

New agents in the treatment of liver cancer

Deep Dive into Liver Cancer – Session IV, 5th DiCE Masterclass 2020

21-10-2020

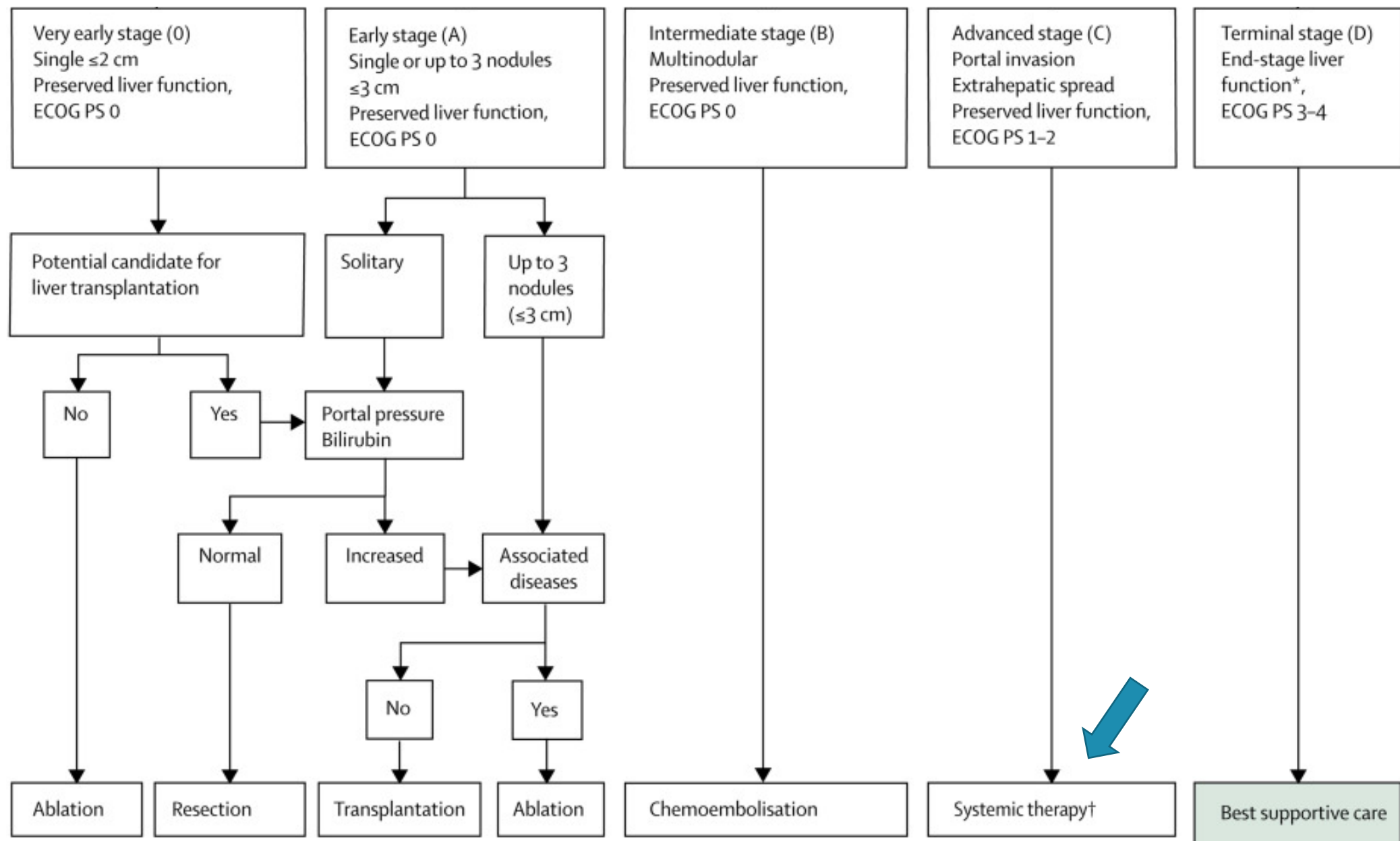


Jeroen Dekervel - MD PhD

Disclosures

Relationships with commercial interests:

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- **Travel grants:** Ipsen, Servier, Roche

