#jornadadigestivo2016

TEMAS DE ACTUALIDAD EN

CÁNCER DIGESTIVO

II JORNADA CIENTÍFICA

Cáncer colorrectal metastásico

Córdoba 13 de Mayo 2016

CÁNCER DIGESTIVO

II JORNADA CIENTÍFICA

#jornadadigestivo2016

Metastasis Hepaticas Colorectales

Nueva técnicas *Quirúrgicas* avanzadas en el tratamiento de la enfermedad metastásica potencialmente resecable

Julio Santoyo Santoyo
Jefe de Servicio de Cirugía General, Digestiva y Trasplantes
Hospital Regional Universitario de Málaga

- **Metástasis Hepáticas en España: problema creciente**
- **Definición de Resecabilidad en la actualidad**
- **Estrategias Onco-quirúrgicas para la enfermedad avanzada**

Metástasis hepáticas por Cáncer Colo-Rectal

SEGÚN INFORME DE la SEOM >32,000 CASOS DE CCR EN ESPAÑA 2014 Y >14.000 MUERTES POR ESTE CANCER

50% Irresecables

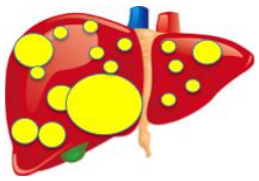
10,000-15,000

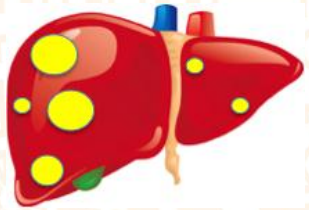
15% Resecables

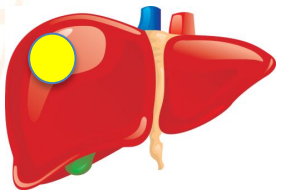
2,000-4,500

35% Potencialmente Resecables

7,000-10,000







Metástasis hepáticas por Cáncer Colo-Rectal

SEGÚN INFORME DE la SEOM >32,000 CASOS DE CCR EN ESPAÑA 2014 Y >14.000 MUERTES POR ESTE CANCER

50% Irresecables

10,000-15,000

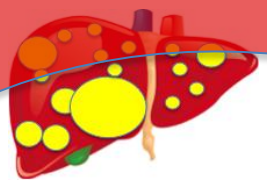
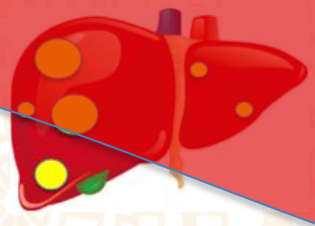
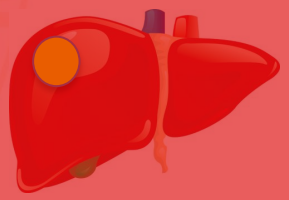
15% Resecables

2,000-4,500

35% Potencialmente Resecables

7,000-10,000

ANTES

Metástasis hepáticas por Cáncer Colo-Rectal

? Irresecables

>50% Resecables?

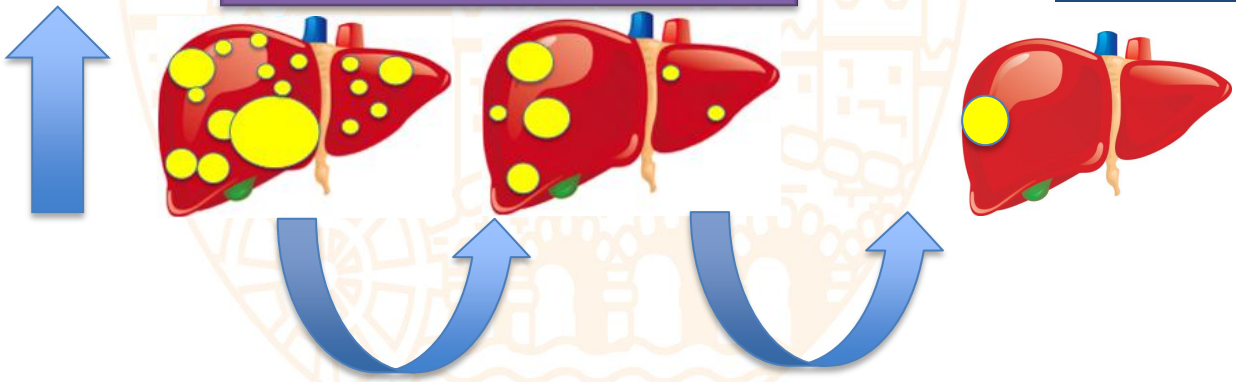
?Potencialmente Resecables

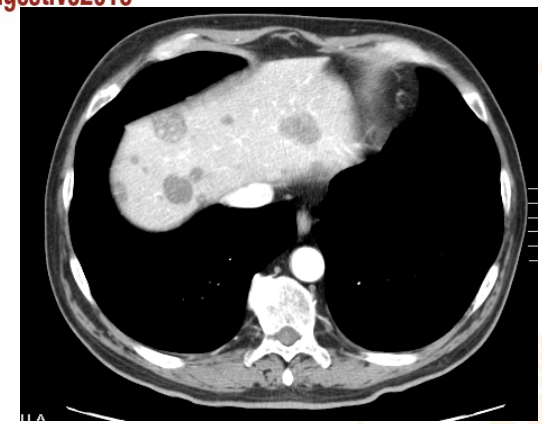
2,000->4,500

7,000-10,000

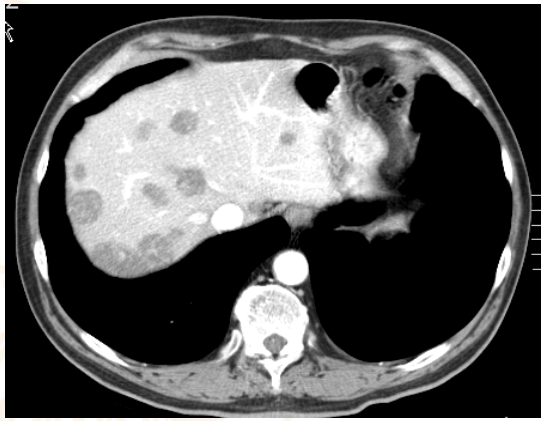
10,000-5,000

Tratamiento Multimodal

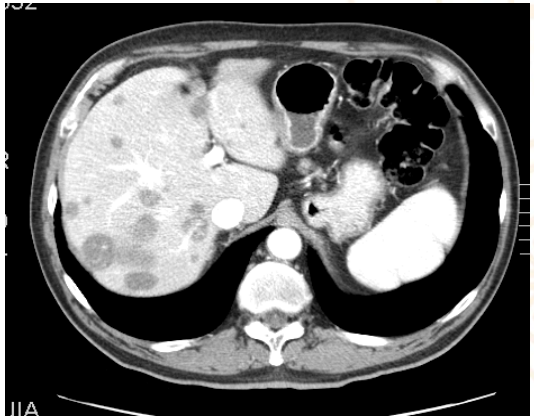


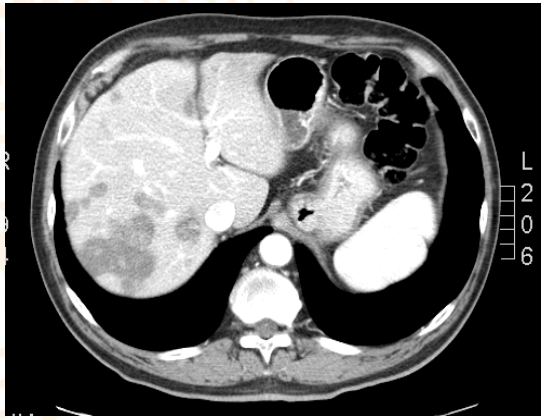


¿?



