The Future Roles of Systemic Therapy in Transplant Oncology

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Sept 23rd 2023

Mount Sinai *Recanati/Miller Transplantation Institute*

The Liver Transplant Symposium 2023

Disclosures

- Bayer
- Boston Scientific
- AstraZeneca

Epidemiology of Liver Cancer

Mount Sinai Recanati/Miller Transplantation Institute

Villanueva et al. NEJM 2019

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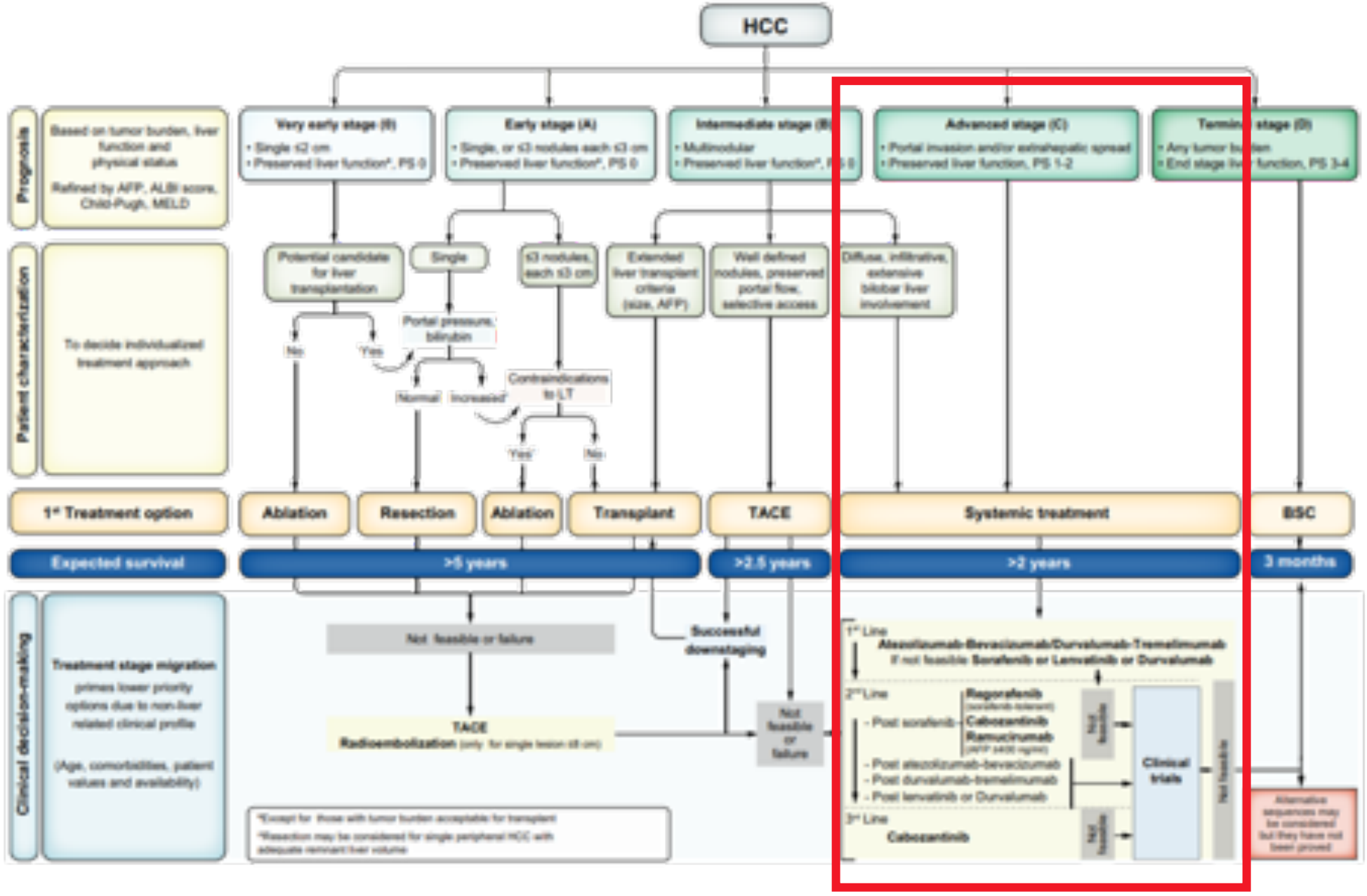


Mount Sinai Recanati/Miller Transplantation Institute

Reig et al, Journal of Hepatology 2022

The Liver Transplant Symposium 2023

Sorafenib: First systemic treatment for HCC

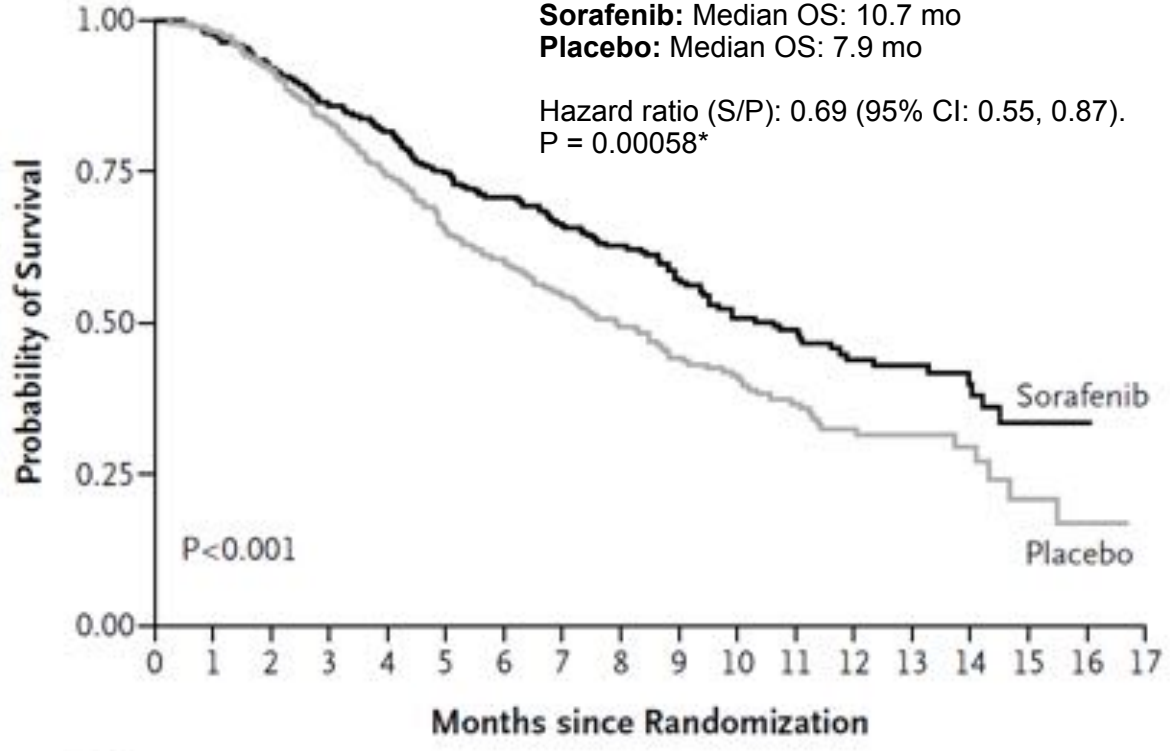
ORIGINAL ARTICLE

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*

Sorafenib: Median OS: 10.7 mo
Placebo: Median OS: 7.9 mo

Hazard ratio (S/P): 0.69 (95% CI: 0.55, 0.87).
P = 0.00058*



No. at Risk

Sorafenib	299	290	270	249	234	213	200	172	140	111	89	68	48	37	24	7	1	0
Placebo	303	295	272	243	217	189	174	143	108	83	69	47	31	23	14	6	3	0

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Llovet et al, NEJM 2008

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Management of advanced HCC

First Line:

1. Sorafenib vs. Placebo
2. Sorafenib +/- Erlotinib
3. Sorafenib vs. Brivanib
4. Sorafenib vs. Sunitinib
5. Sorafenib vs. Linifanib
6. Sorafenib +/- Doxorubicin
7. Sorafenib vs. Lenvatinib
8. Sorafenib vs. Y90
9. Sorafenib vs. Nivolumab

Second Line:

1. Brivanib vs. Placebo
2. Everolimus vs. Placebo
3. Ramucirumab vs. Placebo (AFP > 400 ng/mL)
4. Regorafenib vs. Placebo
5. Tivantinib vs. Placebo
6. Cabozantinib vs. Placebo
7. Pembrolizumab vs. Placebo

- Positive
- Non-inferior

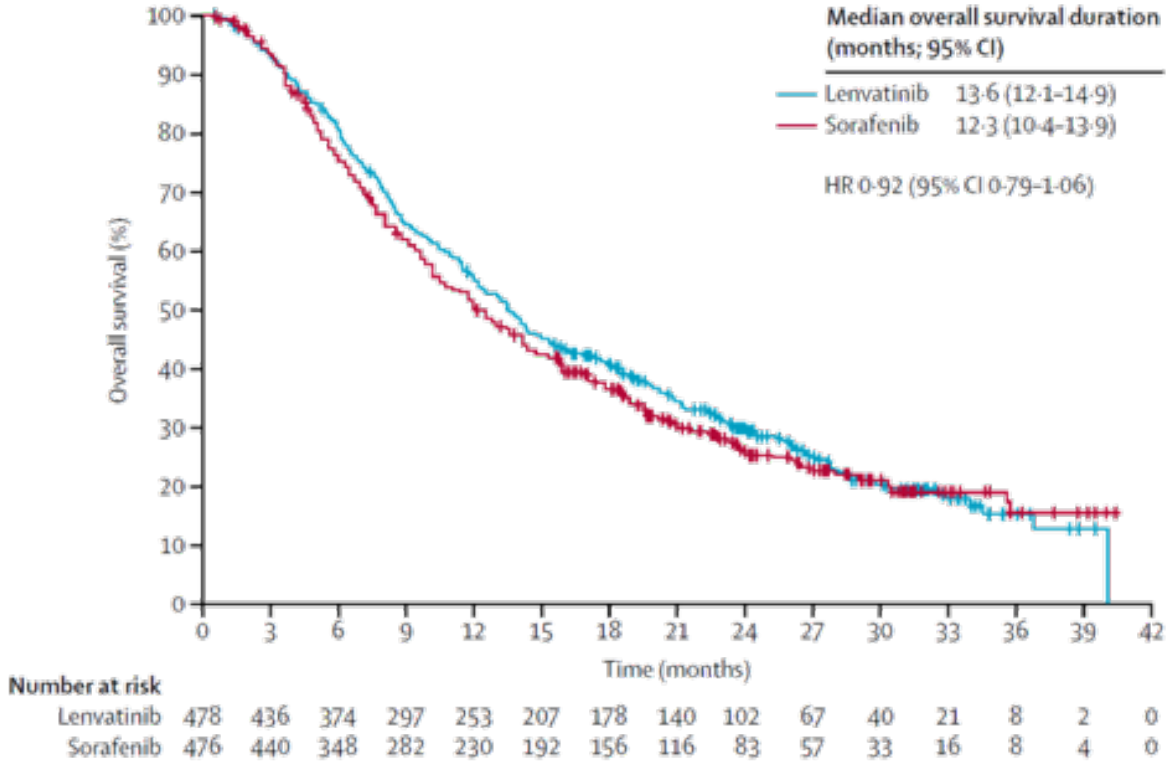
REFLECT: First line treatment: Lenvatinib

Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial

Masatoshi Kudo, Richard S Finn, Shukui Qin, Kwang-Hyub Han, Kenji Ikeda, Fabio Piscaglia, Ari Baron, Joong-Won Park*, Guohong Han*, Jacek Jassem, Jean Frederic Blanc, Arndt Vogel, Dmitry Komov, T R Jeffry Evans, Carlos Lopez, Corina Dutcus, Matthew Guo, Kenichi Saito, Silvija Kraljevic, Toshiyuki Tamai, Min Ren, Ann-Lii Cheng*

Advanced stage (BCLC C: *Portal invasion and/or extrahepatic spread*)
Intermediate stage (BCLC B: *Multinodular*) **progressing upon loco-regional therapies**

1st line	Sorafenib	Levatinib
	OS **HR = 0.69** (*vs.* placebo)	OS **HR = 0.92** (*vs.* Sorafenib)
	Child-Pugh A-ECOG PS ≤ 2 *Higher benefit in HCV infection and lack of EHS	Child-Pugh A-ECOG PS ≤ 1 No invasion main portal vein