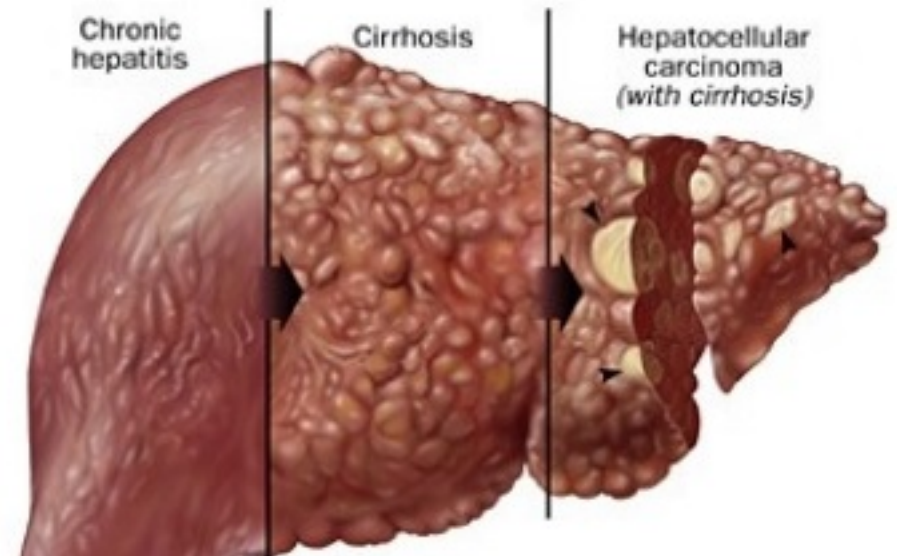


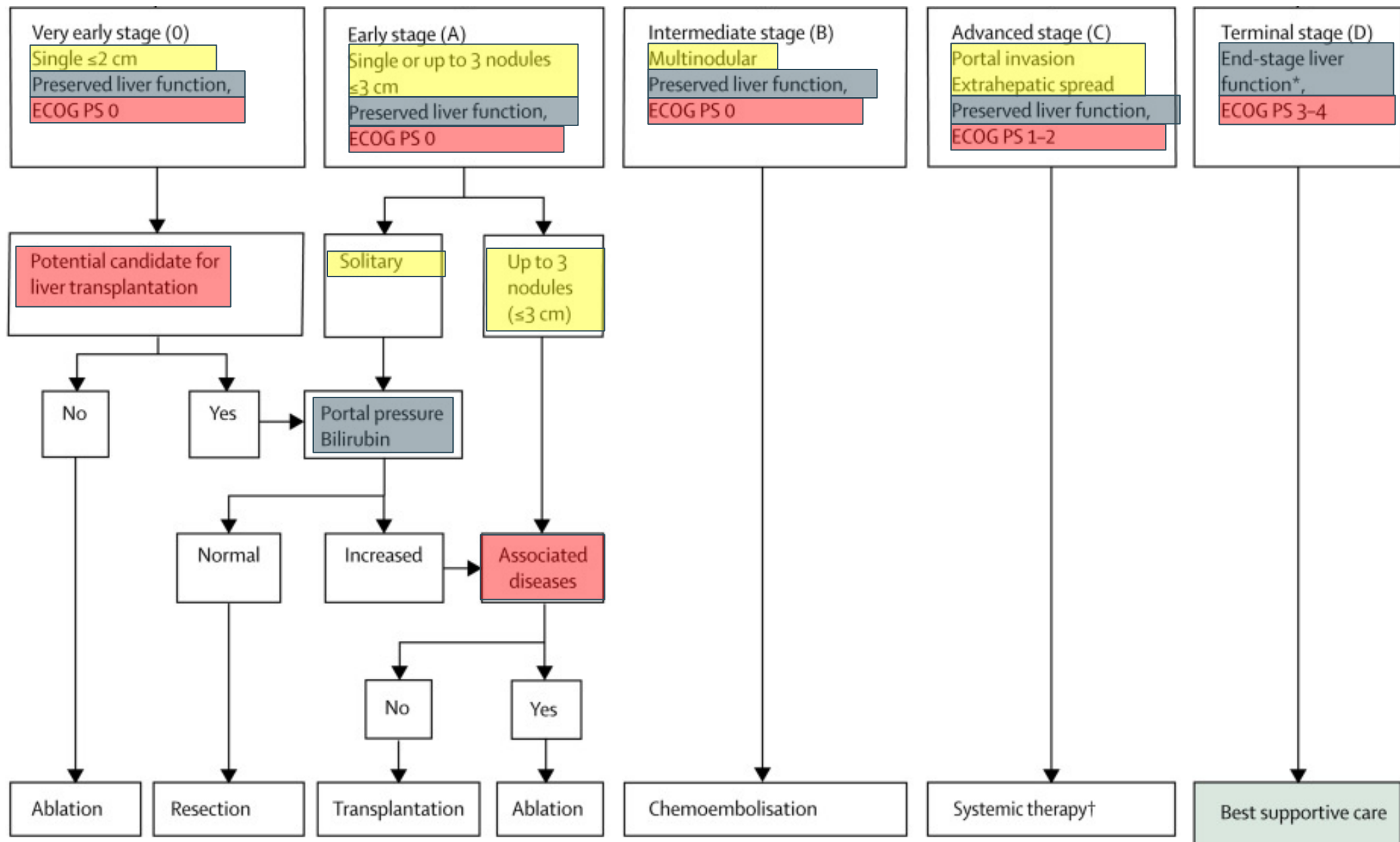
As a comparison: colon cancer

- Very early stage → surgical resection
- Early stage without involved lymph nodes → surgical resection + sometimes chemotherapy
- Lymph nodes involved but no distant metastasis → surgical resection + chemotherapy
- Distant metastasis → chemotherapy

