#### **Rationale**

- Much less frequent than Colorectal liver metastases
- For long a non-surgical entity...
- Outcome as a whole, in pioneering groups not so different than that of Colorectal mets, even for cancers with hematogeneous spread (Breast)
- But still pending questions on the role of liver surgery vs systemic treatment
- Literature: small cohorts, heterogeneity of primaries, inclusion or not of NET...
- Key Question: What should be the place of liver surgery in the context of Liver Metastases of a cancer either of the stomach, the pancreas, the breast, the kidney?...

Should we resect or transplant LM from neuroendocrine tumors and when?

#### Aims of the project

- To collect, on a large scale, the critical information concerning the history of patients <u>surgically treated</u> for both neuroendocrine and non colorectal liver metastases
- To prospectively evaluate the outcome after surgery
- To analyse survival data in relation to pertinent prognostic factors
- To provide information on pending questions regarding the indications to surgical treatment, the type of surgery including liver transplantation, the role of chemotherapy and the usefulness of adjuvant treatments.

## **Protocol**

- To nominate a scientific board including surgeons, medical oncologists, radiologists,
- To define a questionnaire with the most critical informations needed to evaluate predictive factors of outcome
- To offer the possibility to all HPB centers affiliated to IHPBA to contribute, providing a regular feedback regarding transmission of the results of the whole registry as well as of the individual series of each center.
- To make publications from the registry, on behalf of IHPBA with a co-authorship from contributing centers, in relation to the number of patients included in the Registry

#### What is the benefit to contribute?

- To have regular access to all the results of the whole registry
- To maintain your own database within the whole registry with automatized information on the results
- To run any scientific paper on the global cohort of the registry, provided that you routinely update the data from your patients included in the Registry
- To be co-author of the publications made from the global registry

#### Who can access the data?

- All the contributing centers will have access to the whole data of the registry and to their own series but without the possibility to see the data from the other centers.
- The access will be secured by a password and reserved to the head of the center as well as to 3 co-investigators of each center to whom a different password will be attributed.

#### Who is going to regulate it?

- The scientific committee will meet at least once a year, twice ideally under the auspices of the IHPBA and will make an annual report of the registrations and their results.
- These will be examined by the Research committee and transmitted to the executive committee of IHPBA
- Bi-annual Newsletter to the centers (TBD)

#### How the information is going to be used?

Every projected study will be submitted to the approval of the scientific committee, provided that the contributing center which makes the demand, is updated in the inclusion of his patients. The authorship will include:

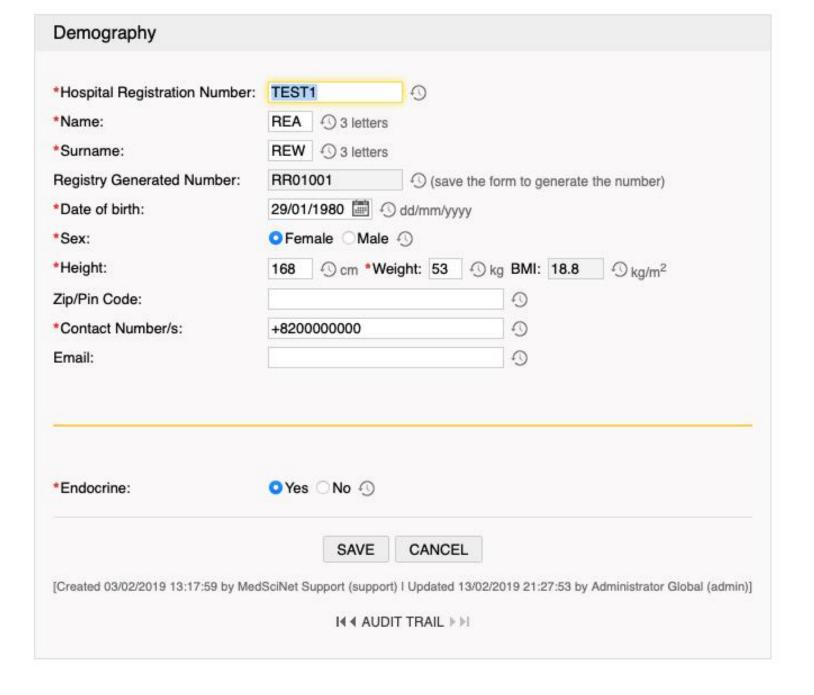
- 3 authors from the center which makes the study (1st, 2<sup>nd</sup> and last author)
- The 3<sup>rd</sup> authorship will be reserved to the member of the scientific committee specifically devoted to the internal review of the paper and
- Then, all the maximum number of co-authors allowed by the journal, by decreasing order of the number of patients included in the registry, with one or two representants by center in relation to the number of inclusions
  - Aknowledgements for centers not included in the authorship

