrine tumors: variables affecting response rates and survival. Cancer. 2005;104(8):1590-1602.

150. Ruutiainen AT, Soulen MC, Tuite CM, et al. Chemoembolization and bland embolization of neuroendocrine tumor metastases to the liver. J Vasc Interv Radiol. 2007;18(7):847-855.

151. Dong XD, Carr BI. Hepatic artery chemoembolization for the treatment of liver metastases from neuroendocrine tumors: a long-term follow-up in 123 patients. Med Oncol 2011;28 Suppl 1:S286-90.

152. Bhagat N, Reyes DK, Lin M, et al. Phase II study of chemoembolization with drug-eluting beads in patients with hepatic neuroendocrine metastases: high incidence of biliary injury. Cardiovasc Intervent Radiol. 36(2):449-59, 2013 Apr.

153. Fiore F, Del Prete M, Franco R, et al. Transarterial embolization (TAE) is equally effective and slightly safer than transarterial chemoembolization (TACE) to manage liver metastases in neuroendocrine tumors. Endocrine 2014;47:177-82.

154. Devcic Z, Rosenberg J, Braat AJ, et al. The efficacy of hepatic 90Y resin radioembolization for metastatic neuroendocrine tumors: a meta-analysis. J Nucl Med. 55(9):1404-10, 2014 Sep.

155. Pericleous M, Caplin ME, Tsochatzis E, Yu D, Morgan-Rowe L, Toumpanakis C. Hepatic artery embolization in advanced neuroendocrine tumors: Efficacy and long-term outcomes. Asia Pac J Clin Oncol 2016;12:61-9.

156. Fan KY, Wild AT, Halappa VG, et al. Neuroendocrine tumor liver metastases treated with yttrium-90 radioembolization. Contemp Clin Trials. 50:143-9, 2016 09.

157. Guiu B, Deschamps F, Aho S, et al. Liver/biliary injuries following chemoembolisation of endocrine tumours and hepatocellular carcinoma: lipiodol vs. drug-eluting beads. J Hepatol. 2012;56(3):609-617.

158. Chen JX, Rose S, White SB, et al. Embolotherapy for Neuroendocrine Tumor Liver Metastases: Prognostic Factors for Hepatic Progression-Free Survival and Overall Survival. Cardiovasc Intervent Radiol. 40(1):69-80, 2017 Jan.

159. Tomozawa Y, Jahangiri Y, Pathak P, et al. Long-Term Toxicity after Transarterial Radioembolization with Yttrium-90 Using Resin Microspheres for Neuroendocrine Tumor Liver Metastases. J Vasc Interv Radiol 2018;29:858-65.

160. Filice A, Fraternali A, Frasoldati A, et al. Radiolabeled somatostatin analogues therapy in advanced neuroendocrine tumors: a single centre experience. J Oncol 2012;2012:320198.

161. Kwekkeboom DJ, de Herder WW, Kam BL, et al. Treatment with the radiolabeled somatostatin analog [177 Lu-DOTA 0,Tyr3]octreotate: toxicity, efficacy, and survival. J Clin Oncol. 26(13):2124-30, 2008 May 01.

162. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 Trial of (177)Lu-Dotatate for Midgut Neuroendocrine Tumors. N Engl J Med 2017;376:125-35.

163. Lin PS, Semrad TJ. Molecular Testing for the Treatment of Advanced Colorectal Cancer: An Overview. [Review]. Methods Mol Biol. 1765:281-297, 2018.

164. Sanchez-Gundin J, Fernandez-Carballido AM, Martinez-Valdivieso L, Barreda-Hernandez D, Torres-Suarez AI. New Trends in the Therapeutic Approach to Metastatic Colorectal Cancer. [Review]. Int J Med Sci. 15(7):659-665, 2018.

165. Ducreux M, Adenis A, Pignon JP, et al. Efficacy and safety of bevacizumab-based combination regimens in patients with previously untreated metastatic colorectal cancer: final results from a randomised phase II study of bevacizumab plus 5-fluorouracil, leucovorin plus irinotecan versus bevacizumab plus capecitabine plus irinotecan (FNCLCC

ACCORD 13/0503 study). Eur J Cancer 2013;49:1236-45.