Hepatocellular carcinoma

- Take into account **disease stage** (like colon cancer)
- Take into account (often) **impaired liver function**
- Take into account (often) impaired **patient performance status**







Surgeon

Nurse
specialist

Oncologist

Pathologist

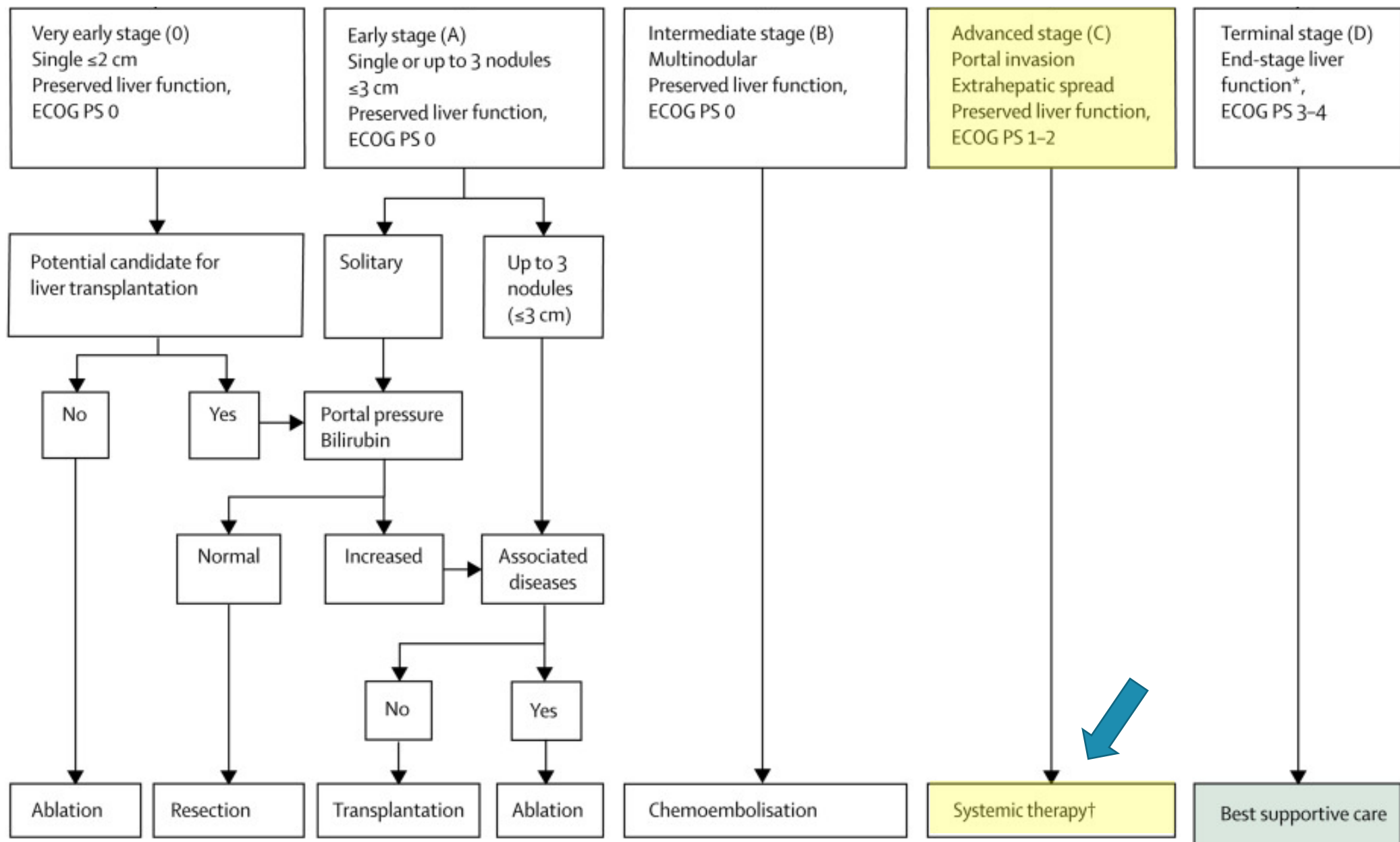
Hepatologist

Transplant
surgeon

Interventional
radiologist

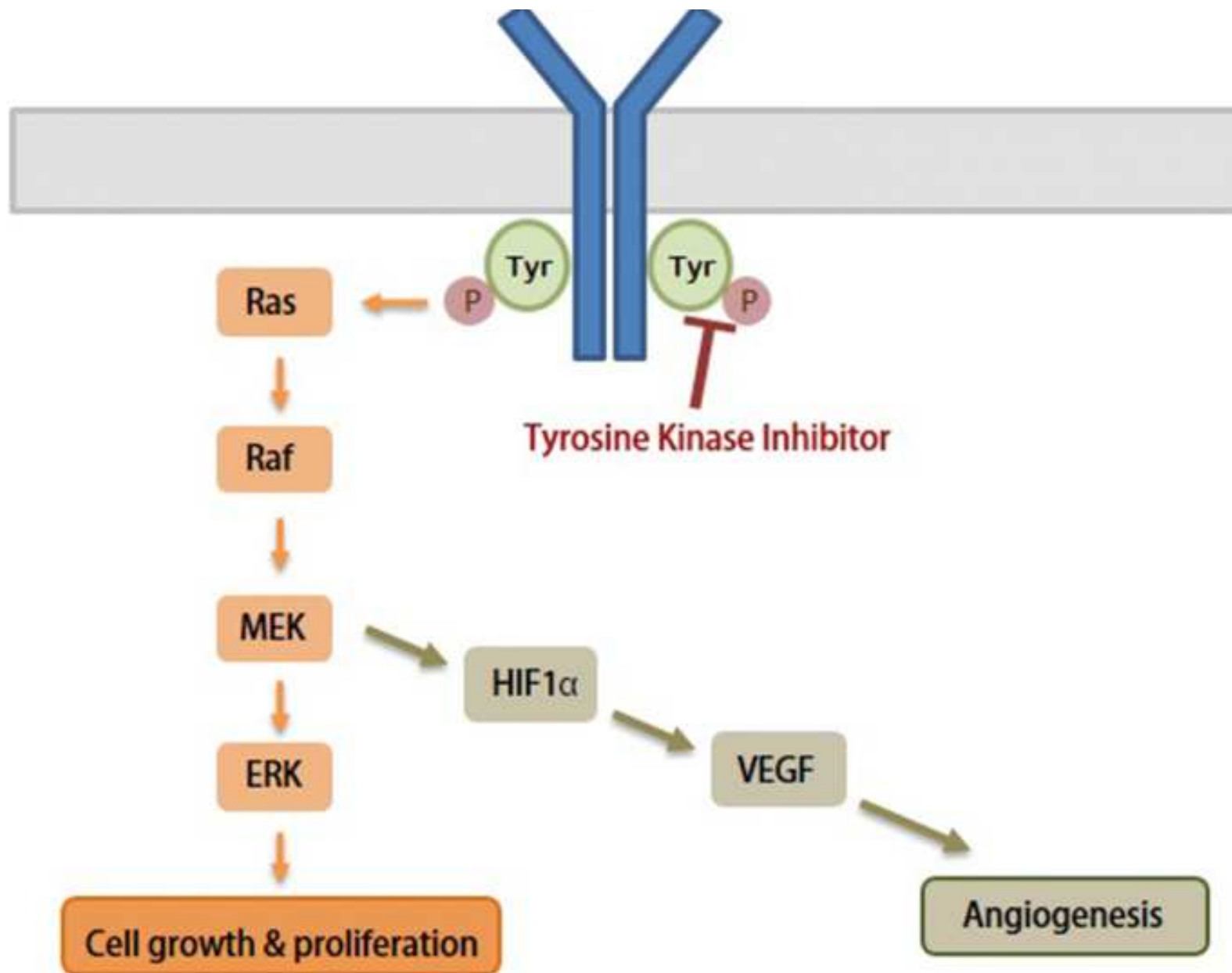
Radiologist

Radiation
therapist



Chemotherapy

Tyrosine Kinase Inhibitors



ORIGINAL ARTICLE

Sorafenib in Advanced Hepatocellular Carcinoma

Josep M. Llovet, M.D., Sergio Ricci, M.D., Vincenzo Mazzaferro, M.D.,
Philip Hilgard, M.D., Edward Gane, M.D., Jean-Frédéric Blanc, M.D.,
Andre Cosme de Oliveira, M.D., Armando Santoro, M.D., Jean-Luc Raoul, M.D.,
Alejandro Forner, M.D., Myron Schwartz, M.D., Camillo Porta, M.D.,
Stefan Zeuzem, M.D., Luigi Bolondi, M.D., Tim F. Greten, M.D.,
Peter R. Galle, M.D., Jean-François Seitz, M.D., Ivan Borbath, M.D.,
Dieter Häussinger, M.D., Tom Giannaris, B.Sc., Minghua Shan, Ph.D.,
Marius Moscovici, M.D., Dimitris Voliotis, M.D., and Jordi Bruix, M.D.,
for the SHARP Investigators Study Group*

N Engl J Med 2008;359:378-90.