#### Scientific Committee of the NCR LM Registry

```
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Others...(TBD)
```

# Questionnaire

## Endocrine Liver Met



Primary disease			
*Date of diagnosis:	20/11/2000 🗐 🕙 dd/mm/yyyy		
Location:	✓ Gastric ④		
	Oesophagus 🕙		
	☐ Colon-rectum ④		
	☐ Small intestine ④		
	□ Pancreas ④		
	☐ Lung ④		
	☐ Undetermined ④		
	Others 🕙		
Circumstances of diagnosis:	✓ Fortuitous ④		
	Occlusion 🕙		
	☐ Hepatomegaly ④		
	☐ Diarrhea ④		
	☐ Flush ④		
	Others 🕙		
Familial syndrome:	Multiple Endocrinopathy Neoplasia type 1 🕙		
	Others 🕙		
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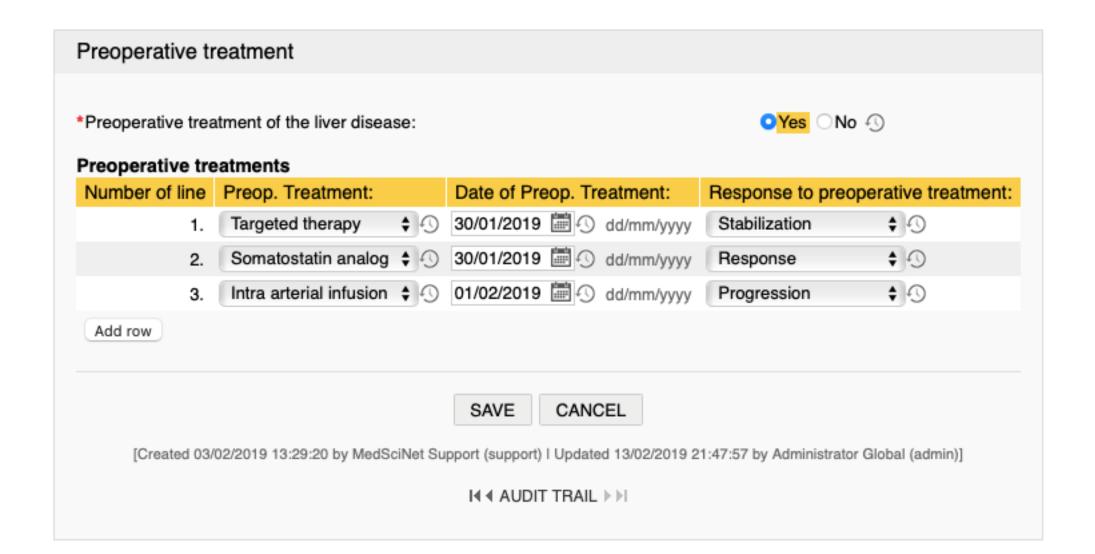
Biomarkers at diagnosis				
Chromogranin A: NSE:	12 ① ng/l 5 ① ng/mL			
5-HIAA (urine collection): 5-HIAA (plasma):	⊕ mg/24 hours ⊕ ng/ml			
Gastrin:				
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I◀ ◀ AUDIT TRAIL ▶ ▶I				