Hombre, 59 años, Ca recto con Metástasis sincrónicas (TC 12xFolfox+Beva)





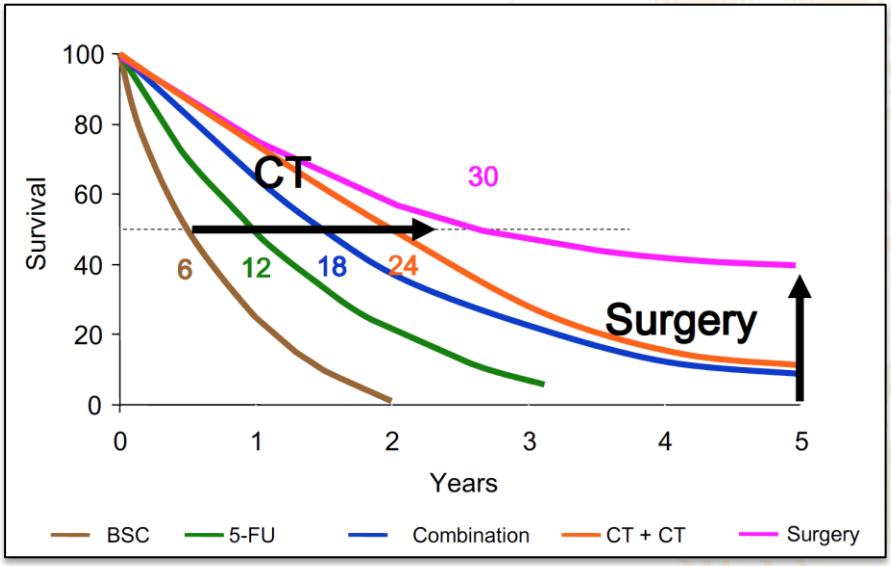
- Metástasis Hepáticas en España: problema creciente
- **Definición de Resecabilidad en la actualidad**
- Estrategias Onco-quirúrgicas para la enfermedad avanzada

Resecabilidad vs. Resultado

- **Ideal** → ***Curación?*** **(20% a 10 años)**
- **Optimo** → ***Supervivencia libre de enfermedad 5años (>30-50% ?)***
- **Aceptable** → ***Supervivencia con de enfermedad 2-3 años (30% ?)***

Resecabilidad vs. Resultado

- Ideal → *Curación?*
- Optimo → *Supervivencia libre de enfermedad 5años>30-50% ?*
- **Aceptable** → ***Supervivencia con de enfermedad 2-3 años 30% ?***

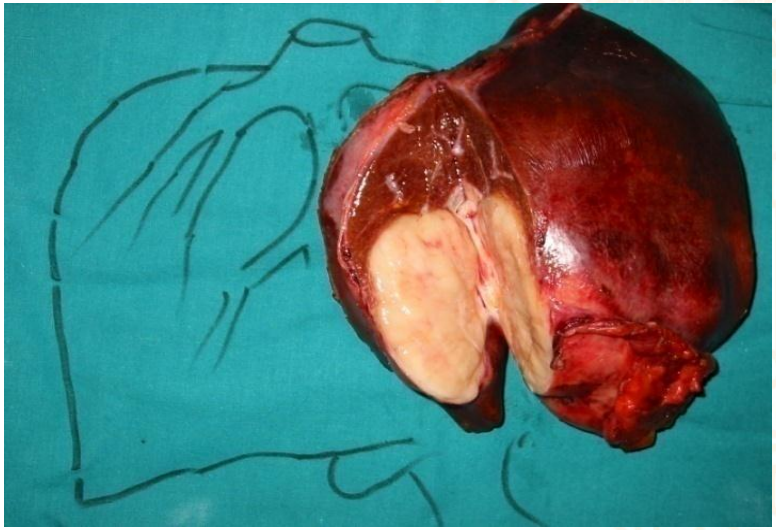


La resección quirúrgica debe conducir a algún beneficio oncológico (supervivencia) sobre el mejor esquema de QT

Criterios actuales de resecabilidad:

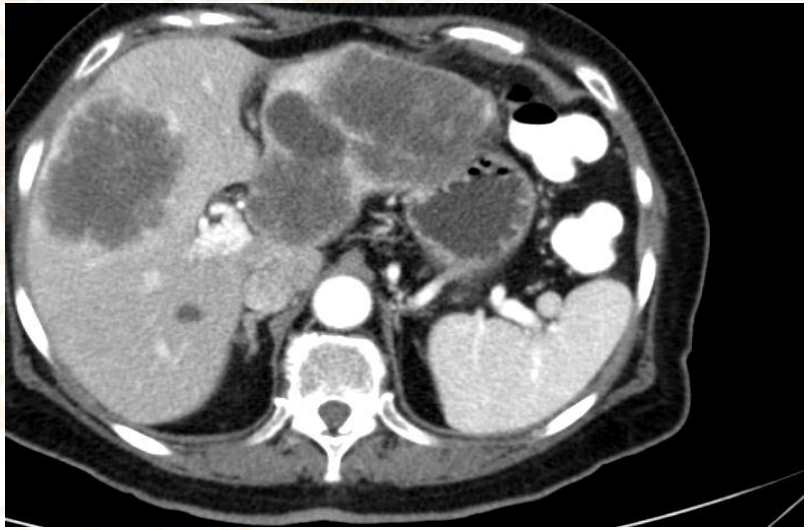
Criterios Técnicos

- Resección R0 posible macro y microscópicamente (Margen 1mm/R1/R2?)
- Remanente suficiente (>20-30% hígado sano; >30-40% hígado QT)



Criterios Oncológicos

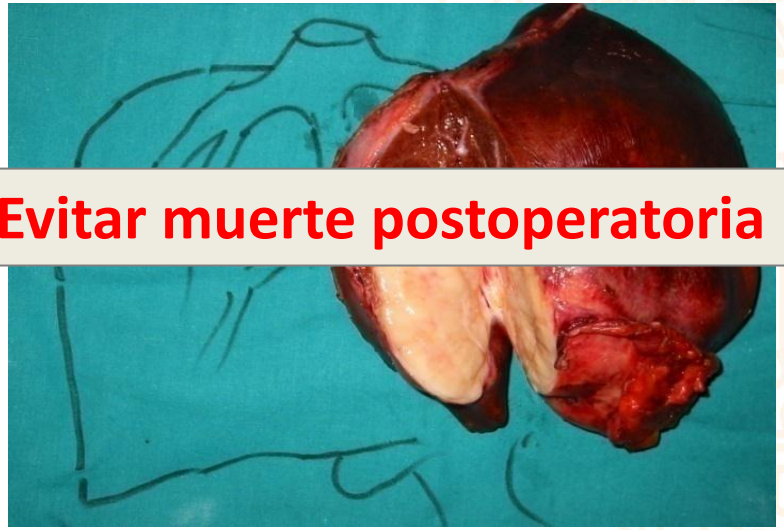
- Enfermedad extra-hepática resecable (pulmonar, peritoneal…)
- Ausencia de progresión de enfermedad (?)



Criterios RECIENTES de resecabilidad:

Criterios Técnicos

- Resección R0 posible macro y microscópicamente (Margen 1mm/R1/R2?)
- **Remanente suficiente (>20-30% hígado sano; >30-40% hígado QT)**



Evitar muerte postoperatoria

Criterios Oncológicos

- **Enfermedad extra-hepática resecable (pulmonar, peritoneal, osea…)**
- Ausencia de progresión de enfermedad (?)