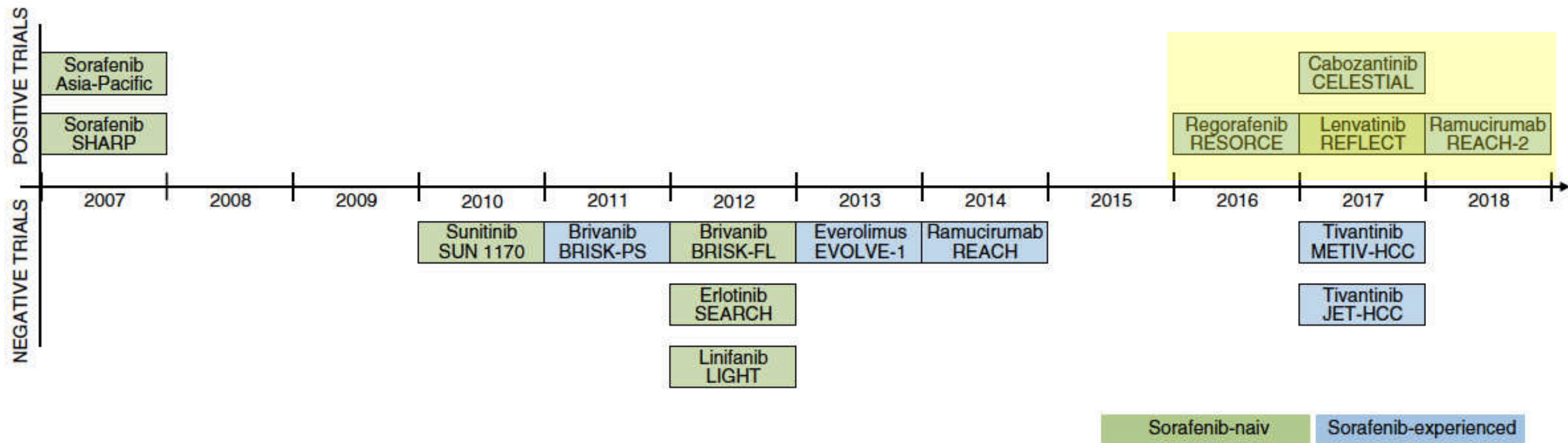
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Median survival without treatment: 5 – 8 months