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Kudo et al, Lancet 2018

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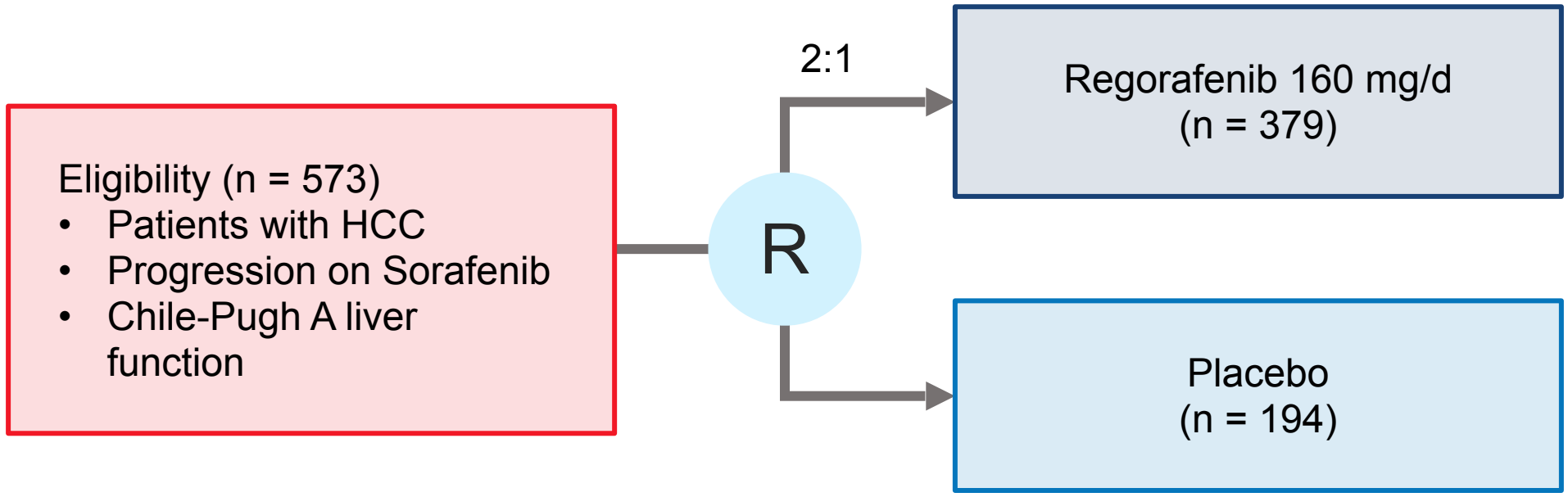
RESORCE trial: Phase III Regorafenib 2nd line



Outcome	Regorafenib (n = 379)	Placebo (n = 194)	HR	*p*-value
Median OS	10.6 mo	7.8 mo	0.63	< 0.0001

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Bruix et al, Lancet 2017

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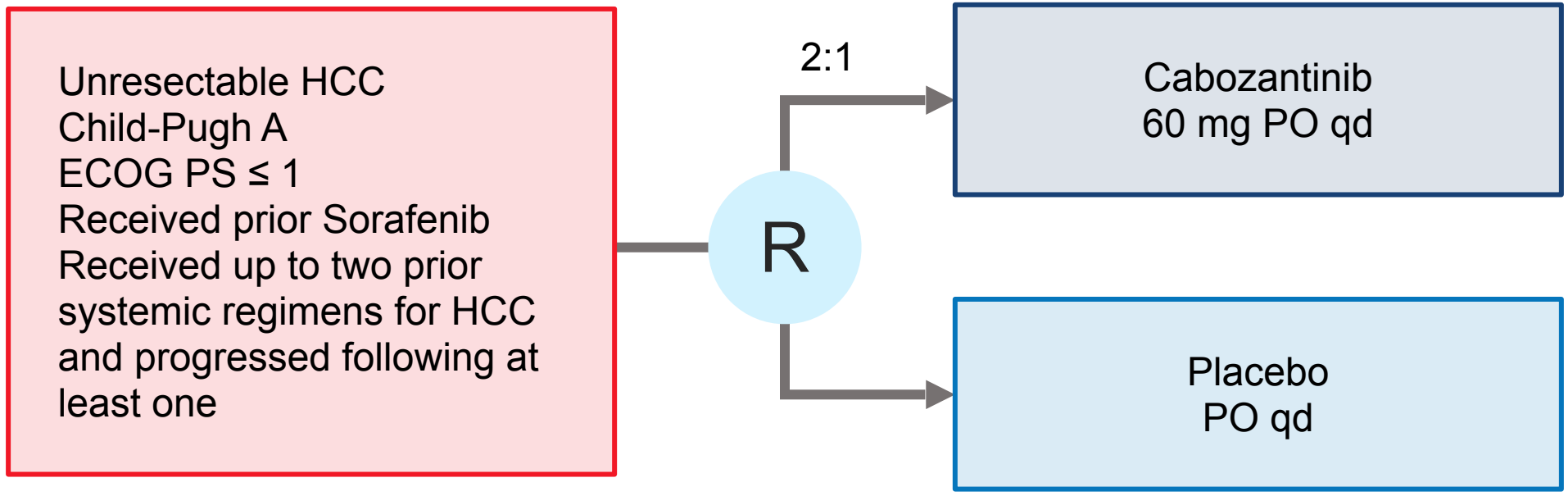
Celestial Trial: Cabozantinib 2nd line



Outcome	Cabozantinib (n = 470)	Placebo (n = 237)	HR	*p*-value
mOS, mo (95% CI)	10.2 (9.1, 12.0)	8.0 (6.8, 9.4)	0.76	0.005
mPFS, mo (95% CI)	5.2 (4.0, 5.5)	1.9 (1.9, 1.9)	0.44	< 0.001
ORR, n (%)	18 (4)	1 (< 1)		0.009

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Abou Alfa et al, NEJM 2018

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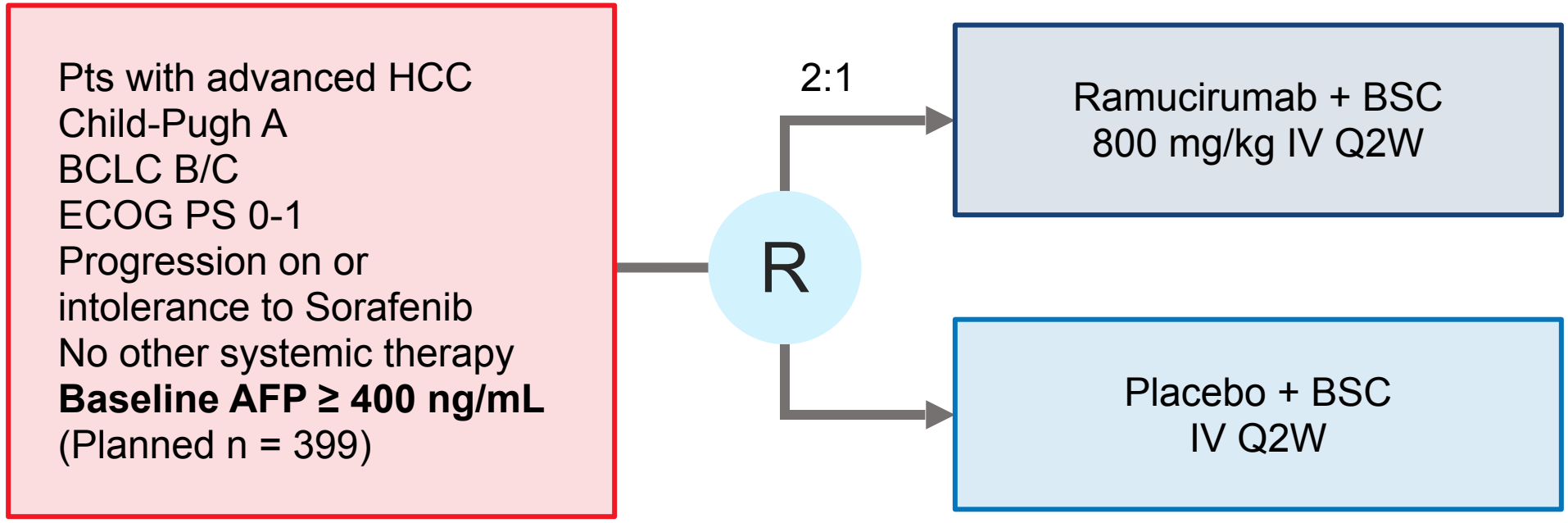
REACH 2: Ramucirumab AFP≥ 400 ng/mL



Primary endpoint: OS

	Ramucirumab (n = 197)	Placebo (n = 95)	Δ
Median, months	8.5	7.3	1.2
HR (95% CI); *p*-value	0.710 (0.531, 0.949); 0.0199		

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Zhu et al, Lancet Oncology 2019

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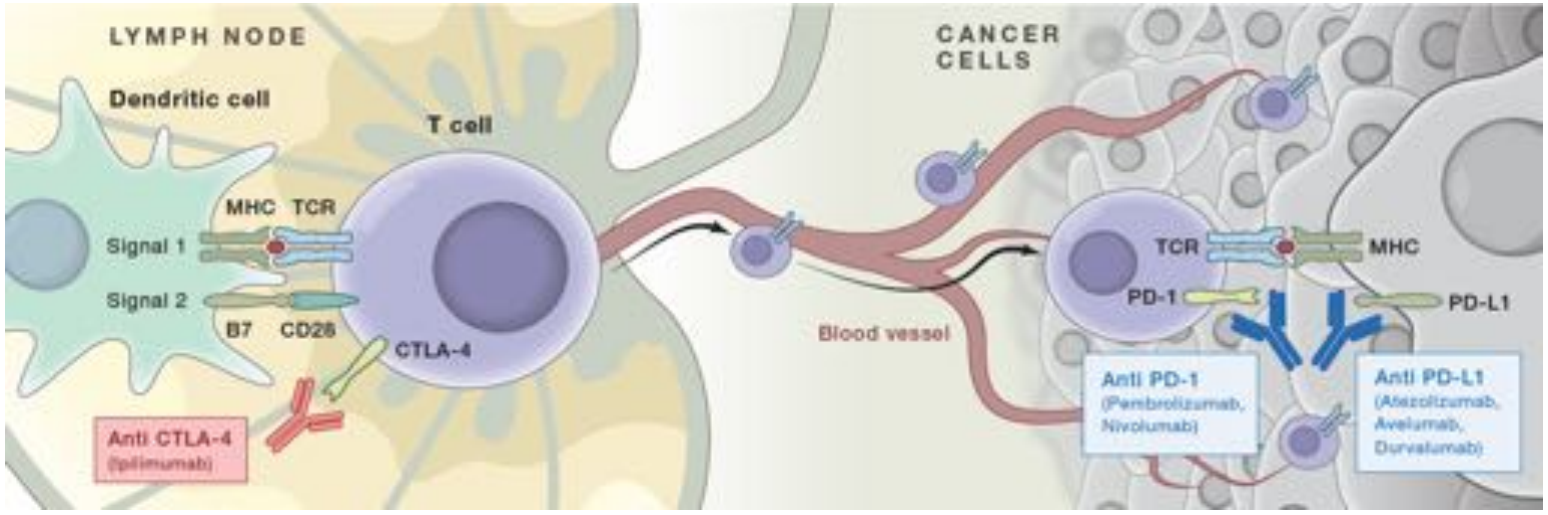
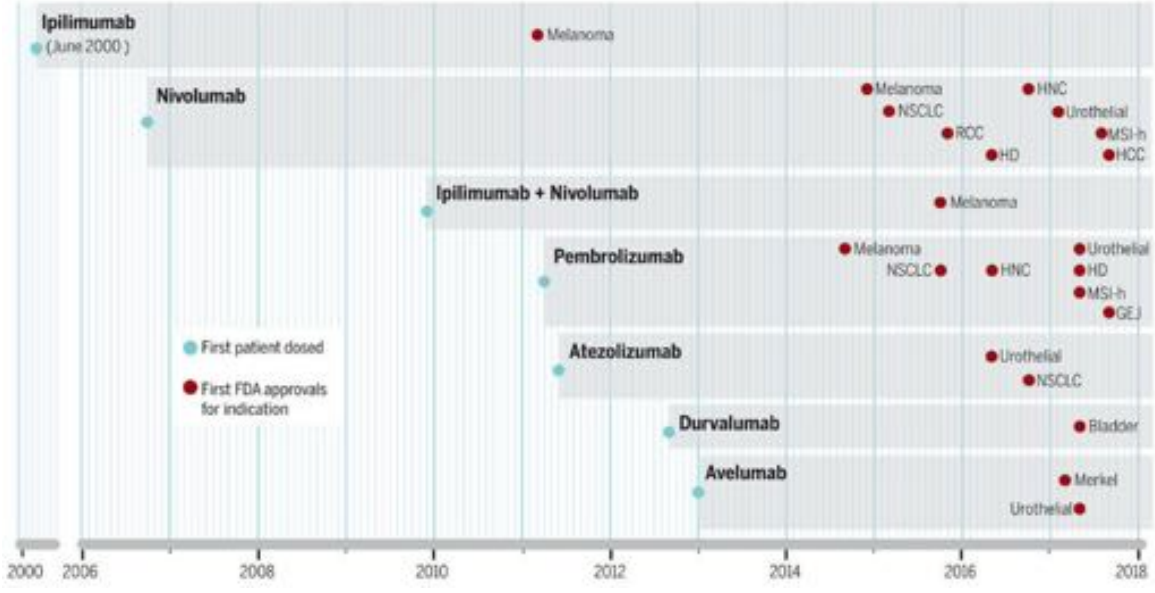
Immune checkpoint therapy





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Abril-Rodriguez et al, Cancer Cell 2017
Ribas et al, Science 2018