Sugery of the primary			
*Resection: *Type: *Date:	OYes ONo ← O  gastrectomy  (ex.: total gastrectomy, partial mastectomy)  22/12/2000 □ ← Odd/mm/yyyy		
*Pathology:	*Endocrine: Yes No ①		
*Tumor size:  *No. of positive LN:  *No. of examined LN:  *Lymph node metastasis left in place	*Adenocarcinoma with neuroendocrine differenciation: Yes No 40  20 mm  2 40  5 40		
*Margin:	Ce: ○ Yes ○ No → ○  ○ Positive ○ Negative ◆ ○		
*Ki-67:	3 49%		
*Classification:	Neuroendocrine G1 Neuroendocrine G2 Neuroendocrine G3 Neuroendocrine carcinoma (poorly differenciated) Other		
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Sugery of the primary				
*Resection:	OYes ○No ④			
*Type:	gastrectomy (ex.: total gastrectomy, partial mastectomy)			
*Date:	22/12/2000 📰 🕙 dd/mm/yyyy			
*Pathology:	*Endocrine: OYes ONo 40			
	*Adenocarcinoma with neuroendocrine differenciation: OYes ONo			
*Tumor size:	20			
*No. of positive LN:	2 ①			
*No. of examined LN:	5 🕙			
*Lymph node metastasis left in place:	∵ ○Yes ○No ·			
*Margin:	OPositive Negative			
*Ki-67:	3 🕚 %			
*Classification:	ONeuroendocrine G1			
	○ Neuroendocrine G2 ○ Neuroendocrine G3			
	Neuroendocrine carcinoma (poorly differenciated)			
	Other			
	SAVE CANCEL			
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*Type:  Date diagnosis of liver disease:	Synchronous • Metachronous •  25/10/2002  dd/mm/yyyy				
Date diagnosis of primary diseas	20/11/2000 dd/mm/yyyy				
Circumstances of diagnosis:	✓ Follow-up ④				
-	□ Fortuitous ⑤				
	□ Symptoms ④				
	Others 🕙				
*Hepatomegaly:	○Yes ○No ④				
*Carcinoid Heart disease:	○Yes ○No ④				
*CT-scan:	○ Yes ○ No ④				
*MRI:	OYes ○No ①				
*FDG-PET scan:	○Yes ○No ⑤				
mean SUV:	①				
Somatostatin receptor scintigraph	y: ○Yes ○No ④				
68Ga-DOTATOC:	○ Yes ○ No ④				
18F-DOPA-PET:	○ Yes ○ No ④				
*Localization:	Ounilobar ○ Bilobar ④				
*Number of lesions:	3 🕠				
*Max tumor size:	4 ① mm				
*Initially resectable disease:	○ Yes ○ No ④				
*Concomitant extrahepatic disea	e (other than primary) at diagnosis: • Yes ONo				
Extrahepatic disease location	ns .				

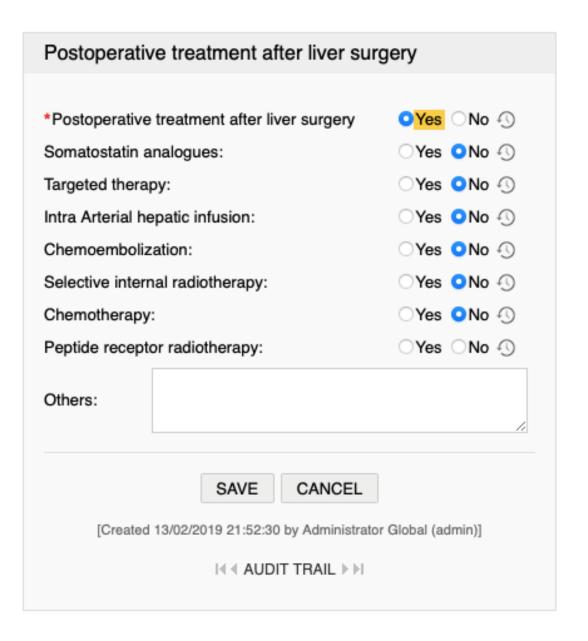
Biomarkers at dia	agnosis	
CgA:	3 ① ng/l	
NSE:	5 ⊕ ng/mL	
	SAVE CANCEL  [Created 13/02/2019 21:43:57 by Administrator Global (admin) I Updated 13/02/2019 21:46:43 by Administrator Global (admin)]  I◀ ◆ AUDIT TRAIL ▶ ▶	Name   Name