FIRST LINE

Sorafenib / Nexavar

+ 2,8 months vs no treatment



Median survival without treatment: 5 – 8 months

FIRST LINE

Sorafenib / Nexavar

+ 2,8 months vs no treatment

Lenvatinib/Lenvima

Equal to sorafenib

SECOND LINE

Regorafenib / Stivarga

+ 2,8 months vs no 2nd line

Cabozantinib / Cabometyx

+ 2,2 months vs no 2nd line

Ramucirumab/Cyramza*

+ 1,2 months vs no 2nd line

Tyrosine Kinase Inhibitors: side effects

Common

Diarrhoea

Fatigue

Induced hypertension

Hepatotoxicity

Skin changes

Nausea

Increased thyroxine dosage
requirement

Changes in taste

Weight loss

Serious

Thrombosis

Bleeding

Heart failure

Hepatotoxicity

GI tract fistula formation

Intestinal perforation

Guidance on HFSR management

GRADE 1: Mild



GRADE 2: Moderate



GRADE 3: Severe

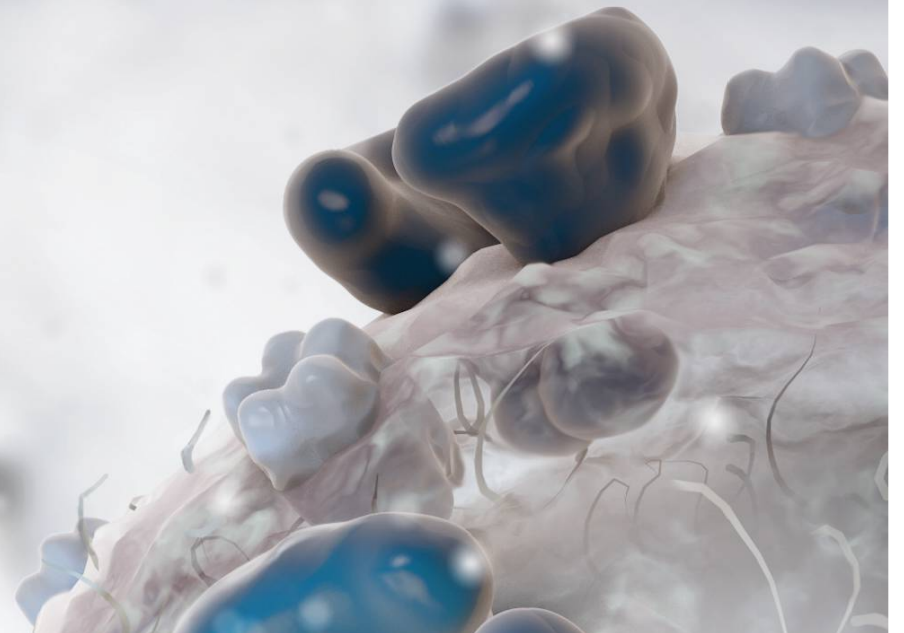


Immunotherapy

20 December 2013 | \$10