Evitar muerte precoz

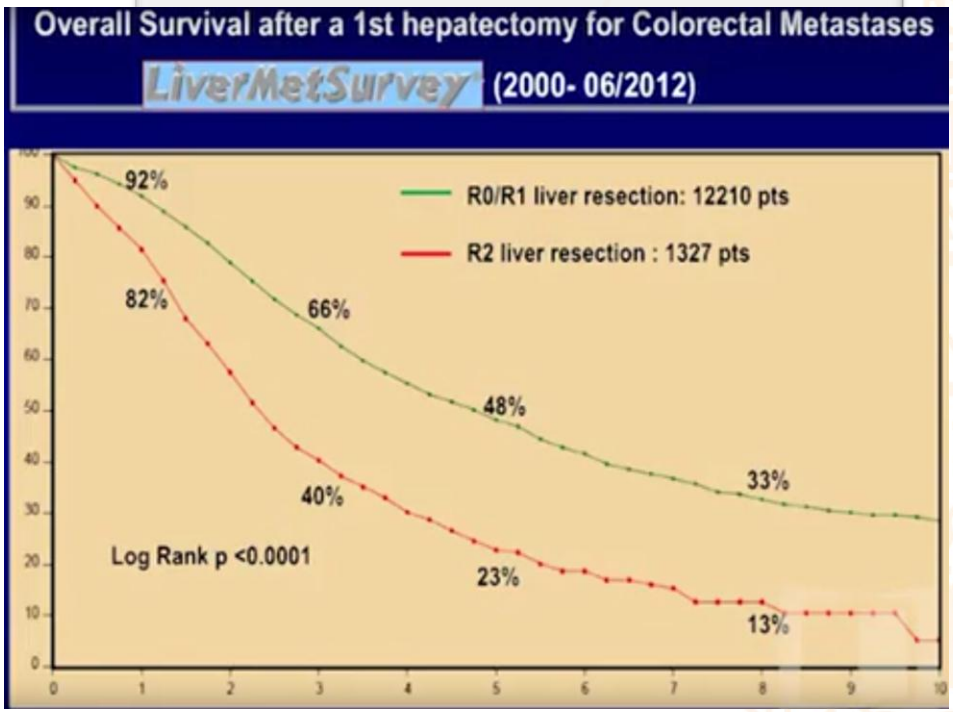
Criterios actuales de resecabilidad

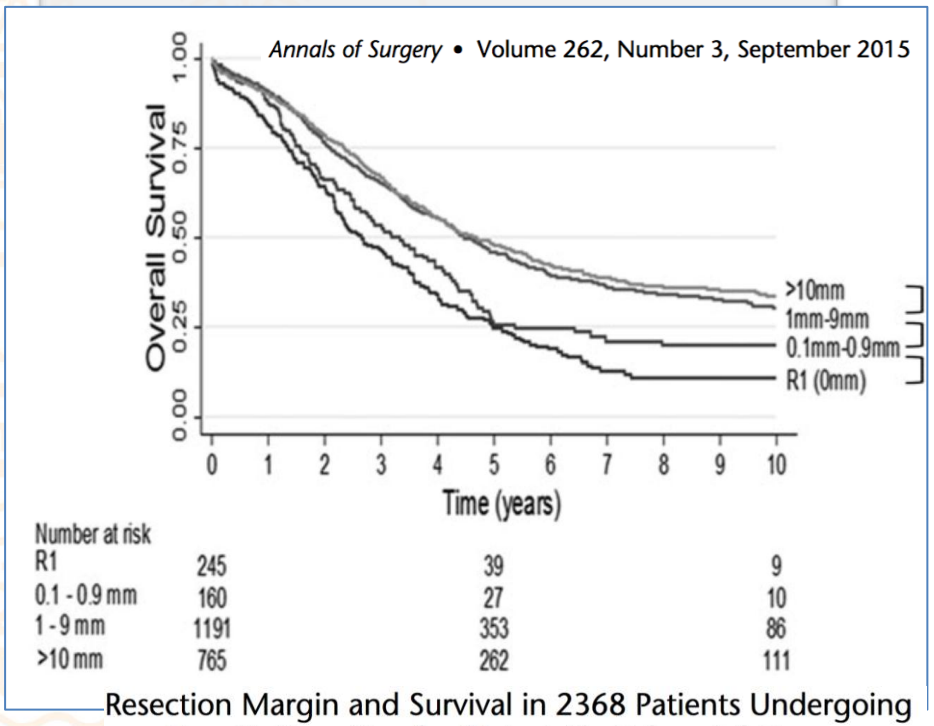
Criterios Técnicos

- **Resección R0 posible macro y microscópicamente (Margen 1mm/R1/R2?)**

Criterios Oncológicos

- **Enfermedad extra-hepática resecable (pulmonar, peritoneal…)**





Resection Margin and Survival in 2368 Patients Undergoing Hepatic Resection for Metastatic Colorectal Cancer

CÁNCER DIGESTIVO

II JORNADA CIENTÍFICA

#jornadadigestivo2016

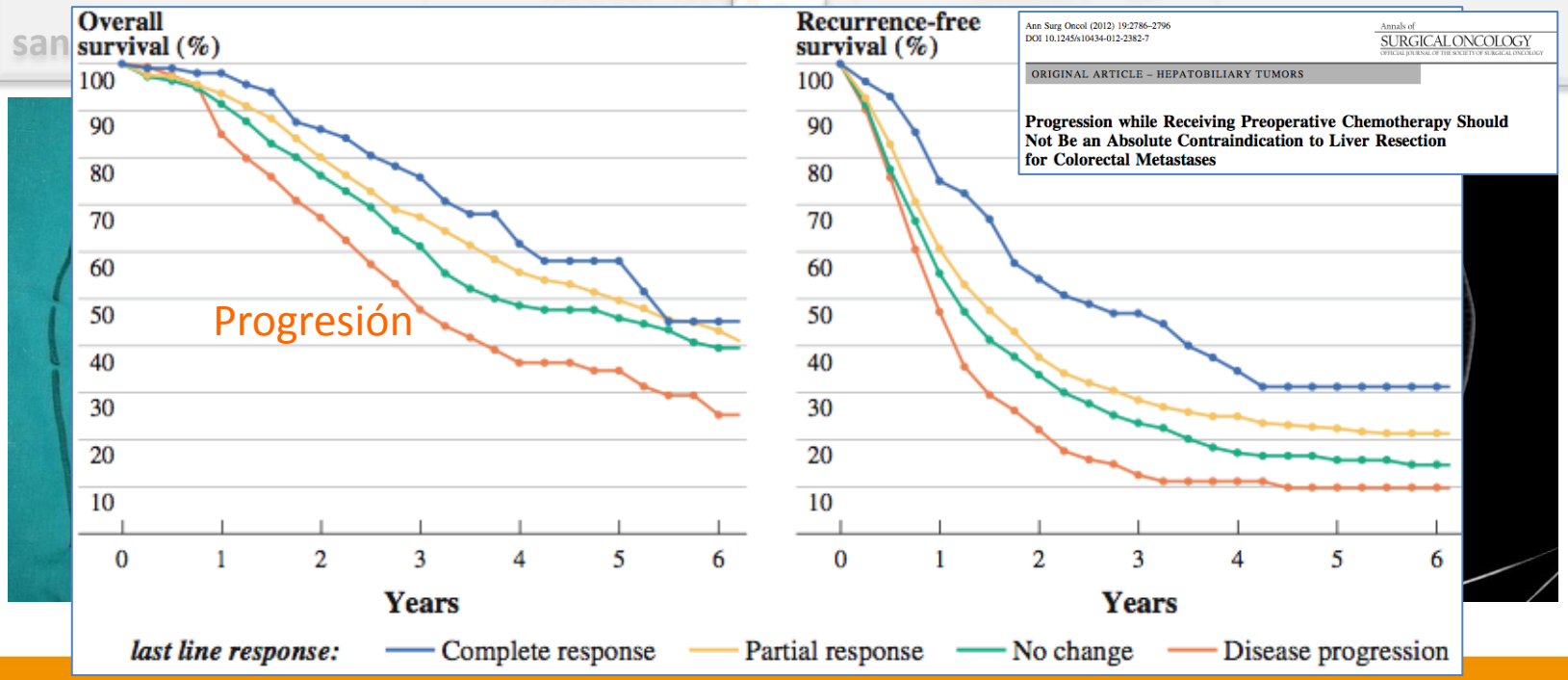
Criterios actuales de resecabilidad

Criterios Técnicos

- Resección R0 posible macro y microscópicamente (Margen 1mm/R1/R2?)
- Remanente suficiente (>20-30% hígado san

Criterios Oncológicos

- Enfermedad extra-hepática resecable (pulmonar, peritoneal…)
- **Ausencia de progresión de enfermedad**



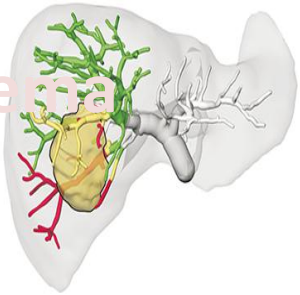
Ann Surg Oncol (2012) 19:2786–2796
DOI 10.1245/s10434-012-2382-7

Annals of SURGICAL ONCOLOGY

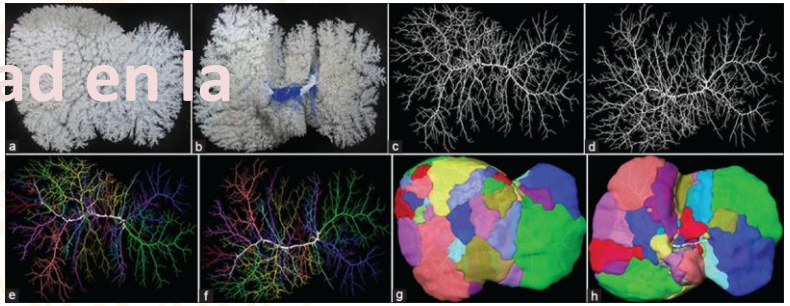
ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Progression while Receiving Preoperative Chemotherapy Should Not Be an Absolute Contraindication to Liver Resection for Colorectal Metastases

- Metástasis Hepáticas en España: problema creciente



- Definición de Resecabilidad en la actualidad



- **Estrategias Onco-quirúrgicas para la enfermedad avanzada**

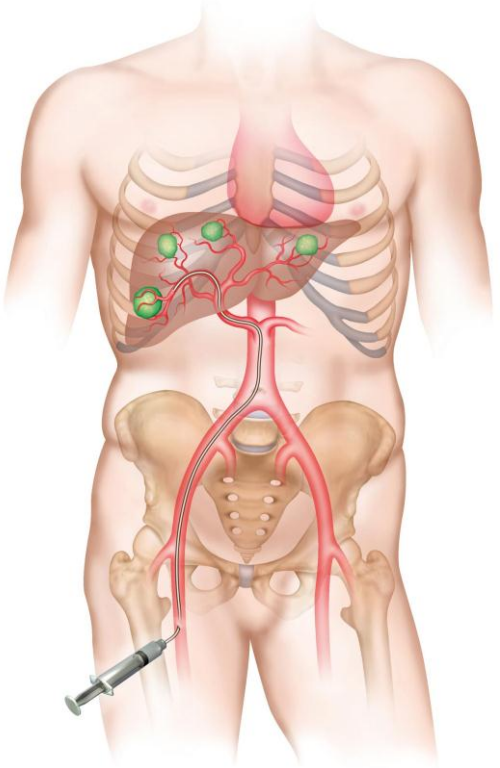
- **Estrategias para disminuir la carga tumoral**
  - QT de conversión
- **Estrategias para preservar el hígado remanente**
  - Hepatectomía mayor + RF/MO
- **Estrategias para aumentar el hígado remanente**
  - Cirugía en 2 tiempos
  - Embolización portal/Radioembolización Y90
  - ALPPS
- **Hepatectomías complejas (localización tumoral)**
  - Resecciones ex o in situ hipotérmicas
  - Resecciones submasivas
- **Trasplante hepatico**