166. Fuchs CS, Marshall J, Mitchell E, et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C Study. J Clin

167. Goldberg RM, Sargent DJ, Morton RF, et al. A randomized controlled trial of fluorouracil plus leucovorin, irinotecan, and oxaliplatin combinations in patients with previously untreated metastatic colorectal cancer. J Clin Oncol 2004;22:23-30.

168. Cremolini C, Loupakis F, Antoniotti C, et al. FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study. The Lancet. Oncology 2015;16:1306-15.

169. Sag AA, Selcukbiricik F, Mandel NM. Evidence-based medical oncology and interventional radiology paradigms for liver-dominant colorectal cancer metastases. [Review]. World J Gastroenterol. 22(11):3127-49, 2016 Mar 21.

170. Wicherts DA, de Haas RJ, Adam R. Bringing unresectable liver disease to resection with curative intent. Eur J Surg Oncol. 2007;33 Suppl 2:S42-51.

171. Guglielmi A, Ruzzenente A, Conci S, Valdegamberi A, Iacono C. How much remnant is enough in liver resection? Dig Surg 2012;29:6-17.

172. Toso C, Pinto Marques H, Andres A, et al. Liver transplantation for colorectal liver metastasis: Survival without recurrence can be achieved. Liver Transpl 2017;23:1073-76.

173. Gillams AR, Lees WR. Radio-frequency ablation of colorectal liver metastases in 167 patients. Eur Radiol 2004;14:2261-7.

174. Khajanchee YS, Hammill CW, Cassera MA, Wolf RF, Hansen PD. Hepatic resection vs minimally invasive radiofrequency ablation for the treatment of colorectal liver metastases: a Markov analysis. Arch Surg. 2011;146(12):1416-1423.

175. Lemke J, Cammerer G, Ganser J, et al. Survival and Prognostic Factors of Colorectal Liver Metastases After Surgical and Nonsurgical Treatment. Clin Colorectal Cancer. 15(4):e183-e192, 2016 12.

176. Shady W, Petre EN, Gonen M, et al. Percutaneous Radiofrequency Ablation of Colorectal Cancer Liver Metastases: Factors Affecting Outcomes--A 10-year Experience at a Single Center. Radiology 2016;278:601-11.

177. Franzese C, Comito T, Clerici E, et al. Liver metastases from colorectal cancer: propensity score-based comparison of stereotactic body radiation therapy vs. microwave ablation. J Cancer Res Clin Oncol. 144(9):1777-1783, 2018 Sep.

178. Ceelen W, Praet M, Villeirs G, et al. Initial experience with the use of preoperative transarterial chemoembolization in the treatment of liver metastasis. Acta Chir Belg 1996;96:37-40.

179. Yamakado K, Inaba Y, Sato Y, et al. Radiofrequency Ablation Combined with Hepatic Arterial Chemoembolization Using Degradable Starch Microsphere Mixed with Mitomycin C for the Treatment of Liver Metastasis from Colorectal Cancer: A Prospective Multicenter Study. Cardiovasc Intervent Radiol. 40(4):560-567, 2017 Apr.

180. Folprecht G, Gruenberger T, Bechstein W, et al. Survival of patients with initially

unresectable colorectal liver metastases treated with FOLFOX/cetuximab or FOLFIRI/cetuximab in a multidisciplinary concept (CELIM study). Ann Oncol. 25(5):1018-25, 2014 May.

181. Ruers T, Van Coevorden F, Punt CJ, et al. Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial. J Natl Cancer Inst 2017;109.

182. Chang DT, Swaminath A, Kozak M, et al. Stereotactic body radiotherapy for colorectal liver metastases: a pooled analysis. Cancer 2011;117:4060-9.

183. Lim A, Le Sourd S, Senellart H, et al. Hepatic Arterial Infusion Chemotherapy for Unresectable Liver Metastases of Colorectal Cancer: A Multicenter Retrospective Study. Clin Colorectal Cancer 2017;16:308-15.

184. Guo JH, Zhang HY, Gao S, et al. Hepatic artery infusion with raltitrexed or 5-fluorouracil for colorectal cancer liver metastasis. World J Gastroenterol 2017;23:1406-11.