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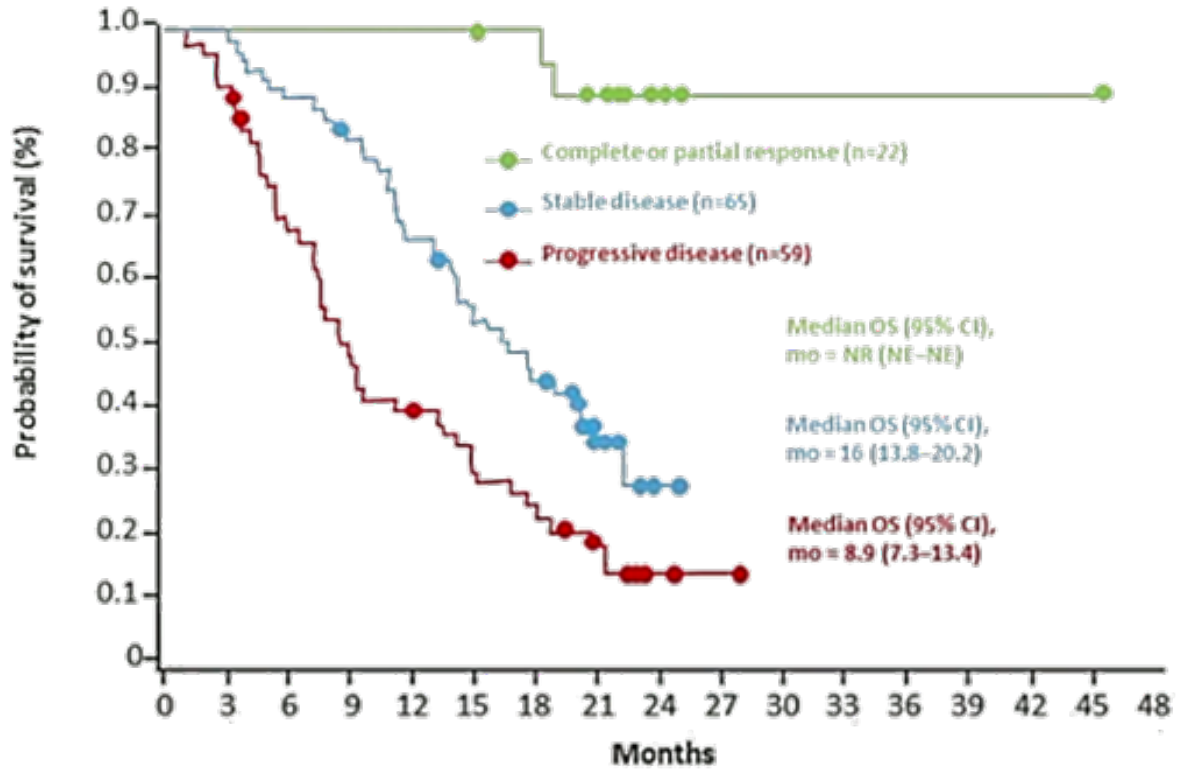
Phase II trial: Nivolumab – CheckMate 040



	Escalation phase (n=44)*	Expansion phase (n=174)*
PD-L1 ≥1%†	11 (25%)	34 (20%)
Objective response	3/11 (27%; 6–61)	9/34 (26%; 13–44)
Complete response	1 (9%)	1 (3%)
Partial response	2 (18%)	8 (24%)
Stable disease	0	16 (47%)
Progressive disease	7 (64%)	9 (26%)
Not determined	1 (9%)	0
PD-L1 <1%†	33 (75%)	140 (80%)
Objective response	4/33 (12%; 3–28)	26/140 (19%; 13–26)
Complete response	2 (6%)	2 (1%)
Partial response	2 (6%)	24 (17%)
Stable disease	19 (58%)	62 (44%)
Progressive disease	8 (24%)	46 (33%)
Not determined	2 (6%)	6 (4%)

Data are n (%); n/N (%; 95% CI). PD-L1=programmed death-ligand 1.
*Four patients in the dose-escalation phase and 40 patients in the dose-expansion phase did not have tumour PD-L1 expression data available.
†PD-L1 membrane expression on tumour cells.

Table 5: PD-L1 expression on tumour cells and response

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El-Khoueiry, Lancet 2017

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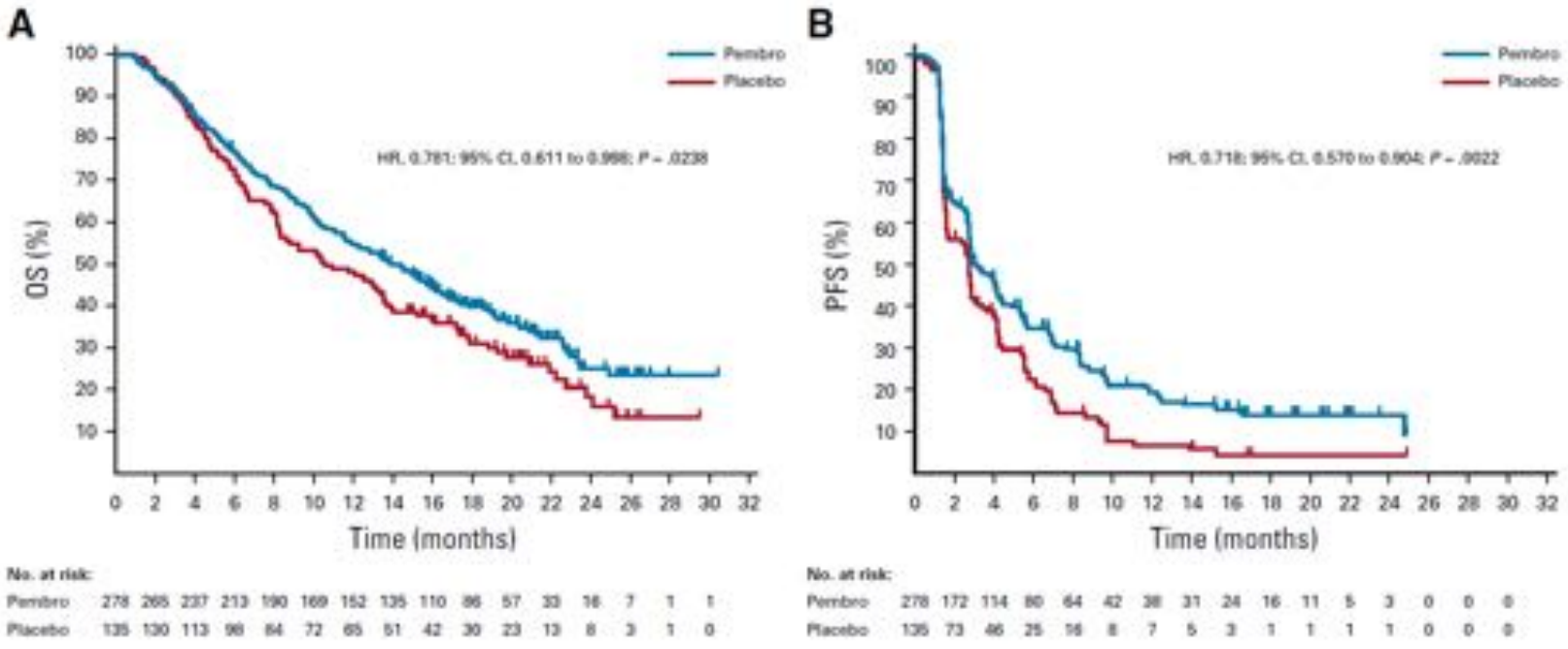
Phase III: Pembrolizumab vs. placebo KEYNOTE-240



Parameter	No. (%) Pembrolizumab (n = 278)	Placebo (n = 135)
Objective response*	51 (18.3)	6 (4.4)
95% CI	14.0 to 23.4	1.6 to 9.4
Estimated treatment difference†	13.8	
95% CI	7.7 to 19.5	
P‡	.00007	
Best overall response§		
CR	6 (2.2)	0 (0)
PR	45 (16.2)	6 (4.4)
SD	122 (43.9)	66 (48.9)
≥ 23 weeks‖	37 (13.3)	20 (14.8)
PD	90 (32.4)	57 (42.2)
Not evaluable	7 (2.5)	3 (2.2)
Not assessable¶	8 (2.9)	3 (2.2)
DCR#	173 (62.2)	72 (53.3)

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Finn et al, J. Clin Oncol. 2020

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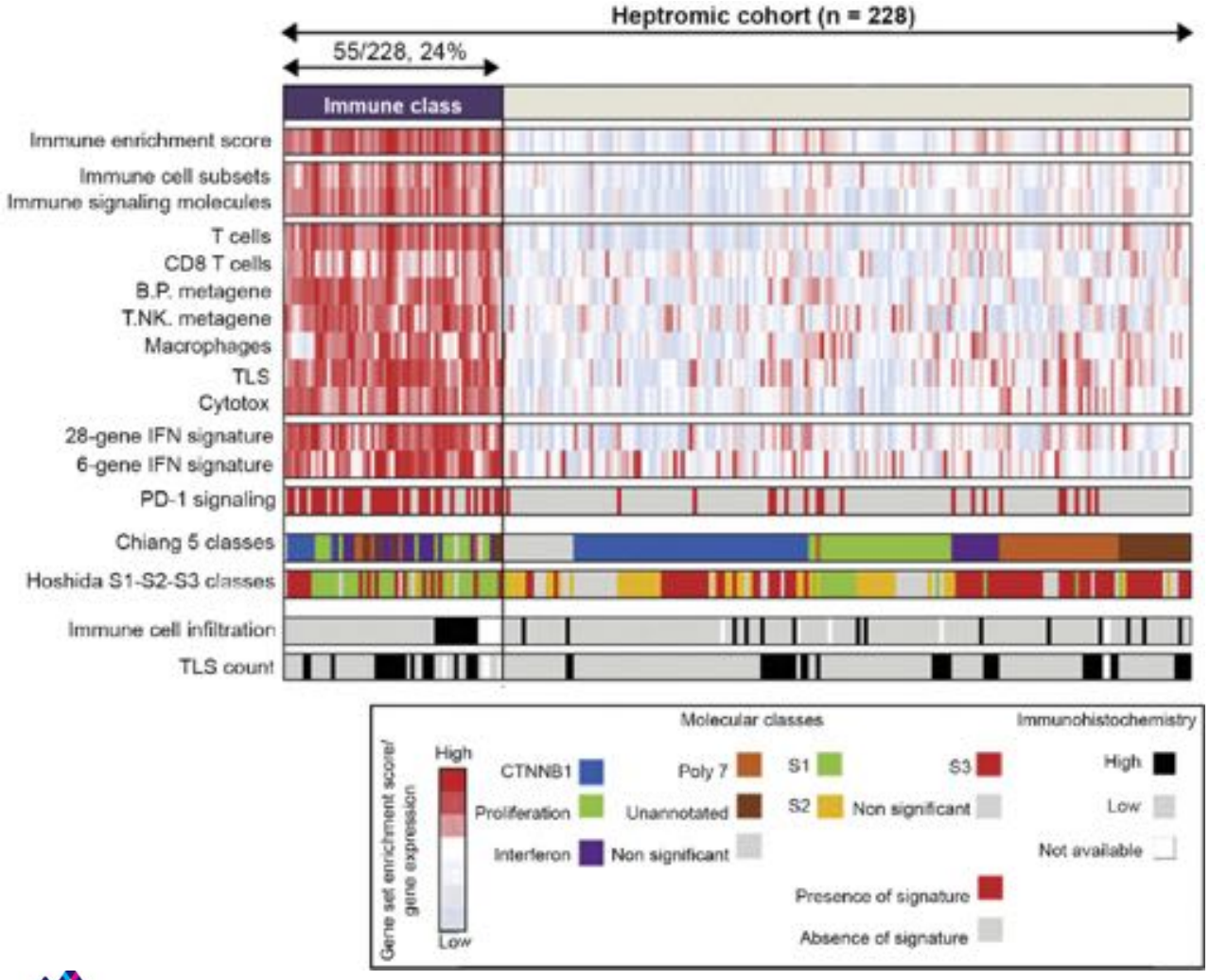
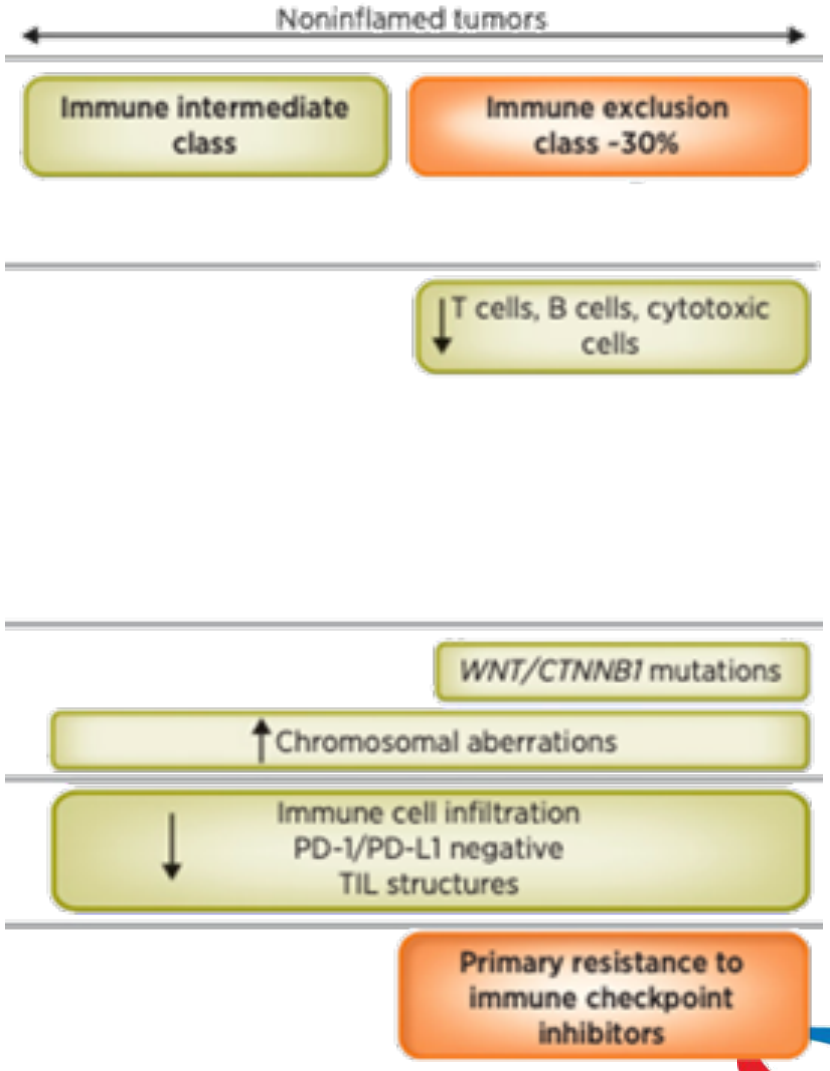
Mechanism of resistance to ICI