Hepatectomy			
*Portal vein embol	ization:	Yes ○ No ◆○	
*Date hepatectomy	y:	//	
*Resected:		Yes ○ No ◆	
No. Resected segr	nents:	•	
*Macroscopically (	Complete:	Yes ○ No ◆	
*Nature of the surg	jery:	Curative  Debulking	
Associated treatme	ents:	✓ RFA ④	
		☐ Cryotherapy ◆	
*Type of hepatecto	omy:	<ul> <li>Trisectionectomy</li> <li>Hemihepatectomy</li> <li>Sectionectomy</li> <li>Segmentectomy</li> <li>Partial hepatectomy</li> <li>Total hepatectomy</li> <li>Others</li> </ul>	
*Strategy:		<ul><li>One hepatectomy</li><li>Two stage</li><li>ALPPS</li><li>Liver Transplantation</li></ul>	
*Approach:  *Combined surger	y of the primary and	Open ORObotic  the liver? Yes No	
	SAVE DRAFT	SAVE CANCEL	
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Histology				
*Number:	2 ①			
*Max size:	15 ① mm			
*Pathological response:	3 % remaining cancer cell			
*Ki-67:	24 %			
*Margins:	○ Positive ○ Negative ○			
*Non tumoral liver:	ONormal Steatosis Fibrosis Other			
*Grade:	○ Poor ○ Moderate ○ Well ④			
*Mitotic Count (10 consecutive high-power fields):	•			
*Lympho vascular invasion	○Yes ○No ◆			
*Mixt features with adenocarcinoma	○Yes ○No ◆			
SAVE DRAFT SAVE CANCEL  [Created 13/02/2019 21:49:57 by Administrator Global (admin)]				

Operative outcomes	
*Complications:	○Yes ○No ◆ ○
If yes, main complication:	Urinary infection Catheter-related infection Mental confusion Cardiovascular Pulmonary embolism Renal failure Carcinoid crisis Others
Liver specific complications:	✓ Liver failure
	☐ Biliary fistula ④
	☐ Hemorrhage ←
	☐ Infected collection ④
*Dindo-Clavien:	○ Grade I
	○ Grade II
	Grade Illa
	Grade IIIb
	Grade IV
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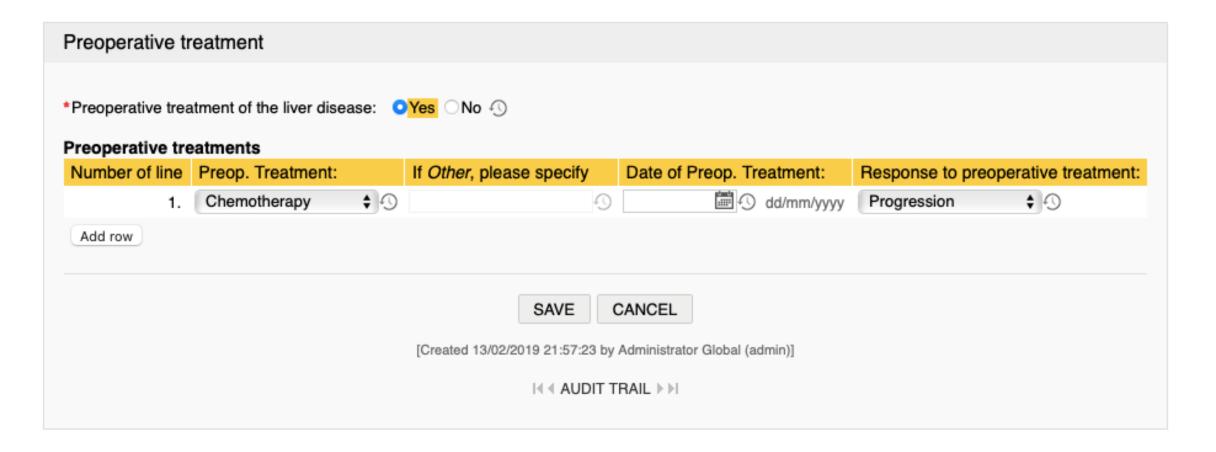