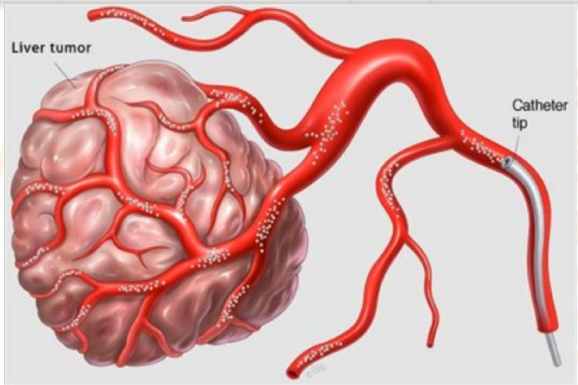
- **Estrategias para disminuir la carga tumoral**
  - **QT de conversión**

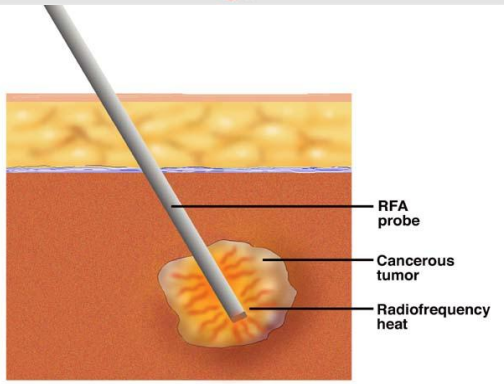
- **Mínimo numero de ciclos (<4-6)**
- **Esperar 3-6 semanas tras el cese de la QT**
- **Buen estudio TC/RM tras el ultimo ciclo**
- **Toxicidad de QT (CASH, SOS…)**
- **Desaparición de las Metástasis**

Estrategias para preservar el hígado remanente

(COMBINADAS: Cirugía + TECNICAS ABLATIVAS)



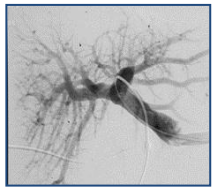
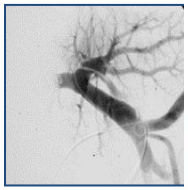
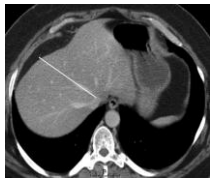
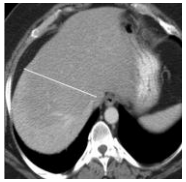
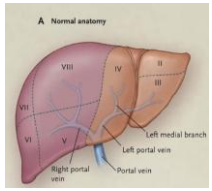


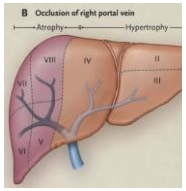


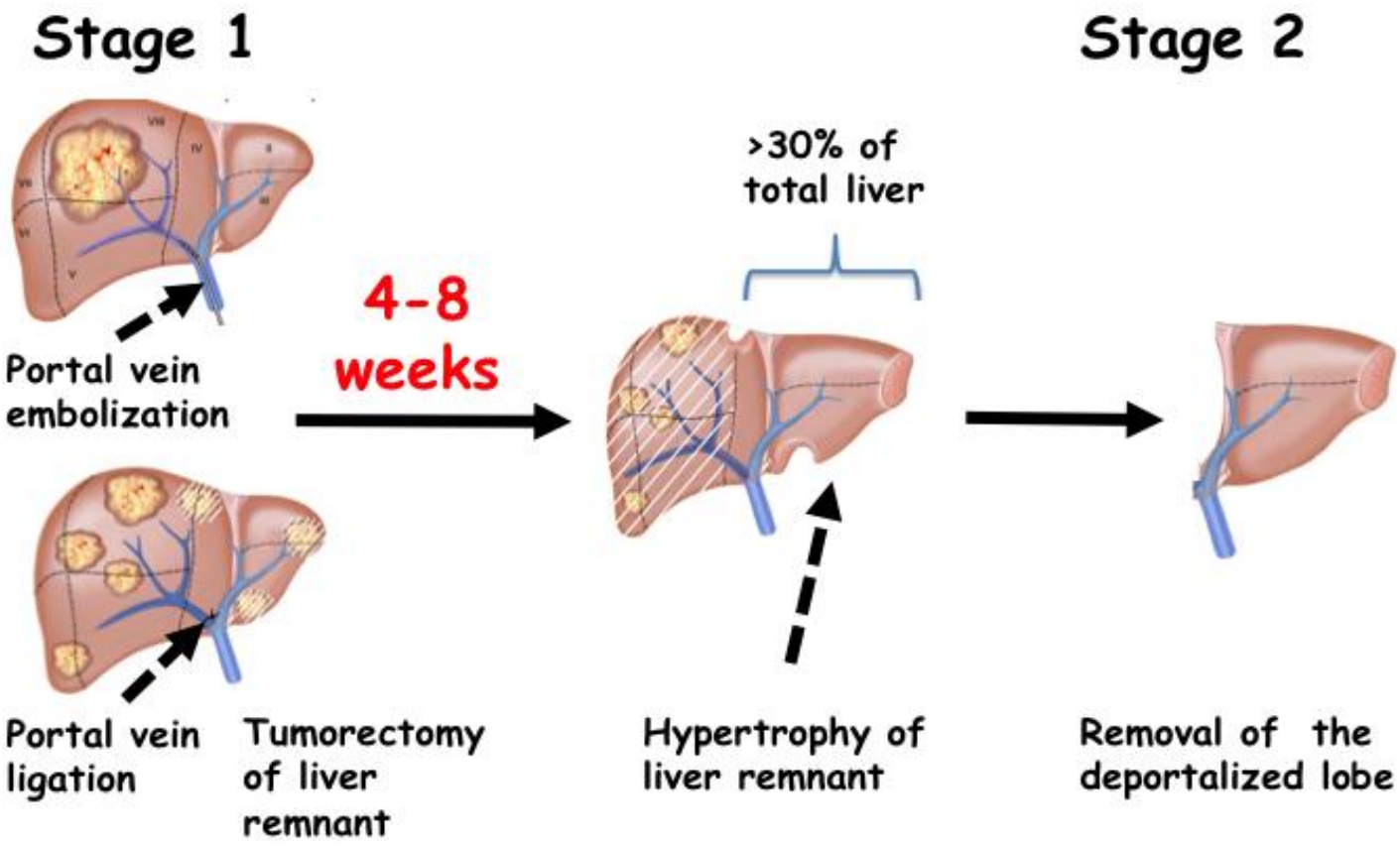
- RADIOFRECUENCIA
- MICROONDAS
- DEBIRI
- RADIOEMBOLIZACION
- ELECTROPORACION
- SABR
- ….