Fujiwara et al. Cancer drug resist 2020

Response/resistance to ICI





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Bassaganyas et al, Clinical Cancer Research 2020
Sia et al, Gastroenterology 2017

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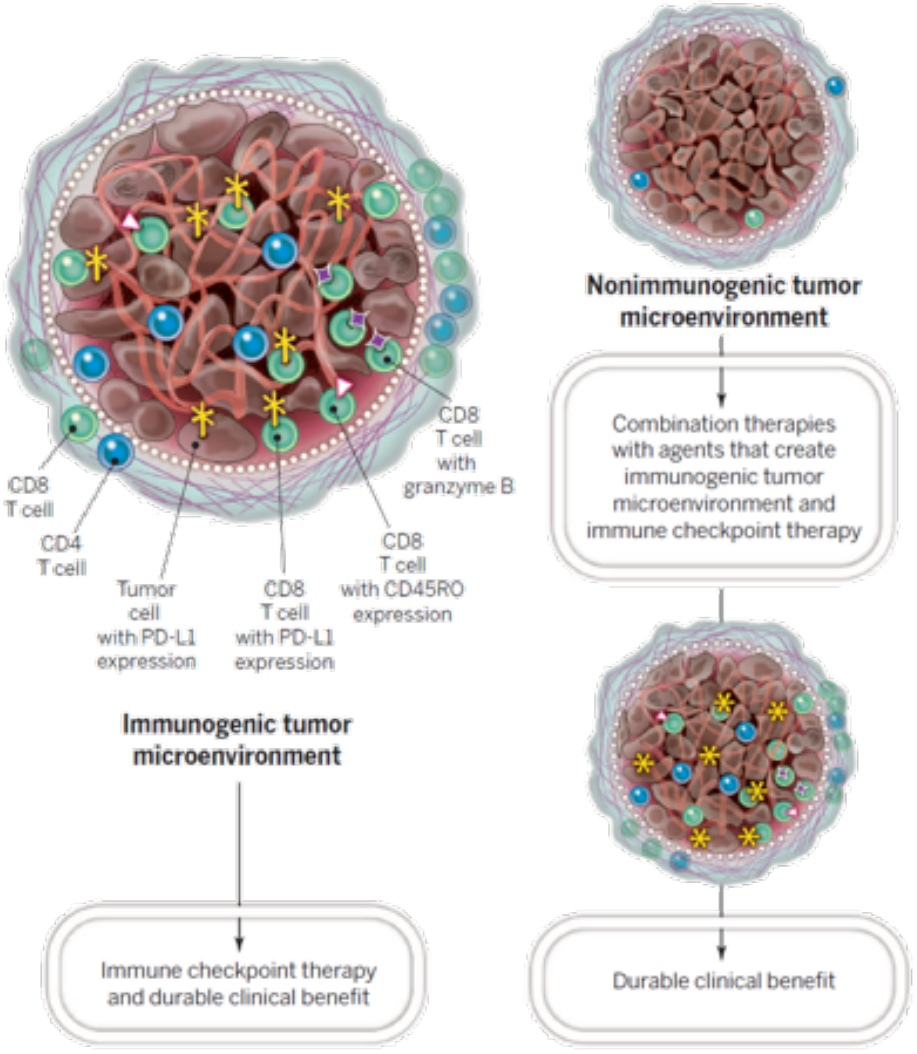
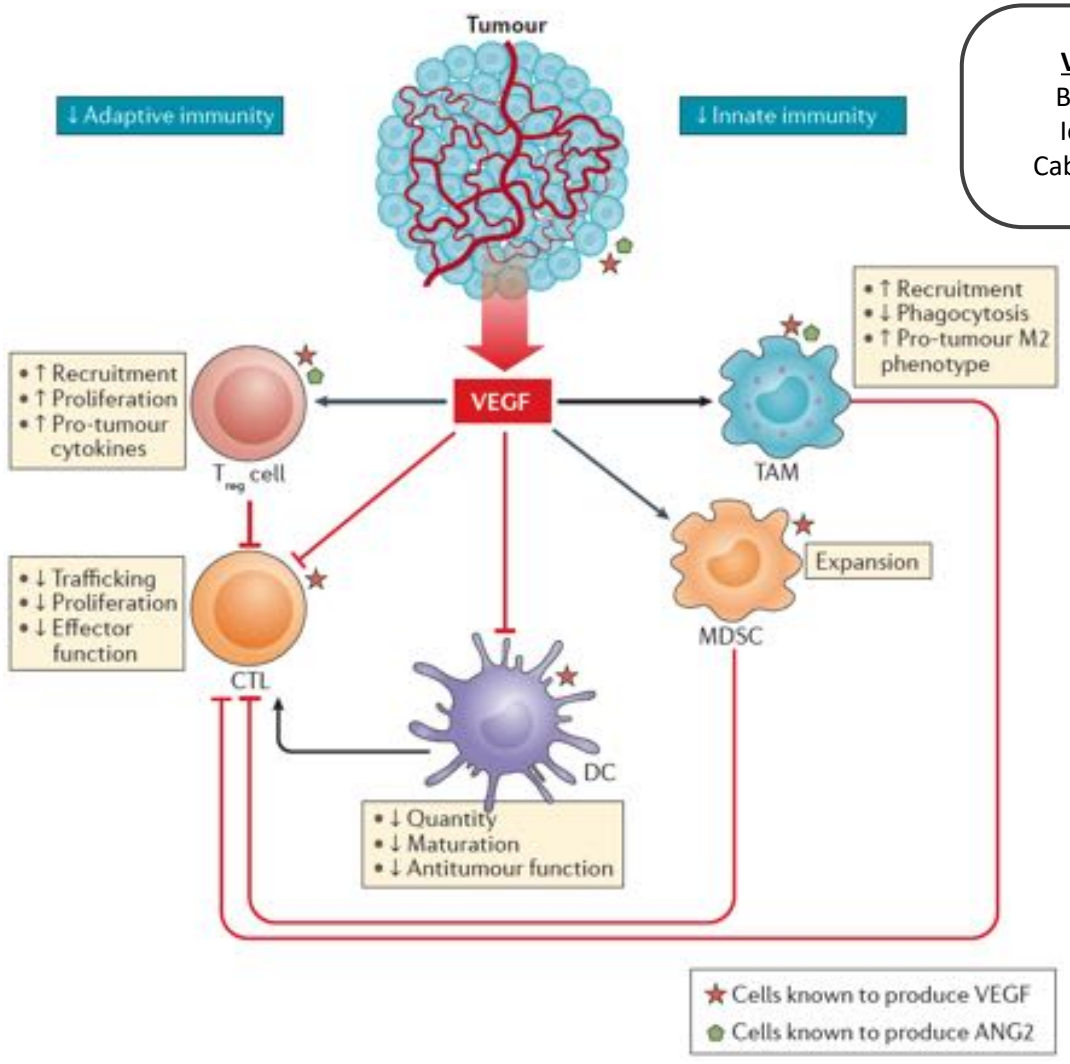
VEGF + checkpoint inhibitors





VEGF inhibitors in HCC
Bevacizumab Sorafenib, Ienvatinib Regorafenib, Cabozantinib Ramucirumab

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Sharma et al, Science 2018
Fukumura et al, Nat Review Clin Oncology 2018

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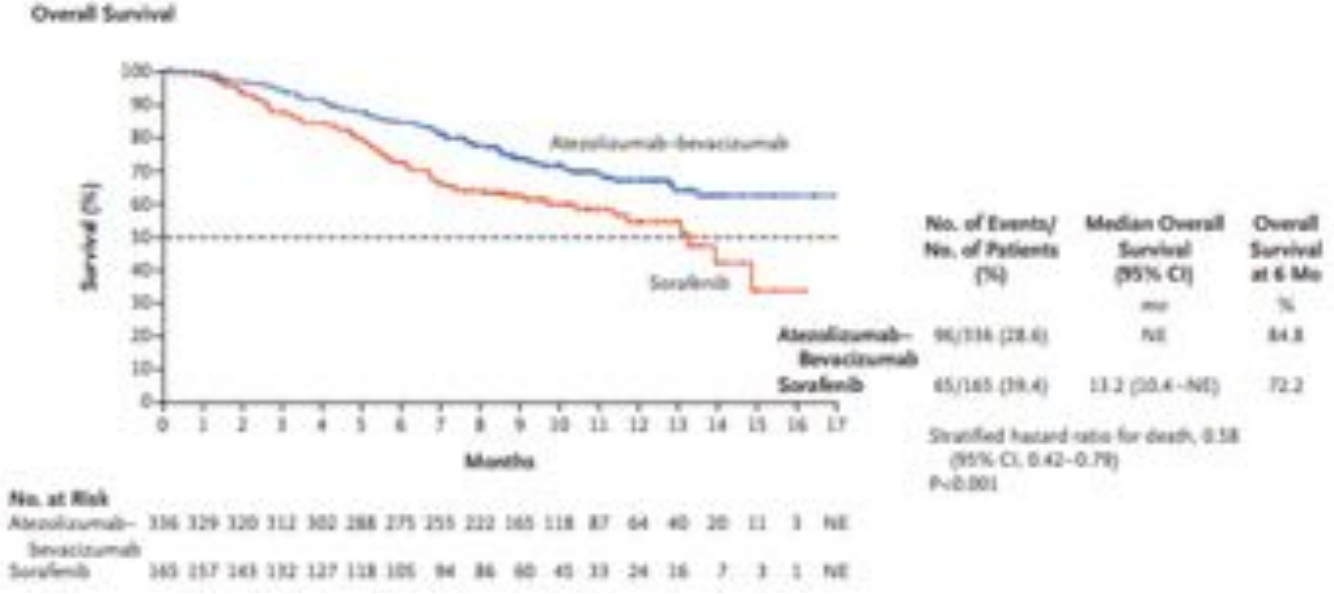
IMbrave150 trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma

Richard S. Finn, M.D., Shukui Qin, M.D., Masafumi Ikeda, M.D., Peter R. Galle, M.D., Michel Ducreux, M.D., Tae-You Kim, M.D., Masatoshi Kudo, M.D., Valeriy Breder, M.D., Philippe Merle, M.D., Ahmed O. Kaseb, M.D., Daneng Li, M.D., Wendy Verret, Ph.D., Derek-Zhen Xu, M.D., Sairy Hernandez, Ph.D., Juan Liu, Ph.D., Chen Huang, M.D., Sohail Mulla, Ph.D., Yulei Wang, Ph.D., Ho Yeong Lim, M.D., Andrew X. Zhu, M.D., Ph.D., and Ann-Lii Cheng, M.D., for the IMbrave150 Investigators*