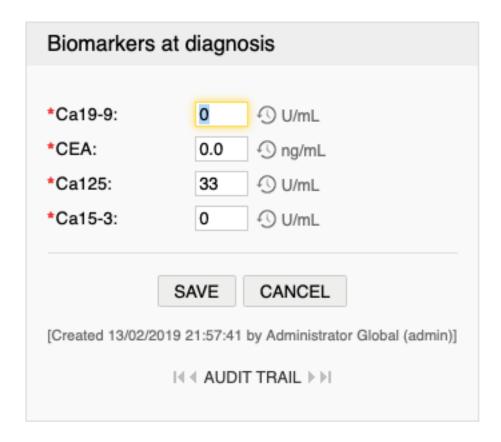
Oncological outcomes				
Date last follow-up:  O6/02/2019 OR Date of death: 06/02/2019 OAlive recurrence-free without ongoing treatment Alive recurrence-free with ongoing treatment Alive with recurrence Dead			ment	
Disease unresected:		○Yes ○No ④		
Dates of relapse				
Date of relapse:	Location:	If Other, please specify:	Treatment:	
dd/mm/yyyy	<b>+</b>		<b>*</b>	
Add row				
Date of relapse surgically untreatable:				
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## NON Endocrine Non colorectal registry

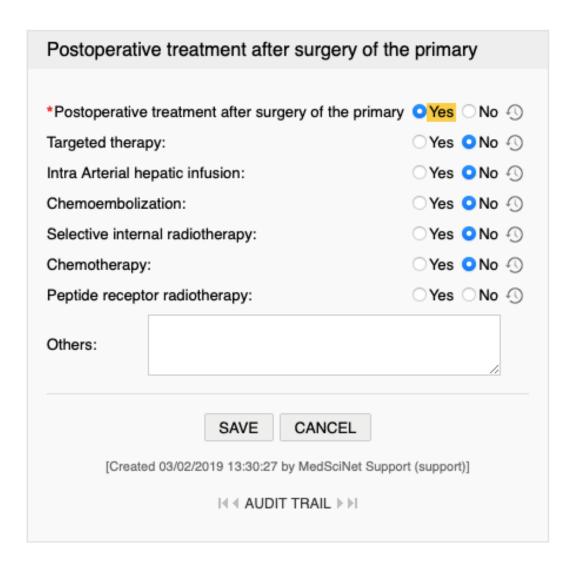
*Hospital Registration Number	er: TEST2			
*Name:	TES 3 letters			
*Surname:	HAR 3 letters			
Registry Generated Number:	TH01002 (save the form to generate the number)			
*Date of birth:	31/01/1988 🗐 🕙 dd/mm/yyyy			
*Sex:	○ Female • Male • ○			
*Height:	189			
Zip/Pin Code:	•			
•	+8200000000			
Zip/Pin Code: *Contact Number/s: Email:				
*Contact Number/s:	+8200000000			
*Contact Number/s: Email:  *Endocrine:	+820000000			
*Contact Number/s: Email:  *Endocrine: *Inherited cancer gene:	+8200000000			
*Contact Number/s: Email:	+8200000000  Yes • No • O  Yes • No • O			