Estrategias para aumentar el hígado remanente

- Cirugía en 2 tiempos + Embolización portal

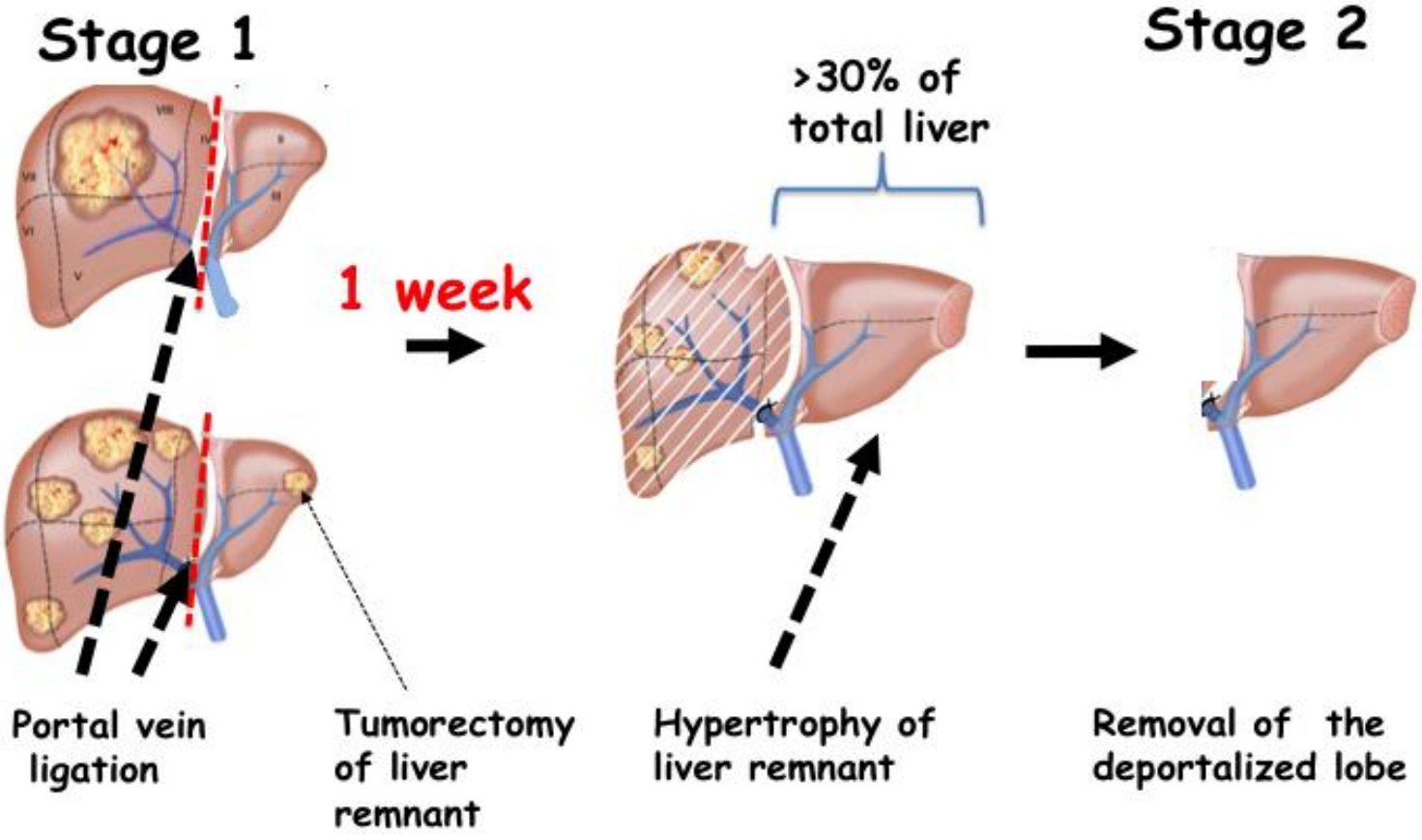










Estrategias para aumentar el hígado remanente

- **ALPPS** (ASSOCIATING LIVER PARTITION AND PORTAL VEIN LGATION FOR STAGED HEPATECTOMY)



ALPPS ACCORDING TO THE STRATEGY

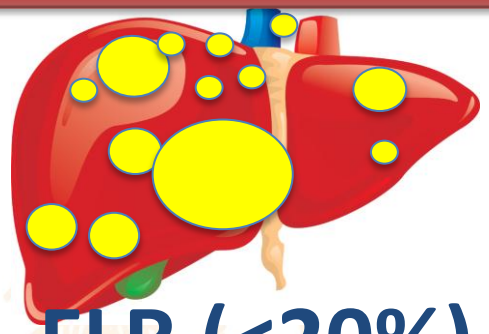
FLR

>20%/BWR>0,5
CALI >30%/>0,7

One stage HEPATECTOMY
R TRISECCIONECTOMY

<20%/BWR<0,5
CALI <30%/BWR<0,7

Two stage HEPATECTOMY
PVE and R TRISECCIONECTOMY



FLR (<20%)

Two stage HEPATECTOMY
PVE or PVL
R TRISECCIONECTOMY

Two stage HEPATECTOMY
ALPPS

FAILURE OF PVE

Feasibility of ALPPS

Performance of stage 2 with macroscopic tumor removal

ALPPS REGISTRY n=197/202 98%

TWO-STAGE HEPATECTOMY (in CRLM)	Year	N=	Feasibility
Lamb *et al* (Systematic review)	2013	459	**76%**
Abbot *et al* (MD Anderson USA)	2013	82	**68%**
Cardona *et al* (MSKCC USA)	2013	40	**88%**
Tsai *et al* (J Hopkins USA)	2010	45	**78%**
Belghiti J (Beaujon- FRANCE)	2008	35	**74%**
Adam *et al* (Paul Brousse-FRANCE)	2008	59	**69%**

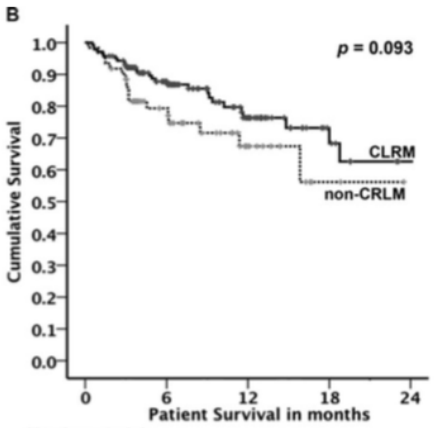
Safety of ALPPS

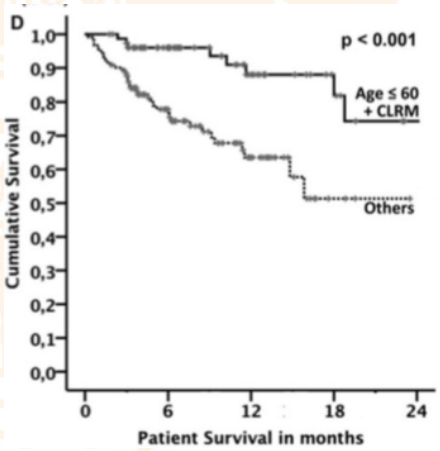
End-points:
Mortality 90 days
Morbidity Clavien >IIIa

	%	CI
90-Day mortality	**11%**	**8-16%**
Complications (>IIIa Clavien-Dindo)	**44%**	**38-50%**

Oncologic efficacy of ALPPS

Oncological data 141 CRLM	N=141	%
Histologically complete resection (R=0)	12/185	91%
2-year survival (KM) median follow-up 9 (IQR 6-13) months	141	62%
2-year disease free survival (KM)	141	41%





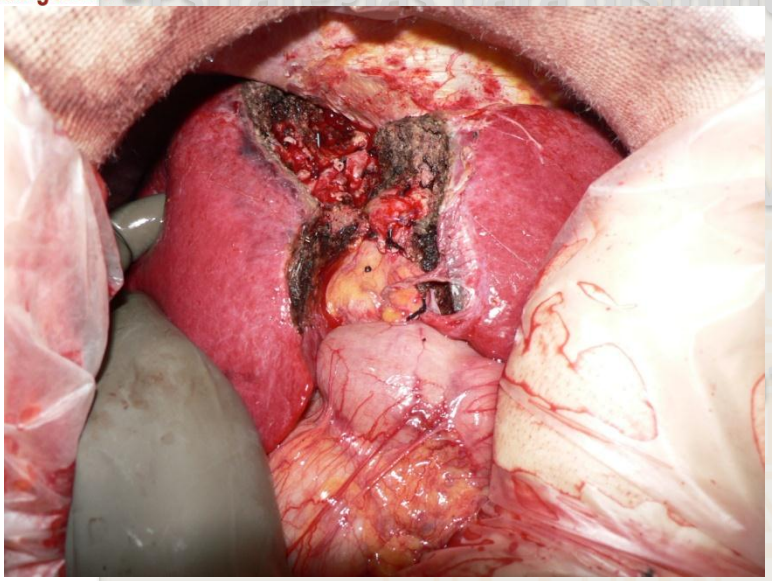
Málaga ALPPS EXPERIENCE (June 2012-April 2016)

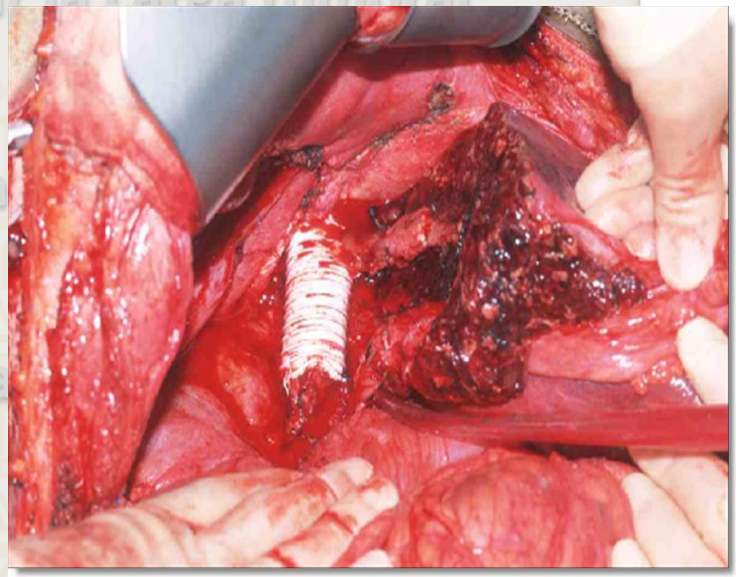
Total liver resections: 275

CRLM resections: 156

% ALPPS: 7,6% of CRLM and 4,3% of All resections

Nº	SEXO	EDAD	DIAGNÓSTICO	CIRUGÍA PRIMARIO			RESECCIÓN	CLAVIEN	EXITUS postop.	ESTANCIA (dias)		SEGUIMIENTO
			Tipo tumor	liver first	INTERVALO	Ciclos				1ª	2ª	VIVO
1	H	57	Metástasis	SI	9 meses	9	TRISEC. DERECHA	I	NO	4	0	NO
2	M	48	Metástasis	NO	2 meses	8	TRISEC. DERECHA		NO	11	4	SI
3	M	45	Metástasis	NO	3 meses	4	TRISEC. DERECHA	IIIB	NO	8	39	SI
4	H	47	Metástasis	NO	2 meses	7	TRISEC. DERECHA	I	NO	10	7	SI
5	M	56	Metástasis	SI	1 mes	4	TRISEC. DERECHA	I	NO	10	14	SI
6	H	67	Metástasis	SI	11 meses	8	TRISEC. DERECHA	V	SI	12	29	NO
7	H	59	Metástasis	NO		12	TRISEC. DERECHA	II	NO	9	11	SI
8	H	52	Metástasis	SI	31 meses	x	TRISEC. DERECHA	I	NO	14	11	SI
9	H	49	Metástasis	si	10 meses	11	HEPATEC DCHA		NO	11	5	SI
10	H	64	Metástasis	si	6 meses	4	TRISEC. DERECHA	IVA	NO	10	60	SI
11	M	36	Metástasis	SI	7 meses	7	HEPATEC DCHA			4		si
12	H	48	Metástasis	No	2 meses	11	HEPATEC DCHA		NO	8	3	si
		52		7		8				11	17	