185. D'Angelica MI, Correa-Gallego C, Paty PB, et al. Phase II trial of hepatic artery infusional and systemic chemotherapy for patients with unresectable hepatic metastases from colorectal cancer: conversion to resection and long-term outcomes. Ann Surg 2015;261:353-60.

186. Chan DL, Alzahrani NA, Morris DL, Chua TC. Systematic review and meta-analysis of hepatic arterial infusion chemotherapy as bridging therapy for colorectal liver metastases. [Review]. Surg Oncol. 24(3):162-71, 2015 Sep.

187. Arai Y, Ohtsu A, Sato Y, et al. Phase I/II study of radiologic hepatic arterial infusion of fluorouracil plus systemic irinotecan for unresectable hepatic metastases from colorectal cancer: Japan Clinical Oncology Group Trial 0208-DI. J Vasc Interv Radiol 2012;23:1261-7.

188. Richardson AJ, Laurence JM, Lam VW. Transarterial chemoembolization with irinotecan beads in the treatment of colorectal liver metastases: systematic review. J Vasc Interv Radiol 2013;24:1209-17.

189. Albert M, Kiefer MV, Sun W, et al. Chemoembolization of colorectal liver metastases with cisplatin, doxorubicin, mitomycin C, ethiodol, and polyvinyl alcohol. Cancer. 2011;117(2):343-352.

190. Wasan HS, Gibbs P, Sharma NK, et al. First-line selective internal radiotherapy plus chemotherapy versus chemotherapy alone in patients with liver metastases from colorectal cancer (FOXFIRE, SIRFLOX, and FOXFIRE-Global): a combined analysis of three multicentre, randomised, phase 3 trials. Lancet Oncol. 18(9):1159-1171, 2017 09.

191. van Hazel GA, Heinemann V, Sharma NK, et al. SIRFLOX: Randomized Phase III Trial Comparing First-Line mFOLFOX6 (Plus or Minus Bevacizumab) Versus mFOLFOX6 (Plus or Minus Bevacizumab) Plus Selective Internal Radiation Therapy in Patients With Metastatic Colorectal Cancer. J Clin Oncol. 34(15):1723-31, 2016 05 20.

192. Gibbs P, Heinemann V, Sharma NK, et al. Effect of Primary Tumor Side on Survival Outcomes in Untreated Patients With Metastatic Colorectal Cancer When Selective Internal Radiation Therapy Is Added to Chemotherapy: Combined Analysis of Two Randomized Controlled Studies. Clin Colorectal Cancer. 17(4):e617-e629, 2018 12.

193. Seidensticker R, Denecke T, Kraus P, et al. Matched-pair comparison of radioembolization plus best supportive care versus best supportive care alone for chemotherapy refractory

liver-dominant colorectal metastases. Cardiovasc Intervent Radiol 2012;35:1066-73.

194. Cosimelli M, Golfieri R, Cagol PP, et al. Multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases. Br J Cancer 2010;103:324-31.

Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

[a]University of Wisconsin, Madison, Wisconsin. [b]Froedtert & The Medical College of Wisconsin, Milwaukee, Wisconsin. [c]Panel Chair, University of Wisconsin, Madison, Wisconsin. [d]Panel Vice-Chair, Duke University Medical Center, Durham, North Carolina. [e]University of Chicago, Chicago, Illinois. [f]Vascular Institute of North Texas, Dallas, Texas; Commission on Nuclear Medicine and Molecular Imaging. [g]Weill Cornell Medicine, New York, New York; RADS Committee. [h]Stanford Medical Center, Stanford, California. [i]Perelman School of Medicine of the University of Pennsylvania, Philadelphia, Pennsylvania; American Association for the Study of Liver Diseases. [j]Providence St. Joseph Health, Eureka, California; Commission on Radiation Oncology. [k]University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; American Gastroenterological Association. [l]University of Wisconsin, Madison, Wisconsin. [m]Stanford University School of Medicine, Stanford, California; Society of Surgical Oncology. [n]Froedtert & The Medical College of Wisconsin, Milwaukee, Wisconsin. [o]Specialty Chair, Froedtert & The Medical College of Wisconsin, Milwaukee, Wisconsin.