Primary disease					
*Date of diagnosis	29/08/2017 🗂 🕙 dd/mm/yyyy				
Location:	☑ Gastric ④ ☐ Ampuloma ④ ☐ Bladder ④				
	Oesophagus (	Anus 🕙	☐ Melanoma ④		
	☐ Cardia ④	☐ Breast ④	☐ Lung ◆		
	☐ Pancreas ④	Ovary 🕚	☐ Head/Neck ④		
	☐ Duodenum ④	Uterus 🕚	☐ Thyroid ◆		
	☐ Small bowel ④	☐ Kidney ④	Others 🕚		
	☐ Gallblader ④	☐ Testis ④			
Histology:	Adenocarcinoma	a 🕙			
	☐ Epidermoid ④				
	Sarcoma 🕙				
	Stromal tumor 4	3			
	Others 🕔				
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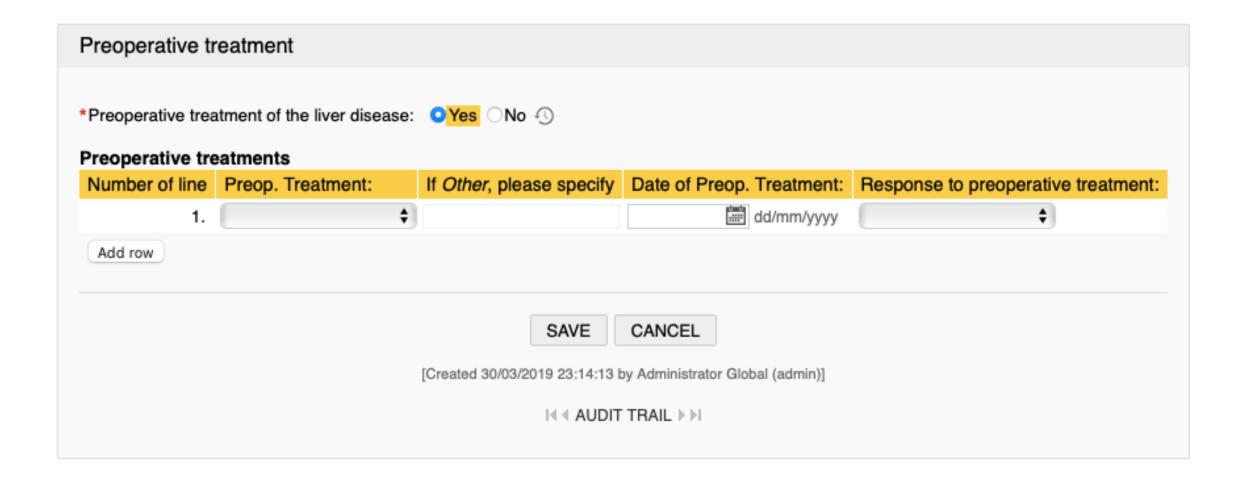




Sugery of the prin	nary			
*Resection:	OYes ○No ④			
*Type:	mastectomy	(ex.: total gastrectomy, partial mastectomy)		
*Date:	05/02/2010 🛗 🕙 dd/mm/yyyy			
*Pathology:	<ul><li>Adenocarcinoma NOS</li><li>Papillary</li><li>Squamous</li><li>Neuroendocrine</li><li>Other</li></ul>			
*Tumor size:	22 ① mm			
*No. of positive LN:	2			
*No. of examined LN:	34			
*Margin:	OPositive ONegative			
SAVE CANCEL  [Created 13/02/2019 22:01:18 by Administrator Global (admin)]  I  AUDIT TRAIL  II				