Science

Breakthrough of the Year
Cancer
Immunotherapy
T cells on the attack



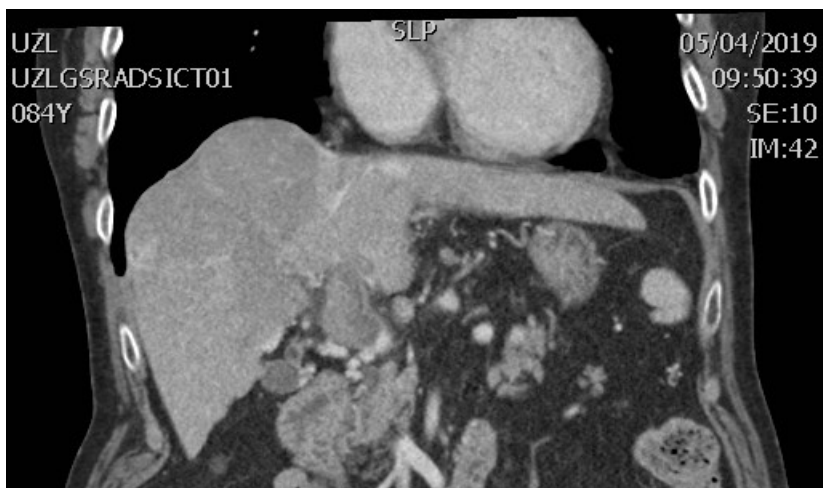
20 December 2013

Science

Vol. 342 | No. 6165 | Pages 1405–1544

83 yo male patient treated with Nivolumab/Opdivo

04/2019



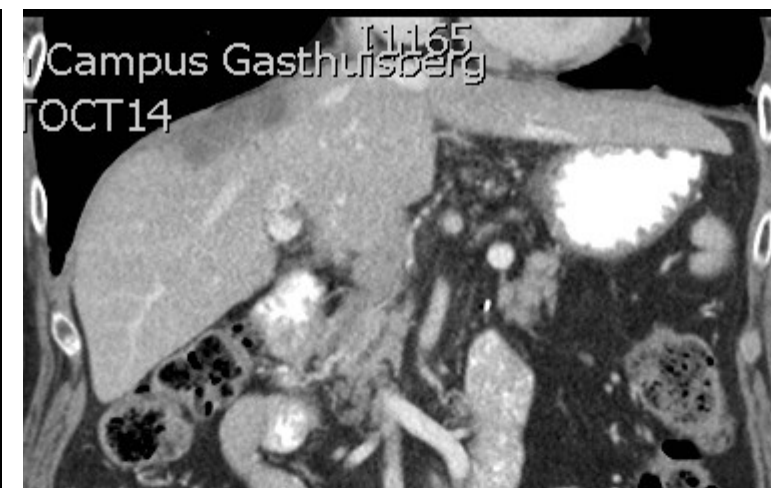
aFP 400800 ug/l

07/2019



aFP 150 ug/l

09/2019



aFP 5 ug/l

Median survival without treatment: 5 – 8 months

FIRST LINE

Sorafenib / Nexavar

+ 2,8 months vs no treatment

Lenvatinib/Lenvima

Equal to sorafenib

Nivolumab / Opdivo

Not better than to sorafenib

SECOND LINE

Regorafenib / Stivarga

+ 2,8 months vs no 2nd line

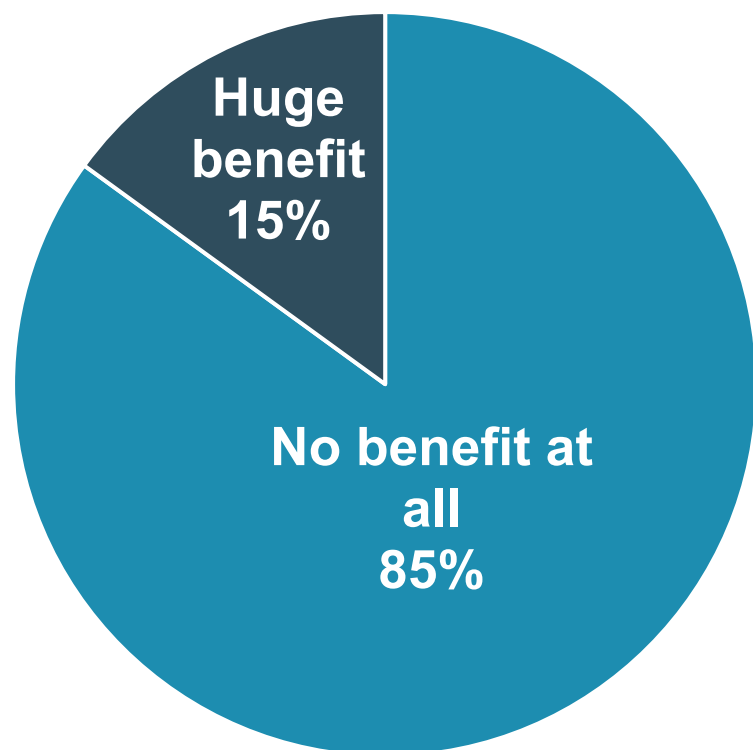
Cabozantinib / Cabometyx

+ 2,2 months vs no 2nd line

Ramucirumab/Cyramza*

+ 1,2 months vs no 2nd line

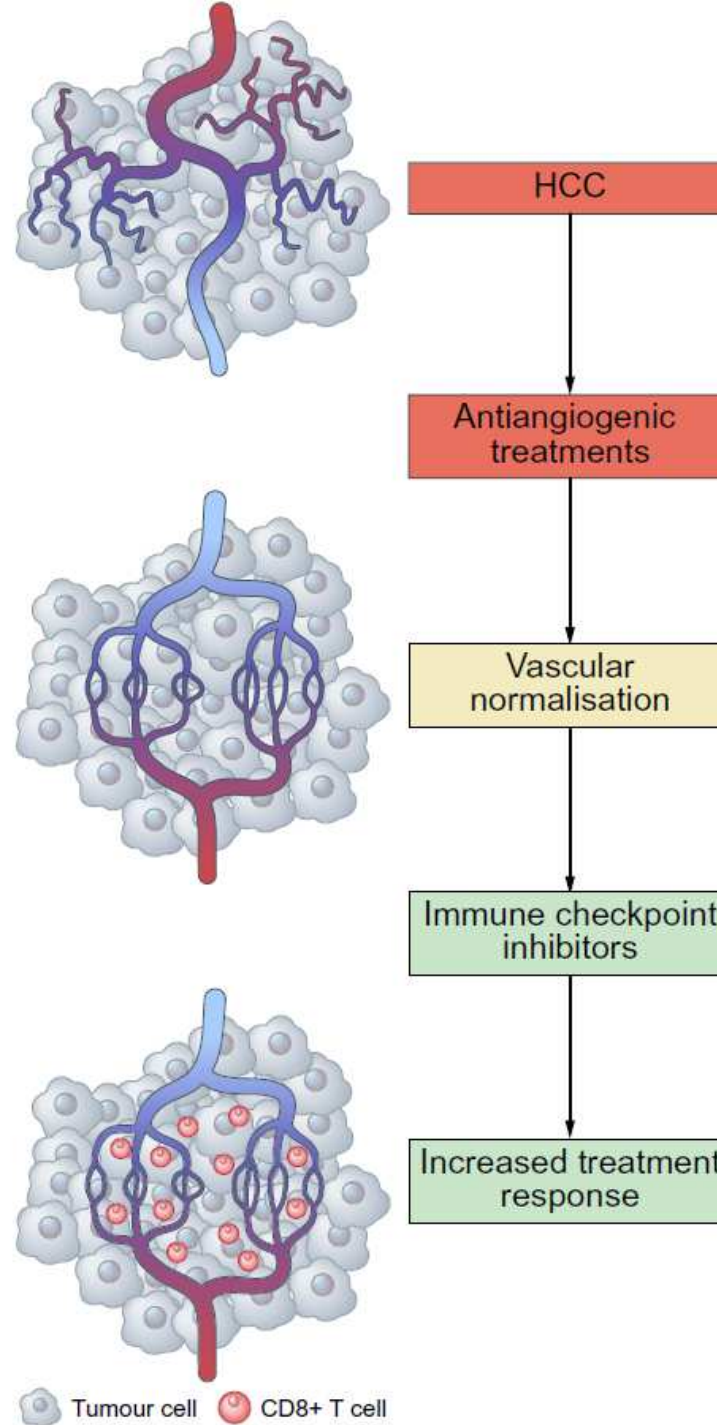
100 people with HCC
treated with immunotherapy



Solution?