Finn et al. NEJM 2020

Safety

Table 1. Patient Characteristics at Baseline.*

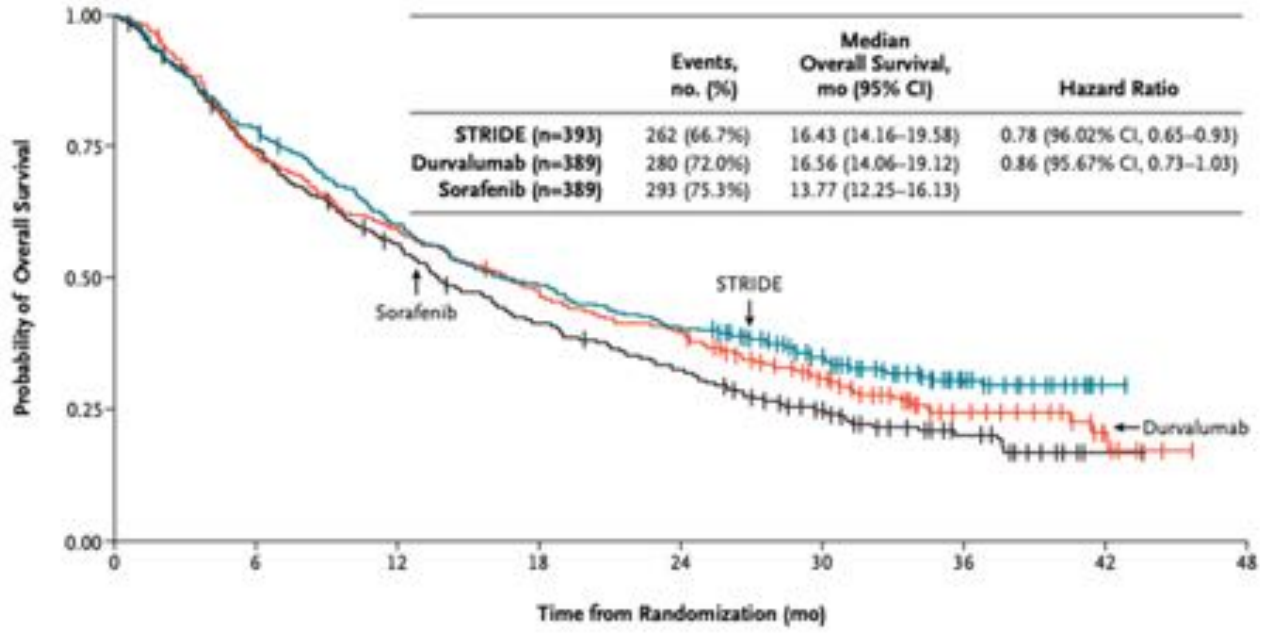
Variable	Atezolizumab–Bevacizumab (N = 336)	Sorafenib (N = 165)
Median age (IQR) — yr	64 (56–71)	66 (59–71)
Male sex — no. (%)	277 (82)	137 (83)
Geographic region — no. (%)		
Asia, excluding Japan	133 (40)	68 (41)
Rest of the world†	203 (60)	97 (59)
ECOG performance status score — no. (%)‡		
0	209 (62)	103 (62)
1	127 (38)	62 (38)
Child–Pugh classification — no./total no. (%)§		
A5	239/333 (72)	121/165 (73)
A6	94/333 (28)	44/165 (27)
Barcelona Clinic liver cancer stage — no. (%)¶		
A	8 (2)	6 (4)
B	52 (15)	26 (16)
C	276 (82)	133 (81)

Table 4. Adverse Events with an Incidence of More Than 10% in Either Group.

Event	Atezolizumab–Bevacizumab (N = 329)		Sorafenib (N = 156)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number (percent)			
Hypertension	98 (29.8)	50 (15.2)	38 (24.4)	19 (12.2)
Fatigue	67 (20.4)	8 (2.4)	29 (18.6)	5 (3.2)
Proteinuria	66 (20.1)	10 (3.0)	11 (7.1)	1 (0.6)
Aspartate aminotransferase increase	64 (19.5)	23 (7.0)	26 (16.7)	8 (5.1)
Pruritus	64 (19.5)	0	15 (9.6)	0
Diarrhea	62 (18.8)	6 (1.8)	77 (49.4)	8 (5.1)
Decreased appetite	58 (17.6)	4 (1.2)	38 (24.4)	6 (3.8)
Pyrexia	59 (17.9)	4 (1.2)	15 (9.6)	2 (1.3)
Alanine aminotransferase increase	46 (14.0)	12 (3.6)	14 (9.0)	2 (1.3)
Constipation	44 (13.4)	0	22 (14.1)	0
Blood bilirubin increase	43 (13.1)	8 (2.4)	22 (14.1)	10 (6.4)
Rash	41 (12.5)	0	27 (17.3)	4 (2.6)
Abdominal pain	40 (12.2)	4 (1.2)	27 (17.3)	4 (2.6)
Nausea	40 (12.2)	1 (0.3)	25 (16.0)	1 (0.6)
Cough	39 (11.9)	0	15 (9.6)	1 (0.6)
Infusion-related reaction	37 (11.2)	8 (2.4)	0	0
Weight decrease	37 (11.2)	0	15 (9.6)	1 (0.6)
Platelet count decrease	35 (10.6)	11 (3.3)	18 (11.5)	2 (1.3)
Epistaxis	34 (10.3)	0	7 (4.5)	1 (0.6)
Asthenia	22 (6.7)	1 (0.3)	21 (13.5)	4 (2.6)
Alopecia	4 (1.2)	0	22 (14.1)	0
Palmar–plantar erythrodysesthesia syndrome	3 (0.9)	0	75 (48.1)	13 (8.3)

Tremelimumab Plus Durvalumab in Unresectable Hepatocellular Carcinoma

Ghassan K. Abou-Alfa, M.D., M.B.A.,[1,2] George Lau, M.D., F.R.C.P.,[3] Masatoshi Kudo, M.D., Ph.D.,[4] Stephen L. Chan, M.D.,[5] Robin Kate Kelley, M.D.,[6] Junji Furuse, M.D., Ph.D.,[7] Wattana Sukeepaisarnjaroen, M.D.,[8] Yoon-Koo Kang, M.D., Ph.D.,[9] Tu Van Dao, M.D., Ph.D.,[10] Enrico N. De Toni, M.D., Ph.D.,[11] Lorenza Rimassa, M.D.,[12,13] Valeriy Breder, M.D., Ph.D.,[14] Alexander Vasilyev, M.D.,[15] Alexandra Heurgué, M.D.,[16] Vincent C. Tam, M.D.,[17] Kabir Mody, M.D.,[18] Satheesh Chiradoni Thungappa, M.D.,[19] Yuriy Ostapenko, M.D.,[20] Thomas Yau, M.D.,[21] Sergio Azevedo, M.D.,[22] María Varela, M.D., Ph.D.,[23] Ann-Lii Cheng, M.D., Ph.D.,[24] Shukui Qin, M.D., Ph.D.,[25] Peter R. Galle, M.D., Ph.D.,[26] Sajid Ali, M.D.,[27] Michelle Marcovitz, Ph.D.,[27] Mallory Makowsky, Pharm.D.,[27] Philip He, Ph.D.,[27] John F. Kurland, Ph.D.,[27] Alejandra Negro, Ph.D.,[27] and Bruno Sangro, M.D., Ph.D.,[28] for the HIMALAYA Investigators*



	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

No. at Risk									
STRIDE	393	308	235	190	158	98	32	1	0
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

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LEAP-002: Phase III Lenvatinib +Pembrolizumab

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Finn et al. Ann Oncol 2022

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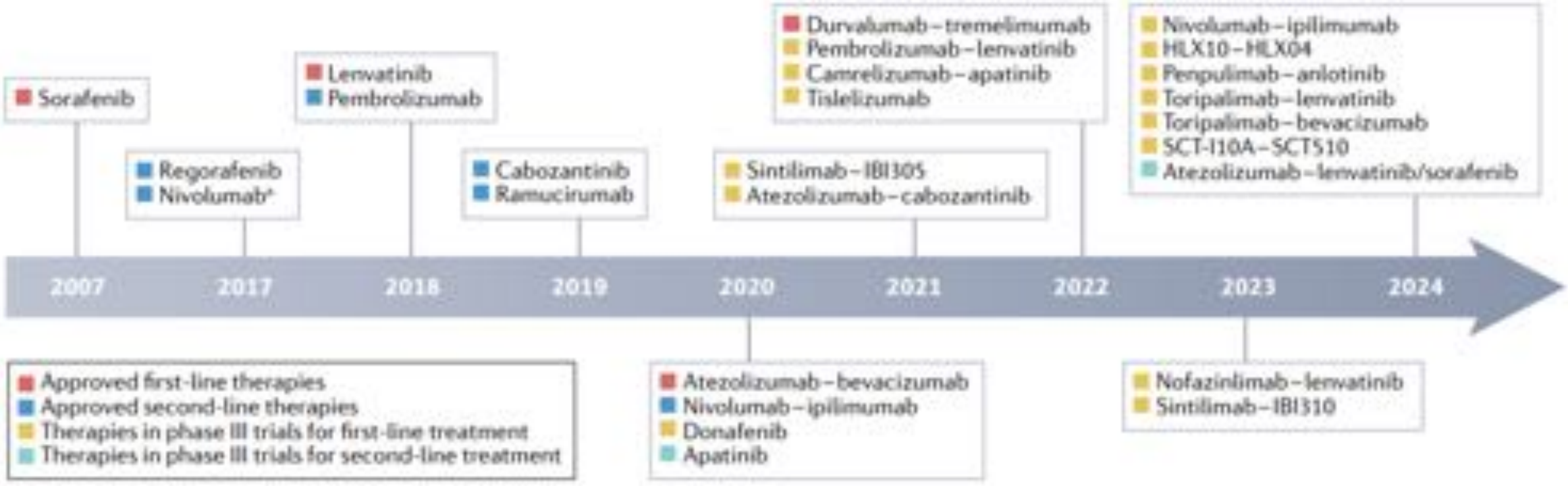
Therapeutic landscape of advanced HCC



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Yang et al. Nature Reviews Gastroenterology and Hepatology 2022

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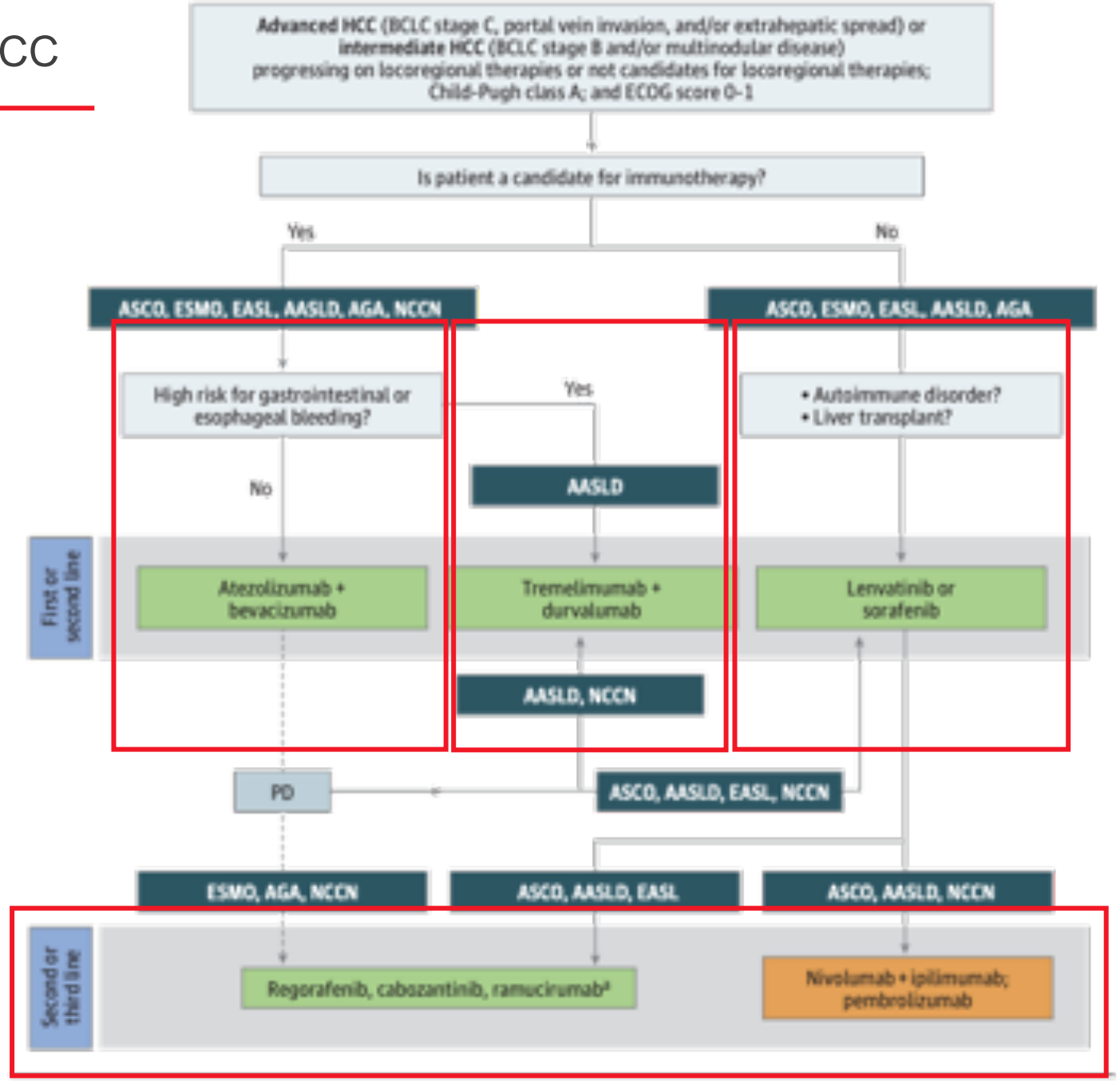
Proposed Treatment Algorithm for Advanced HCC