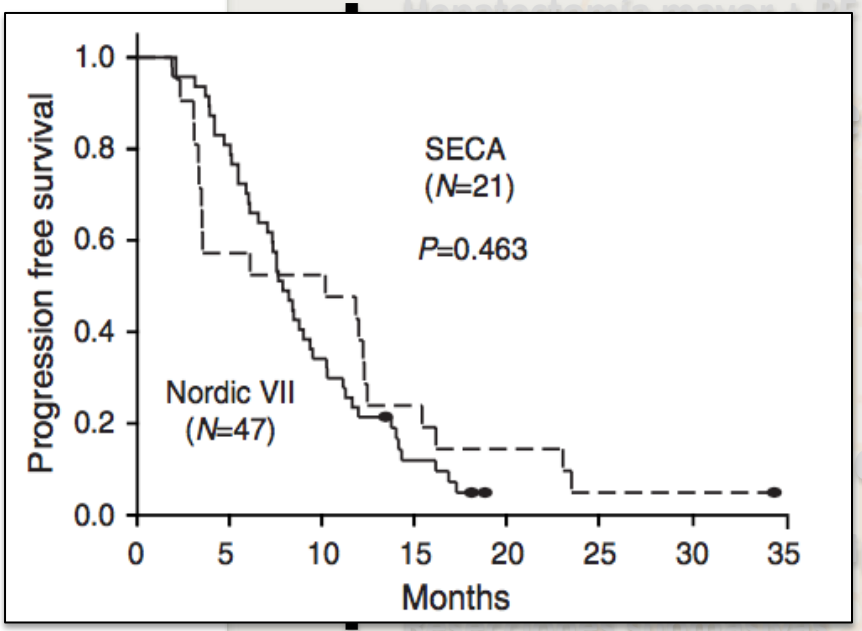
- ALPPS

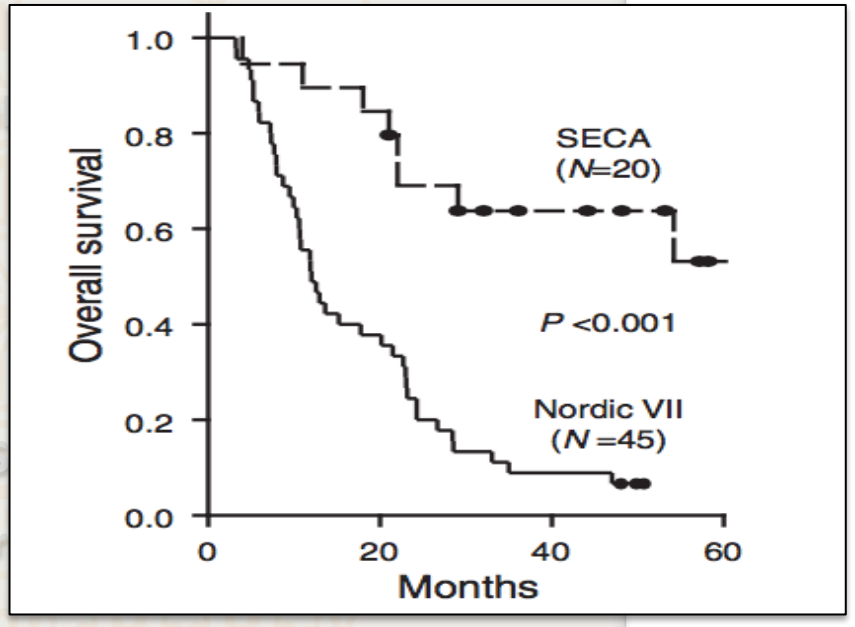
- **Hepatectomías complejas**
  - **Resecciones ex o in situ hipotérmicas**
  - **Resecciones submasivas**
- **Trasplante hepatico**

Chemotherapy or Liver Transplantation for Nonresectable Liver Metastases From Colorectal Cancer?

Svein Dueland, MD, PhD, Tormod K. Guren, MD, PhD,* Morten Hagness, MD, PhD,†‡ Bengt Glimelius, MD, PhD,§ Pål-Dag Line, MD, PhD,† Per Pfeiffer, MD, PhD,¶ Aksel Foss, MD, PhD,†‡ and Kjell M. Tveit, MD, PhD*‡*

Annals of Surgery • Volume 261, Number 5, May 2015



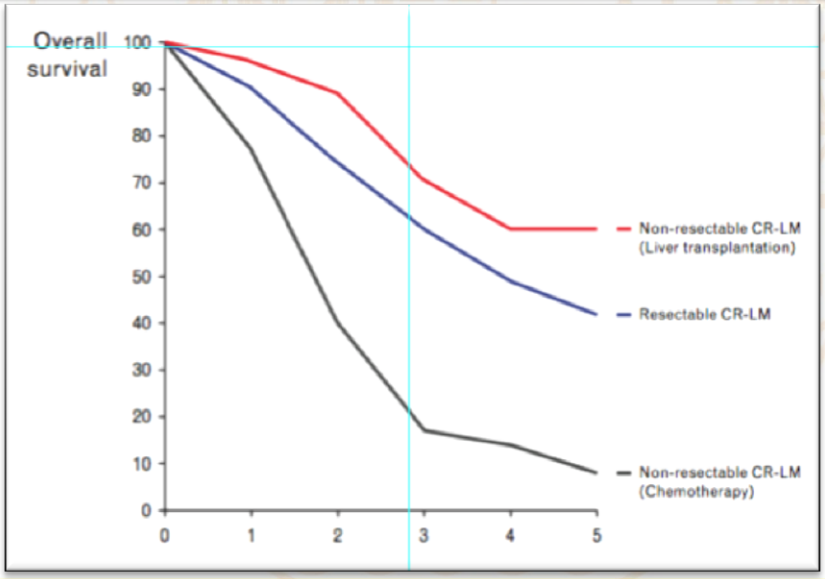


- **Trasplante hepatico**

Liver Transplantation for Nonresectable Liver Metastases From Colorectal Cancer

Morten Hagness, MD,† Aksel Foss, MD, PhD,*† Pål-Dag Line, MD, PhD,* Tim Scholz, MD, PhD,*
Pål Foyn Jørgensen, MD, PhD,* Bjarte Fosby, MD,*† Kirsten Muri Boberg, MD, PhD,‡
Øystein Mathisen, MD, PhD,§ Ivar P. Gladhaug, MD, PhD,†§ Tor Skatvedt Egge, MD,¶
Steinar Solberg, MD, PhD,‖ John Hausken, MD,** and Svein Dueland, MD, PhD††*

Conclusions: OS exceeds by far reported outcome for chemotherapy, which is the only treatment option available for this patient group. Furthermore, OS is comparable with liver resection for resectable CLMs and survival after repeat liver transplantation for nonmalignant diseases.



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

DIGESTIVO

II JORNADA CIENTÍFICA

Liver Transplantation and Colorectal Cancer

This study is currently recruiting participants. (see Contacts and Locations)

Verified October 2015 by Oslo University Hospital

Sponsor:
Oslo University Hospital

Information provided by (Responsible Party):
Oslo University Hospital

ClinicalTrials.gov Identifier:
NCT01479608

First received: November 22, 2011
Last updated: October 21, 2015
Last verified: October 2015
History of Changes

Liver Transplantation in Patients With Unresectable Colorectal Liver Metastases Treated by Chemotherapy (TRANSMET)

This study is currently recruiting participants. (see Contacts and Locations)

Verified October 2015 by Assistance Publique - Hôpitaux de Paris

Sponsor:
Assistance Publique - Hôpitaux de Paris

Information provided by (Responsible Party):
Assistance Publique - Hôpitaux de Paris

ClinicalTrials.gov Identifier:
NCT02597348

First received: October 23, 2015
Last updated: November 5, 2015
Last verified: October 2015
History of Changes

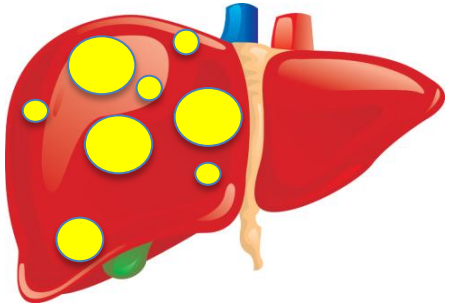
Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

This is a multicentric randomized parallel group open trial comparing 5-year survival of chemotherapy followed by LT (Group LT+C) versus chemotherapy alone (Group C) in patients with confirmed unresectable liver-only metastases, w
chemotherapy (no progression) and extensively explored by modern imaging techniques. The primary objective of the trial is to validate in a large multicentric cohort of selected patients the possibility to obtain at least 50% 5-years surv
chemotherapy compared to around 10% with chemotherapy alone.