Find test to identify those 15%
that benefit

Combine immunotherapy with
other drug to increase efficacy



Median survival without treatment: 5 – 8 months

NEW FIRST LINE

Atezolizumab + Bevacizumab / Tecentriq + Avastin

42% less risk of death vs sorafenib

FIRST LINE

Sorafenib / Nexavar

+ 2,8 months vs no treatment

Lenvatinib/Lenvima

Equal to sorafenib

SECOND LINE

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+ 2,8 months vs no 2nd line

Cabozantinib / Cabometyx

+ 2,2 months vs no 2nd line

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+ 1,2 months vs no 2nd line

Side effects immunotherapy

RESPIRATORY

Pneumonitis
Pleuritis
Sarcoidosis

EYE

Uveitis
Conjunctivitis
(epi)Scleritis
Blepharitis
Rétinitis

ENDOCRINAL

Hypothyroïdy
Hyperthyroïdy
Hypophysitis
Adrenal insufficiency
Diabetes

HEPATICAL

Hepatitis
Cholangitis

GASTROINTESTINAL

Colitis
Ileitis
Pancreatitis
Gastritis

CUTANEOUS

Eruption
Prurit
Psoriasis
Vitiligo
Stevens Johnson

HEMATOLOGICAL

Hemolytic anemia
Thrombocytopenia
Neutropenia
Hemophilia

- New
- Diverse
- Rare
- Managable

CARDIOVASCULAR



RENAL

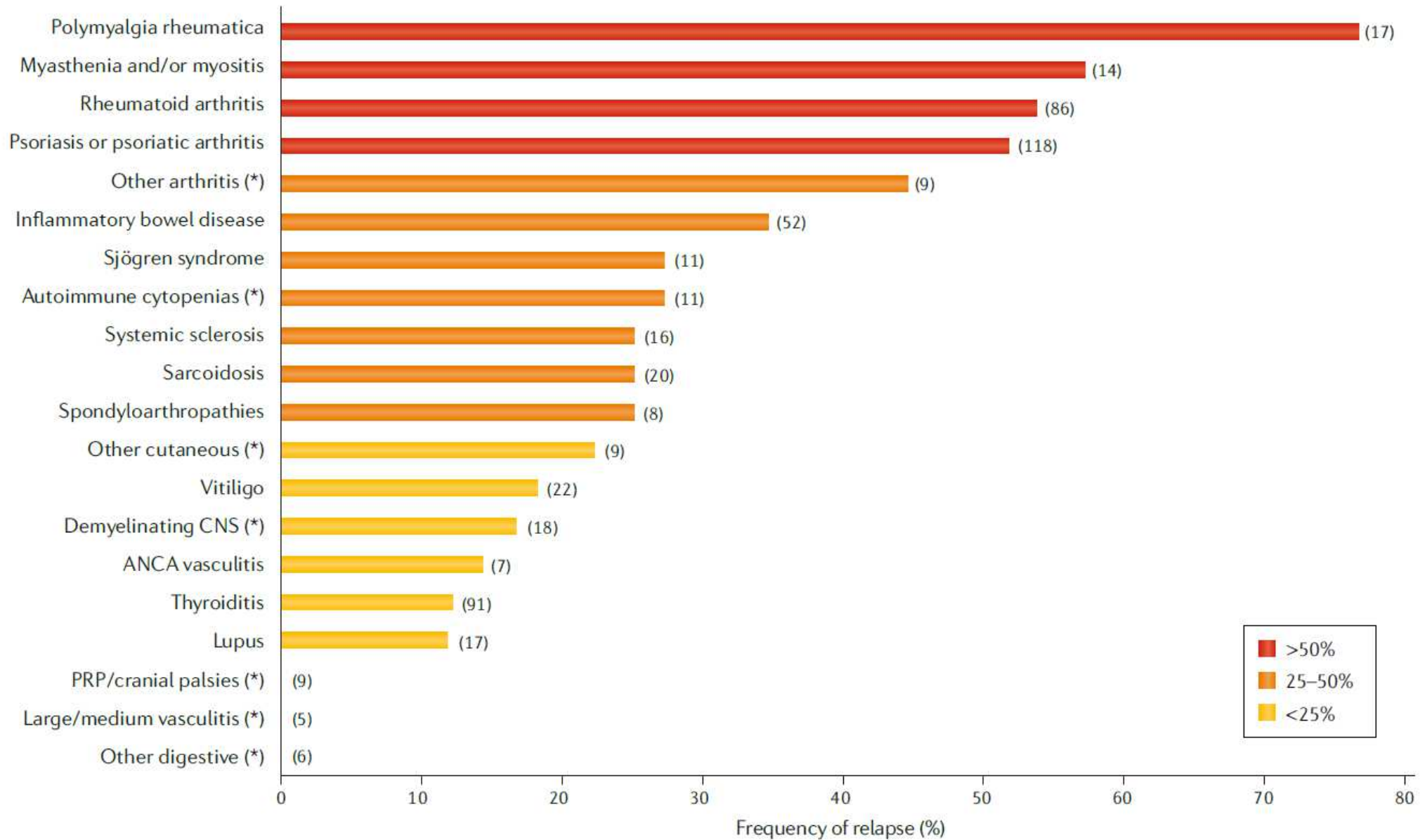
Nephritis

NEUROLOGICAL



RHEUMATOLOGICAL

Arthritis
Myositis



New agents in the treatment of HCC: summary

Developing drugs for patients with hepatocellular carcinoma has proven to be difficult due to **chemoresistance** of the disease, **impaired liver function** and/or **functional status**

Tyrosine kinase inhibitors were the first drugs to **lengthen life of HCC patients**, albeit with modest effect

Immunotherapy have dramatic effects in this disease, but **identifying those likely to benefit** remains the challenge

Very recently, a **combination treatment** of immunotherapy and anti-angiogenesis has become the **new standard of care** for treatment of HCC.



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