*Date diagnosis of liver disease	06/02/2019	06/02/2019 📰 🕙 dd/mm/yyyy				
Circumstances:	Follow-up	0				
	<ul><li>Fortuitous</li></ul>	0				
	Symptoms	0				
	Others 🕔					
*PET-CT:	O Yes O No	0				
*CT-scan:	Yes ○ No	○Yes ○No ④				
*MRI:	Yes ○ No	○ Yes ○ No ④				
*Localization on imaging:	Unilobar	○ Unilobar ○ Bilobar ④				
*Number of lesions:	3					
*Max tumor size:	- ⊕ mm					
iviax tumor size:	100	nm				
*Max tumor size:  *Initially resectable:	○Yes ○No					
	○Yes ○No	0	No 🕙			
*Initially resectable:  *Concomitant extrahepatic disea	• Yes O No	0	No 🕙			
*Initially resectable:  *Concomitant extrahepatic disea  Extrahepatic disease location	• Yes O No		No ①  Treatment:	Date res	ection:	Complete
*Initially resectable:  *Concomitant extrahepatic disea  Extrahepatic disease location	• Yes • No ase (other than prin			Date res	ection:	Complete
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location  If Other	• Yes • No ase (other than prin	mary) at diagnosis • Yes • Date of diagnosis:				
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location:  If Other	• Yes • No ase (other than prin	mary) at diagnosis • Yes • Date of diagnosis:				
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location  Location:  If Other  Add row	• Yes • No ase (other than prin	mary) at diagnosis • Yes • Date of diagnosis:				
*Initially resectable:  *Concomitant extrahepatic disease location  Location: If Other  Add row  Biomarkers at diagnosis	Yes No No ase (other than print ons r, please specify	mary) at diagnosis • Yes • Date of diagnosis:				
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location  If Other	Yes No No ase (other than print ons r, please specify	mary) at diagnosis • Yes • Yes • Date of diagnosis:				
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location:  If Other  Add row  Biomarkers at diagnosis  *Alpha-Fetoprotein:  *Ca19-9:	• Yes • No ase (other than print ons r, please specify	mary) at diagnosis • Yes • Date of diagnosis:  dd/mm/yyyy				
*Initially resectable:  *Concomitant extrahepatic disease  Extrahepatic disease location  Location:  If Other  Add row  Biomarkers at diagnosis  *Alpha-Fetoprotein:	• Yes • No  ase (other than print  ons  r, please specify	mary) at diagnosis • Yes • Date of diagnosis:  dd/mm/yyyy				



Hepatectomy	
*Date hepatectomy:	//
*Resected:	○Yes ○No ◆
*Macroscopically Complete:	○Yes ○No ④
If No:	< 10% residual disease >= 10% residual disease
Associated treatments:	□ RFA ⊙
	Cryotherapy 🕙
*Type of hepatectomy:	Trisectionectomy Hemihepatectomy Sectionectomy Segmentectomy Partial hepatectomy Total hepatectomy Others
*Strategy:	One hepatectomy Two stage ALPPS Liver Transplantation
*Approach:	○ Laparoscopy ○ Open ④ ○ Robotic
*Combined surgery of the primary and the liver?	○Yes ○No ④
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Histology	
*Number:	
*Max size:	mm
*Pathological response:	% remaining cancer cell
*Margins:	OPositive ONegative
*Non tumoral liver:	<ul><li>Normal</li><li>Steatosis</li><li>Fibrosis</li><li>Other</li></ul>
*Grade:	○ Poor ○ Moderate ○ Well
*Mitotic Count (10 consecutive high-power field	ds):
*Lympho vascular invasion	○ Yes ○ No
*Mixt features with adenocarcinoma	○Yes ○No
SAVE DRAFT SAVE	CANCEL

Operative outco	omes	
*Complications: *Dindo-Clavien:	Gra Gra Gra Gra Gra	No ade I ade II ade IIIa ade IIIb ade IV ade V
SAVE DRAFT	SAVE	CANCEL

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Postoperative treatment after liver surgery					
*Postoperative treatment after liver surgery ONO					
Targeted therapy:   Yes No					
Intra Arterial hepatic infusion:					
Chemoembolization: Yes • No •					
Selective internal radiotherapy:					
Chemotherapy: Yes ONo					
Peptide receptor radiotherapy:	○Yes ○No ④				
Others:					
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