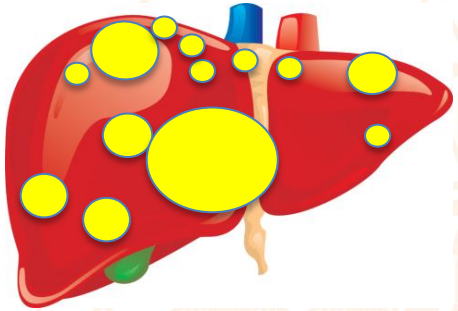
Condition	Intervention	Phase
Liver Metastasis Colorectal Cancer Metastasis	Procedure: Liver Transplantation	Phase 3

RESECABLE

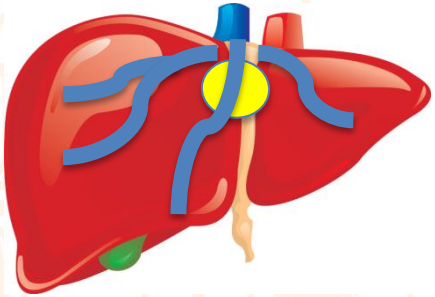


- Hepatectomia Extendida
- PVE+Hepatect.
- RY90E+Hepatect.

INICIALMENTE IRRESECABLE

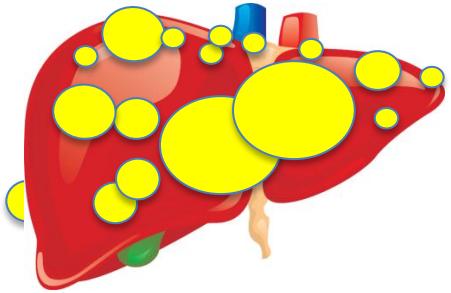


- PVE+ Hepatecto
- ALPPS
- RF +Hepatectomi



- Cirugía ex situ Hipotérmica
- Hepatectomia central

NO RESECABLE



- Trasplante Hepático?