Cappuyns et al. JAMA Oncol 2023

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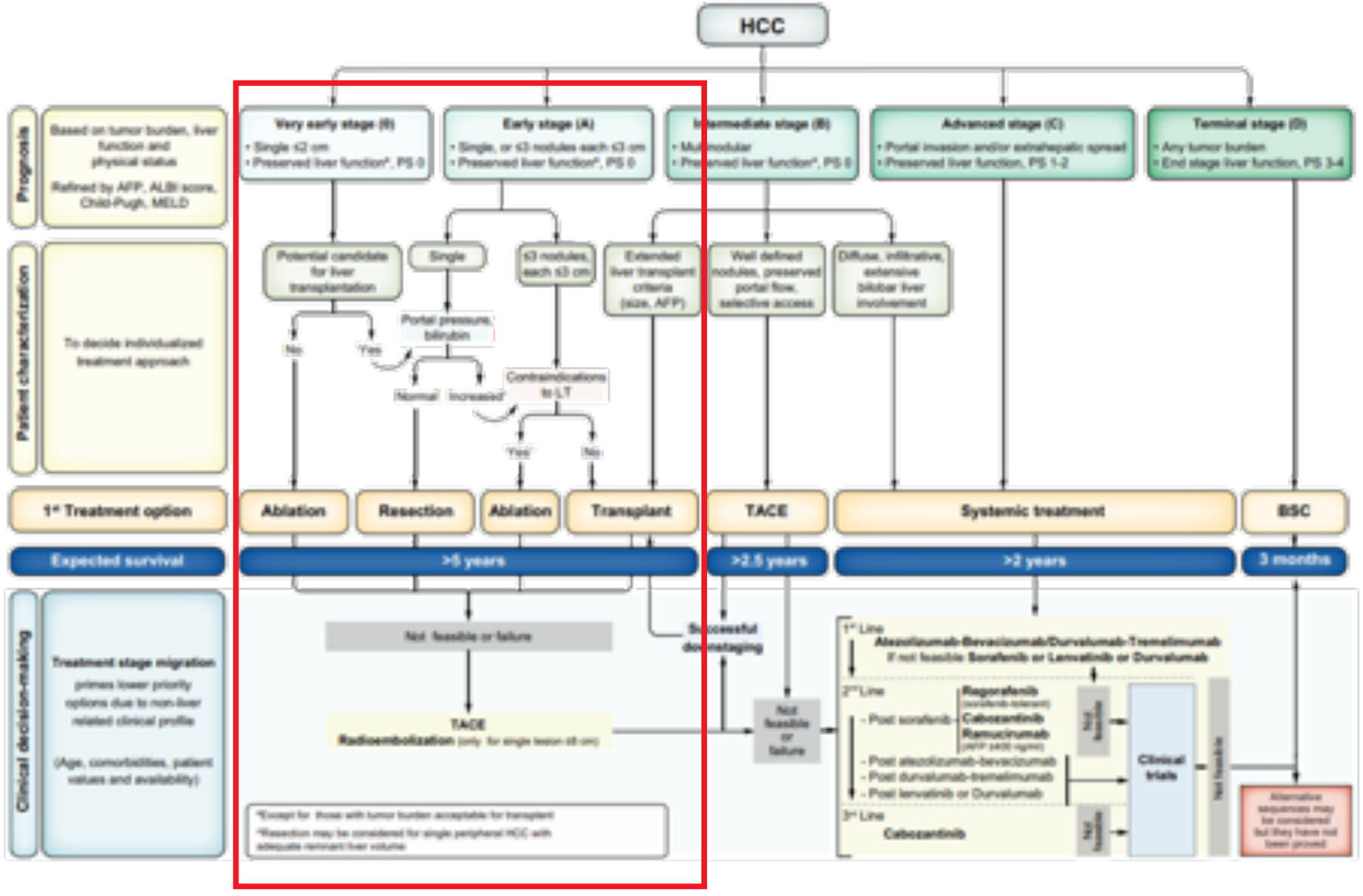

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Reig et al, Journal of Hepatology 2022

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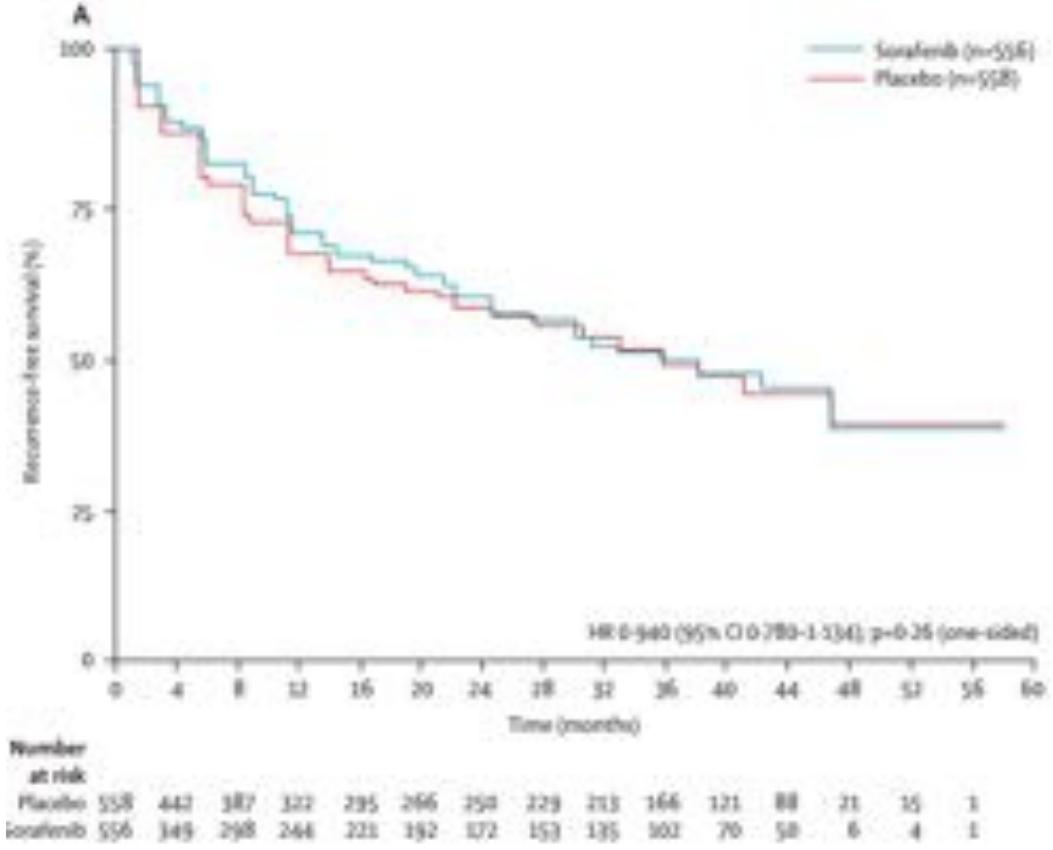
STORM: Adjuvant therapy post resection in HCC



	Sorafenib (n=556)	Placebo (n=558)
Events, n (%)	**194 (34.9)**	270 (48.4)
Median RFS (95% CI)	**33.4 months (27.6-44.0)**	33.8 months (27.6-39.0)

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Bruix et al, Lancet Oncol 2015

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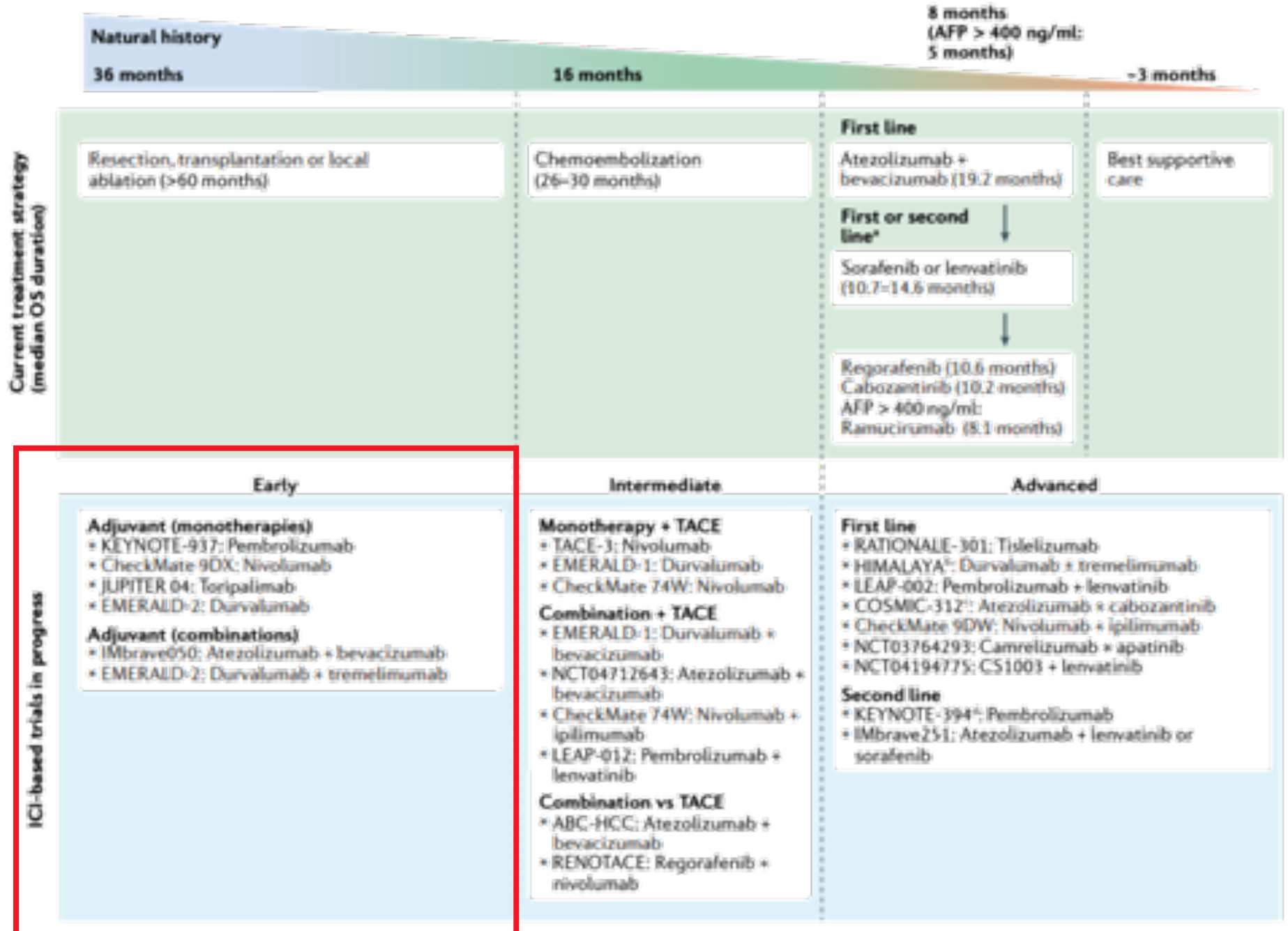


Llovet et al, Nat Review Clinic Oncol 2022

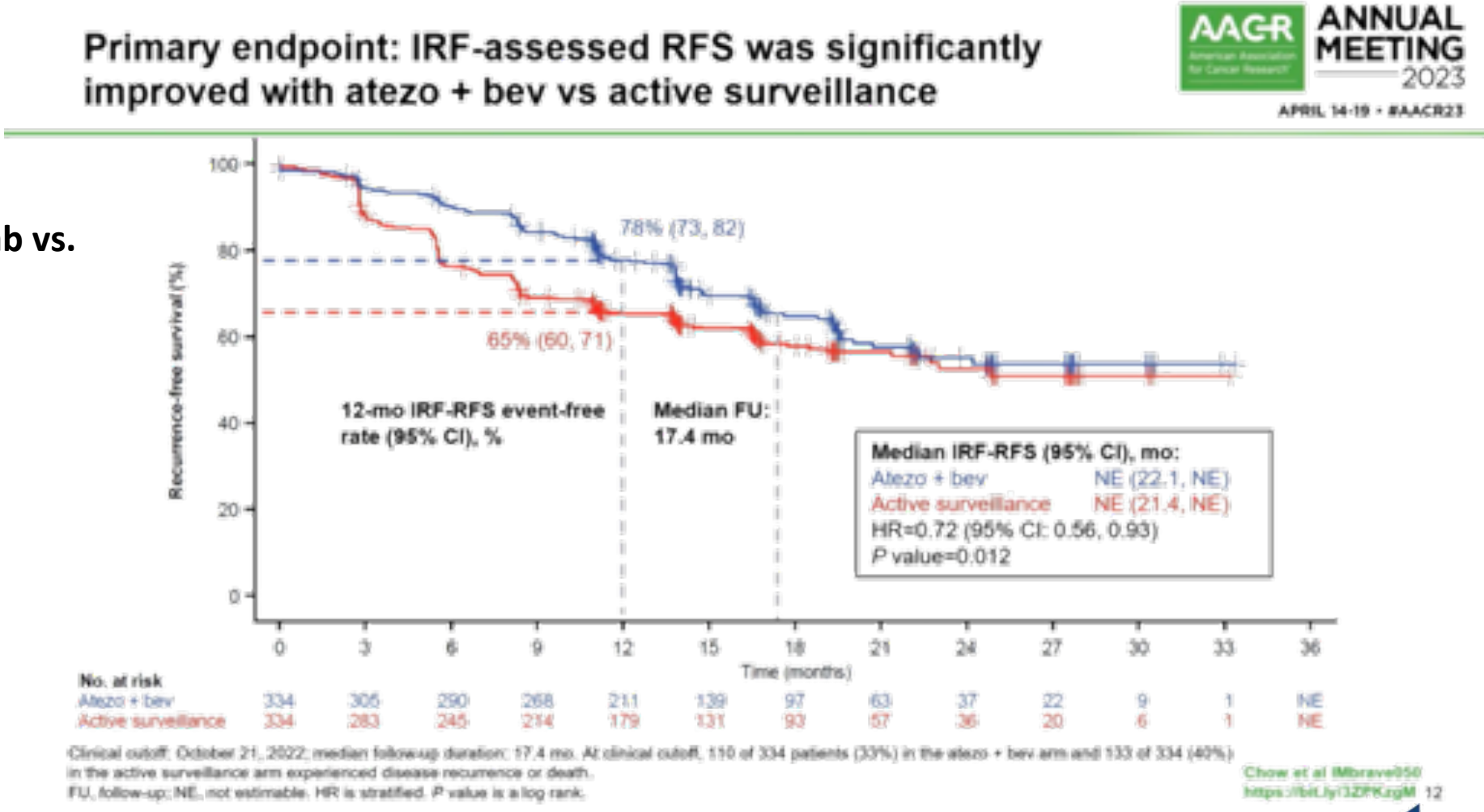
IMBRAVE 050

RFS Atezolizumab + Bevacizumab vs. placebo (HR: 0.72, *p* = 0.01)