CÁNCER DIGESTIVO

II JORNADA CIENTÍFICA

#jornadadigestivo2016

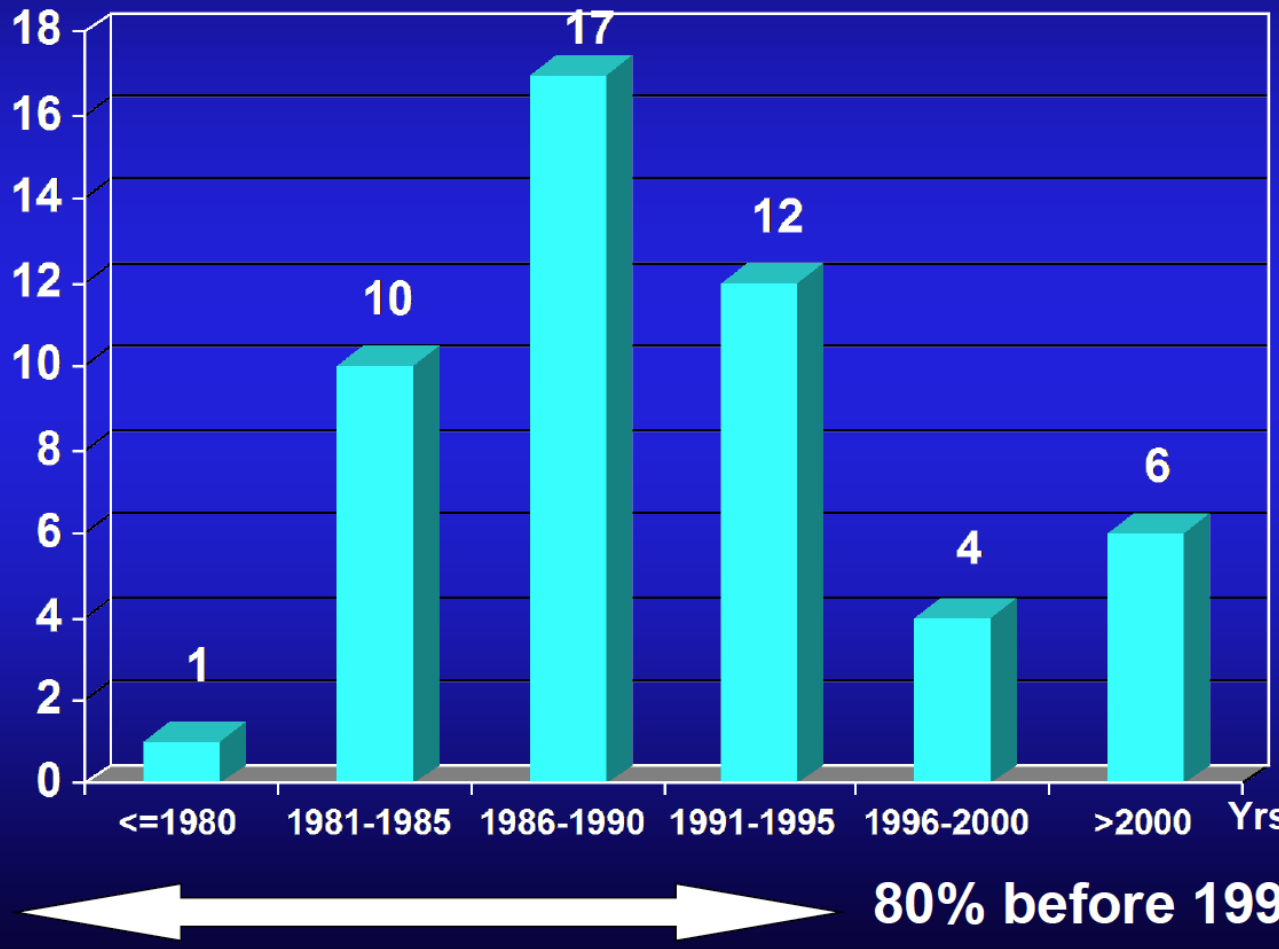
CÁNCER DIGESTIVO

II JORNADA CIENTÍFICA

#jornadadigestivo2016

Evolution of Liver Transplantation for Colorectal Metastases

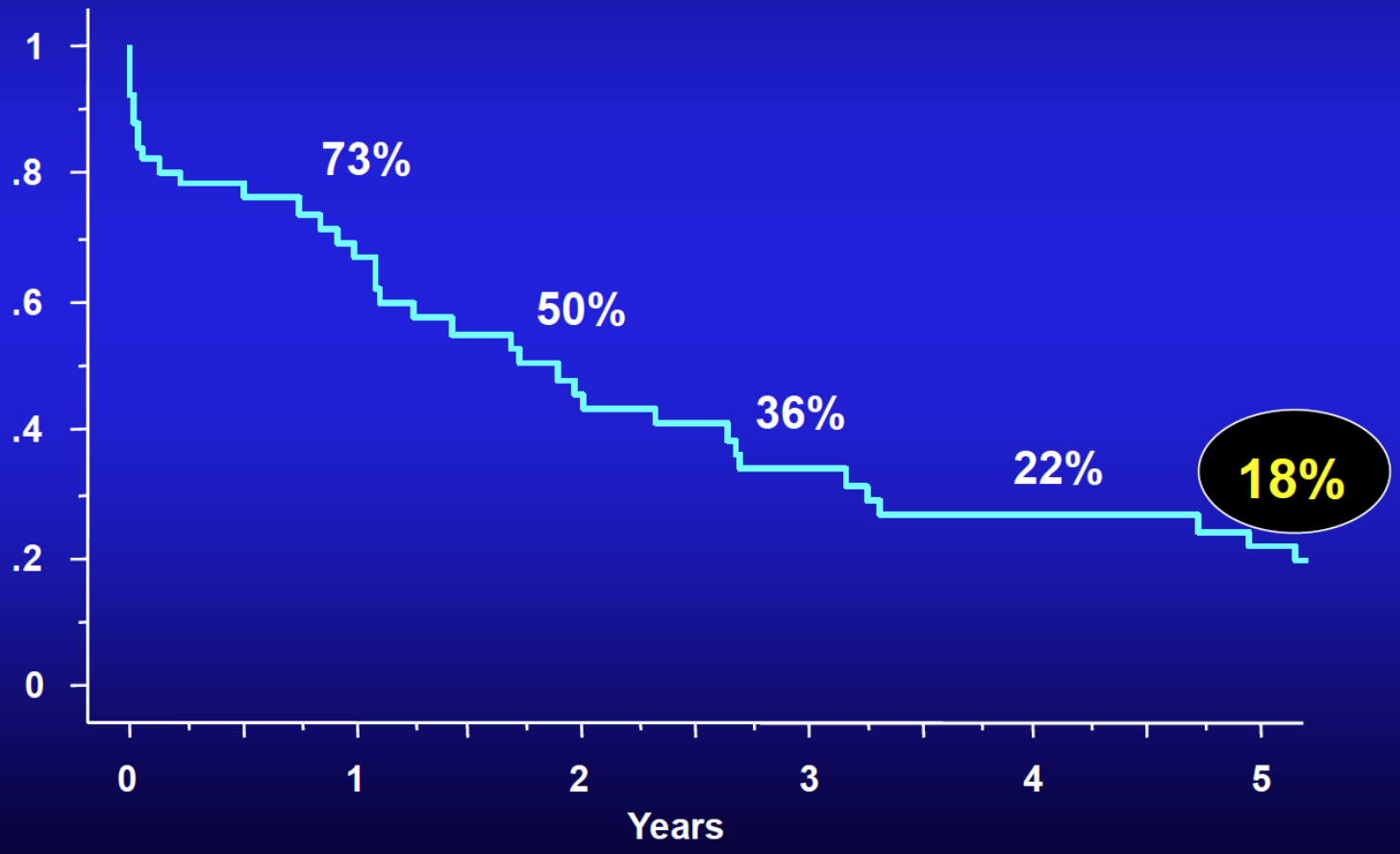
N=50, Feb. 1977 – Dec. 2004



Courtesy of Pr. Rene Adam

Patient Survival after LT for Colorectal Metastases

N=50, Feb. 1977 – Dec. 2004



ELTR 12/04

Courtesy of Pr. Rene Adam

Liver Transplantation for Colorectal Liver Metastases

ELTR 12/04

Past experience…

5-year survival 18% overall, but…

- Mainly for historical cases (< 1995)
- No real patient selection
- Almost 50% graft loss : non tumoral causes
- No “standard indication” or adjuvant Tt

Survival was possible at long-term

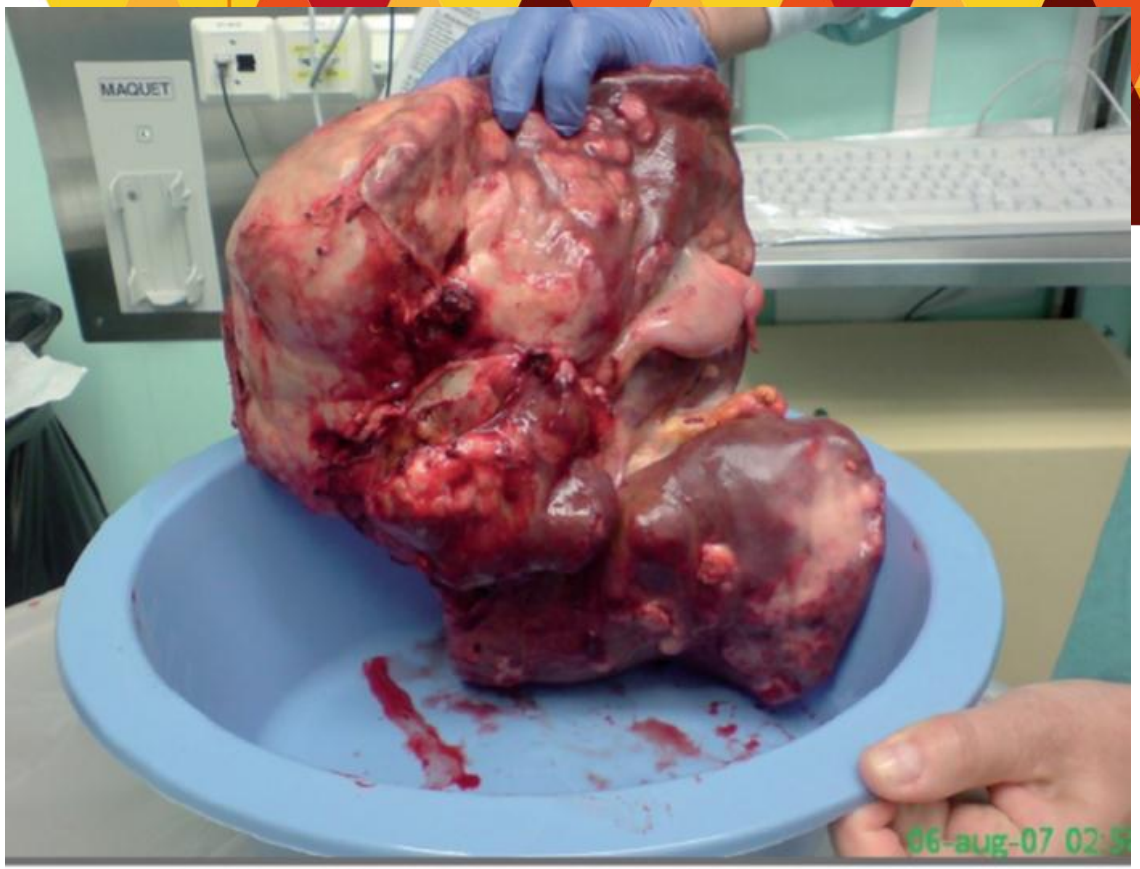


Figure 3 Explanted liver from study patient.

Female 54 years at time of transplantation, body weight 58 kg. The weight of the liver is 4.6 kg. The liver/body weight ratio is 8% which was the highest ratio in the study population. The histology showed breaching of liver capsula at several places. She was the patient with shortest survival in the study, 6 months post transplantation.

Liver Transplantation for Nonresectable Liver Metastases From Colorectal Cancer

Morten Hagness, MD,† Aksel Foss, MD, PhD,*† Pål-Dag Line, MD, PhD,* Tim Scholz, MD, PhD,* Pål Foyn Jørgensen, MD, PhD,* Bjarte Fosby, MD,*† Kirsten Muri Boberg, MD, PhD,‡ Øystein Mathisen, MD, PhD,§ Ivar P. Gladhaug, MD, PhD,†§ Tor Skatvedt Egge, MD,¶ Steinar Solberg, MD, PhD,‖ John Hausken, MD,** and Svein Dueland, MD, PhD††*

- Estudio prospectivo piloto (Universidad Oslo)
- 2006-2011

- N 21 pacientes
  - *PS 0*
  - *Cirugía radical del primario*
  - *No enfermedad extrahepatica*
  - *AL menos 6 semanas de QT*
  - *Mts irresecables (media 8 nodulos)*

- Intervalo Primario-TH
  - *Mts Sincronicas 16 meses*
  - *Mts Metacronicas 36 meses.*

Annals of Surgery • Volume 257, Number 5, May 2013

Liver Transplantation for Nonresectable Liver Metastases From Colorectal Cancer

Morten Hagness, MD,† Aksel Foss, MD, PhD,*† Pål-Dag Line, MD, PhD,* Tim Scholz, MD, PhD,* Pål Foyn Jørgensen, MD, PhD,* Bjarte Fosby, MD,*† Kirsten Muri Boberg, MD, PhD,‡ Øystein Mathisen, MD, PhD,§ Ivar P. Gladhaug, MD, PhD,†§ Tor Skatvedt Egge, MD,¶ Steinar Solberg, MD, PhD,‖ John Hausken, MD,** and Svein Dueland, MD, PhD††*

- Estudio prospectivo piloto (Universidad Oslo)
- 2006-2011 (N 21 pacientes)
  - *IS: Simulect+Sirolimus+MMF+Esteroides*
  - *No QT (hasta progresión)*

- Recurrencia 19/21 media de 6 meses (2-24)

- Factores mal pronostico:
  - Tumor mayor >5,5cms.
  - Intervalo <2 años
  - CEA >80
  - Enfermedad en progresión en el TH

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

DIGESTIVO

II JORNADA CIENTÍFICA

#jornadadigestivo2016

PHRC : Multicentric Randomised Trial

Towards a better Patient Selection …

- ≤ 65 years
- Confirmed non resectable liver metastases of colorectal cancer,
- High standard carcinological resection of the primary (≥ 12 lymph N)
- No extrahepatic tumor localisation
- Treatment by ≥ 3 months of optimal chemotherapy
- Stable or Partial Response while on ≤ 3 lines of chemotherapy
- No BRAF mutation
- Serum CEA levels < 100 ng/ml or 50% decrease from baseline

Independant Validation of the indication…

by the steering committee of the study including oncologists, radiologists and hepatologists / Transplant surgeons

Tailored Immunosuppression…

OncoSurgical Approach…

PHRC : Multicentric Randomised Trial

- 1ry End Point: 5-yr OS
- Objective : ≥ 50% with LT
- 80 Pts (40 in each group) to demonstrate a 40% diff (50 vs 10%)
- 14 French centres
- 10 European centres
- Additional centres…