High-risk population:

- Micro/macro VI
- Poor differentiation

- Single > 5 cm
- > 3 tumors



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Chow et al. *AACR meeting*. April 2023

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Neoadjuvant trials may elucidate intratumoral IO effect

For the patient:

- Lower tumor burden - better response rates?
- Smaller tumors → less heterogeneity
- Earlier stage (and smaller tumors) → better immune fitness
- Downstage

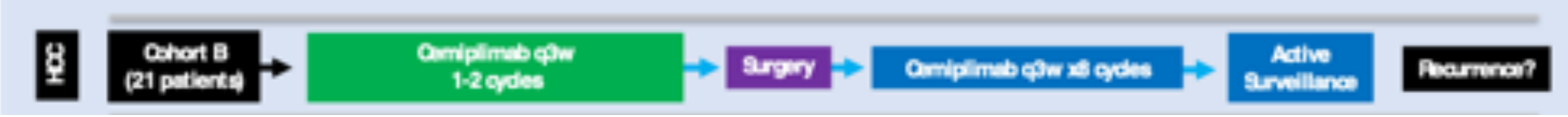
→ Higher chance for “cure” with IO

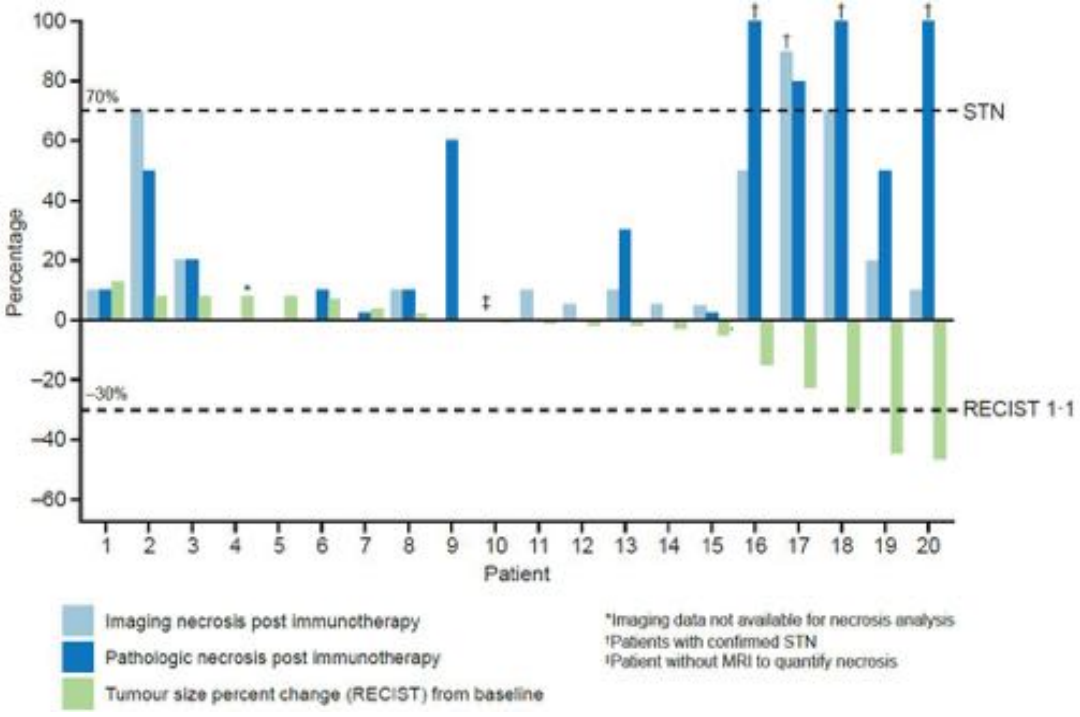
For research purposes:

- Define mechanism of action/resistance
- Define biomarkers (responders vs non responders)
- Smaller trials
- Propose rational combinatorial approaches

→ Help cure MORE people

TCI neoadjuvant Cemiplimab trial





Pathologic tumour necrosis	n (%)
STN (>70%)	4 (20)
Complete tumour necrosis (100%)	3 (15)
Tumour necrosis ≥50%	7 (35)
Tumour necrosis <50%	13 (65)

STN=significant tumour necrosis.

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Marron et al. Lancet Gastroenterology and Hepatology 2021

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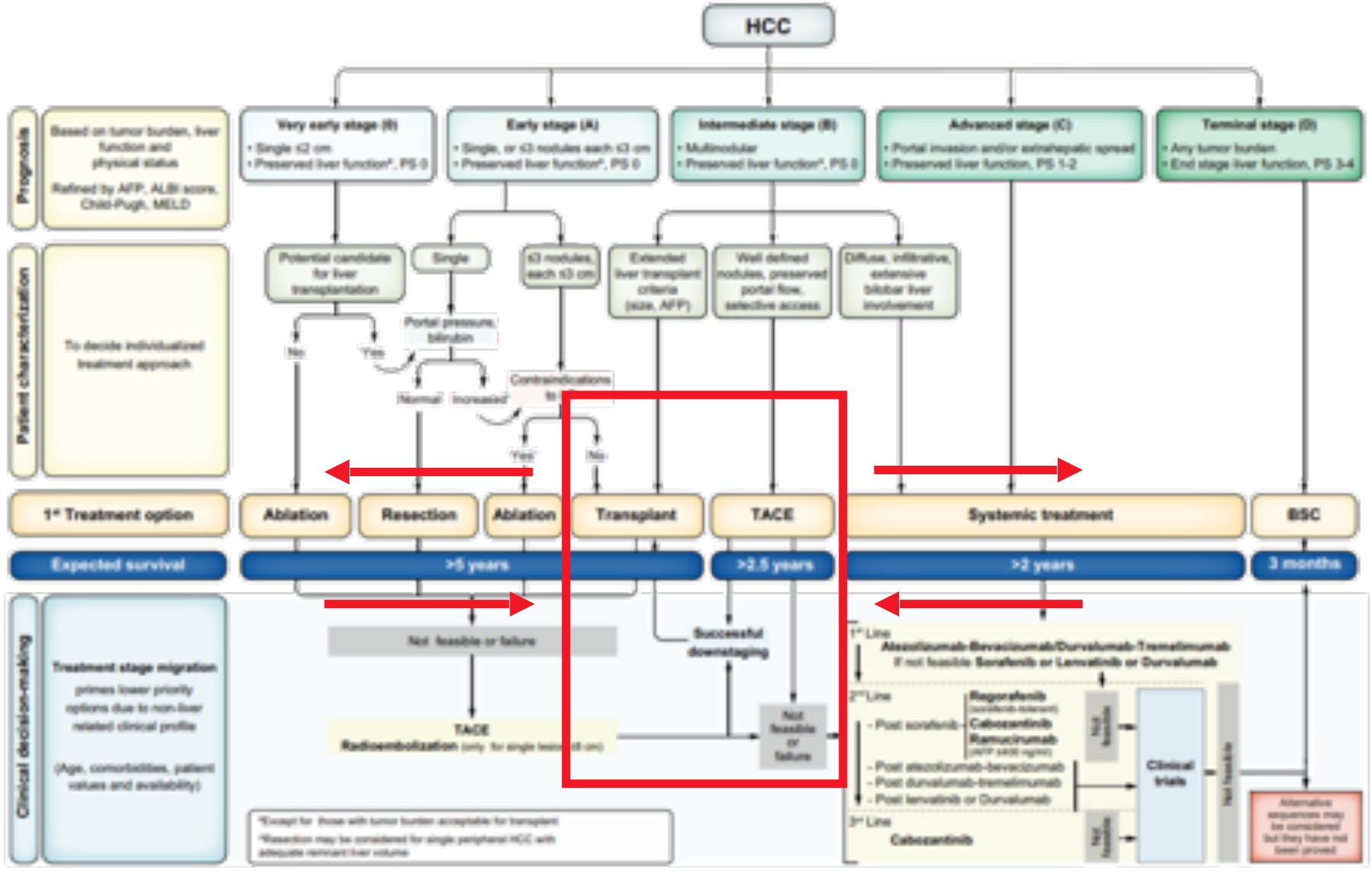

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Reig et al, Journal of Hepatology 2022

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Solid organ transplant recipients treated with ICI

Age	Gender	Immune-suppression	Years after LT	Doses	Graft outcome	Pathology of graft	Treatment of rejection	Outcome of cancer	Overall outcome
20	M	Sirolimus	3	Nivo, 2	Loss of function	Cellular/AB mediated rejection	Prednisone, IVIG	N/A	Death after 5 weeks
14	M	Tacrolimus	3	Nivo, 1	Loss of function	Cellular/AB mediated rejection	Prednisone	N/A	Death after 4 weeks
53	F	Everolimus	3	Nivo, 1	Loss of function	Cellular	Steroids	Progression	Death after 4 weeks
41	M	Tacrolimus	1	Nivo, 15	No rejection	N/A	N/A	Progression	Death > 7 mo
57	M	Tacrolimus	4	Pembro x10	No rejection	N/A	N/A	Radiologic resolution	Alive at 10 mo

n = 29, 14/29 kidney, 11/29 liver, 3/29 heart, 1 cornea
Graft loss/acute rejection: 45%

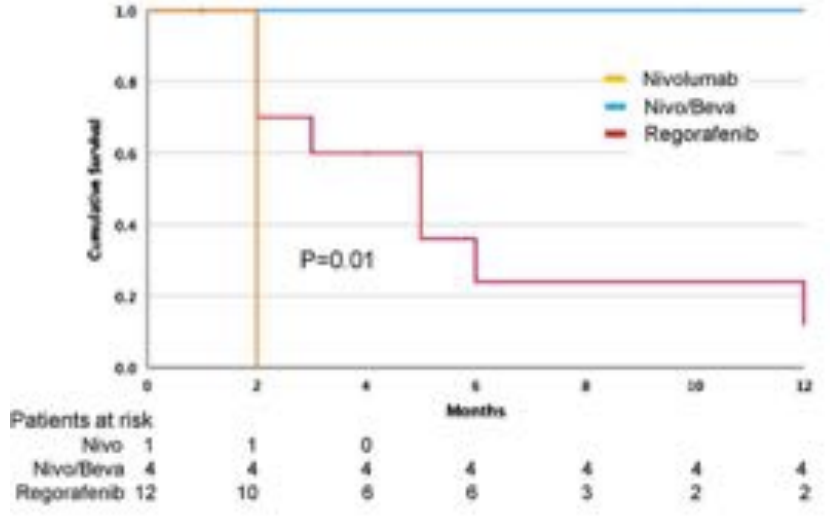
Gassmann et al. Transplantation direct 2018

Feasibility, safety, and outcome of second-line nivolumab/bevacizumab in liver transplant patients with recurrent hepatocellular carcinoma

- Proof-of concept study 2018-2021
- Analyze the safety of nivolumab/bevacizumab in 22 patients HCC recurrence post LT, **progressed on sorafenib** therapy.
- Nivolumab 2 infusions→ Atezo/Bevacizumab
- Unsuitable for nivolumab/ bevacizumab → regorafenib

- 18 % best supportive care, 81% sorafenib
- N=12 regorafenib, n=1 nivo, n=4 Nivo/Bev (AE: moderate rejection, ALT increase, proteinuria)

- OS from the initiation of sorafenib has been
- 26.5±10.4 for patients on nivolumab/bevacizumab
- 9.5±5.5 for those on regorafenib (p=0.02)



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DiMarco et al. Liver Transplantation 2023

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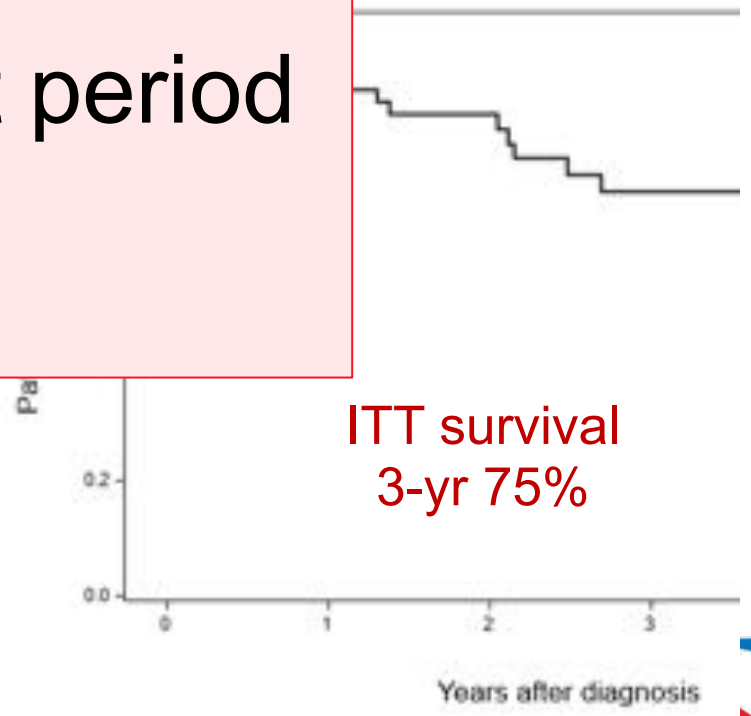
Immunotherapy and liver transplant

PD-1 inhibitor as bridge therapy to liver transplantation?

American Journal of TRANSPLANTATION

No majo
No m
50%
> 90 % major pathologic necrosis

- Heterogeneous
- Case series/reports
- ICI type and washout period
- Lack of biopsy
- Immunosuppression



ITT survival
3-yr 75%

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Tabrizian et al. AJT 2020

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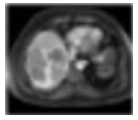
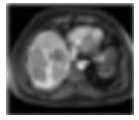
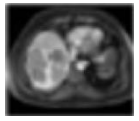
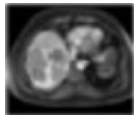
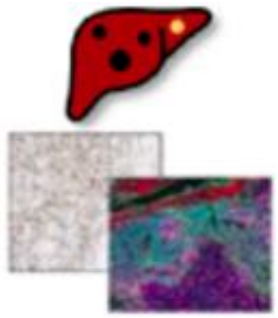
Diagnosis ← Listing Time → Downstaged → Transplant

Patient selection:

- High risk
- High tumor burden
- AFP
- Number LRT
- Long wait list
- Downstaging/all comers
- Underlying liver disease?

- Choice of IO
- Observation period
- Washout period
- Living donor?

- Choice of Immunosuppression
- Induction therapy?

- Risk of Rejection and management
- Adjuvant use?

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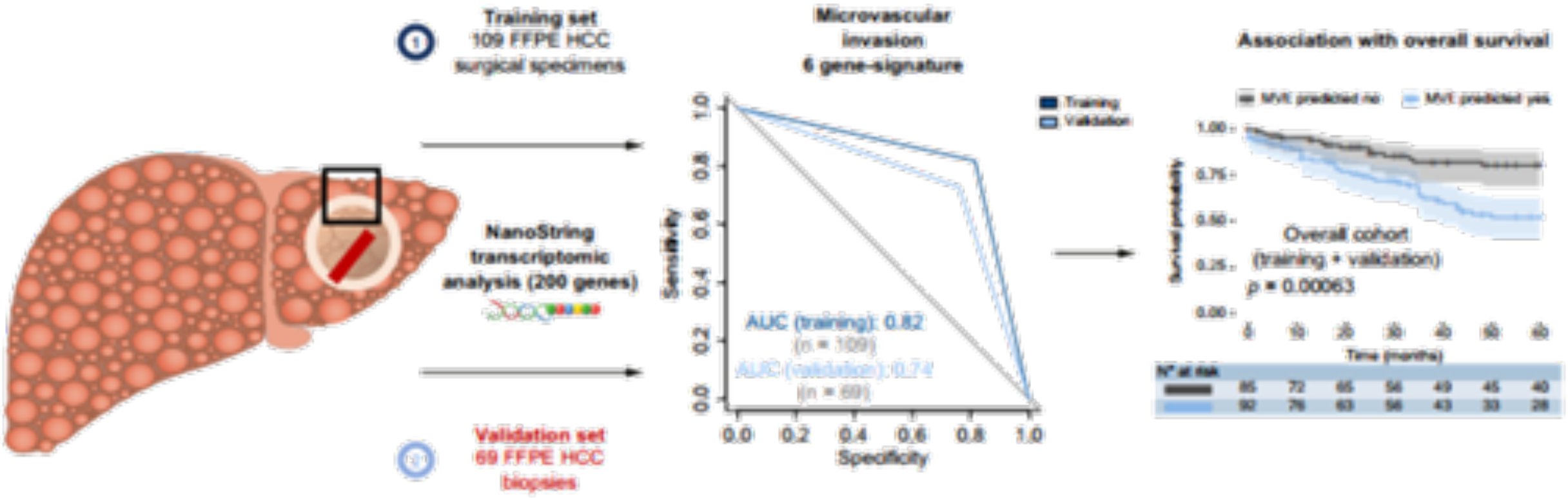
Future directions

Trial	NCT	Phase	Treatment arms	Endpoint	Adjuvant	N=
Neoadjuvant pre LT						
PLENTY202001	NCT04425226	Phase 2	Pembro/Len	RFS	No	192
	NCT05185505	Phase 2	Atezo/Bev	Feasibility % rejection	No	24
	NCT05027425	Phase 2	Durva/Tremi	30d rejection rate	No	30
	NCT04443322	NA	Durva/Len	PFS/RFS	No	20

Gene expression signature



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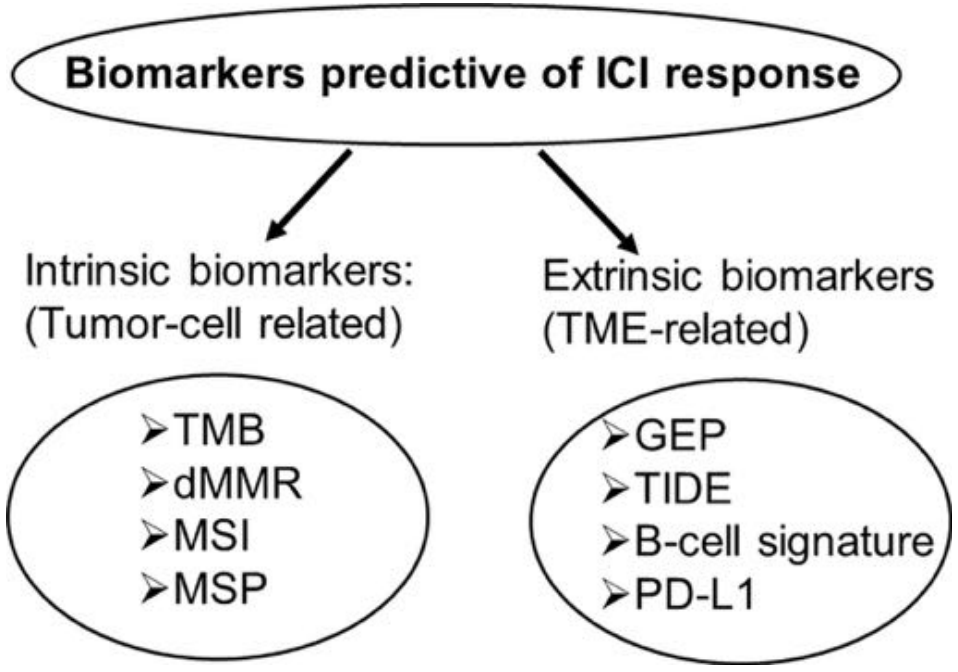
Beaufrere et al, J hep 2022

The Liver Transplant Symposium 2023

FDA-Approved and Emerging Next Generation Predictive Biomarkers for Immune Checkpoint Inhibitors in Cancer Patients

Ye Wang[1†], Zhuang Tong[2†], Wenhua Zhang[1], Weizhen Zhang[3], Anton Buzdin[4,5,6], Xiaofeng Mu[1,7], Qing Yan[1], Xiaowen Zhao[1], Hui-Hua Chang[8], Mark Duhon[8], Xin Zhou[9], Gexin Zhao[8], Hong Chen[9] and Xinmin Li[8*]*



Tumor Mutational Burden (TMB); defective MisMatch Repair (dMMR); MicroSatellite Instability (MSI); β-MicroSeminoProtein (MSP); T-cell inflamed Gene Expression Profile (GEP); Tumor Immune Dysfunction and Exclusion gene signature (TIDE); Melanocytic Plasticity Signature (MPS); B-cell focused gene signature

Selected ongoing phase I–III trials for advanced HCC

Agent(s) (targets)	Primary endpoint	Line of treatment	Phase	Sample size	NCT
ICI combinations with targeted therapies					
Pembrolizumab (PD1), lenvatinib (VEGFR1–VEGFR3, PDGFR, FGFR1–FGFR4, RET)	OS, PFS	First	III	750	NCT03713593
Atezolizumab (PD-L1), cabozantinib (VEGFR1–VEGFR3, MET, RET)	OS, PFS	First	III	740	NCT03755791
AK105 (PD1), anlotinib (VEGFR1–VEGFR3, FGFR1–FGFR4, PDGFR, KIT receptor)	OS	First	III	648	NCT04344158
Camrelizumab (PD1), apatinib (VEGFR2)	OS, PFS	First	III	510	NCT03764293
Tislelizumab (PD1), lenvatinib (VEGFR1–VEGFR3, PDGFR, FGFR1–FGFR4, RET)	ORR	First	II	66	NCT04401800
Nivolumab (PD1), sorafenib (VEGFR1–VEGFR3, PDGFR, RAF kinase, KIT receptor)	ORR, MTD	First	II	12	NCT03439891
Pembrolizumab (PD1), sorafenib (VEGFR1–VEGFR3, PDGFR, RAF kinase, KIT receptor)	ORR	First	I/II	27	NCT03211416
HX008 (PD1), bevacizumab (VEGFA), lenvatinib (VEGFR1–VEGFR3, PDGFR, FGFR1–FGFR4, RET)	ORR	First	II	72	NCT04741165
CS1001 (PD-L1), fisogatinib (FGFR4)	ORR, DLT	First or second	Ib/II	52	NCT04194801

Selected ongoing phase I–III trials for advanced HCC

ICI combinations with other ICIs					
Durvalumab (PD-L1) plus tremelimumab (CTLA4)	OS	First	III	1,504	NCT03298451
Nivolumab (PD1) plus ipilimumab (CTLA4)	OS	First	III	650	NCT04039607
Nivolumab (PD1), relatlimab (LAG-3)	ORR	Second	II	250	NCT04567615
Triplet combinations involving ICIs and targeted therapies					
Atezolizumab (PD-L1), bevacizumab (VEGFA), tiragolumab (TIGIT), tocilizumab (IL-6R), SAR439459 (TGF-β), TPST-1120 (PPAR-α), RO7247669 (PD1, LAG-3)	ORR	First	Ib/II	280	NCT04524871
Pembrolizumab (PD1), quavonlimab (CTLA4), lenvatinib (VEGFR1–VEGFR3, PDGFR, FGFR1–FGFR4, RET)	ORR, DLT, incidence of AEs/SAEs, hepatic AEs, discontinuation due to AEs	First	II	110	NCT04740307
Nivolumab (PD1), ipilimumab (CTLA4), cabozantinib (VEGFR1–VEGFR3, MET, RET)	ORR, incidence of AEs/SAEs	First or second	I/II	1,097	NCT01658878
New immunologic targets					
Voyager V1 (VSV oncolytic virus), cemiplimab (PD1)	ORR	Second	II	152	NCT04291105
Talimogene laherparepvec (T-VEC, HSV oncolytic virus), pembrolizumab (PD1)	DLT, ORR	Second	I/II	206	NCT02509507
GNOS-PV02 (personalized neoantigen), INO-9012 (IL-12), pembrolizumab (PD1)	Incidence of AEs, immunogenicity	Second	I/II	24	NCT04251117
ET140203 T cells (AFP)	Incidence of AEs, DLTs, RP2D	Third+	I/II	50	NCT04502082
ECT204 T cells (GPC3)	Incidence of AEs, DLTs, RP2D	Third+	I/II	12	NCT04864054

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Llovet et al, Nature Cancer 2022

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Summary

- Criteria of LT for HCC continues to evolve
  - Include surrogates of biological behavior into decision-making
  - Ongoing research to develop better biomarkers
  - Liquid biopsy, gene expression, imaging
- Systemic therapies are game changers→ Controlled clinical trial in transplant oncology
  - What is the upper limit ?
  - What is an acceptable survival rate?
  - Should LDLT be used?
  - ICI pre transplantation?


Thank you